Elżbieta Kalisińska *Editor*

Mammals and Birds as Bioindicators of Trace Element Contaminations in Terrestrial Environments

An Ecotoxicological Assessment of the Northern Hemisphere

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We dedicate this book to all animals that help us recognize the threats to our environment and hopefully prevent a global catastrophe.

Preface

This monograph includes a collection of data on the role and concentrations of 17 trace elements occurring in wild warm-blooded vertebrates inhabiting the Northern Hemisphere. These elements include those that are essential or potentially essential for the lives of birds and mammals, as well as those that are commonly regarded as toxic.

Since the mid-twentieth century, we have witnessed rapid development in the field of animal biology, including ecology, biogeography, physiology, genetics, and ecotoxicology, fields of science dealing with the increasing number of environmental issues related to the overwhelming growth of the human population. The consequences of this demographic explosion include profound changes in land use, disruption of the natural geochemical cycles of many elements and their large-scale mobilization from deposits as a result of economic activity, the release of anthropogenic pollutants into the environment, and the spread of some species and decline in the abundance and ranges of other species. These environmental changes have many adverse effects on humans and other vertebrates living in terrestrial environments with different geological structures and varying levels of anthropogenic pressure.

In this context, we endeavored to analyze the available ecotoxicological literature (mainly in English and published between 1960 and 2016), focusing on terrestrial bird and mammal species of different trophic levels to identify the most universal bioindicators of pollution. We also aimed to identify the usefulness of different types of biological samples in biomonitoring of certain elements and to assess the present state of knowledge in this area.

Szczecin, Poland
January 2019

Elżbieta Kalisińska

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Part I
Introduction

Chapter 1
Human Population Increase and Changes in Production and Usage of Trace Elements in the Twentieth Century and First Decades of the Twenty-First Century

Elżbieta Kalisińska

Abstract People currently live in a unique time, the Anthropocene. Since the acceleration of the Industrial Revolution (~1850), humans have become a huge geological force. In 1800, 1 billion people lived in the world, but in 2018 the global human population exceeded 7.6 billion. The beginning of large-scale human impacts during the 1950s was related to the dynamics of global population growth thus far unprecedented in human history. The years 1950–1970 were defined by a quickly expanding chemical industry and the widespread popular belief that so-called progress would result in seemingly endless improvement in the quality of everyday life but that led to destruction and pollution of environment with huge amounts of chemicals (including metals) from industry, agriculture and transport. Anthropogenic metal emission still persists in the world, but its main sources are no longer located in Europe and North America, however, in Asia where half of the global population live. For example, in 2015 aluminium ore mining increased 33 times compared to 1950 and the mining of other economically important metals [iron (Fe), copper (Cu), zinc (Zn)] >6 times. In the case of highly toxic metals such as cadmium (Cd) and lead (Pb), this increase was 4.3 higher, respectively, but there was a 50% decrease in mercury (Hg) production. It is estimated that at least 60 elements (out of 118 naturally occurring on Earth) were mobilized from minerals and introduced into biogeochemical cycles on a larger scale (>50%) as the result of human activity rather than natural causes. Never in Earth's history a single species has dominated the biosphere the way *Homo sapiens* population does now.

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1 Population Growth in the Twentieth Century

In the twentieth century, especially its later decades, we witnessed the highest growth dynamics of the global population, unprecedented in the recorded history of mankind. Its exponential course began in the late eighteenth century with the advent of the Industrial Revolution. It is estimated that in 1800, 1 billion people lived in the world. During the following 150 years, the number of people on Earth increased more than two and a half times, reaching 2.58 billion in 1951. Even before the end of the twentieth century, the number of people had doubled more than twice, amounting to 6 billion in 1999 (Fig. 1.1). In less than 12 subsequent years, the next billion people appeared, and in 2011 we had a global population of 7 billion (Bongaarts 2009; UNEP 2012).

According to current data, in 2018 the number of people in the world exceeded 7.6 billion and is expected to reach 8 to 9 billion by 2023 and 2037, respectively. Annual natural growth rate had the highest value in the late 1960s, when it was ~2%. The rate of increase has nearly halved since then and will continue to decline in the coming years. It is estimated to reach 1% by 2023. The world population will continue to grow in the twenty-first century, but at a much slower rate in comparison to the twentieth century. It is estimated that by 2055, the global population will reach 10 billion (http://www.worldometers.info). This means that in about 100 years, the human population will have increased almost four times (from 2.58 to 10 billion).

Both in 1950 and 2017, and probably also in 2050, the largest part of the world's population (>50%) inhabited and will inhabit Asia (Fig. 1.2). In 2017, over 4.5 billion people (almost 60% of the global population) lived there, with the greatest number of people in China and India, 1.41 and 1.34 billion, respectively, which amounts together to about 36% of the world's population. The continent with the

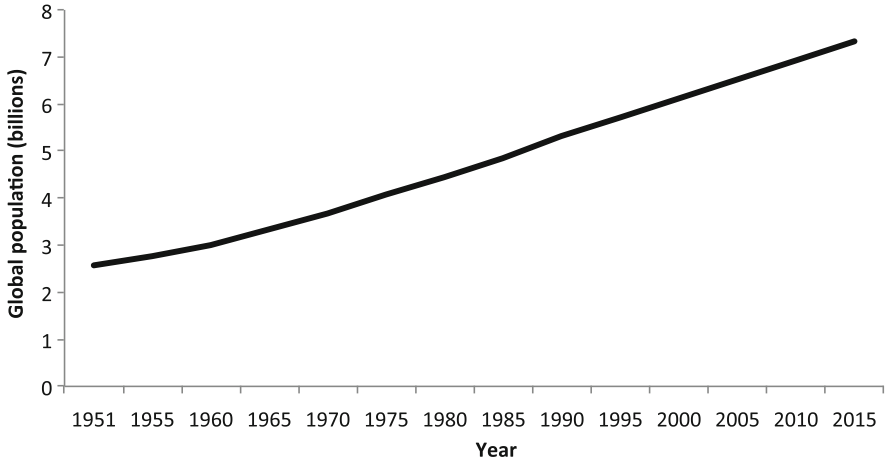
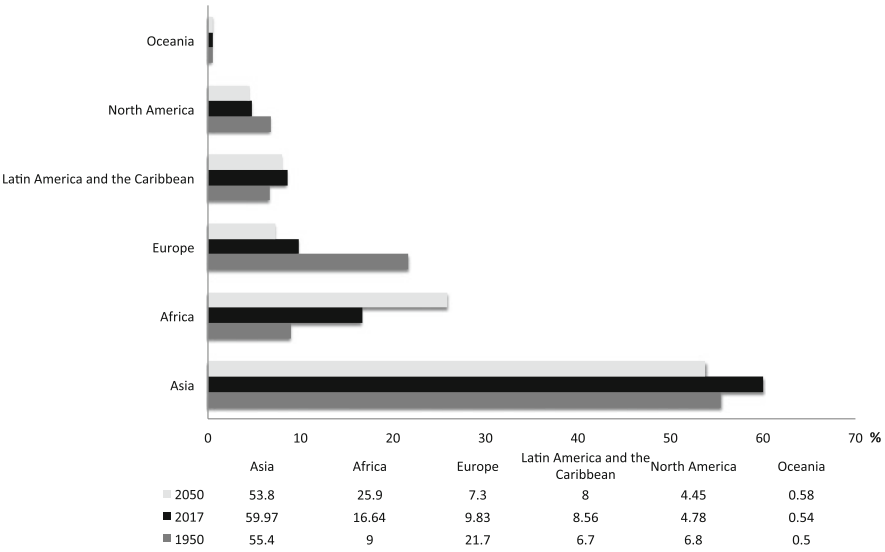


Fig. 1.1 Increase of global population in years 1951–2015 (Source of data UN WPP 2017)



	Asia	Africa	Europe	Latin America and the Caribbean	North America	Oceania
2050	53.8	25.9	7.3	8	4.45	0.58
2017	59.97	16.64	9.83	8.56	4.78	0.54
1950	55.4	9	21.7	6.7	6.8	0.5

Fig. 1.2 Regional share of the global population in years 1950, 2017 and 2050 with total number of people 2.54, 7.55 and 9.77 billion, respectively (Source: UN WPP 2017; www.worldometrics.info)

second largest number of people is Africa, where almost 17% of the global population live.

In 2017, the group of the ten most populous countries of the world, besides China and India, included three other Asian countries (Indonesia, Pakistan and Bangladesh), two countries in Latin America (Mexico and Brazil), one in North America (USA), one in Africa (Nigeria) and one in Europe (Russian Federation). The biggest growth rate between 2017 and 1950 was observed in Pakistan and Nigeria, as the number of people in these countries increased about five times (Table 1.1).

In 2050, the human population in Asia and Africa will presumably amount to 54% and 26% of the world's population, respectively (Fig. 1.2). In the subsequent few decades, population growth in Asia will slow down, but growth will probably accelerate on the African continent as a result of high fertility as expressed in number of live births per woman. Between 2010 and 2015, only 8% of the world's population lived in countries where fertility was $\geq$5 live births per woman. Of 22 countries with such high levels of fertility in the mentioned period, 20 are found in Africa and 2 in Asia (UN WPP 2017). Ninety-five percent of current global population growth (75–80 million annually) occurs in developing countries and only 5% in developed countries. As most demographers have forecast, in approaching decades, the world's population will become larger, older and more urban than it was in the twentieth century, but with much more variance among different regions and across the world (Cohen 2010; United Nations 2004).

Table 1.1 Total population in the ten most populous countries in 2017, the number of their inhabitants in 1950, differences between population size and population ratio 2017/1950

Continent	Country	Population (millions)		Difference between 2017 and 1950	Increase ratio 2017/1950
		2017	1950		
Asia	China	1410	554	+856	2.55
	India	1339	376	+963	3.56
	Indonesia	264	70	+194	3.77
	Pakistan	197	38	+159	5.18
	Bangladesh	165	39	+126	4.23
North America	USA	324	159	+165	2.04
Latin America	Mexico	129	28	+101	4.61
	Brazil	211	54	+157	3.91
Africa	Nigeria	191	39	+152	4.90
Europe	Russian Federation	144	103	+41	1.40

Source of data UN WPP (2017)

2 Main Reasons for, and Natural Consequences of Overpopulation

The rapid growth of the global population in the second half of the twentieth century, unprecedented in the history of mankind, was the result of progress in many areas of life, including medicine, hygiene and healthcare, as well as better access to food and increasing material prosperity, which have all created conditions favourable to the extension of the life span. However, at the same time, this demographic increase has caused dramatic environmental changes, especially in ecosystems and resources (Gardner et al. 2015). In the middle of the last century, the countries of North America (the USA and Canada) and Western Europe, including the UK, France, Germany, Sweden, Denmark, the Netherlands and Norway, dominated the world economic map. While the world was recovering from the aftermath of the Second World War, the production of material goods was growing, which was directly related to the increasing demand for mineral and energy resources (mainly coal, oil and natural gas). This development was accompanied by a huge expansion of the chemical industry and a popular belief that it would bring unending improvement to everyday life. At the same time, huge amounts of chemical pollutants from industry, agriculture, transport and increasingly numerous and populous cities—some of which grew into gigantic agglomerations with slums—were introduced into the environment in an uncontrolled manner. As it turned out, pesticides that were commonly used in agriculture for the protection of crops (insecticides, herbicides, fungicides, bactericides) had very toxic effects not only on pathogenic fungi, bacteria, weeds and the insect pests of plants but also on vertebrates, such as birds and mammals (including humans). Dozens of scientific papers have been written on

pesticides and other pollutants and their adverse influence on the natural environment. One of the most important environmental science works that drew the attention of the general public to the problem (especially in the USA) was the groundbreaking book *Silent Spring* by Rachel Carson (1962). She wrote: "The most alarming of all man's assaults upon the environment is the contamination of air, earth, water, and sea with dangerous and even lethal materials". Unfortunately, more than 55 years later, the processes of releasing thousands of different chemicals into the environment on a tremendous scale still continue, albeit with altered geographical distribution. Since the late 1970s, mainly in developed countries, certain environmental monitoring systems have gradually been created, and legal restrictions concerning the anthropogenic emissions of pollutants on national and multinational levels were introduced (Gorman and Conway 2005; OECD 2011; Kuklinska et al. 2015). Additionally, such countries have prohibited the use of some of the most dangerous pesticides in agriculture, including DDT (UNEP/FAO UN 1991; Bouwman et al. 2013). Over the last 30 years, the greatest problems with chemical emissions in the Northern Hemisphere have been pushed onto the emerging economies of China and India (Tian et al. 2015; Stokes et al. 2016; Gong et al. 2017). The last analysis carried out by Bernhardt et al. (2017) showed that the use of synthetic chemicals, including pesticides, is increasing just as fast as other agents of global change do or even more rapidly. What is more, the range of substances of concern has dramatically expanded since Carson's days, including not only pesticides other than DDT (dichlorodiphenyltrichloroethane), heavy metals and food contaminants but now even many pharmaceuticals as well as substances which act as endocrine disruptors to vertebrates and invertebrates (Cox 1991; Balmford 2013; Goulson 2014; Hayes and Hansen 2017; Bernhardt et al. 2017). Since 1900, roughly 10 million chemical compounds have been synthesized, with some 150,000 or so put to commercial use—although nobody knows the exact number (Gardner et al. 2015).

Classic examples of the dramatic effects of anthropogenic environmental pollution, mainly in the years 1950–1970, include human and animal mercury poisonings originating from industrial sources (including cases in Minamata Bay, Japan, and in Ontario, Canada) and agricultural sources (Sweden and other developed countries of Western Europe), as well as cadmium and pesticide poisonings, including DDT, in Japan (Borg et al. 1969; Ikeda et al. 2015; Blus 2011; Bouwman et al. 2013; Köhler and Triebskorn 2013; Carvalho 2017; Mosa and Duffin 2017). The history of lead poisoning of people and wildlife has been very well documented in different ways, including various pieces of research focusing on automotive fuels, paints and hunting ammunition containing this metal (Tong et al. 2000; Franson and Pain 2011; Ma 2011; Assi et al. 2016; ATSDR 2017).

The aforementioned substances and many others have contributed directly or indirectly to a decline in the population of some animal species in different parts of the world and thus to the increasing rate of their extinction (Sodhi et al. 2008; Acevedo-Whitehouse and Duffus 2009; Bernanke and Kohller 2009; Mitra et al. 2011; Kohler and Triebskorn 2013; Goulson 2014). Other relevant factors pertaining to global population growth and human activity, which are closely related to the loss of biodiversity and extinction of species, are deforestation, desertification, climate

change (including global warming, increased atmospheric methane and dioxide concentrations and enlargement of the hole in the ozone layer over Antarctica), acid rains, habitat loss, overfishing, hunting and the introduction of alien species. According to new research, all these factors pose a threat to life on Earth, raising the risk of extinction by 20–25%, and it is estimated that the current rates of extinction are about 1000 times the background rate of extinction (Nott et al. 1995; McKee et al. 2004; Gaston 2005; Castello 2015; McCauley et al. 2015). It is generally assumed that the rate of extinction in terrestrial and freshwater ecosystems, which are in greater danger of direct anthropopressure and which are better known in this respect, is nine times higher than in the seas (Pimm et al. 2014; Webb and Mindel 2015).

3 Changes in Production and Usage of Trace Elements

The dynamic growth of the global population is reflected by a huge increase in demand for food, freshwater and the natural resources necessary for the production of energy and the material goods on which the functioning of various sectors of the economy is based. Many forecasters ask themselves how many people can live on Earth and what is Earth's carrying capacity. The UNEP study (2012) analysed 65 estimates in that respect from the years 1971–2012, according to which the number of human beings that could possibly exist on our planet falls into a wide range from below 2 to over 1000 billion. However, the most frequently (24/65) estimated number ranged between $\leq$8 and $\leq$16 billion. There are many indications that in this century, between 2055 and 2070, the world's population will reach 10 billion, thus becoming ten times larger than it was in 1800 (Bongaarts 2009; http://www.worldometers.info). However, the UNEP study (2012) shows that predictions concerning the growth of human population tend to be uncertain, and the further into the future they are made, the more uncertain they become. Unquestionably, since the 1950s there have been enormous technological advances in various areas of life, but as numerous studies indicate, the increase in demand for and exploitation of many resources is faster than the growth of the global population because everyone wants a good quality of life, including the residents of the most populous countries in Asia and Africa (Steffen et al. 2011; Balatsky et al. 2015; Meinert et al. 2016). As stated in a report by Ewing et al. (2010), "if everyone lived the lifestyle of the average American, we would need five planet Earths". Future trends in demography, biosphere exploitation and environmental pollution depend largely on today's policies (UNEP 2012).

Releasing a multitude of elements from different minerals and introducing them into geochemical circulation, landscape transformations, soil erosion, climate warming and changes in water relations in many regions of the world as well as the gigantic amounts of pollutants emitted as the result of economic activity, degenerations of ecosystems and extinction of various species are happening on a scale and at a pace that has never occurred during the 4.5 billion years of Earth's history. Since the acceleration of the Industrial Revolution around 1850, over a

period of less than two centuries, which by the geological time clock is merely a fraction of a second, people have become a huge geological force (van der Pluijm 2014). The rapid changes on our planet caused by people have prompted scientists to introduce the term "Anthropocene" into the timescale of Earth's history. This informal term refers to the new epoch, which follows the Holocene (or postglacial epoch) and which began about 11,700 years ago. However, geologists still debate when the exact beginning of the Anthropocene would be (Crutzen and Stoermer 2000; Monastersky 2015). Some scientists identify its onset with the arrival/acceleration of the Industrial Revolution, and this idea has been popularized by environmentalists, politicians and the media (Clemencon 2012; Syvitski 2012; van der Pluijm 2014; Corlett 2015; Monastersky 2015; Olsson et al. 2017).

Out of 118 elements naturally occurring on Earth, only a small number are considered essential to the life of organisms. All living creatures have four basic elements (the big four) in their organisms, carbon (C), hydrogen (H), oxygen (O) and nitrogen (N), which amount to more than 95% of their body masses. Aside from the big four, other major elements include phosphorus, sulphur, sodium, chlorine, potassium, calcium and magnesium. These make up the remaining 3.5% of the body mass of living things. The other elements essential for life, which amount to about 0.5% of the body mass of living organisms, are said to belong to the group of microelements. Individual eukaryotic and prokaryotic taxonomic groups may vary considerably between themselves, mainly with regard to their demand for microelements. Microelements performing important physiological functions in all plants include chlorine (Cl), boron (B), iron (Fe), manganese (Mn), copper (Cu), zinc (Zn), nickel (Ni) and molybdenum (Mo), while the number of all elements essential for life is 17 (Soetan et al. 2010; White and Brown 2010). It is estimated that the bodies of vertebrates, including humans, are composed of about 21–25 elements, while the group of microelements include B, cobalt (Co), Cu, Fe, iodine (I), Mn, Mo, selenium (Se) and Zn. In addition, several further elements such as arsenic (As), fluorine (F), Ni, silicon (Si) and vanadium (V) are believed to have beneficial effects on human health (Nielsen 1984, 1998; WHO 1996; Chellan and Sadler 2015). However, some microelements may become harmful at high levels of exposure or may cause malnutrition in case of deficiency. At the same time, it should be noted that some non-essential elements penetrate from the environment into various organisms, of which human beings are the best known, but also including domesticated animals and arable crops. Their physiological role is not always known. Some are considered neutral; others have proven toxic effects, such as lead (Pb), cadmium (Cd) and mercury (Hg). For many decades some of the non-essential elements, such as As, Cd, Hg and Pb, have attracted attention worldwide because of their toxicity to living organisms.

Numerous interactions among elements in the inanimate environment, and acid rains containing elevated levels of S and N oxides, facilitate increased mobilization of heavy metals in soil and consequently their uptake by plants, which leads to increased supply and absorption of various metals and non-metals by herbivores, then omnivores and predators. There might also be a new environmental menace related to nanomaterials or particles with at least one dimension of 100 nm or less.

Some of them are natural nanoparticles (NPs), but ecotoxicologists specializing in nanoecotoxicology raise concern over the possible adverse influence of nanomaterials on living systems due to increasing diversity within and amounts of engineered NPs. These engineered materials such as carbonaceous NPs, metal oxides, zero-valent metals, semiconductor materials and nanopolymers are introduced into the environment both unintentionally and intentionally (Viswanath and Kim 2016). For a few decades now, many metals and their oxides have been used for the manufacture of NPs, including Cd, Cu, Fe, Mn, Zn, aluminium (Al), titanium (Ti), silver (Ag) and gold (Au) due to the ever-broadening use of these elements in consumer products, chemical and medical equipment, information technology and energy production, among other things. Present knowledge on the behaviour of metals containing NPs and other such materials in the natural environment and their possible effect on biota is extremely limited, but many scientists think that NPs are a class of newly emerging environmental pollutants (Peralta-Videa et al. 2011; Thiery et al. 2012; Ray et al. 2009; Ding et al. 2015; Viswanath and Kim 2016; Giese et al. 2018). Perhaps nanomaterials, along with other new anthropogenically manufactured or used elements such as synthetic chemicals and radionuclides, as well as the man-made enrichment of biogeochemical cycles with dozens of metals and non-metals released from mineral deposits, will become hallmarks of the Anthropocene (Whitmee et al. 2015; Brondizio et al. 2016).

The manufacture of NPs and their dissemination by humans in nature span only the last two or three decades, but these processes have a tendency towards rapid increase (Salata 2004; Inshakova and Inshakov 2017). On the other hand, the acquisition of metal ores and other minerals on a gigantic scale, including those used in the production of energy or for various economic purposes, has been taking place for an incomparably longer time (at least extending to the last two centuries). Metals have long been used by humans since prehistoric times, but their application on a mass scale is a relatively recent phenomenon. In the first part of the twentieth century, world metal production rose from 30 million tons in 1900 to 198 million tons in 1950. After reaching 740 million tons in the 1970s, the output levelled off for the following 20 years. But then, driven mainly by economic expansion in China, another phase of rapid growth occurred. The bulk of these figures are connected with steel production, which expanded at least 56 times since 1900 (Gardner et al. 2015). In 1950 and 2015, steel production reached 134 and 1640 million tons, respectively, which means an over 12-fold increase in this period (Norwood et al. 1951; US GS 2016). As a result of very intense economic activity, including metal acquisition and processing, numerous elements have been introduced into the biogeochemical cycles in quantities often far greater than those resulting from natural biotic and abiotic factors or processes, such as weathering of rocks, erosion, volcanic eruptions and fires. The most attention has been devoted to this problem with regard to biogenic elements (C, N, P, S) and their influence on climate changes, engineered metals (e.g. Ag, Al, Cr, Cu, Fe, Ni, Pb and Zn, among which the major industrial metals are Al, Cu, Fe and Zn in the human-built environment) and toxic elements such as lead (Pb), cadmium (Cd), mercury (Hg) and arsenic (As), which are of interest because of the health hazards they pose to humans and ecosystems (Nriagu and Pacyna 1988; Mackenzie and Chris 1993;

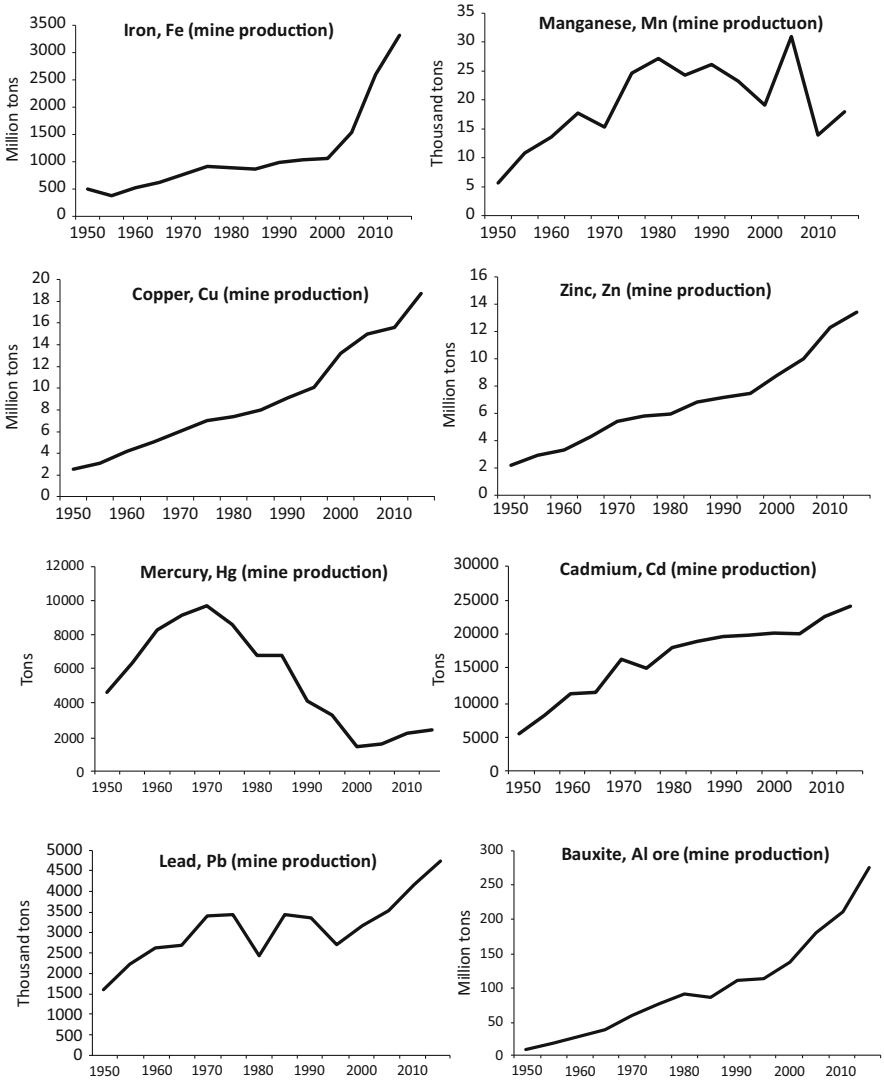


Fig. 1.3 Selected metal mine production in years 1950–2015 (Source of data: Bureau of Mines, Minerals Yearbook: 1951, 1956, 1961, 1966, 1971, 1981, 1986, 1991, 1996, 2001, 2006, https://minerals.usgs.gov/minerals/pubs/usbmmyb.html; US GS 2011, 2016. Mineral commodity summaries. US Geological Survey, p 202, https://doi.org/10.3133/70140094)

Candelone et al. 1995; Wang et al. 2010; Klee and Graedel 2004; Rauch 2009; Rauch and Pacyna 2009; Sen and Peucker-Ehrenbrink 2012; Galloway et al. 2014; Gardner et al. 2015; Nishijo et al. 2017; Obrist et al. 2018).

Figure 1.3 depicts selected metals (Fe, Mn, Zn, Cu, Hg, Cd, Pb, Al) with varying dynamics in their ore mining in the years 1950–2015, usually with an upward trend.

The exception to this is Hg (characterized by very high toxicity and atmospheric mobility), which when carried by air masses can travel thousands of kilometres and cover distances between continents. Owing to mercury toxicity and concerns for the environment and human health, and as the result of the long-term efforts of some international bodies, the world's nations have adopted the Minamata Convention on Mercury to protect humans and nature from mercury pollution. The Convention came into force on 16 August 2017. In many countries with large mercury ore deposits, including those belonging to the European Union and the USA, extraction of Hg had already been discontinued. The exception is China, where most Hg is currently mined (US GS 2016; UN Environment 2017). In 2015, about 50% less Hg was extracted globally when compared to 1950–2340 and 4605 tons, respectively (Fig. 1.3). It should be noted, however, that mercury had previously been intensively produced, among other things, for the purposes of extracting precious metals (silver and gold) using an amalgamation method that utilizes mercury's ability to form alloys with them, from which it is later evaporated. Particularly large amounts of Hg were used in the period of the gold and silver rushes in North America at the turn of the nineteenth and twentieth centuries, as is reflected by deposits found on this continent containing elevated levels of the toxic metal (Hylander and Meili 2003; Strode et al. 2009; Horowitz et al. 2014).

During the last 65 years, the largest increase in production of the aforementioned metals has occurred with aluminium ore (bauxite)—over 33 times, from 8.2 to 274 million tons. In 2015, the world smelter production of aluminium (the third most abundant element after O and silicon, Si, and the most abundant metal in the Earth's crust) reached over 58 million tons, caused by a huge demand for this metal due to its versatile applications (US GS 2016). During the discussed period, iron ore production increased >6 times (from 498 to 3.320 million tons), copper production (from 2.5 to 18.7 million tons) and zinc (from 2.2 to 13.4 million tons). Furthermore, manganese ore production increased 3.2 times (from 5.6 to 18,000 tons, with a maximum value of 31,000 tons in 2005) and cadmium 4.3 times (from 5.666 to 24.200 tons). In the case of lead, its production increased ~2.9 times (from 1.640 to 4.710 thousand tons), but during the discussed period, there were two distinct decreases, in 1980 and 1995. They were at least partly related to the withdrawal of lead additives to gasoline and paints in well-developed countries. On the other hand, a persistent and clear upward trend continues after 1995, mainly due to the growing demand for lead for battery manufacturing, including those used in vehicles (Davidson et al. 2016; US GS 2016; Mohr et al. 2018). Some experts believe that despite the increase in production of various metals over the past 50 years, their reserves have remained largely unchanged. Additionally, in the case of most metals, recycling currently satisfies 10–20% of demand, and new technologies play an important role in the more economical management of metals (Bloodworth and Gunn 2012; Arndt et al. 2017; Mohr et al. 2018).

These examples of the increased mining of metal ores (except for Hg) in the last 65 years are closely related to the growth of the human population and the extremely intense anthropogenic mobilization of those and many other elements found in the Earth's crust (Halada et al. 2008; van der Voet et al. 2013; Meinert et al. 2016). Their

mobilization is the result not only of mining and smelting but also processing (including processing metals from recycling), use in various economic sectors, combustion of fossil fuels and biomass, deforestation and improper agricultural uses of soil conducive to their erosion. These processes are accompanied by the emission of metallic and non-metallic pollutants into the air, water and soil. Various elements are partly subject to redeposition processes on land and ocean surfaces and remineralization in soils and sediments, but they are also partly remobilized, which is well known and broadly described in the case of a small group of elements, including those mentioned above. The most comprehensive current studies in this field include Klee and Graedel (2004) and Sen and Peucker-Ehrenbrink (2012), which analysed 91 and 77 elements, respectively. These reports estimated, among other things, anthropogenic mobilization (AM) and natural mobilization (NM), the ratio between them (AM/NM), total mobilization (TM = AM + NM) and percentage share of AM in TM (AM/TM). According to Klee and Graedel (2004), the anthropogenic mobilization of almost 3/4 of the elements they analysed exceeds natural mobilization, and the AM/TM ratio exceeds 50%. However, Sen and Peucker-Ehrenbrink (2012) suppose that the value >50% of the ratio may concern up to 80% of the elements (62/77), while in anthropogenic contributions, soil erosion and eolian dust (results of unsustainable farming practices and deforestation in large scale) are considered.

In Table 1.2, based on the research by Klee and Graedel (2004), 17 elements are listed, which are discussed in more detail in this book. In the case of Cu, Cr, Fe, Hg, Pb and Sn, it can be assumed that 75–99% of their amounts present in the natural environment were mobilized as the result of human activity. This includes Hg (AM/TM = 95%) and Pb (AM/TM = 84%), i.e. two metals with remarkably toxic effects, as well as Cr (AM/TM = 99%) which is mobilized 140 times more due to human activity than to natural processes. Hazards to both human and animal health and threats to entire ecosystems are caused not only by the increasing amount of metals mobilized from minerals but also by their transformations in the environment affecting the oxidation state and the occurrence of various inorganic and organic compounds with different biochemical properties. For example, Cr(III) is a micronutrient, while Cr(VI) is a carcinogenic and mutagenic mammalian agent. Inorganic Hg forms are less bioavailable than organic methyl mercury (Adriano 2001; Gall et al. 2015; Mikulewicz et al. 2017). Anthropogenic mobilizations of silver (Ag), arsenic (As), fluorine (F), iodine (I) and nickel (Ni) also exceed natural mobilizations. The values of their AM/TM ratio range between 51 and 75%. In the case of six elements (Al, Cd, Mn, Mo, Se, Zn), the values of their AM/TM ratios fall below 50% (range 17–47%).

Since the 1950s humanity has been developing new technologies to meet its rapidly growing needs, which have effected not only quantitative but also qualitative changes in the demand for various raw materials and the methods of their use. The search for new deposits of metal ores and improvements in acquisition of various elements from poorer minerals is ongoing (Halada et al. 2008; Balatsky et al. 2015; Arndt et al. 2017). The world is changing at an unusually fast pace under the enormous pressure of the incessantly growing human population. Many raw materials are being depleted, including fossil fuels and the ores of some metals, natural

Table 1.2 Calculation of mobilization rates and dominance of selected elements

Element	Anthropogenic mobilization, AM (Tg/year)	Natural mobilization, NM (Tg/year)	Total mobilization, TM = AM + NM (Tg/year)	Anthropogenic vs. natural ratio (AM/NM)	Anthropogenic as % of total (AM/TM × 100%)
Ag	0.02	0.01	0.03	1.4	58
Al	80	228	309	0.4	26
As	0.08	0.05	0.1	1.7	63
Cd	0.03	0.1	0.16	0.2	17
Cu	13	2.3	16	5.9	85
Cr	15	0.1	15	139	99
F	3.0	1.4	4.4	2.2	69
Fe	762	86	848	8.9	90
Hg	0.06	0.003	0.07	18.5	95
I	0.05	0.02	0.07	1.9	66
Mn	8.8	32	40	0.3	22
Mo	0.2	0.6	0.8	0.3	24
Ni	1.6	0.7	2.3	2.3	69
Pb	3.3	0.6	3.9	5.2	84
Se	0.01	0.05	0.05	0.2	17
Sn	0.3	0.07	0.3	3.5	78
Zn	9.4	10	20	0.9	47

Tg, tetragram = 1,000,000 tons
Source of data: Klee and Graedel (2004)

ecosystems are shrinking and biodiversity is decreasing, while environmental pollution increases, which results in adverse climate changes. According to geological research, five great extinctions of species have occurred in the history of the Earth, the causes of which are still being investigated. Probably one of the most important ones was climate warming and increasing emissions of volcanic dusts and gases containing many toxic substances, including mercury (Bond and Grasby 2016; Racki et al. 2018). The sixth extinction that we are currently witnessing is accompanied by climate warming and anthropogenic emissions of Hg and many other heavy metals, as well as many synthetic pollutants.

In the face of the numerous deep and unfavourable changes taking place on Earth as the result of human activity in such a relatively short period of time and on such a large scale, efforts have been made, at least since the 1970s, to stop them. Public awareness in this field increased greatly with the publication of a report by the United Nations World Commission on Environment and Development. This report, entitled *Our Common Future* (Brundtland 1987), contained the definition of the term "sustainable development" (development that meets the needs of the present without compromising the ability of future generations to meet their own needs). The term became very popular in later years (e.g. in economy, politics, sociology and environmental sciences), but its definition was imprecise and concerned an unspecified period of time, measured by the length of a human lifetime (Bartlett 1998). Referring to the first two laws of sustainability, the author emphasized that population growth cannot be sustained in any society and that the larger the population, the more difficult it will be for the society to achieve sustainability. According to subsequent scientific studies and analyses, reality has turned out to be much more complicated and destructive for Earth than anyone suspected while preparing Brundtland's report and later documents for the United Nations Conference on Environment Development (also known as the Rio de Janeiro Earth Summit) in 1992 or the United Nations Conference on Sustainable Development in 2012 held in Rio again and commonly called Rio + 20 or Rio Earth Summit 2012. The analysis of demographic and economic trends between the first and second Rio Earth Summits shows that the global population increased during this period by 30%, but the production of cement, plastics and steel by 170%, 130% and 100%, respectively. In the two aforementioned decades, one of the few beneficial changes that have taken place in anthropogenic environmental impact has been the decreasing use of ozone-depleting substances by 93% (Clemencon 2012; Gardner et al. 2015; www.worldometers.info). The incessant demographic increase of the global population has rapidly eroded Earth's biosphere (de Sherbinin et al. 2007; Bradshaw and Brook 2014; Balatsky et al. 2015; Fagerberg and Srholec 2017). Unfortunately, most people in the world live only in the shell of their own personal and local problems, focusing on satisfying their own needs and dreaming about "American style" prosperity. Vast masses of people, especially those living in developing countries, but also the majority of political and economic decision-makers at various levels seem not to comprehend the severity of the situation indicated by only too abundant evidence and arguments presented by scientists pertaining to increasing environmental degradation and resource shortages occurring at a rate that can no longer be sustained.

The first manifesto concerning this problem, called *World Scientists' Warning to Humanity*, was penned in 1992, and the second was published 25 years later, in 2017. Many examples of the diverse and effective steps humanity can take to transition to sustainability were presented in the first manifesto. One of the most important ones should be to further reduce fertility rates by ensuring that women and men have access to education and voluntary family-planning services, since the environmental problems of our planet are closely related to progressing overpopulation. Unfortunately, we have not heeded the recommendations presented in the list of very important steps to be taken, so well-articulated by the world's leading scientists who first warned humanity 25 years ago. Time is running out, and soon it will be too late to shift our course away from its present disastrous trajectory (Ripple et al. 2017).

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Chapter 2
Endothermic Animals as Biomonitors of Terrestrial Environments

Elżbieta Kalisińska

Abstract Since the late 1980s, wildlife toxicology has grown considerably as an important field of laboratory and field research. It focuses on the effects of various chemicals on the reproduction, health, and well-being of wildlife, including essential and nonessential elements. Deficiency of essential elements (e.g., copper, manganese, nickel, zinc, selenium) can lead to adverse effects in endothermic vertebrates, while their excess may result in significant intoxication or even death. However, the greatest concern is the contamination with highly toxic nonessential elements such as mercury, lead, cadmium, and arsenic.

Human activity results in the introduction of large amounts of essential and nonessential trace elements into biogeochemical cycles. Particularly exposed to excessive levels of trace elements are top avian and mammalian predators at the end point of biological pathways along which contaminants may accumulate in increasing concentrations. Determinations of trace elements in samples from selected species serving as biomonitors can be used to indirectly assess the condition of terrestrial ecosystems, including herbivorous, omnivorous, and predatory wildlife. Biomonitors are usually native species common in the area (involving hunted animals) but also invasive species (in Europe American mink and raccoon from North America; in the USA and Canada wild boar and common starling from Europe). Biomonitoring using terrestrial birds and mammals can be local, regional, or continental and is well developed in many countries of the Northern Hemisphere, especially in North America and Europe.

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1 Introduction

Since the 1950s, the dynamic growth of the world's population has been accompanied by growing levels of environmental pollution, resulting in a multifaceted destruction of natural biological systems, as observed both locally and globally. This has been accompanied by an increase in interest in environmental phenomena and developments in ecology, including ecotoxicology. Research has shown that measurements of the levels of various substances in air, water, and soil from chemical monitoring of the environment are still not sufficient to properly assess the health hazards to humans, animals, plants, and entire ecosystems. Currently, the use of living or deceased organisms in biotesting, bioindication, and biomonitoring is an established method of determining inorganic and organic contaminants and pollutions (Burger 2006a; Bealey et al. 2008; Holt and Miller 2011; Markert 2013).

The terms "bioindicator," "biomonitor," "bioaccumulator," and "biomarker" have all been used in varying ways to describe different approaches and techniques for studying biological responses to pollution of the air and other environmental components. In ecological and environmental sciences, the terms "biomonitor" and "bioindicator" have been and still are used interchangeably, and the terminology in this area can be ambiguous. However, since the early 1990s, we may observe a certain distinction in the use of these terms (Burger 2006a, b; Wilkomirski 2013; Sidding et al. 2016). Biomonitoring can include both a qualitative (bioindicator) and quantitative (biomonitor) approach in pollution control. For example, chemical analysis of biomonitors (an organism or its part or a community of organisms) contains information on the quantitative aspects of quality of the environment. A biomonitor is also a bioindicator, except that it quantifies the impact or eventual outcome on an organism or ecosystem and their health (O'Brien et al. 1993; Markert et al. 2003; Burger 2006a; Bealey et al. 2008). Large-scale biomonitoring uses plant and animal bioaccumulators, or organisms that accumulate various chemicals (including contaminants) in the tissues. Bioaccumulation is result of the biological sequestering of many substances often at a higher concentrations than that at which they occur in the surrounding environment or/and in food of animals.

2 Trace Elements

Some elements present in inorganic/organic forms in organisms are essential elements and others nonessential. In biochemistry, an essential trace element (or micronutrient) is a dietary mineral that is needed in very minute quantities (expressed in micrograms or milligrams) for the proper growth, development, and physiology of the organism. In humans the requirement per day is below 100 mg, with a deficiency leading to disorders that may even prove fatal.

In endothermic vertebrates, the biochemical functions of essential trace elements include enzyme activity, transport of oxygen (iron and copper), organization and

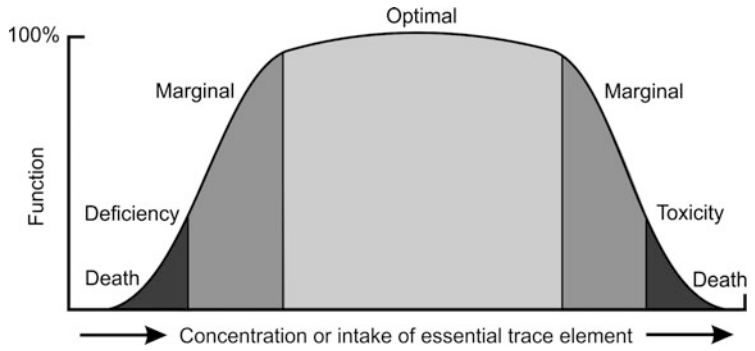

Fig. 2.1 Dependence of biologic function on the tissue concentration of essential trace elements (according to Aras and Ataman 2006)

structure of macromolecules, vitamin activity (cobalt and vitamin B_{12}), or hormonal activity, e.g., iodine and thyroid hormones (Taylor 1996). All essential elements may even be toxic in animals and humans if ingested at sufficiently high levels and for a long enough period (Fig. 2.1). This aspect has been well recognized in humans, domesticated and laboratory animals, yet very poorly in wildlife (WHO 1973; Wada 2004; NRC 2005; Aras and Atman 2006; Lopez-Alonso 2012; Yatoo et al. 2013; Prashanth et al. 2015; Bhattacharya et al. 2016).

According to the National Research Council (NRC 2005), heavy metals (accepting as a criterion a density of at least 5.0 g cm^{-3}) such as cobalt (Co), chromium (Cr), copper (Cu), iron (Fe), manganese (Mn), molybdenum (Mo), and zinc (Zn) and two nonmetal elements (iodine (I) and selenium (Se)) are considered essential trace elements for higher animals. NRC (2005) classified nickel (Ni) as a possible essential element, while in the case of fluorine (F), which is nonmetallic, opinions are divided. Some researchers believe that F is an essential element for animals and humans while others consider the available evidence for indispensability to be insufficient. Elements essential to domestic, laboratory, or wild mammals and birds may not be essential to humans and vice versa.

In the document by the WHO (2002), the following trace elements are described as essential for human health: Cu, Zn, Fe, Cr, Mo, Se, Co, and I (the list includes Cr but its status as an essential element is controversial, where CrIII is beneficial for animals and humans but CrVI is a human carcinogen). The next smaller group is composed of Si (silicon), Mn, Ni, B (boron), and V (vanadium) with those elements classified as probably essential elements for humans. There are some differences between the NRC (2005) and WHO (2002) reports concerning the essentiality of elements for animals and humans, and the discussion on essentiality of some of those elements is still open (Aras and Ataman 2006; Bhattacharya et al. 2016; Maret 2016).

The term "trace element" is also used in analytical chemistry and geochemistry. In analytical chemistry it is an element whose average concentration is less than 100 mg kg^{-1} (<100 ppm) but in geochemistry it is less than 1000 mg kg^{-1}

(<1000 ppm) or 0.1% of a rock's composition. Elements from mineral deposits are activated as a result of natural processes, but their contribution to the biogeochemical cycles is very much driven by human economic activity, especially over the last 100–150 years (Klee and Graedel 2004). The natural distribution and concentration of elements in the Earth's crust are very diverse as a result of the geological structure, but they are subject to strong anthropogenic modification having a significant impact on the mineral composition of plants, animals, and people and consequently on their condition, health, and reproduction (Adriano 2001; Yaroshevsky 2006; Steinnes 2009; Kabata-Pendias 2011). Among the elements, which can occur in living creatures, special attention is paid to all the essential and some of the nonessential trace elements, the latter having no biological function. For a long time, the greatest concerns have been triggered by heavy metals which are highly toxic to endothermic vertebrates, such as cadmium (Cd), lead (Pb), mercury (Hg), and arsenic (As), the latter being metalloids (Nriagu and Pacyna 1988; Adriano 2001; Anke et al. 2001; Jarup 2003; Hubner et al. 2010; Tchounwou et al. 2012). Additionally, for several decades, there has been an increasing interest on other metallic xenobiotics such as silver (Ag) and aluminum (Al) due to their high neurotoxicity and increasing distribution in the environment, including man-made Ag and Al nanoparticles (Ray et al. 2010; Stensberg et al. 2011; Jaishankar et al. 2014; Karmakar et al. 2014). Table 2.1 summarizes the concentrations and densities of selected trace elements found in the Earth's crust, which in varying amounts accumulate in wild-living endothermic vertebrates (Selinus and Finkelman 2011). Some of them are classified as essential elements and some as nonessential elements, all of which are discussed in more detail in the respective chapters of this book. In the case of wildlife, the ranges of mean concentrations of elements are shown for the liver, because this organ plays a key role in trace element regulation, bioaccumulation, and detoxification (Vikøren et al. 2005; Horai et al. 2006; Neuschwander-Tetri 2007). In addition, the liver is one of the most extensively used biological materials in ecotoxicological studies for quantifying trends in medium- to long-term contaminant exposure, with most data in this field existing from hepatic tissue (Burger et al. 2000; Gamberg et al. 2005; Braune and Malone 2006; Taggart et al. 2006; Vikøren et al. 2011; Gall et al. 2015; Espin et al. 2016; Kitowski et al. 2017).

In the group of essential elements, mean concentrations in the liver may in some cases reach one (Cr, Cu, Mo, Zn) or three (Se) orders of magnitude higher than their level in the Earth's crust. Liver concentrations of nonessential and highly toxic elements such as Cd, Hg, Ag may also be three orders of magnitude higher than in the crust. In the case of As and Sn, average hepatic concentrations may exceed those in the crust by two or one order of magnitude, respectively.

Eukaryotic organisms, including vertebrates, have evolutionarily developed mechanisms that enable them to maintain a proper level of various essential trace elements and homeostasis (Zhang and Gladyshev 2010). Terrestrial vertebrates via physiological and anatomical means have regulated and/or stored essential elements, including heavy metals up to certain exposure levels such that metals may not be present in their bodies in a concentration, form, or place that can result in a toxic effect. In such regulation, the gastrointestinal tract and the liver play crucial roles in

Table 2.1 Density and concentration of selected elements in the upper continental crust (according to Yaroshevsky 2006), their biochemical status (NRC 2005), and range of mean hepatic levels in wild endothermic animals

Element	Density (g cm^{-3})	Crust concentration	Biochemical status and range of mean hepatic concentration (ppm dw)			No. of chapters in this book
			Essential	Probably essential	Non-essential	
Ag, silver	10.49	0.07 ppm			<DL–44.0	18
Al, aluminum	2.70	8.05%			0.20–25.35	12
As, arsenic	5.73	1.70 ppm			0.05–122.6	13
Cd, cadmium	8.65	0.13 ppm			0.05–163.2	14
Cr, chromium	7.14	83.0 ppm	0.05–150.0			3
Cu, copper	8.92	47.0 ppm	10–790			4
F, fluorine	1.70[a]	660 ppm			<2.6–270[b]	15
Fe, iron	7.87	4.65%	<100–4920			6
Hg, mercury	13.53	0.08 ppm			<DL–35	17
I, iodine	4.94	0.40 ppm	0.17–0.35[c]			5
Mn, manganese	7.47	1000 ppm	2.20–38.3			7
Mo, molybdenum	10.28	1.10 ppm	0.9–13.0			8
Ni, nickel	8.91	58.0 ppm		0.01–13.0		9
Pb, lead	11.34	16.0 ppm			0.30–48.0	16
Se, selenium	4.82	0.05 ppm	<0.20–23.0			10
Sn, tin	7.31	2.50 ppm			<0.01–15.0	19
Zn, zinc	7.14	83.0 ppm	21.0–297.4			11

ppm parts per million or mg kg^{-1}, *dw* dry weight, *DL* detection limit

[a]Density of F in g L^{-1}

[b]In literature no data on wild animals was found, just fluoride concentrations in the livers of control laboratory rat and fatal human cases because 99% of fluorine is retained in bones and teeth (Inkielewicz and Krechniak 2003; NRC 2005; Martinez et al. 2007)

[c]Data available for farm animals only

the uptake and transport of cations (e.g., Cu, Fe, Zn). The anionic group such as Mo and Se is more water-soluble and is less reactive with nitrogen, sulfur, phosphorus, and oxygen, as well as hydroxide groups, than are cations. They are absorbed very efficiently through the intestine. In general, total body burden is regulated by renal excretion (WHO 1996; Rutherford and Bird 2004; US EPA 2007; Lopez-Alonso 2012; Sakulsak 2012; Kim and Oh 2013). Toxic elements strongly affect some essential element metabolisms because they compete for binders for these elements in the biological system. Concentrations of various essential and nonessential elements in birds and mammals depend on many factors and processes, including their forms, oxidation state, and the amount in habitats; biotransformation, bioavailability, diet, and position in the food chains of endothermic vertebrates; absorption (in which the intestinal route is the most important); and the duration of exposure (Chapman 1996; Adriano 2001; Martelli et al. 2006; Diaz-Bone and van de Wiele 2010; García-Barrera et al. 2012; Bhargava and Bhargava 2013). Heavy metals (both essential and nonessential) and metalloids (such as Se, As) in wildlife are the most often analyzed pollutants (Burger 2006b; Jaishankar et al. 2014; Stankovic et al. 2014; Gall et al. 2015; Espin et al. 2016), wherein pollution is defined as contamination that does or can result in adverse biological effects to resident communities. All pollutants are contaminants (substances which are present at places where they should not be or at concentrations above background), but not all contaminants are pollutants (Chapman 2007). Unlike plants and lichens, domestic and wild animals do not usually show qualitative morphological and/or physiological changes as a consequence of chronic bioabsorption of trace elements and the undesirable effects caused by them, which would allow these animals to be considered as bioindicators. There are only a few examples in this field from areas where a natural excess of these elements is noticed. These include loss of hair and malformations of hooves as a result of excessive selenium in food sources and dental fluorosis as a result of a high uptake of fluoride dissolved in groundwater (James and Shupe 1984; Al-Dissi et al. 2011; Choubisa et al. 2011). Wildlife is very often used as a biomonitor where they chronically bioaccumulate trace elements and other substances, but the reaction of the animals to them are generally invisible. These substances qualitatively and quantitatively can be assayed in laboratories using highly specialized and sensitive equipment, from samples of the appropriate biota (Markert et al. 2003).

3 Terrestrial Endothermic Vertebrates as Biomonitors

Since the 1970s there has been a steady and dynamic growth in research and implementation of biomonitoring programs that use organisms from various taxonomic groups as biomonitors of environmental pollution. Of the terrestrial endothermic vertebrates, mainly wild animals but sometimes also breeding birds and mammals (including furbearers) are chosen (Wren 1984; O'Brien et al. 1993; López Alonso et al. 2002; Golden and Rattner 2003; Tataruch and Kierdorf 2003; Ji et al.

2006; Wolfe et al. 2007; Rabinowitz et al. 2009; Reis et al. 2010; Rajaganapathy et al. 2011; Kalisinska et al. 2012a). The consequence of this has been an increase in the number of reports in this field concerning wildlife. Of particular interest are persistent organic pollutants (including organochlorine pesticides and polychlorinated biphenyls (PCBs)), but much attention is also devoted to trace elements (Golden and Rattner 2003; Markert et al. 2003, 2008; Stolen et al. 2005; Burger 2006b; Hollamby et al. 2006; Holt and Miller 2011). Warm-blooded biomonitors can be used for information on:

- Essential and nonessential element concentrations and relations between them in selected species (especially in rare and threatened birds and mammals, common species, including game animals, which are used by humans as food and potentially valuable source of minerals but may also contained toxic contaminants)
- Concentrations and bioavailability of essential elements in an area of interest important for the detection of their deficiency or excess and which may be referenced in proper steps in the management and health protection both in animals and humans (e.g., level of selenium is significant in protection against mercury toxicity)
- Bioindicators can be used as information about various temporal and spatial changes occurring in a specific area (including those from anthropogenic and natural sources such as atmospheric deposition, floods), especially in the case of xenobiotic metals and metalloids
- Differences in trace element concentrations among animals from the same area (or from control and contaminated sites) and the various trophic levels
- Ecotoxicological situation of selected species which are widely distributed in various provinces, states, countries, and even continents

Depending on the purpose of the research or the biomonitoring program being implemented, one or several of the above points may be taken into account, but there may also be others not mentioned above (Talmage and Walton 1991; Stolen et al. 2005; Burger 2006a; Smith et al. 2007; Zhang and Ma 2011; Garcia-Fernandez 2014; Espin et al. 2016; Herzke et al. 2017). Species that are targeted as candidates of bioindicators of trace elements should have desirable characteristics including:

- Are sensitive and indicative of change
- Broad distribution with accompanying data
- Easily measured and readily observable
- Well-known ecology and life history
- Suitable for lab studies
- Significant to humans
- Economical/cost-effective
- Well-developed and usable with existing data
- Common enough not to impact populations

Lists of characteristics may differ from one another to a certain point, and a potential or suitable terrestrial candidate may fulfill only some of the desired features (O'Brien et al. 1993; Hollamby et al. 2006; Espin et al. 2016; Herzke et al. 2017). It

seems that the list of avian species is much longer than that of mammalian species. This is due not only to the greater number of bird species found in the world, which is almost twice as much as mammals (9993 and 5416 species, respectively), but also from a much larger and more active group of people professionally and amateurly researching and observing birds (ornithologists, volunteers, and bird-watchers) compared to the analogous "mammalian" group (Jones and Safi 2011; Jetz et al. 2012). The highest biodiversity of birds and mammals is recorded in tropical regions. Mammalian and avian fauna in Europe in comparison to other parts of the Northern Hemisphere is poorly diversified, with the avifauna of eastern Asia about 50% richer than Europe and North America, and Western North America the richest region with 14% and 44% more species than eastern Asia and Europe, respectively (Monkkonen and Viro 1997). However, wildlife researchers and observers mainly operate in Europe and North America, which are dominated by animal species of temperate and boreal biomes, with a much better knowledge of their biology. For example, in Europe about 270 mammalian species and 400 avian species are noticed, and in continental North America (USA and Canada) over 710 and 540 species, respectively (Leveque and Mounolou 2003; Arita et al. 2005; Thuiller et al. 2014; Sauer et al. 2017). For biomonitoring goals, much more numerous and more diverse avian samples and information on them than mammalian have been gathered. It concerns terrestrial wildlife too (Frank 1986; Ma et al. 1991; Furness and Greenwood 1993; Golden and Rattner 2003; Rattner et al. 2005; Burger 2006b; Smith et al. 2007; Schmeller et al. 2012; Carneiro et al. 2016; Sauer et al. 2017).

3.1 Mammals as Biomonitors

In Europe, North America, and Asia (mainly in Korea and Japan), samples in which trace elements are determined usually come from several or a dozen selected species of wildlife found on those continents. Among inland mammals there are mainly representatives of the following animal groups: even-toed ungulates (ordo Artiodactyla), lagomorphs (ordo Lagomorpha including hares and rabbits), carnivores (ordo Carnivora), bats (ordo Chiroptera), and Micromammalia, which comprises both rodents (ordo Rodentia) and insectivores (ordo Insectivora). Many researchers prefer micromammals because of their frequent occurrence in the environment, small individual areas, relatively easy acquisition for research, and the possibility of comparison and/or verification of laboratory rodent species results. In addition, their small size makes it possible to assess trace element content in the whole body and an assessment of their transmission to predatory animals (Wren 1986; Ma et al. 1991; Talmage and Walton 1991; Shore and Douben 1994; Kramarova et al. 2005; Sánchez-Chardi et al. 2007; Wijnhoven et al. 2007; Mendez-Rodriguez and Alvarez-Castaneda 2014; Gall et al. 2015). In addition, micromammals are an important part of the diet of avian and mammalian predators and participate in the transmission of trace elements between the links of terrestrial food chains (Gall et al. 2015; Knopper et al. 2006; Herzke et al. 2017). However, the

transformation of trace elements in these small mammals is poorly correlated with that occurring in humans and medium-sized long-lived mammals because micromammals have a much higher metabolic rate, usually a short life (1–2 years), and the samples taken, e.g., kidneys or brain, have very low mass, which may cause some analytical problems, including the risk of contamination of the research material (Speakman 2005; Wijnhoven et al. 2007).

Trace elements in the environment generally occur in low concentrations (including highly toxic metals), but their impact on long-lived organisms, including many animals and humans, lasts many years. In the indirect evaluation of their chronic impact on mammals, medium-sized carnivores have been used successfully such as canids (family Canidae: red fox (*Vulpes vulpes*), Arctic fox (*V. lagopus*), golden jackal (*Canis aureus*), and raccoon dog (*Nyctereutes procyonoides*)), mustelids (family Mustelidae: river otter (*Lontra canadensis*), Eurasian otter (*Lutra lutra*), American mink (*Neovison vison*) (previously *Mustela vison*), voloine (*Gulo gulo*), European badger (*Meles meles*), and martens among others), and raccoon (*Procyon lotor*) belonging to family Procyonidae (Wren 1984, Van den Brink and Ma 1998; Lord et al. 2002; Hoekstra et al. 2003; Millan et al. 2008; Heltai and Markov 2012; Kalisinska et al. 2016; Markov et al. 2016; Herzke et al. 2017). They are positioned on the top of the food pyramid, and their feed consists of field and forest rodents, hares, birds, seeds, fruits, or fish in various amounts in semiaquatic species (otters, American mink, raccoon). Many medium-sized carnivores are widely distributed in forest, agricultural, and urban landscapes of the Northern Hemisphere, with some species introduced into areas beyond their natural occurrence (Gehrt et al. 2011; Lesmeister et al. 2015; Poessel et al. 2017). For example, native North American raccoon and American mink are common as alien species in many European countries, while the raccoon dog present in Eastern and Central Europe originated from Asia (Genovesi et al. 2009). Fish-eating wildlife is particularly exposed to mercury biomethylated in water and sediments, and methylmercury product undergoing biomagnification in food chains. For this reason Hg achieves its highest concentrations in fish and piscivorous birds and mammals from the ends of food chains. In inland ecosystems fish-eating carnivores are preferred in studies on mercury contamination. Many reports concerning Hg (and sometimes other heavy metal levels) in American minks, river otters, and raccoons inhabiting North America have been published over the years (e.g., Wobeser and Swift 1976; Wren et al. 1980; Wren 1986; Lord et al. 2002; Wolfe et al. 2007; Sleeman et al. 2010; Basu 2012), but increasing numbers of European studies using American minks and raccoons have also been observed (Norheim et al. 1984; Kalisinska et al. 2012a, 2016, 2017; Brzezinski et al. 2014; Lanocha et al. 2014; Ljungvall et al. 2017).

In contrast to mesocarnivores, publications on trace element concentrations in large predatory Northern Hemisphere mammals, such as cats, are rare (e.g., Eurasian lynx (*Lynx lynx*), North American cougar (*Puma concolor*), bears, and wolves) due to their usually small population sizes, dispersion, and very large anthropogenic limitations of natural ranges, making it difficult to obtain biological samples from them and perform spatiotemporal comparisons (Gamberg and Braune 1999; Shore

et al. 2001; Newman et al. 2004; Millan et al. 2008; Celechovska et al. 2006; Noel et al. 2014; Lazarus et al. 2017).

In ecotoxicology, herbivorous game mammals (especially deer; red deer (*Cervus elaphus*), roe deer (*Capreolus capreolus*), mule deer (*Odocoileus hemionus*), white-tailed deer (*O. virginianus*) among others), moose/elk (*Alces alces*), reindeer/caribou (*Rangifer tarandus*), and hares play an important role. Determination of trace elements in these species allows not only identification of the adverse effects connected with excess or deficiency of micronutrients in the animals themselves and on their populations, identification of the contamination of the food chains by nonessential elements, and estimation of human health risks (Adriano 2001; O'Hara et al. 2003; Tataruch and Kierdorf 2003; Vikøren et al. 2005; Mysłek and Kalisińska 2006; Pedersen and Lierhagen 2006; Kursa et al. 2010; Al-Dissi et al. 2011; Ertl et al. 2016). Venison (mainly muscle and to a lesser extent the liver and other offal) is consumed as an important source of protein and micronutrients, but when it contains elevated amounts of toxic elements (e.g., Pb incorporated in tissues), this may contribute to consumer intoxication (Strmiskova and Strmiska 1992; Borch-Iohnsen et al. 1996; Frank et al. 2000; Wolfe et al. 2010; Roug et al. 2015; Skibniewski et al. 2015; Ertl et al. 2016) and a threat to wild mammalian and avian raptors and scavengers, including threatened species (Rogers et al. 2012; Haig et al. 2014; Behmke et al. 2015; Arnemo et al. 2016; Herring et al. 2016).

Omnivorous animals occupy an intermediate trophic position between herbivorous and carnivorous mammals. In Eurasia, one of the most widespread hunted species in this group is wild boar *Sus scrofa*, the progenitor of the domestic pig, and is very often used in European ecotoxicological studies (Santiago et al. 1998; Kursa et al. 2010; Rudy 2010; Amici et al. 2012; Danieli et al. 2012; Dlugaszek and Kopczynski 2013; Gasparik et al. 2017). In North America, the wild boar (feral hog) is classified as an invasive rapidly spreading species and is now abundant in the south and southwest of the USA (Snow et al. 2017; McClure et al. 2018). Although it is a hunted animal in the USA and its meat is often consumed by people, its tissues are rarely tested for the presence of trace elements. Therefore, this type of data is very seldom used for indirect assessment of environmental pollution and consumer health exposure in North America (Oldenkamp 2016; Oldenkamp et al. 2017; Smith et al. 2018). The trophic chain position of the raccoon in North America and Europe is similar to that of the wild boar. In an effort to protect native fauna, the populations of these (and other) species are being deliberately reduced outside their natural ranges, so their tissues can be easily obtained for ecotoxicological studies and intercontinental comparisons. Selenium concentration comparisons in this aspect in omnivorous wild-living mammals seem particularly interesting. Selenium is an element with a very uneven distribution in the earth's crust. Much of Central and Northern Europe's soils are Se-deficient, while North American soils are generally rich in this microelement; in some areas its levels are even excessive. A comparison of Se concentrations in wild boar muscles from Europe (Czech Republic) and the USA (Georgia) indicates that Se levels in the European population are an order of magnitude smaller than in the USA, at 0.10 mg kg^{-1} vs 1.0 mg kg^{-1} dw (Kursa et al. 2010; Oldenkamp 2016). Considering that Se counteracts the absorption of Hg from

the diet, areas with an elevated amount of Hg and food poor in Se (e.g., fish) would exhibit increased Hg intoxication of animals compared to individuals of the same species from areas of comparable Hg concentration but more abundant in Se. In relation to raccoon and American mink from Poland, such a suggestion was put forward by Kalisinska et al. (2017) after comparisons of data on Se and Hg in the muscles of these species in Europe (NW Poland) and North America.

3.2 Birds as Biomonitors

Avifauna, especially inland birds, is the longest (over 100 years) and the most intensively methodically observed group of animals in Europe and North America. In contrast, in Asia large-scale observations were initiated as late as the 1970s–1980s (Bibby 2003; Li and Mundkur 2006; Keck 2015). Various bird monitoring programs in Europe and North America, from local to pancontinental, have been introduced for at least 50 years, and some of them include pollution testing (Lambert et al. 2009; Schmeller et al. 2012; Gomez-Ramirez et al. 2014; Ahrestani et al. 2017; Sauer et al. 2017). There are many examples in the history of ecotoxicology where birds have been used as sentinels of environmental and human health. Canaries used to be taken to mines to indicate dangerous concentrations of methane. A dramatic reduction in the populations of birds of prey showed the dangers associated with the widespread use of pesticides in agriculture, including DDT (dichlorodiphenyltrichloroethane), organochlorine substances, and alkyl mercury compounds. The use of the latter, highly neurotoxic and undergoing biomagnification in the trophic chains, resulted in the considerable exposure of piscivorous wildlife and humans to mercury (Scheuhammer 2008; Rabinowitz et al. 2009; Rattner 2009; Basu 2012; Holt et al. 2012; Espin et al. 2016).

Yet another and very spectacular example is the impact of lead contained in hunting ammunition on the health and fitness of individual birds and its effects at the population level. Waterfowl such as ducks and geese (also some landfowls) are a unique group in this respect, because they swallow small pebbles as gastroliths, which are retained in the gizzard and used to grind food. However, the birds do not distinguish pebbles from spent lead shot pellets. Incidental mortality from waterfowl hunting reached population-level effects when over two million ducks and geese (~2% of all waterfowl) in North America were poisoned annually by ingestion of spent lead shot deposited on the grounds and in sediments (Bellrose 1951). Waterfowl, in addition to shot pellets, also swallow leaded fishing gear used in recreational fishing, which eventually also results in the intoxication of animals and people. In addition, waterfowls and other game animals may retain hunting ammunition in their bodies, which can then be swallowed by predators and scavengers. Thanks to numerous field observations of professionals, bird watchers, volunteers, and ecotoxicological research, the use of DDT and pesticides containing mercury was eventually banned in many developed countries (Smith et al. 2007; Espin et al. 2016; Movalli et al. 2017). In the USA, the use of lead pellets in waterfowl hunting was

discontinued, as in a few European Union countries. The scientific arguments and the strong voice of the public resulted in a change of policy in the USA and Canada which used the prevalence of lead poisoning among birds as the basis of policy and law introduced to reduce lead use at the continental level, including leaded petrol (Thomas and Guitart 2010; Golden et al. 2016). However, the problem of metallic lead poisoning of rare, endangered birds and the so-called flagship species remains one of the most important in wildlife toxicology, because lead pellets scattered in the environment are still swallowed by waterfowl and landfowl, and lead bullets used in large-game hunts contaminate viscera (offal) left by hunters in the field (Pain et al. 2009; Haig et al. 2014; Espin et al. 2016; Herring et al. 2016). Tranel and Kimmel (2009), based on data from Minnesota (USA), estimated that among terrestrial vertebrates such as reptiles, mammals, and birds, lead ammunition had the greatest effect on birds (about 95%), mostly water birds (38%), raptors, and scavengers (24%). In this respect, the situation may be similar in other parts of the world where hunters use lead ammunition (Pain et al. 2009; Saito 2009; Nadjafzadeh et al. 2013; Golden et al. 2016). Another source of intoxication of birds and humans with lead are remnants of paint containing this metal and leaded gasoline (Nriagu 1990; Cai and Calisi 2016). Therefore, birds are also used in the biomonitoring of cities, e.g., urban pigeons (Ohi et al. 1981; Dauwe et al. 2005; Deng et al. 2007; Roux and Marra 2007; Behmke et al. 2015; Cai and Calisi 2016; Pollack et al. 2017).

In addition to a large number of studies on lead in birds, there is also a considerable body of research on mercury, especially in North America (Rattner et al. 2000, 2005). In inland ecosystems, exposure to mercury is the highest among piscivorous species, and in North America key research in this field includes common loon (*Gavia immer*), bald eagle (*Haliaeetus leucocephalus*), osprey (*Pandion haliaetus*), mergansers, and grebes (DesGranges et al. 1998; Scheuhammer et al. 1998; Stout and Trust 2002; Mierzykowski et al. 2011, 2013; Rutkiewicz et al. 2011; Shore et al. 2011; Depew et al. 2012; Schoch et al. 2014). There are also many studies on other aquatic birds, especially game waterfowls (Gerstenberger 2004; Rothschild and Duffy 2005; Braune and Malone 2006). For a long time, it was thought that mercury is only marginally accumulated in terrestrial songbirds. This view changed after the publication of Cristol et al. (2008) which showed that in areas historically anthropogenically contaminated with mercury it is transferred from the river (the South River, Virginia, USA) and riverside areas to arthropods (spiders and insects) and then songbirds feeding on them. This discovery inspired broader studies on songbirds as sentinels of mercury in terrestrial habitats (Jackson et al. 2015). The flagship species in European studies on mercury contamination is the white-tailed eagle (*Haliaeetus albicilla*) (Norheim and Frøslie 1978; Falandysz et al. 2001; Kenntner et al. 2001; Kalisinska et al. 2016; Kitowski et al. 2017), but observational studies show this species is not at risk of mercury intoxication, as opposed to lead. However, elevated amounts of this metal were found in some of the common merganser (*Mergus merganser*) wintering on the southern coast of the Baltic Sea (Kalisinska et al. 2010).

In ecotoxicological studies, elements are rarely determined in many types of samples from wild birds to characterize their distribution in the body. Such

exceptions include two papers describing the distribution of Hg and trace elements in piscivorous great cormorants (*Phalacrocorax carbo*) (Nam et al. 2005; Misztal-Szkudlińska et al. 2018) and one report concerning Hg in young osprey (DesGranges et al. 1998). The muscles of an adult cormorant had the largest amount of Cu (>65%), a significant part of Hg and Cr (about 35%), as well as about 30% of Se and Co accumulated in the body (Nam et al. 2005). In osprey nestlings, about 85% of absorbed Hg gets to feathers during their growth, and from the remaining a dozen or so percent, half of them accumulate in muscles (DesGranges et al. 1998). The quoted works show that the highest amount of Hg in soft tissues is found in the muscles of birds, but its distribution is strongly influenced by the intense transfer of Hg to feathers during their growth.

The usefulness of various bird tissues to monitor the abundance of the environment with elements essential to life and its contamination with toxic metals is constantly discussed. Although the samples most frequently selected in biomonitoring include liver and kidneys, it is important to study their concentration in the muscles and target tissues because of the transfer of various elements up the terrestrial food chains. Interpretation of the obtained concentrations of elements in avian samples requires their reference to threshold values, as in the book by Beyer and Meador (2011) for Cd, Hg, Pb, and Se. However, most trace elements have not been researched in such a thorough fashion for very large and species-diverse clusters of birds. Due to this lack of data, certain reference may come from values calculated for unanalyzed tissues based on the known concentration in the examined tissues through the use of appropriate equations (when the concentrations between these tissues correlate with each other) (Mochizuki et al. 2011; Ackerman et al. 2016; Evers 2018).

3.3 Tissues of Terrestrial Vertebrates Used in Biomonitoring

In wildlife toxicology, various types of biological samples may be collected from live animals captured then released (mainly feathers, hair/fur, blood; less frequently fragments of claws or oil from the uropygial gland) or from dead birds and mammals (most of all internal tissues such as liver, kidney, muscle, bone, and brain, but also external tissues). Studies on environmental contaminants, including toxic trace elements, often use avian eggs, with one egg usually taken from individual broods, assaying contaminants in the eggshell, whole egg content, or white and yolk separately (Leonzio and Massi 1989; Burger and Gochfeld 2003; Hashmi et al. 2015; Ackerman et al. 2016; Orlowski et al. 2016; Movalli et al. 2017; Pollack et al. 2017). In addition, researchers often use feathers (e.g., in nests or nearby), hair, mammalian scat, cervid antlers, and avian pellets. Those biological materials are taken mainly from endangered, threatened, or sensitive species; such noninvasive sampling methods are recommended as valuable tools to monitor wildlife and minimally affect free-ranging animals. So-called “postlethal” animal samples are obtained from those already killed by hunters, trappers, museum collectors, or

vehicles or found in the field (Kierdorf and Kierdorf 2003; Pokorny 2006; Pauli et al. 2010; Movalli et al. 2017; Trapp and Flaherty 2017).

Different trace elements are deposited in different wildlife tissues at different rates and amounts. The liver, kidney, muscle, and bone from internal tissues are major locations where the largest part of the absorbed essential trace elements are deposited, but concentrations in these tissues are not necessarily representative of the entire body burden, and it can be difficult to detect trace element deficiencies within critical organs (Taylor 1996; Demesko et al. 2018). Essential and nonessential trace elements in different tissues and organs may be subject to temporary or long-term accumulation in various body parts, biotransformation (including methylation and demethylation), and removal mainly with feces and urine, and to a small extent also with saliva, sweat, tears and respiration (Nollet et al. 2008; Lopez-Alonso 2012; Jan et al. 2015; Prashanth et al. 2015). Additional methods of metal and metalloid excretion in birds are eggs and feathers and in mammals the fur (Burger et al. 1993; Burger 1994; Leonzio et al. 2009; Rendón-Lugo et al. 2017). The organ or tissue in which trace metal/metalloid toxicity occurs may differ from the organ or tissue(s) where the element bioaccumulates, which may be connected with its kinetics. Target organs (where the toxic effects are produced) may differ between species of endothermic vertebrates, mainly owing to differences in absorption, distribution, and excretion (US EPA 2007). Table 2.2 presents the main target organs/tissues of nonessential elements and internal body parts where the elements achieve typically highest levels in terrestrial endothermic animals.

Among the internal tissues of wildlife, a number of essential and nonessential elements are predominantly measured in the liver and kidney; however, fluoride and lead are mainly investigated in the bones (Mateo et al. 2003; Demesko et al. 2018). For the past two to three decades, nondestructive samples (hair, feathers, and blood) have been preferred, which are often taken from birds and bats (Russo and Jones 2015; Pauli et al. 2010; Wada et al. 2010; Langner et al. 2012; Lodenius and Solonen 2013; Stankovic et al. 2014; Gall et al. 2015; Flache et al. 2015; Ackerman et al. 2016). Sampling of live animals does not reduce the population, which is important in the case of their small numbers, especially with regard to protected species, and such action is usually socially acceptable. It is estimated that plumage and mammalian pelts contain the largest part of methylmercury (MeHg) accumulated in the body. Therefore these tissues are frequently used in the detection of mercury exposure in wildlife, but many other heavy metals are also investigated in these keratin structures. Feathers (similar to hair) are metabolically inert after their formation, so for those avian species with well-known molt schedules, the analyses of specific individual feathers provide unique chemical information of a very discrete time. For many bird species, the molt schedules are poorly recognized, and metal concentrations in feathers are highly variable within an individual bird. Therefore, proper interpretation of chemical results is very difficult or impossible. For these reasons some researchers state that feathers and hair have a low priority as preferred tissues for sampling in ecotoxicological studies (Furness and Greenwood 1993; Leonzio et al. 2009; Ackerman et al. 2016; Rendón-Lugo et al. 2017).

Table 2.2 Main target organ or tissue as well as internal body parts of terrestrial endothermic animals where nonessential trace elements are accumulated following chronic oral chronic

Element	Target organ or tissue	Organ or tissue with typically highest concentration	References
Ag, silver	Probably brain and liver	Bones	Connors et al. (1972), Horai et al. (2006), and Kuo et al. (2000)
Al, aluminum	Brain and bone	Brain, liver	Llacuna et al. (1995), Krewski et al. (2007), Al-Ganzoury and El-Shaer (2008), and Lucia et al. (2010)
As, arsenic	Liver	Liver	Liu and Waalkes (2008), Sanchez-Virosta et al. (2015), and Mandal (2017)
Cd, cadmium	Kidneys	Kidneys, liver	Martelli et al. (2006) and Wayland and Scheuhammer (2011)
F, fluorine	Skeleton and kidneys	Bones	Bird et al. (1992), Tsunoda et al. (2005), and Kurdi (2016)
Hg, mercury	Kidneys for inorganic Hg; brain for organic Hg	Kidney, liver	Evers et al. (2005), Clarkson and Magos (2006), Bridges and Zalups (2010), and Sleeman et al. (2010)
Pb, lead	Nervous system, mainly brain	Bones	Silbergeld et al. (1993), Nemsadze et al. (2009), Franson and Pain (2011), Flora et al. (2012), and Kalisinska et al. (2016)
Sn, tin	Probably bones and liver	Bones, liver	Kannan and Falandysz (1997), Harding et al. (1998), Nath (2000), ATSDR (2005), and Mizukawa et al. (2009)

Generally, metal levels in blood samples reflect short-term exposure (immediate dietary intake), the liver and kidney reflect longer terms, while the bones reflect the longest because their mineral remodeling occurs very slowly (Stankovic et al. 2014; Gall et al. 2015; Espin et al. 2016). Cadmium is bioaccumulated in bird and mammal kidneys almost over the entire lifetime, and a strong correlation between nephric Cd level and animal age is observed (Wayland and Scheuhammer 2011; Rendón-Lugo et al. 2017). Many trace elements achieve their highest concentrations in the liver and kidneys, (Table 2.2), but together these organs constitute no more than 4%–6% of the animal's body weight. The muscles (40%–50% of body weight) are most significant in the transfer of trace elements between animals from different trophic levels, depending on the type of consumer (Kalisinska et al. 2017). This is especially important in the case of Hg. The level of intestinal absorption of Hg in terrestrial vertebrates depends on its chemical form, and in animal muscle about 90% Hg is present as MeHg, which is almost completely absorbed from the digestive tract. Hg in the liver and kidney is mostly inorganic Hg with low intestinal absorption (<10%). In the kidneys and liver, the percentage of MeHg in total mercury (THg) can be small (especially when THg reaches high concentrations), which is why these organs play a small role in the transfer of Hg between animals. Unfortunately, few papers provide information about the absolute and relative weight of tissues and

organs as well as the percentage composition of the consumer's diet, so it is difficult to estimate the amount of transfer of trace elements between different trophic levels. Among terrestrial birds and mammals, Hg concentration increases from herbivores to omnivores and carnivores, but in the case of other trace elements, this type of regularity is not always clearly determined (Tete et al. 2013; Stankovic et al. 2014; Kalisinska et al. 2017).

The most numerous group of ecotoxicological studies concerns a small group of trace elements (<10). They are dominated by toxic elements (Cd, Hg, Pb, As), usually analyzed in 1–3 types of biological samples. Publications in which several or dozens of elements were determined in samples obtained from terrestrial birds and mammals are much less numerous, but this has been made possible due to technical progress in chemical analysis (e.g., Harding et al. 1998; Falandysz et al. 2001; Horai et al. 2006; Deng et al. 2007; Dailey et al. 2008; Zimmerman et al. 2008; Ertl et al. 2016; Lazarus et al. 2017). In literature, data concerning trace elements in soft and hard tissues tend to be presented as mean wet/fresh or dry weight. In scientific studies, the diversity of samples and the multiplicity of the elements determined are subject to various comparisons and discussions. Then it is necessary to present concentrations of elements not only in the same units (mainly expressed as mg kg^{-1}, which is analogous to μg g^{-1} or ppm) but also selecting dry or wet weight. Conversion of wet weight to dry weight (or vice versa) requires knowledge of the percentage of water in the samples, but such information is seldom presented in the reports. Furthermore, samples are dried at temperatures ranging from 50 °C to 105 °C (not always to constant weight), depending on the methodology and the analytical requirements. Therefore, various comparisons use the average percentage of water in vertebrate tissues (Ackerman et al. 2016; Zukal et al. 2015). For the purposes of this book, the average water content in the four most commonly analyzed tissues of birds and mammals was calculated using data from seven and ten species, respectively (data for birds were taken from Honda et al. 1985; Cosson et al. 1988: Kalisinska et al. 2010, 2014; Binkowski et al. 2013; for mammals from Weiner 1973; Reinoso et al. 1997; Blus and Henny 1990; Gamberg et al. 2005; Rudy 2010; Sleeman et al. 2010; Kalisinska et al. 2012a, b; Lanocha et al. 2014). Table 2.3 shows the average percentage of water in the tissues of birds and mammals and also proposed coefficients for wet to dry mass conversion.

When collecting samples from wild mammals and birds, it is advisable to obtain and record important information about them, including species, sex, age, location (latitude and longitude), and season/year. This kind of data is needed for intra- and

Table 2.3 Mean moisture content in tissues of endothermic vertebrates and proposed conversion factors (CF) for normalization of wet weight assay results from tissue samples to dry weight

Parameter	Liver	Kidney	Muscle	Brain
Mammals				
Moisture in tissues (%)	70.9	75.5	74.6	77.0
CF	3.0	2.5	2.5	2.0
Birds				
Moisture in tissues (%)	70.2	74.3	71.4	79.9
CF	3.0	2.5	3.0	2.0

interspecies analyses of differences in the concentration of trace elements and may reveal time-spatial changes on a regional, continental, and even global scale (Tataruch and Kierdorf 2003; Hollamby et al. 2006; Burger 2007; Traas and van Leeuwen 2007; Zukal et al. 2015; Gochfeld 2017).

Depending on the assumed objective of research in wildlife toxicology, samples used in analysis may come from one or more species representing the same or different trophic categories (e.g., herbivores, omnivores, predators). Particularly important are studies analyzing the concentration of selected highly toxic elements (Hg, Pb, Cd) due to the range of research and the very large number of samples (sometimes exceeding 1000). For example, a study on Hg levels in North American birds analyzed blood samples of 102 songbird species from terrestrial habitats (Jackson et al. 2015). The review by Ackerman et al. (2016) compiled literature data on Hg in approximately 27,000 samples (eggs, blood, liver, muscle, and feathers) from 225 species of birds from various systematic groups found in western North America. They concluded that avian Hg concentrations were greatest in ocean and salt marsh habitats and lowest in terrestrial habitats. Their analysis identified multiple hotspots contaminated by the metal in the western part of North America. Finally, Jackson et al. (2016) studied Hg in the blood of 20 avian piscivorous species (including a few target species: bald eagle, osprey, common loon) and those species turned out to be much more exposed to Hg than non-piscivorous species including songbirds.

Biomonitoring of heavy metals in Europe uses bird species on a smaller scale. The leading role is played by diurnal and nocturnal avian raptors, mostly tested for lead and to a lesser extent mercury, the two most preferred metals in such studies (Gomez-Ramirez et al. 2014; Espin et al. 2016). Unlike birds, it is difficult to find extensive studies on toxic metals in North American and European mammals that would allow intra- and intercontinental comparisons (Tranel and Kimmel 2009; Yates et al. 2014). Such publications can only be found for mercury in otters. Mercury in white-tailed eagle and Eurasian otter has been of great interest in Europe for years and sporadically in Asia. In relation to these two species, their North American counterparts are the bald eagle and river otter, which have also been extensively studied. Below we present an example of intercontinental comparisons concerning hepatic mercury concentrations in these species (Fig. 2.2). Median hepatic Hg concentrations in both otter species were similar, but Hg levels in the bald eagle were higher than in the white-tailed eagle (Mann-Whitney U test, $p < 0.05$).

Also other piscivorous wildlife species are used in Hg biomonitoring, including both native and alien species occurring in Europe and North America, with well-known biology and reactions to Hg (Table 2.4). However, the volume of European research is much smaller than in North America (e.g., because of lower Hg contamination), and it is difficult to perform comprehensive intercontinental comparisons. For example, there are many American and Canadian papers on Hg in species such as American mink or raccoon (native mammals from North America introduced in Europe), but in Europe the research has been scarce so far. Birds such as common loon or common merganser are native to both continents, but the volume of research

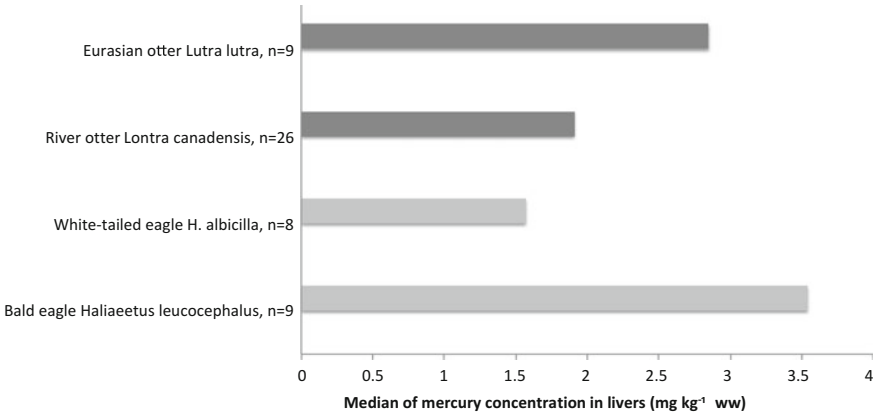

Fig. 2.2 Hepatic mercury concentrations in counterpart piscivorous species of Europe (Eurasian otter and white-tailed eagle) and North America (river otter and bald eagle). Data sources of Eurasian otter, Madsen et al. (1999), Kruuk et al. (1997), Gutleb et al. (1998), Lemarchand et al. (2010), Walker et al. (2010, 2011), Lodenius et al. (2014); river otter: Wren et al. (1980), Sheffy and Amant (1982), Kucera (1983), Halbrook et al. (1994), Evans et al. (2000), Facemire et al. (1995), Mierle et al. (2000), Fortin et al. (2001), Yates et al. (2005), Grove and Henny (2008), Klenavic et al. (2008), Strom (2008), Sellers (2010), Stansley et al. (2010), Mayack (2012), Keeyask Hydropower Limited Partnership (2012), Dornbos et al. (2013); white-tailed eagle, Norheim and Frøslie (1978), Holt et al. (1979), Falandysz et al. (2001), Kenntner et al. (2001), Kalisinska et al. (2014), Krone et al. (2004, 2006), Kitowski et al. (2017); bald eagle, Evans (1993), Wood et al. (1996), Stout and Trust (2002), Weech et al. (2003), Evers et al. (2005), Mierzykowski et al. (2011, 2013), Rutkiewicz et al. (2011)

Table 2.4 Candidates of mercury bioindicator species from terrestrial mammals and birds in North America and Europe

North America	Distribution category and remarks	Europe	Distribution category and remarks
Mammals		Mammals	
American mink *Neovison vison*	Native	American mink *Neovison vison*	Alien, common in Europe
Raccoon *Procyon lotor*	Native	Raccoon *Procyon lotor*	Alien common in Europe
River otter *Lontra canadensis*	Native	Eurasian otter *Lutra lutra*	Native, counterpart species to river otter
Birds		Birds	
Common loon *Gavia immer*	Native	Common loon *Gavia immer*	Native, mainly in Scandinavia
Common merganser *Mergus merganser*	Native	Common merganser *Mergus merganser*	Native
Bald eagle *Haliaeetus leucocephalus*	Native	White-tailed eagle *Haliaeetus albicilla*	Native, counterpart species to bald eagle

in North America is also much greater than in Europe (especially with regard to common loon). With time, when the number of European studies on Hg in their bodies will become sufficiently large (especially American mink and raccoon in Europe), it will be possible to deepen intercontinental comparative studies.

Biomonitoring potential is one of the few acceptable effects of introducing alien game animals. It is associated with good knowledge of the biology of most of these species (e.g., American mink, raccoon, wild boar, red fox), social approval for acquiring material for research from specimens during culling of their populations. Nevertheless, in various European countries and some parts of North America (rarely in Asia), biomonitoring programs for various contaminants in terrestrial ecosystems, including trace elements, are created mainly on the basis of selected native species of birds and mammals. An interesting European example is the Norwegian program "Environmental pollutants in the terrestrial and urban environment," now having been conducted for several years and based mainly on the research on the following animals: earthworms, brown rat (*Rattus norvegicus*), red fox, fieldfare (*Turdus pilaris*), Eurasian sparrowhawk (*Accipiter nisus*), and tawny owl (*Strix aluco*) (Herzke et al. 2017).

4 Conclusions

The collection and analysis of a sufficiently large number of diverse data on trace elements determined in many species of wildlife allow, among other things, to select candidate species as biomonitors accumulating specific elements in their tissues (e.g., piscivorous species for mercury biomonitoring) and identify existing threats from toxic substances for endangered species, localization of hotspots, and levels of human exposure to trace elements. In order to carry out comparisons in this respect on a large scale, i.e., covering the large terrestrial areas of the Northern Hemisphere, it would be necessary to focus on widespread and numerous species representing different trophic levels.

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Part II
Selected Trace Elements

Chapter 3
Chromium, Cr

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Abstract In 1957 chromium(Cr) was proposed as an essential element, vital for the life and normal development of animals and humans. In the natural environment, the activity of compounds containing chromium in the third and the sixth oxidation states differs substantially, Cr(III) and Cr(VI), respectively. Trivalent Cr is essential for humans and animals; it shapes the proper glucose metabolism through participation in the glucose tolerance factor (GTF) and is involved in metabolism of hydrocarbons, proteins, and lipids. Chromium supplementation brings positive results only at small doses though. Chromium-deficient nutrition impairs glucose tolerance and insulin function, alters protein metabolism, and negatively affects both growth and reproduction.

Hexavalent Cr is a strong oxidant, easily penetrating into living organisms, being reduced to Cr(III) in cells. Industrial production is a source of Cr-containing wastes, which contaminate the water and air and, in consequence, the soil. Emission of chromium to the atmosphere is mainly due to combustion of coal and other fossil fuels but also results from iron and nonferrous metal smelting. Hexavalent Cr, which acts oxidatively, is very toxic. Anthropogenic Cr soil contamination is a result of atmospheric deposition of dust but also industrial wastes discharged into the soil from paint factories, tanneries, sewage treatment plants, and chrome-steel scrap piles. Chromium is toxic to plants and accumulated in the roots and is to a limited extent transferred to overground parts of plants. In the cells of mammals and birds, Cr(VI) is reduced to Cr(III), which produces highly toxic-free radicals. Hexavalent Cr is carcinogenic to homeothermic vertebrates. Reproduction disorders were observed in mammals. In males, exposure to high Cr level deteriorates the quality of semen, leads to testicular disorders, and reduces libido. In females, Cr negatively affects fertility. A high level of Cr in the environment is mutagenic, carcinogenic, and teratogenic to birds; concentration of chromium in avian lungs increases with age, which implies equivalence of diet and air as sources of Cr intoxication. Studies

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show that chromium exhibits no biomagnification. On the contrary, with an increase in the trophic level, the concentration of Cr considerably decreases. This is referred to as "biominification." In this chapter are presented the effect of exposure to hexavalent Cr and chromium content in avian and mammalian soft tissues as well as in feathers and hair.

1 Introduction

More than half a century after chromium was recognized as an essential nutrient (Mertz and Schwarz 1957), experiments yield results that may undermine the opinion that chromium really is a necessary component for the normal development of warm-blooded organisms (Nielsen 2007; Zaccaroni et al. 2008a; Di Bona et al. 2011).

Varied assimilation and toxicity of trivalent and hexavalent chromium has been a major issue in the discussion on the topic (Anke et al. 2005). On the one hand, chromium is a key metal in many industries, including metallurgy, electroplating, chemical industry, leather tanning, pigment production, and wood preservation (Cotton et al. 1999; Gheju and Balcu 2010; Kabata-Pendias 2011; Pati et al. 2014). On the other hand, the toxic, mutagenic, and carcinogenic properties of chromium are well known too (Bartlett 1991; Irwin 1997; Barałkiewicz and Siepak 1999; Dhal et al. 2013; Singh et al. 2015). Chromium induces an oxidative stress and kills cells, damages DNA, and modifies gene expression (Bagchi et al. 2002; Pechova and Pavlata 2007; Gheju and Balcu 2010; Cantu et al. 2014). Hexavalent chromium is toxic to plants, animals, and humans (Borel and Anderson 1984; Mertz 1993; Cohen et al. 1993; Mancuso 1997; Wise et al. 2002; OSHA 2006; Islam et al. 2007; Wise et al. 2008; Singh et al. 2015). It is the most mobile, reactive, and toxic form of chromium (Bartlett 1991; Tribovillard et al. 2006; Dhal et al. 2013). The main mechanism underlying the toxicity of Cr(VI) is the oxidative stress (Bagchi et al. 2003; Cantu et al. 2014). In endothermic vertebrates, long-lasting exposure to chromium(VI) leads to neurotoxic, dermatoxic, and genotoxic effects and to carcinogenic and mutagenic changes; in humans, it additionally leads to skin allergies, ulcers, and kidney failures (Bagchi et al. 2002; Thacker et al. 2006; Singh et al. 2015).

Most authors have confidence that trivalent chromium is an essential element and emphasize its positive influence if included in the nutrition of both humans and animals (Gheju and Balcu 2010; Weksler-Zangen et al. 2012; Lewicki et al. 2014).

Experiments carried out in the 1990s confirm that chromium is a necessary nutrient for various groups of animals, such as cattle, sheep, pigs, and poultry (Pechova and Pavlata 2007).

In animals, Cr(VI) rapidly converts to Cr(III) (Anke et al. 2005). The environmental mobility of chromium(III) is lower, and it is 1000 times less toxic for living cells as compared with hexavalent Cr (Bagchi et al. 2003; Suwalsky et al. 2008;

Gheju and Balcu 2010; Singh et al. 2015). Trivalent, non-resorbable chromium is used as a marker (Anke et al. 2005).

Chromium was identified as a component of biological tissues in the 1940s. Mertz and Schwarz (1957) observed developmental abnormalities in a population of rats fed with a chromium-deficient diet and hypothesized that the feed lacked the glucose tolerance factor (GTF). This has been confirmed in other studies (Schwarz and Mertz 1959; Mertz 1993; Grela et al. 1997; Pechova and Pavlata 2007; Vincent and Stallings 2007).

GTF has been confirmed to contain an active form of trivalent chromium (Mertz 1993). According to Grela et al. (1997), GTF is a trivalent chromium-nicotinic acid occurring in combination with glutamic acid, glycine, and cysteine. It improves insulin binding to its receptors, with the participation of hydrogen sulfide. Trivalent chromium enhances the action of insulin, both in vitro and in vivo. Many experiments on animals, studies on human diabetic patients, and in vitro trials have shown that Cr(III) improves the efficacy of insulin and enhances the actions of tyrosine kinase and the transmembrane tyrosine phosphatase of insulin receptors. As a result, glucose is more efficiently absorbed and utilized by the cells of the body (Krejpcio et al. 2007). The maximum in vitro activity requires a specific chemical form of GTF and is initially identified as chromium-niacin complex (Mertz 1993; Piva et al. 2003). The importance of chromium in terms of human diabetes has been confirmed in a number of studies (Mertz 1993; Grela et al. 1997; Kurył and Dębski 2001; Krejpcio et al. 2007; Pechova and Pavlata 2007).

The results of experiments demonstrate that chromium is an essential micronutrient in the metabolism of carbohydrates, lipids, and proteins in mammals (NRC 1989; Anderson et al. 1991; Anderson 1993; Mertz 1993; Morris et al. 1995; Mordenti and Piva 1997; Şahin et al. 2001; Pollard et al. 2002; Brown 2003; Lewicki et al. 2014). In addition, chromium is involved in the antioxidant processes, RNA and DNA synthesis, and the immune response and also has an effect on the secretion of hormones and some vitamins (Grela et al. 1997; NRC 1997; Thor et al. 2011).

It has been demonstrated in various livestock animals that a diet low in chromium leads to such deficiency symptoms as reduced feed intake, lower weight gains, reproduction disorders, and a higher lipid content in blood serum (Frank et al. 2000; Anke et al. 2001; Bagchi et al. 2002). Parenterally nourished patients showed symptoms of diabetes (including reduced glucose tolerance, weight loss, and neurological disorders), which were subsequently effectively alleviated with chromium administration (Anderson 1995; Gammelgaard et al. 1999). Insufficient intake of chromium leads to symptoms similar to those observed in diabetes and cardiovascular disorders. Chromium is a nutrient, not a medication; thus it is beneficial only for patients diagnosed for its deficiency (Anderson 1997). In endothermic vertebrates, including humans, such cases are rare (Anderson et al. 1991). Chromium deficiency may mostly occur due to low dietary intakes of chromium, less often due to stress (Grela et al. 1997). Children with protein-energy malnutrition, diabetic patients, as well as the elderly and middle-aged definitely require supplementation with chromium (Borel and Anderson 1984).

Chromium supplementation, regardless of its form, produces beneficial outcomes only at low doses; its excess in the diet interferes with the development of animals (Pollard et al. 2002). Supplements of Cr enhance the binding of insulin and increase the number of insulin receptors and their phosphorylation (Anderson 1998; Brown 2003).

Chronic stress may alter the daily requirement for micronutrients, including chromium. Stress situations in animals result from transport, high temperatures in the premises, rapid growth rate, aging, and diets requiring full activation of insulin; also the species and/or breed of the animal may induce the symptoms of chromium deficiency if its intakes are short. Stress factors affecting chromium metabolism in humans include heavy glycemic load, a diet high in monosaccharides, lactation, infection, or injuries. The response of the human body in such situations consists in elevated chromium urinary excretion. If these stress factors, which lead to reduced renal reabsorption of chromium and its increased excretion with urine, add to a reduced Cr level in the diet, all this may result in the symptoms of chromium deficiency (Anderson 1997). Under increased stress, such as fatigue, injuries, and pregnancy, but also as a result of dietary, metabolic, physical, environmental, or emotional stress, the chromium requirement increases (Burton 1995; Piva et al. 2003).

The role of chromium in cholesterol metabolism remains unexplained (Wang et al. 1989; Press et al. 1990; Abraham et al. 1992; Pechova and Pavlata 2007; Hua et al. 2012). A slight chromium deficiency increases the risk of ischemic heart disease and myocardial infarction (Mertz 1993). Grela et al. (1997) suggest that the condition is an important risk factor in the coronary heart disease, since it is accompanied by high blood pressure, high plasma triglyceride levels, and low plasma high-density lipoproteins (HDL) levels.

The animal daily requirement for chromium is probably 300 μg Cr kg dry weight (dw) of feed and is usually covered by the feed ration. If the demand is met, any chromium supplements will fail to improve the health status of the animal (Anke et al. 2005).

Chromium reduces total body weight but can increase lean body mass (Morris et al. 1995; Bielicka et al. 2005). It has been found that Cr also improves lean body mass in animals, enhances growth rate and feed conversion, and stimulates feed intake and energetic efficiency (NRC 1996). Chromium may accelerate the growth rate of skeletal musculature and cardiac muscle (Morris et al. 1995). Studies on farm animals (Grela et al. 1997; Pollard et al. 2002) have shown that chromium yeast supplementation improves their production parameters (better carcass lean content, lower fat percentage, improved weight gains, more effective feed conversion, higher content of polyunsaturated fatty acids). Organic chromium reduces the mortality of piglets and chicks, reduces disease incidence in bulls, and improves reproduction performance. It increases the immunity of the body and improves the response to vaccination (NRC 1997). It enhances the immune response and reduces blood levels of cortisol, which is an indicator of stress. This form of chromium improves milk yields in dairy cows, and increases equine endurance in exercise, reducing muscle lactate content in horses, which improves muscle efficiency (Grela et al. 1997). Chromium ions stimulate lipid metabolism in broiler chickens (Kurył and Dębski 2001; Krejpcio et al. 2007).

A risk of chromium contamination of the natural environment on a global scale does not seem real. However, due to its increased use and significant local introduction of chromium to the atmosphere, water, and soil, an excessive share of chromium in the biogeochemical cycle and increased risks to the environmental health should be anticipated (Kabata-Pendias and Mukherjee 2007). Hence, it is reasonable to collect and study data on chromium concentrations in a variety of organisms, including wild birds and mammals.

2 General Properties

Chromium(Cr) was discovered by Vauquelin in 1798, who isolated the element from crocoite, $PbCrO_4$ (Barceloux 1999). In the periodic table of elements, chromium is a member of Group 6 (previously VIb). The valence of chromium may vary from −2 to +6. Its most common forms found in the environment are trivalent, Cr(III), and hexavalent, Cr(VI), and both have a significant impact on living organisms, including humans (WHO 1988; Miksche and Lewalter 1997; Thacker et al. 2006; Oliveira 2012). Divalent chromium ion is rapidly oxidized to trivalent chromium and therefore does not occur in living organisms (Borel and Anderson 1984; Pechova and Pavlata 2007).

Chromium is a hard, heavy, and brittle metal, steely-gray in color with a bluish tint. Its atomic number is 24, and its atomic weight is 51.996 g mol^{-1}. There are more than 20 chromium isotopes (with atomic weight from Cr^{42} to Cr^{67}), but only four of them are stable (Cr^{50}, Cr^{52}, Cr^{53}, Cr^{54}). The most common in nature chromium isotopes are Cr^{52} (83.76%) and Cr^{53} (9.55%) (Borel and Anderson 1984; Rosman and Taylor 1998; Stoecker 2004; Hammond 2005; Izbicki et al. 2008). The melting point and the boiling point of chromium are, respectively, 1857 °C and 2672 °C. Chromium dissolves in dilute sulfuric and hydrochloric acids and passivates in concentrated nitric acid. It forms a range of complex ions (Borel and Anderson 1984; Greenwood and Earnshaw 1997). In complex compounds, the element occurs in the oxidation states from −2 to +6, of which the substances containing Cr in the +2 and +3 oxidation states are most common (Borel and Anderson 1984).

In the rank representing the abundance of elements in the Earth's crust, chromium occupies the 21st place (McGrath and Smith 1990; Barnhart 1997; Cervantes et al. 2001; Zou et al. 2006; Thacker et al. 2006; Pechova and Pavlata 2007; Ebdon et al. 2001), but it is the seventh most abundant element within the globe's surface layer (McGrath and Smith 1990; Kirklin 1999; Cervantes et al. 2001; Anke et al. 2005). Its average content in the Earth's crust is 100 mg kg^{-1} (Cervantes et al. 2001; Anke et al. 2005; Emsley 2011), but it attains its highest concentrations in ultrabasic igneous rocks, 1600–3400 mg kg^{-1}, and the lowest in acidic volcanic rocks, limestones and dolomites, 5–16 mg kg^{-1} (Papp 1994; Kabata-Pendias and Mukherjee 2007). Metallic chromium(0) does not occur in the Earth's crust and is biologically neutral (Pechova and Pavlata 2007).

The environmental effects of the compounds of chromium in the third and sixth oxidation state are fundamentally different, and therefore these two should definitely be considered independently (Bielicka et al. 2005).

Trivalent Cr is the most stable ion in the biological system (Borel and Anderson 1984; Mertz 1993; Irwin 1997; Thacker et al. 2006; Pechova and Pavlata 2007) and does not penetrate cell membranes (Mertz 1993). Trivalent Cr tends to form ligand complexes. Chromium hydroxide [$Cr(OH)_3$], which contains Cr(III), is nearly insoluble in water within the range of pH 6–9, and its migration through the soil to the groundwater is limited (Jeyasingh and Philip 2005; Cantu et al. 2014).

Biologically active chromium(III) form, low-molecular-weight chromium-binding substance (LMWCr) may take part in the insulin-signaling pathway (Hua et al. 2012; Vincent 2015). Studies on laboratory and farm animals indicate that organic and inorganic compounds of Cr are beneficial to carbohydrate and lipid metabolism, improve the growth of animals, and reduce mortality (NRC 1989; Anderson 1993; Grela et al. 1997; Şahin et al. 2001; Pollard et al. 2002; Lewicki et al. 2014).

On the other hand, the dietary guidelines for daily chromium intake in the USA were in 2001 lowered from 50–200 μg (for an adult person) to 35 μg for an adult male and to 25 μg for an adult female (Thor et al. 2011).

Hexavalent chromium is highly soluble and reactive; therefore, the ion easily penetrates into living organisms, causing changes in their functioning (Bartlett 1991; Peterson et al. 2008; Wuana and Okieimen 2011; Dhal et al. 2013). The hexavalent form is a strong oxidant; in acidic soils, with a high content of organic matter, this ion can easily convert to the trivalent, nontoxic form of chromium (Borel and Anderson 1984; Cervantes et al. 2001; Jianlong et al. 2004). The reverse process of Cr(III) converting into Cr(VI) is also possible, particularly in the presence of common minerals containing manganese (Mn) oxides, mainly of Mn (IV) (Bielicka et al. 2005). Cr(VI) chromates, which prevail under pH-neutral conditions, are absorbed by cells via sulfate channels and are subject to nonenzymatic activation involving ubiquitous ascorbate and small thiols (Zhitkovich 2011).

On entering the cell, hexavalent chromium degrades to Cr(III), which has a stronger binding affinity to DNA, RNA, proteins, and lipids (De Flora et al. 1990; McGrath and Smith 1990; Cervantes et al. 2001; Pechova and Pavlata 2007). In this process, however, other transitional products are generated, including long-persisting Cr(IV) and Cr(V) (Shi and Dalal 1989, 1990).

A high concentration of hexavalent Cr may suppress environmental capacity able to reduce the ion to Cr(III) and so may create a serious pollution problem. Moreover, Cr(III) can be oxidized to Cr(VI) as a result of excess oxygen (Cervantes et al. 2001).

3 Chromium Minerals, Production, and Uses

Industrial production of chromium is based on chromium-rich ore called chromite or ferrochromite ($FeCr_2O_4$) (Irwin 1997) (Fig. 3.1). Chromite may contain up to 55% Cr_2O_3. Most chromite deposits, which are of economic importance, contain at least

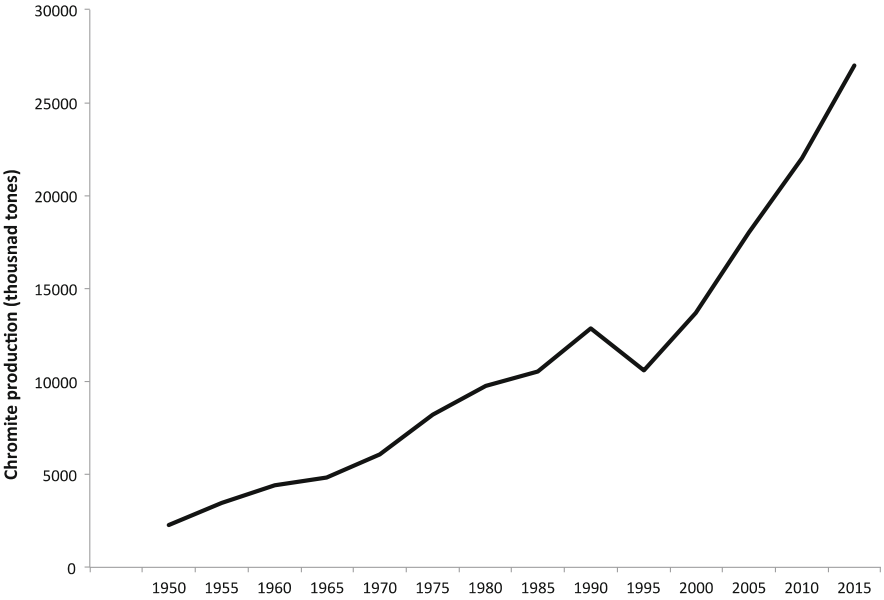

Fig. 3.1 World chromite production in 1950–2015 (Source of data: US Geological Survey https://minerals.usgs.gov/minerals/pubs/commodity/chromium/index.html#myb)

25% of the mineral (Irwin 1997; Papp and Lipin 2006). Another source of chromium is crocoite ($PbCrO_4$), known as a secondary mineral found in the oxidized zones of lead deposits (Gaines et al. 1997). Chromium was first detected in crocoite by Vauquelin in 1798 (Bequer et al. 2003; Shanker et al. 2005). Crocoite occurs in chromite deposits, coal seams, and quartz veins (Zhangsheng et al. 2001; Bequer et al. 2003). It contains hexavalent form of chromium (Irwin 1997). Another mineral containing chromium is magnesiochromite ($MgCr_2O_4$), belonging to the spinel group, takes part in the process of oxidation and is used in flotational chromite ore beneficiation. Magnesiochromite is an industrially important mineral (Sobieraj and Laskowski 1973; Vert 2016).

The metallurgical, refractory, and chemical industries are the fundamental users of chromium (Jacobs and Testa 2005; ATSDR 2012; Vert 2016). About 60–70% of chromium is used in the production of alloys, including stainless steel, and another 15% is used in chemical industrial processes (US Geological Survey 2010; Papp 2005, 2016). The main applications of Cr involve the production of nonferrous alloys, decorative finishes, metal plating, and green-colored glass (Jacobs and Testa 2005). The aircraft manufacturing industry has been using chromium for aluminum anodizing. Cr is also used as a catalyst in chemical reactions (ATSDR 2012). Oxidizing agents containing Cr are used for qualitative analysis (Jacobs and Testa 2005).

According to the Mineral Commodity Summaries 2015 (US Geological Survey 2015), global reserves of Cr-rich chromite ore are estimated at over 480 million tons,

Fig. 3.2 Chromium pollution of Earth regions from tanneries (Based on https://www.worstpolluted.org/projects_reports/display/88)

most of which is located in Kazakhstan, South Africa, and India (230, 200, and 54 million tons, respectively). South Africa, India, Kazakhstan, and Turkey, which together make up about 80% of the world chromite production (Papp 2011, 2016), have been the leading chromite mining countries for many years.

Industrial wastes carry large amounts of chromium in the form of chromates, dichromates, and other compounds, which threaten the aquatic environments. Both air and water become polluted by industrial plants that combust liquid fuels or wastes. US EPA (2010) has listed chromium as a priority pollutant (Rauch and Pacyna 2009; Friis 2012; Pati et al. 2014).

Dyestuffs and leather tanning agents discharged directly into waste streams, either as liquids or solids, are considered as the main source of chromium pollution (Fig. 3.2).

Both industrial residential sewage treatment plants discharge substantial amounts of Cr. Thus, COPR (chromite ore processing residue) is one of the greatest environmental threats in some regions (Kabata-Pendias and Mukherjee 2007; ATSDR 2012).

4 Chromium in Nature

The sources of chromium present in the natural environment are both natural and anthropogenic. Table 3.1 shows the chromium content in the environment and its various components.

Table 3.1 Global mean chromium concentrations in abiotic reservoirs

Reservoir	Chromium (mg kg^{-1})
Upper continental crust	92
Oceanic crust	320
Continental sediment	74
Oceanic sediment	79
Loess	59
Soil	130
Coal	16
Crude oil	0.19
Rivers (particulate)	100
Rivers (dissolved)	0.00085
Freshwater lakes (dissolved)	0.00025
Groundwater (dissolved)	0.0007
Greenland ice	0.000038
Antarctic ice	0.000007
Ocean (dissolved)	0.00026
Air	0.015–0.03 mg m^{-3}
Air	Average 0.6 ng m^{-3}, urban, industrial 1–1100 ng m^{-3}

Data sources: Kamaludeen et al. (2003), Shanker et al. (2005), Kabata-Pendias and Mukherjee (2007), and Rauch and Pacyna (2009)

An air concentration of chromium in the range 0.01–1 ng m^{-3} is considered normal; however, it may vary greatly depending on the anthropogenic impact (Barałkiewicz and Siepak 1999; Kabata-Pendias 2011; Pati et al. 2014). The average concentration of the metal in the atmosphere ranges from 1 ng m^{-3}, in rural areas, to 10 ng m^{-3}, in polluted urban sites (Bielicka et al. 2005). If we look at the Northern Hemisphere, chromium concentrations in the air vary as follows (according to Kabata-Pendias 2011): the cleanest air, 0.6–0.8 ng m^{-3}, can be found in Greenland, 1–140 in Germany, and 1.3–167 in Japan, and the highest chromium concentrations are found in North America, ranging between 5 and 1000 ng m^{-3}. In heavily polluted areas, chromium concentrations in the air may exceed 1000 ng m^{-3}. Maximum acceptable yearly average chromium air concentrations are 0.4 for cities and 0.08 for protected areas (Barałkiewicz and Siepak 1999). According to Wise et al. (2008), a chromium level in the range 1–100 ng m^{-3} poses a threat of exposure to hexavalent Cr and afflicts human lungs with 2 μg of chromium per day.

The United States Environmental Protection Agency (EPA 2000) estimated the lifetime cancer risk due to exposure to chromium(VI) to be 1.2×10^{-2}. According to IARC (1990), neither metallic nor trivalent chromium is classified as a human carcinogen, contrary to the carcinogenic hexavalent form of chromium.

Chromium occurring in the atmosphere is in 60–70% of the anthropogenic origin, including that of iron and steel production and, to a lesser extent, fossil fuel combustion. The remaining 30–40% of chromium in the air occurs naturally (Talebi 2003; Bielicka et al. 2005).

Global emission of chromium to the atmosphere is estimated at about 30,000 tons, most of air pollution from combustion of coal and other fossil fuels, as well as from the smelting of iron and nonferrous metals (Kabata-Pendias 2011). According to the US Agency for Toxic Substances and Disease Registry (ATSDR), chromium VI accounts for approximately one third of the 2700–2900 tons of chromium emitted to the atmosphere annually in the USA (ATSDR 2012). Total atmospheric emissions of chromium in China during the period from 1990 to 2009 were estimated at approximately 1.92×10^5 tons, at annual growth rates of 8.8% since 1990. Coal combustion was identified as the largest contributor, though a decrease from 60.2% in 1990 to 42.2% in 2009 was noted; nevertheless, a contribution of oil combustion has grown slightly during these years (Cheng et al. 2014). The European Union emission inventory report informs that between 1990 and 2013, Cr emissions in the EU-28 dropped by 74% (EEA 2015).

Hexavalent Cr is very toxic and soluble in water and can migrate down to the groundwater. The pollution of groundwater by Cr(VI) is related to the widespread industrial activity, like the usage of hexavalent chromium in various processes and discharges of Cr-bearing wastes. For the USA, a median value of 10 μg L^{-1} in fresh water is reported (ATSDR 2012). Chromium concentrations in riverine waters, according to Kabata-Pendias and Mukherjee (2007), range between 0.29 and 11.46 μg L^{-1}. Barałkiewicz and Siepak (1999) report that chromium concentrations in unpolluted lakes are on average 1–2 μg L^{-1} and in rivers from 5 to 50 μg L^{-1} (e.g., Germany 2.5–15.5, Russia-Siberia $>$ 10, Italy 0.1–1.2 μg L^{-1}). Also Bielicka et al. (2005) report that the chromium concentration in lakes and rivers is usually between 1 and 10 μg L^{-1}, regardless of the estimated 6.7 million kg of Cr discharged annually into the sea with industrial wastes. A total of 13,400 tons of Cr was discharged to the water in China during the years 1990–2009, mainly by fabricated metal products manufacturers and the leather tanning industry, accounting for 68.0% and 20.0% of the total emission, and representing increases of 15.6% and 10.3% annually, respectively (Cheng et al. 2014).

Over the last decade, there have been many reports on very high levels of Cr(VI) naturally occurring in groundwater. For example, in Cazadero County (California, USA), 12–22 μg L^{-1} of Cr(VI) was found in spring water from ultramafic rock; in La Spezia (Italy), 5–73 μg L^{-1} was found in groundwater from ophiolite complex (McNeill and McLean 2012). The US EPA regulates total chromium in drinking water and has set a maximum contaminant level (MCL) of 0.1 mg L^{-1} and 100 and 50 μg L^{-1}, respectively, for Cr(III) and Cr(VI) (Das and Singh 2011; Dhal et al. 2013). The World Health Organization (WHO) guideline is 0.05 mg L^{-1} for total chromium.

Chromium in soils occurs mainly in its trivalent oxidation state, which is poorly absorbed by vegetation (Bielicka et al. 2005). In strongly acidic soils, trivalent chromium dissolves well, whereas Cr(VI) is well soluble in both acidic and alkaline soils. Chromium(III) mobility is reduced through adsorption by loam and mineral oxides at pH <5 and low solubility at pH $>$ 5 due to formation of $Cr(OH)_3$. Chromium in soil is reduced by a number of organic compounds, primarily by reduced sulfur compounds and Fe(II) compounds (Buerge and Hug 1999). In the

presence of organic ligands (humic and fulvic acids), trivalent chromium may undergo complexation, which increases the solubility of trivalent chromium compounds and, therefore, leads to its higher mobility and better accessibility for living organisms (Wyszkowski and Radziemska 2009; Wuana and Okieimen 2011). The most mobile forms of chromium in the soil are CrO_4^{2-} and $HCrO_4^-$ ions (Dhal et al. 2013). Thakur et al. (2007) describe the average content in the soils of the world (Table 3.2).

Barnhart (1997) estimated the average soil Cr concentration in the USA at 40 mg kg^{-1}, whereas in the Czech Republic from 4.16 to 7.50 mg kg^{-1} (Mazanec 1996). The concentration range in the soil and regulatory guidelines have been established for some heavy metals, including chromium: 0.05–3950 mg kg^{-1}, regulatory limits 100 mg kg^{-1} (Riley et al. 1992; NJDEP 1996; Wuana and Okieimen 2011). Anke et al. (2005) ranked the soils in terms of chromium content as follows (in descending order): Rotliegend, granite, syenite, peat and muck soils, phyllite, shale, sand and Buntsandstein soil, glacial till clays, and sandy alluvial soil.

Canada's chromium in soil guidelines for the protection of environmental and human health is generally lower than soil standards in other countries. On Canadian agricultural, residential, and park soils, the total Cr should be below 64 mg kg^{-1} and Cr(VI) below 0.4 mg kg^{-1}. For industrial and commercial lands, the limits are 87 mg kg^{-1} total Cr and 1.4 mg kg^{-1} Cr(VI). The upper limits of typical Ontario chromium concentrations in uncontaminated soils are slightly higher than the

Table 3.2 Chromium concentrations in soils

Region	Soil	Concentration (mg Cr kg^{-1})	References
World	Natural	10–15	Thakur et al. (2007)
World	Serpentine	634–125,000	Thakur et al. (2007)
World	World soils	200 (mean value)	Thakur et al. (2007)
World		100–300	Thakur et al. (2007)
World		10–150	Thakur et al. (2007)
USA	Generally	25–85	Thakur et al. (2007)
Urban soils			
China, Beijing		35.60	Su et al. (2014)
China, Shanghai		107.90	Su et al. (2014)
China, Changsha		121.00	Su et al. (2014)
USA, Cincinnati		37.00	Su et al. (2014)
France		42.08	Su et al. (2014)
Finland, Turku		59.00	Su et al. (2014)
Arable soils			
China, Beijing		75.74	Su et al. (2014)
China, Guangzhou		64.65	Su et al. (2014)
China, Wuxi		58.60	Su et al. (2014)
India		1.23–2.19	Su et al. (2014)
USA		48.5	Su et al. (2014)
Spain		63.48	Su et al. (2014)

Canadian guidelines, with 0.66 mg kg^{-1} Cr(VI) and 67–70 mg kg^{-1} total chromium. The Ontario Site Condition Soil Standards have set higher limits than the Canadian guidelines. Limits for soils of all property uses are 160 mg kg^{-1} total chromium and 8–10 mg kg^{-1} Cr(VI). Lower limits for soil within 30 m of a water body are set at 67–70 mg kg^{-1} total chromium and 0.66 mg kg^{-1} Cr(VI) (CCME 1999).

Hexavalent chromium significantly affects biological properties of soil, including the content of nitrogen compounds—has an oxidizing effect and, moreover, penetrates the cell membranes of soil organisms. Due to its high solubility in the soil solution, this species is considered more readily available to plants than Cr(III). It is believed that Cr is not essential for microorganisms or plants and may even be toxic in higher concentrations (Samantaray et al. 1998; Cervantes et al. 2001; Singh et al. 2013). A typical ratio of Cr content in plants to Cr content in soil is estimated at the level 0.0045 (0.45%). It has been demonstrated that Cr in plants, especially in crop plants, occurring in low concentrations in the substrate (0.05–1 mg L^{-1}) stimulates plant growth and crop yield. Once Cr is present in the soil solution at a concentration of 1–5 mg L^{-1}, it causes adverse changes in the metabolism of plants, leading to growth inhibition and reduction in the chlorophyll synthesis; it also contributes to the development of chlorosis (Cervantes et al. 2001; Dube et al. 2003; Peralta-Videa et al. 2009). Some plant species tend to accumulate the metal in their tissues extensively, without any visible symptoms of poisoning. Those include the crimson-spot rockrose (*Cistus ladanifer*), a shrub native to the western Mediterranean region, which grows on serpentine soils. More than 2600 mg Cr kg^{-1} has been detected in this particular plant (Wuana and Okieimen 2011; Favas et al. 2014). Plants capable of accumulating and tolerating high concentrations of Cr are sometimes found in some areas of high chromium anthropogenic pollution, such as that near a Chinese electroplating facility. The grass *Leersia hexandra* growing in this area had more than 1600 mg Cr kg^{-1} dw (Liu et al. 2011).

In animal bodies, chromium has been estimated in the range from 0.02 to more than 1500 mg kg^{-1} dw, depending on a large number of biotic and abiotic factors (Eisler 1986; Shanker et al. 2005).

Absorption and transport of chromium may be modified by such factors as soil pH, organic matter content, or chelating agents (Han et al. 2004). Geochemical and reductive conditions of the substrate jointly shape chromium solubility, mobility, and bioavailability to organisms (Martello et al. 2007; Peralta-Videa et al. 2009). With the surface runoff, chromium may be transported into water bodies in a soluble form or as a sediment. The soluble and unadsorbed chromium complexes may be washed from the soil to the groundwater. Leeching of Cr(VI) increases with the soil pH. Most of chromium entering natural water bodies binds to various particles and, eventually, is deposited in the sediment (Wuana and Okieimen 2011). The most common anthropogenic chromium soil pollution comes from the atmospheric deposition of dust emitted by electroplating, steel, and automobile manufacturing industries, as well as from any industrial wastes that are introduced to the soil, in particular all kinds of sludge from paint factories, tanneries, sewage treatment plants, or chrome-steel scrap piles. Estimates are that approximately 80–90% of leather is tanned using a chromium-containing substance, of which approx. 40% of Cr is

discharged with wastewater as Cr(VI) and Cr(III) (Anke et al. 2005; Dhal et al. 2013). In the USA, Cr(VI) represents approximately 35% of all chromium released from anthropogenic sources (Das and Singh 2011; Dhal et al. 2013).

5 Biological Status of Chromium

Chromium(III) is probably an important micronutrient for the glucose metabolism, whereas Cr(VI) is a carcinogenic factor (Peterson et al. 2008).

It has never been considered as essential nutrient in plants; however, positive effects of small Cr doses in terms of growth stimulation were found (Kimborough et al. 1999; Zayed and Terry 2003; Sharma et al. 2003). Also a negative impact of Cr on plants has been reported (Samantaray et al. 1998; Hood 2010; Singh et al. 2013). Toxic effects on plants from chromium exposure are well known, especially in those growing on serpentine soils or in heavily chromium-polluted areas (Anke et al. 2005). Plants can accumulate Cr(III) and Cr(VI) from soil, sediment, water, and atmospheric deposition on leaves. Plant exposure to excess Cr(III) or Cr(VI) can negatively affect plant health and survival. The complex influence of soil chemistry and differences between plant species make it impossible to generalize (Kimborough et al. 1999; Zayed and Terry 2003; Sharma et al. 2003). It has been found that Cr(III) is more toxic against certain plant species as compared to the Cr(VI), unlike in humans (Suwalsky et al. 2008). Higher concentrations of Cr(III) inhibited plant growth or even killed some more susceptible plants (Samantaray et al. 1998; Singh et al. 2013). According to Eisler (1986), chromium is beneficial but not essential to growth in higher plants.

Chromium accumulates mostly in roots, and its transport to shoots, leaves, or fruits of trees and shrubs is limited. Toxic chromium doses hinder plant growth efficiency even by 50% (Samantaray et al. 1998). Toxic effects to plants exposed to excess chromium include reduced growth; decreased chlorophyll production causing yellow leaves, narrow leaves, and small root systems; decreased or complete inhibition of seed germination; delayed growth; decreased seed yield; wilting; and death (Dube et al. 2003; Zayed and Terry 2003; Anke et al. 2005; Mining Watch Canada 2012). Excess chromium damages root membranes and a plant's ability to take up water. It also alters uptake and translocation of essential elements such as nitrogen, iron, potassium, magnesium, manganese, phosphorous, calcium, sulfur, copper, and zinc (Zayed and Terry 2003; Dube et al. 2003; Gardea-Torresdey et al. 2005). It disturbs enzymatic activity and leads to formation of reactive oxygen species, which destroy lipids and DNA in the plant (Singh et al. 2013). Not only is this detrimental to plant health, but a change in plant nutrient balances may also affect wildlife and human health. Sensitivity and effects vary between species, making toxicity predictions difficult without extensive plant studies.

Some researchers suggest that there is a "soil-plant barrier" that protects the terrestrial food chain from excess chromium due to (a) the insolubility of most chromium in soils, (b) >90% of chromium that is taken up is stored in plant roots,

and (c) plant toxicity occurring below levels thought to affect plant consumers (Zayed and Terry 2003).

It has been demonstrated that plant bioavailability of Cr(VI) in the soil is about 35% of its total concentration, and *Streptomyces* bacteria are able to transform hexavalent chromium in such a way that 90% of the ion present in soil will be bioavailable to plants (Polti et al. 2009, 2011). Anke et al. (2005) found that parts of plants—such as shoots and bark of various trees and shrubs, shoots of raspberries and blackberries, as well as crop plants—eaten by wild animals in winter contain from 0.70 to 2.80 mg Cr kg^{-1} dw. Chromium toxic concentrations have also been found in tobacco leaves (18–24 mg kg^{-1} dw), maize leaves (4–8 mg kg^{-1} dw), and barley and rice stems (10 and 10–100 mg kg^{-1} dw, respectively). Plant toxicity limit is assumed at the level 10 mg Cr kg^{-1} dw (Anke et al. 2005). Sanyal et al. (2015), who studied aquatic ecosystems of water bodies and rivers, found a high rate of Cr accumulation in the water. The highest concentration of chromium was found in the roots of aquatic plants (877.5 mg kg^{-1}). Studies have shown Cr(VI) toxicity to algae and aquatic plants exposed to as little as 1–10 μg L^{-1} (Mining Watch Canada 2012). According to Marchese et al. (2008), Cr(III) induces toxic effects in algae at the level 320 μg L^{-1}. Most studies have found Cr(VI) effects occur at lower concentrations and with greater severity. Chromium toxicity to plants has been observed at exposure as low as 160 μg L^{-1} of Cr(VI) (Adema and Henzen 1989) and 104 μg L^{-1} of Cr(III) (Pawlisz et al. 1997) when grown in soilless solution and 1.8 mg kg^{-1} (added as Cr(VI)) when grown in soil (Adema and Henzen 1989).

Anthropogenic chromium pollution of soil in the areas located in the vicinity of cement factories and phosphate-fertilizer plants can significantly increase chromium content in plants, as shown by the example of vegetables as well as legumes and herbs that are eaten on pasture by grazing animals. Chromium content in vegetables collected in an area near a cement factory was from 0.76 to 1.63 mg Cr kg^{-1} dw as compared to non-contaminated areas: 0.34–1.03 mg Cr kg^{-1} dw (Anke et al. 2005).

Fruit and grain eaten by humans and animals usually contain from 0.15 to 0.65 mg Cr kg^{-1} dw and represent a good source of chromium (Anke et al. 2005). There is evidence that plants can convert Cr(VI) to Cr(III) in their roots (Zayed et al. 1998; Howe et al. 2003; Zayed and Terry 2003) though there are differences in observed rates and extent of reduction to Cr(III). Some studies support the concept that plants can quickly convert all Cr(VI) to Cr(III) (Lytle et al. 1998; Zayed et al. 1998; Wang et al. 2011), while other studies have found evidence of Cr(VI) and its intermediates, Cr(V) and Cr(IV), persisting in plants and algae (Micera and Dessi 1988; Liu et al. 1995; Mishra et al. 1995; Aldrich et al. 2003; Howe et al. 2003). As Cr(VI) intermediates are implicated in Cr toxic effects (Stearns et al. 1995), their presence in plants could "produce dangerous effects to ecological cycles" (Micera and Dessi 1988). According ATSDR (2008), there is no documented evidence for biomagnification of Cr from soil to plant to animal, though researchers also acknowledge there is a lack of study regarding the risk of chromium in the food chain (Lind et al. 2001; ATSDR 2008; Peralta-Videa et al. 2009).

The binding of Cr(III) by microalgae is higher at pH ranging 3.5–5.5 than the binding of Cr(VI) at pH $\leq$ 2.0. Reduction of Cr(VI) to Cr(III) increases at a

temperature 25–55 °C (Wilde and Benemann 1993). Laboratory tests on *Scenedesmus*, *Selenastrum*, and *Chlorella* algae have shown that Cr(III) is more efficiently removed from an aqueous medium (83–99%) than Cr(VI) (18–22%) (Brady et al. 1994).

Both Cr(III) and Cr(VI) are efficiently removed from aqueous solution through adsorption on various nanomaterials. Cantu et al. (2014) have shown that sorption of Cr(VI) by the oxides of the nanomaterials is in fact reduction to Cr(III), which is next adsorbed on the surface of a metal oxide. Besides metal oxides, multiwalled carbon nanotubes are also effective here.

Chromium is actively transported through cell membranes in prokaryotes and eukaryotes. Most cells are impermeable to Cr(III), which is probably due to the insolubility of its compounds in an alkaline medium (Jianlong et al. 2004). The amount of chromium taken up and stored in living tissue and its effects depend on factors such as species, organism size, sex and developmental stage, water characteristics, and presence of other contaminants (Eisler 1986; Mining Watch Canada 2012).

Yeast exposed to Cr revealed various phenomena inside their cellular processes, including oxidation and reduction reactions, interactions with cellular organelles, binding cytosolic molecules, forming DNA proteins, Cr-DNA adducts, breaks in the DNA strand, and DNA-DNA cross-links (Kaszycki et al. 2004). It has been shown that yeast is able to accumulate high concentrations of both forms of Cr in line with their concentration in the medium (Brady et al. 1994). In *Saccharomyces cerevisiae*, the concentration of chromium may reach as high as 30 mg g^{-1} dw (Batic and Raspor 1998), being usually lower in other species and ranging from 0.45 to 10 mg Cr g^{-1} dw (Muter et al. 2001; Kaszycki et al. 2004; Ksheminska et al. 2005). Yeast Cr tolerance depends on the physiological growth phase, biomass density, and exposure time (Kaszycki et al. 2004).

Soil organisms are important in creating soil structure and cycling organic matter and elements in the environment. Relatively small amounts of Cr(VI) (1–10- mg kg^{-1}) and Cr(III) (25–100 mg kg^{-1}) can negatively impact the number, type, health, and activity of soil organisms and so impact the health of the soil ecosystem (MOE 2011; Viti et al. 2006). Tests conducted under and near a steel alloy plant slag heap in China found that chromium was related to decreased microorganism numbers and enzyme activity (Huang et al. 2008). Ten thousand to fifteen thousand μg L^{-1} of Cr(VI) in water applied to soil was lethal to two species of earthworms (Eisler 1986). Total chromium levels of 671–1400 mg kg^{-1} killed 50% of a tested earthworm population (*Eisenia fetida*), and 1000 mg Cr kg^{-1} significantly reduced earthworm (*Eisenia andrei*) growth and cocoon production (CCME 1999).

Concentrations of chromium were measured in insects such as Coleoptera, Diptera, Hemiptera, and Hymenoptera captured at ultramafic and non-ultramafic sites in the Highlands of Scotland. Hemiptera showed the greatest concentration differences between the ultramafic and non-ultramafic sites in Cr, with greatly increased levels in ultramafic sites. Coleoptera and Hymenoptera had lower levels of Cr at the ultramafic site than at the non-ultramafic sites. Diptera showed no difference in Cr levels from any site (Davison et al. 1999). Studies by Corbi et al.

(2011) confirm that Cr may also bioaccumulate in the Odonata larvae. Their experiment revealed a higher concentration of Cr in the larvae inhabiting the lower reaches of the river, which is related to its higher concentration in the riverine sediments. The studies on invertebrates did not reveal significant differences in Cr concentrations, though it was noted that habitats more heavily polluted with Cr lack stoneflies (Plecoptera), which are otherwise present in cleaner parts of the river. This may be due to a particular sensitivity of these taxa to chromium pollution (Corbi et al. 2011). Canada has set a quality criteria for agricultural irrigation water and livestock water. The Canadian Water Quality Guideline for the Protection of Freshwater Aquatic Life for Cr(VI) at 1 μg L^{-1} is based on toxicity to a sensitive invertebrate (*Ceriodaphnia dubia*) (Mining Watch Canada 2012). Azam et al. (2015) found that the concentration of toxic metals in insects (a libellulid dragonfly, *Crocothemis servilia*; an acridid grasshopper, *Oxya hyla hyla*; and a nymphalid butterfly, *Danaus chrysippus*) is highest in industrial areas and lowest in places most distant from cities. This implies that these insects represent good bioindicators of environmental pollution (Azam et al. 2015). Long-time exposure of insects to toxic metals may inhibit their growth, impair their development, and lead to reproductive disorders and lower proliferation. Industrial effluent discharged in eastern France contained about 25 mg L^{-1} Cr, which significantly reduced the fertility of the pond snail *Lymnaea palustris* (Coeurdassier et al. 2005). Aquatic organisms may be exposed to various forms of chromium present in both sediments and water column. Crustaceans accumulate chromium in their exoskeleton (Marchese et al. 2008; Peralta-Videa et al. 2009). Weegman and Weegman (2007) investigated whether the population decline of the lesser scaup *Aythya affinis* was related to the diet (zebra mussels, fingernail clam *Sphaerium transversum*, chironomid larvae, gastropods, and amphipods). The authors propose that chromium accumulated in the bivalves, and amphipods may have caused the scaup decline.

Chromium III in water seems to be more toxic to fish than Cr(VI). It can decrease fertilization success and deposit onto gills which damages tissue and function and can cause death at relatively low doses. Trivalent Cr has caused toxic effects on fish at 5 μg L^{-1} and on invertebrates at 44 μg L^{-1} (Marchese et al. 2008). The Canadian Water Quality Guideline for the Protection of Freshwater Aquatic Life for Cr(III) is set at 8.9 μg L^{-1} which is based on toxicity to rainbow trout *Oncorhynchus mykiss*. There are currently no tissue residue guidelines for the protection of animals and people who consume fish (Mining Watch Canada 2012). The one field study located that examined wild fish found no difference between the Cr concentration in unexposed fish and bluegill *Lepomis macrochirus* and largemouth bass *Micropterus salmoides* exposed to hexavalent chromium (0.10–0.30 mg L^{-1}). Researchers acknowledge there is still little information on chromium uptake and effects in freshwater species (Marchese et al. 2008). Studies have observed Cr(VI) toxicity on fish exposed to as little as 10 μg L^{-1}. Chromium(VI) does not deposit on gills but enters the fish and exerts toxic effects on internal organs such as the kidney (Mining Watch Canada 2012). Fish exposed to hexavalent chromium have shown changes in physical and biochemical conditions, increased hatching time, DNA damage, and reduced survival (Mining Watch Canada 2012).

In Chinook salmon *Oncorhynchus tshawytscha*, the kidney is the most vulnerable organ in terms of exposure to Cr(VI), which causes necrosis of the renal tubular epithelium (Farag et al. 2006). Pathological changes caused by Cr were also found in the spleen and blood. Exposure to hexavalent Cr in a teleost *Channa punctata* led to changes on gills, kidney, and liver (Mishra and Mohanty 2009a) and resulted in an increased blood serum cortisol level (Mishra and Mohanty 2009b). The fish caught near petrochemical industry centers contained 0.72 mg Cr kg^{-1} (Copat et al. 2012). Edible fish collected in Karai and Puliyankannu (southern India) had a Cr concentration at a level 0.8–1.66 mg kg^{-1} (Imam Khasim et al. 1989). According to Ciftci et al. (2010), the highest Cr concentration was detected in the liver of *Glossogobius giuris* (679.7 mg kg^{-1}) during monsoon season, followed by the gills of *Mystus bleekeri* (190.0 mg kg^{-1}) and intestines of *Glossogobius giuris* (123.7 mg kg^{-1}) in summer. The liver and gills were found to be the most Cr-contaminated tissues (Ciftci et al. 2010). Sanyal et al. (2015) observed that Cr also accumulates in the piscine gut and kidney. The authors also propose that the muscles of fish escape Cr contamination.

Mozambique tilapia *Oreochromis mossambicus* exposed to trivalent chromium chloride and hexavalent potassium dichromate showed no humoral and cellular response of lymphoid cells. Both forms suppressed the antibody response, though Cr(VI) is more stronger than Cr(III). Supplementation of Cr(VI) and Cr(III) also reduced the weight of the spleen and the percentage of lymphocytes in blood (Arunkumar et al. 2000). It has been demonstrated that trivalent chromium can also cause changes and mutations in DNA (Costa and Klein 2006; Peralta-Videa et al. 2009). Experiments indicate that a high Cr content in the diet affects the growth and survival rates of birds, e.g., the brood of American black ducks *Anas rubripes* (Eisler 2000; Koivula and Eeva 2010).

In some poultry species (broiler chickens, turkeys, laying hens), Cr supplements improved weight gains and egg production while reducing the cholesterol levels in the muscles. On the other hand, a decrease in the concentration of serum glucose, fat, and total cholesterol was observed in laying hens (Şahin et al. 2001; Anke et al. 2005). Puls (1994) adds improved quality of egg contents to the positive effects of poultry feed Cr(III) supplementation.

Information on the doses of Cr in water or food that cause health problems in mammals come mostly from toxicology lab tests done on mice and rats. Effects observed on animals in experimental doses through food, water, or injection include cancers, reproductive harm, behavioral changes, reduced growth, and reduced survival (Nriagu and Kabir 1995). The liver may be the most important depot of biologically active Cr, including GTF, which is secreted into the bloodstream in response to increased amounts of plasma insulin (Outridge and Scheuhammer 1993).

Although in vitro tests reveal mutagenicity of Cr(III), in vivo studies have never indicated any carcinogenic properties of the ion, irrespective of the route of exposure (Juturu and Komorowski 2003). A 90-day period of exposing rats to a dose that was 30,000 times greater than that recommended as dietary supplementation in humans (as Cr picolinate) revealed no adverse health consequences of Cr bioaccumulation (Anderson et al. 1997). Staniek et al. (2010) observed that rats fed with Cr(III)

propionate showed no genotoxic effects, based on the comet assay of lymphocytes, in contrast to Cr(VI) in the form of $K_2Cr_2O_7$.

Experiments on rats (both in vitro and in vivo) demonstrate that 80% of blood Cr is bound to transferrin—the protein transporting and regulating iron concentration (Feng et al. 2003). Chromates are accumulated through a system of sulfate uptake and influence their metabolism (Peitzsch et al. 1998; Juhnke et al. 2002; Nies 2004). Just like in the case of the abiotic reactions, cellular reduction of Cr(VI) results in the thermodynamically stable Cr(III) (Zhitkovich 2011). Chromate reduction to Cr(III) forms free radicals, which make the metal very toxic (Nies 2004).

Chromium metabolism in endothermic vertebrates depends on the degree of oxidation and the properties of the compounds it forms. Most of Cr found in the organisms is ingested with food, in which it is present in the form of Cr(III). Chromium absorbed in blood leaves it quickly; therefore, the blood Cr concentration does not reflect the content of Cr in the tissues (Suwalsky et al. 2008). Cr(VI) and Cr (III) differ in the ability to penetrate cell membranes (Miksche and Lewalter 1997). It has been shown that chromium picolinate and other compounds of Cr(III) have a limited ability to penetrate the cell membrane to get access to DNA, in contrast to Cr (VI), which is carcinogenic (Juturu and Komorowski 2003).

Animal studies have used various experimental models, and various forms (picolinate, propionate, chromium-L-methionine) and concentrations of Cr were applied in the diet (Lewicki et al. 2014). Chromium affected the metabolism of glucose and fat, reduced cholesterol levels, reduced the risk of atherosclerosis, and reduced mortality due to stress in cats, monkeys, guinea pigs, rabbits, squirrels, pigs, cows, calves, poultry, and humans (Anderson 1988; Moonsie-Shageer and Mowat 1993; Piva et al. 2003; Arvizu et al. 2011; Lewicki et al. 2009, 2014). In livestock animals, Cr supplements improved reproductive performance, weight gains, and carcass quality (Mooney and Cromwell 1997; Pollard et al. 2002). Kurył et al. (2006) demonstrated a significant increase in glucose transport in erythrocytes and β-oxidation of fatty acids in the lymphocytes of healthy rats fed with a diet containing fructans and chromium(III), with the effects increasing with the level of these components in the diet.

In pigs, an addition of 200 μg of Cr improved glucose tolerance, increased glucose production, and decreased the half-life of glucose. Such results have not been confirmed in lambs (Anke et al. 2005). Lewicki et al. (2009) demonstrated in vitro (murine C2C12 myocytes) that chromium supplementation had a positive effect (more potent stimulation of chromium chloride than picolinate) on the increase in the intensity of β-oxidation. Cattle fed with a Cr-supplemented feed showed an increased ($p > 0.05$) cellular immunity, a reduced blood cortisol levels, and a higher antibody titer (Mallard and Borgs 1997; Pollard et al. 2002).

The most widely accepted theory explaining the mechanism of Cr effect on glucose metabolism involves chromodulin (Vincent 1999; Peterson et al. 2008). One of the more recent concepts of chromium action is its effect on cell membrane fluidity and—in consequence—on the regulation of glucose uptake by cells. This effect is associated with a lower membrane cholesterol level, which is thought to be a glucose transport inhibitor controlled by the insulin receptor (Pattar et al. 2006). It is

also possible that the mechanism of Cr action depends on estrogen receptor activation (Song et al. 2004). The molecular mechanism of estrogen influence on insulin secretion is not fully understood. It can be divided into two parts: a fast signal (associated with membrane estrogen receptor activation) and slow signal (associated with activation of nuclear estrogen receptors) (Lewicki et al. 2014).

It has been demonstrated that Cr may enhance insulin activity through a hypothetic mechanism which consist in:

- Formation of chromodulin (LMWCr), which—after binding to tyrosine kinase—is supposed to stabilize the active conformation of the insulin receptor and amplify insulin signal approx. eightfold, until the blood concentration of this hormone decreases; thereafter, the bonds with tyrosine kinase loosen and chromodulin is secreted from cells to blood, which is followed by its urinary excretion (Chen et al. 2006; Peterson et al. 2008).
- Decrease in the concentration of tyrosine phosphatase, which—by dephosphorylation of tyrosine residues—inactivates the proteins of insulin receptor stimulation cascade, so quenching the effect of insulin (Wang et al. 2006; Krzysik and Grajeta 2010).
- Regulation of translocation of GLUT4 (transmembrane glucose transporter in insulin-dependent cells) by Cr(III), which may occur independently from the insulin-signaling pathway proteins and is associated with changes in cell membrane fluidity resulting from excessive loss of membrane cholesterol (Ginsberg 2000).

The mechanism of hypotriglyceridemic action of chromium has not been precisely explained. It has been proposed that the mechanism is necessary to maintain the antilipolytic effect of insulin, which involves activation of lipoprotein lipase resulting in the hydrolysis of triglycerides, competitive inhibition of lipolysis, and consequent reduced use of free fatty acids in the biosynthesis of triglycerides (Ginsberg 2000; Krzysik and Grajeta 2010).

Chromium deficiency has been described in rats, guinea pigs, and squirrel monkeys; signs include reduced growth, decreased life span, elevated serum cholesterol, increased formation of aortic plaques, and signs resembling those of diabetes mellitus (Eisler 1986). Some of the first symptoms of Cr deficiency are diminution of insulin function and glucose metabolism disturbances. Further changes involve altered metabolism of proteins, general weakness, and circulatory system damage (Kabata-Pendias and Mukherjee 2007).

Various animal species fed with a chromium-deficient diet exhibited reduced glucose tolerance. A dietary Cr level reduced to below 0.31 mg kg^{-1} dw applied to male goats resulted in lower feed intake, reduced glucose tolerance, and poor weight gains. Bucks fed on chromium-deficient diet produced semen with impaired sperm motility, had lower libido, and suffered from skin diseases (Anke et al. 2005). Chromium deficiency in rats results in increased serum cholesterol level and accelerates platelet formation; in rats, mice, and guinea pigs, it hampers growth rate and shortens the life span (Anke et al. 2005). Some researchers suggest that certain level of dietary chromium is necessary for the normal growth of the heart

(Morris et al. 1995). Experiments on male Sprague-Dawley rats fed with a diet supplemented with chromium picolinate at 300 and 1500 ppb demonstrate that even a fivefold increase of the recommended daily dose of chromium does not cause change in the mass of the heart, total protein content in the heart, and the number of myofibrils but reduces by 11% the amount of high ATPase myosin isoform—V1 (Morris et al. 1995).

Chromium ingestion by humans may be a result of contamination of foods and beverages during the processing and from their packaging. Acids in fruits (malic and citric acids) may wash chromium out from the stainless steel of a cooling vat in the process of canned fruit production (Krzysik et al. 2008; Peralta-Videa et al. 2009). Fish and shellfish are common seafood products, which are regarded as Cr transporters in the trophic chain (Marchese et al. 2008; Peralta-Videa et al. 2009).

Chromium is present in the tissues of human fetuses and infants. Its content decreases with age in all organs except the lungs, where a small increase in the content of chromium is detectable from 10 years of age, probably due to an increase in the Cr levels inhaled into the lungs. The highest accumulation of Cr levels (0.2–2.0 mg kg^{-1}) was found in hair (Bielicka et al. 2005).

On the whole, the levels of chromium in the diets of wild mammals and birds seem to be meeting their daily requirements. Chromium deficiency cases in animals are rare, and those documented most often involve experimental mammals (Anke et al. 2001, 2005).

6 Toxicity of Various Chromium Forms in Homeothermic Animals

Chromium is listed on the Superfund Priority List of Hazardous Substances; it has been among of the top 20 contaminants for the last 15 years (Chrysochoou and Johnston 2012; Friis 2012; Dhal et al. 2013). Humans and animals take chrome into the body with food, water, and air. Chromium excess in drinking water may pose a health threat.

According to Puls (1994), hexavalent chromium is toxic for cattle at the doses 3000 mg kg^{-1} (chromium oxide) and 1000 mg kg^{-1} (CrCl). A dose causing chronic toxicity is 30–40 mg kg^{-1} of zinc chromate for 1 month. Puls (1994) gives the following data on Cr content in poultry feed, eggs, and tissues of chickens (Table 3.3).

A content of 5 mg kg^{-1} Cr as potassium chromate fed to 2-week-old chicks caused 50% mortality in 3 weeks (Puls 1994). Consumption of Cr^{6+} by hens reduced the hatchability of chicks (Kirklin 1999). Chromium transferred vertically by hens into the eggs inhibits the growth of bone in the embryos (Hui 2002). The content of Cr in avian muscles ranges from 0.1 to 15 μg g^{-1} dw, in unpolluted areas, and from 1 to 700 mg kg^{-1} dw, in polluted habitats. The authors conclude that birds inhabiting chromium-polluted areas tend to accumulate the metal. The same cannot be said about mammals (Outridge and Scheuhammer 1993).

Table 3.3 Content of chromium, Cr, in the feed, eggs, and tissues of laying hens

Cr level (mg kg^{-1})	Diet	Eggs	Liver	Kidney	Muscle
Deficient	<3.0				
Adequate	5.0–20	0.05–0.15	0.05–0.40	0.19–0.29	0.05–0.10
High	100	1.25		1.43	0.10
Toxic (chromate)	400–5000		13.0–150.0	>18.6	2.5–14.0

Puls (1994)

Table 3.4 Content of chromium, Cr, in the tissues of rabbit

Diet	Liver	Kidney
Normal	0.3–1.0	0.42–1.58
High/toxic		
Trivalent	6.0–50	17.0–30.7
Hexavalent	10–50	3.3–11.2

mg kg^{-1} wet weight, Puls 1994

A normal Cr content in equine hair ranges between 1.5 and 3.3 mg kg^{-1}. Hair is a better indicator of Cr level in the body than blood serum (Puls 1994). According to Outridge and Scheuhammer (1993), the concentration of Cr in the fur of wild mammals inhabiting uncontaminated areas ranges from 0.1 to 10 mg kg^{-1} dw. However, samples collected in Cr-polluted sites varied in Cr content from 0.3 to 20 mg kg^{-1} dw. The authors observed large differences in the hair of the same species animals collected from a close distance from each other, which is difficult to explain. Cr concentrations in the muscle of marine and terrestrial mammals were similar (Outridge and Scheuhammer 1993). Data by Puls (1994) on the content of Cr in the liver and kidneys of rabbits are shown in Table 3.4.

Only for a few species or groups of mammals and birds, mainly domesticated, have been developed the ranges of normal, high, and toxic levels of Cr in the liver, kidneys, blood, and other biological samples. The Wisconsin Veterinary Diagnostic Laboratory regularly publishes important information on various substances, including Cr (WVDL 2015). Table 3.5 shows the reference values and toxic levels for birds and same mammalian groups.

According to the data summary presented by ATSDR (2012), at acute dermal exposure in rabbits, depending on the mode of exposure to Cr(VI), a LOAEL (lowest-observed-adverse-effect level)—LD_{50}—ranged from 30 mg kg^{-1} (24 h) to 426 mg kg^{-1}, in males, and 553 mg kg^{-1}, in females (2-day exposure). At a single incident of exposure, LD_{50} was 763 mg kg^{-1}. With a 4-h exposure in rabbits, a LOAEL occurred at a dose of 42–55 mg kg^{-1} resulting in necrosis, erythema, and edema. This was similar to other experiment with guinea pigs administered with 0.04 mg kg^{-1} once, which caused erythematous reaction. In terms of inhaled Cr(VI), a serious LOAEL in rats was observed after 4-h inhalation at a dose of 29–137 mg m^{-3} (LC_{50}). Inhaled doses of Cr(VI) in rats resulted in NOAEL at 0.49 mg m^{-3}, causing nasal hemorrhage. In another experiment on rats, the results observed at

Table 3.5 Normal and toxic ranges of Cr in avian, lapine, ursine, and bovine tissues

Animal group	Tissue	Normal	Toxic	Unit	Normal values expressed as mg kg^{-1} dw[a]
Avian	Blood	<0.03	3.9–25	mg dL^{-1}	
	Serum	0.19–0.29	–		
	Kidney	0.05–0.1	19–170	mg kg^{-1} ww	0.25–0.50
	Liver	0.05–0.40	13–150	mg kg^{-1} ww	0.17–1.33
Lapine	Serum	<0.10	1–6		
	Kidney	0.42–1.60	3.3–31	mg kg^{-1} ww	2.1–8.0
	Liver	0.30–1.00	6–50	mg kg^{-1} ww	1.0–3.3
Ursine	Kidney	0.01–0.52	–	mg kg^{-1} ww	
	Liver	0.01–0.53	–	mg kg^{-1} ww	
Bovine	Blood	<0.07	1–4	mg dL^{-1}	
	Kidney	0.05–6.20	15	mg kg^{-1} ww	
	Liver	0.04–3.80	30	mg kg^{-1} ww	

WVDL (2015)

[a]We assumed (according to Kalisinska suggestion) that livers and kidneys of mammals and birds contain 70% and 80% moisture, respectively

0.4 mg m^{-3} were defined as NOAEL in the gastrointestinal, hematological, hepatic, and renal systems.

Laboratory studies on mammals show the following LOAELs for Cr(VI) in drinking water: 100 mg L^{-1} for mice, 70 mg L^{-1} for rats, and 62.7 mg L^{-1} for dogs. LOAELs of Cr(III) in drinking water of rats (28 mg L^{-1}) and mice (5 mg L^{-1}) are notably lower than those of Cr(VI) (Pawlisz et al. 1997).

Carcinogenicity of Cr(VI) was discovered in the late nineteenth century, when cases of nose tumor in workers handling chromium pigments in Scotland were described (Cohen et al. 1993). Research on lung cancer carried out in the 1930s has led to the recognition of chromium as an occupational disease-causing agent for Cr-exposed workers in Germany. Since then, the mainstream research on Cr has been focused on its toxic effects in humans (Pechova and Pavlata 2007). Hexavalent Cr has been introduced in the environment nearly entirely by human activity, and the literature is dominated by reports on its toxicity studies. Over time, a number of experimental studies have shown that Cr(VI) is also carcinogenic for other homeothermic vertebrates (Mertz 1993; Eisler 2000; Koivula and Eeva 2010; Friis 2012). Currently, Cr(VI) is a well-established carcinogen associated with lung, nasal, and sinus cancer, and the International Agency for Research on Cancer (IARC) has classified Cr(VI) compounds as Group 1 substances carcinogenic to humans (WHO/IPCS 2013).

Chromium compounds may damage the respiratory system and gastrointestinal tract; may cause skin lesions; have carcinogenic, mutagenic, embryotoxic, and teratogenic effects; and affect the postnatal development of neonates (Elbetieha and Al-Hamood 1997; Friis 2012). Women occupationally exposed to chromium may encounter impaired fetal maturation and complications during pregnancy and childbirth (Kanojia et al. 1998). Analogous effects have been observed in

experimental mammals exposed to hexavalent chromium compounds (Kanojia et al. 1998; Eisler 2000; Jeyasingh and Philip 2005; Koivula and Eeva 2010; Dhal et al. 2013). A high content of chromium in the environment can have mutagenic, teratogenic, and carcinogenic effects on various avian species (Eisler 2000; Koivula and Eeva 2010).

A LD_{50} based on chromium intake in rats ranges from 50 to 100 mg kg^{-1} for Cr (VI) and from 1900 to 3000 mg kg^{-1} for Cr(III) (De Flora et al. 1990; Dhal et al. 2013).

Chromium exposure of the body reduces the numbers of white cells and, consequently, impairs immunity (Vasylkiv et al. 2010). It has been demonstrated in pregnant female rats exposed to chromium that Cr(VI) level in their embryos and fetuses is ten times higher compared to Cr(III) (Kanojia et al. 1998).

Hexavalent chromium compounds studied in vivo exhibit relatively strong mutagenicity, whereas trivalent Cr may cause chromosomal damage only at very high doses. However, studies on isolated DNA demonstrated that trivalent chromium has a more than tenfold stronger mutagenicity compared to chromium(VI). Hence, a direct mutagenic action is attributed to Cr(III). In conclusion, Cr(VI) easily penetrates into the cell where it is next reduced to chromium III. When the reduction takes place outside the cell (or even outside the nucleus), the mutagenic activity of Cr(III) is lower (De Flora 2000; Sobański et al. 2007).

Clinical trials and animal research reveal that Cr accumulates also in the testes, which causes their damage and a decrease in weight, leads to degeneration of the seminiferous tubules, reduces the volume of semen, and lowers the libido (Wise et al. 2008). Numerous experiments on rodents have shown adverse effects of Cr in relation to testicular and epididymal functions and the semen quality (Ernst and Bonde 1992; Saxena et al. 1990). Presumably, an increase in the production of hydrogen peroxide (H_2O_2) during Cr supplementation may result in an increased lipid peroxidation of epithelial cells in the gut, liver, brain, and kidney, as well as in the membranes of sperm cells (Subramanian et al. 2006). Loss of germ cells from the seminiferous epithelium and accumulation of Cr in the lumen of the tubules result from a chronic exposure to Cr (Aruldhas et al. 2005). Male mice exposed to Cr(III) compounds showed a significant decrease in fertility but also damages in the epithelial cells of the intestine, liver, brain, and kidney. The number of implantation sites and the number of viable embryos were significantly reduced in the females fertilized by males exposed to Cr(VI) compounds. The incidence of embryonic resorption and fetal mortality was higher in females fertilized by males exposed to both Cr(III) and Cr(VI) (Elbetieha and Al-Hamood 1997). The body weight, the weight of the seminal vesicles, and the prostate gland were significantly reduced in males receiving Cr(III) and Cr(VI), whereas the weight of the testes increased substantially. Females receiving Cr(III) and Cr(VI) exhibited a significant increase in ovarian weight, while the uterine weight was considerably lower under Cr(III) (Elbetieha and Al-Hamood 1997). Exposure to Cr in female mice resulted in a lower number of embryonic implantations and, in consequence, reduced fertility (Kanojia et al. 1998). A high level of Cr in the placenta and increased chromium transport to the fetus directly affect its organs (Kanojia et al. 1998). In conclusion,

chromium may have a negative impact on fertility and reproduction (Elbetieha and Al-Hamood 1997).

The most serious global problem of human and environmental health is exposure to carcinogenic metals, including Cr(VI), mainly due to their content in the water. Chronic exposure to Cr(VI) raises the risk of lung cancer, diseases of the gastrointestinal tract and central nervous system, as well as disorders of the reproductive and respiratory systems (Coogan et al. 1991; Koivula and Eeva 2010; Wang et al. 2012b). Chromium(VI) passes through the cell membrane more easily than Cr(III) and binds to the intracellular proteins in various tissues, which explains the higher toxicity of this form (Coogan et al. 1991). The mechanism of carcinogenic activity of Cr(VI) has not been explained, though primary genotoxic effects are most likely to be the case (Wise et al. 2008; Kimura et al. 2010). Elevated Cr(VI) in the body causes a decrease in antioxidant enzymes and an increase in reactive oxygen species in mammals and birds (Koivula and Eeva 2010; Wang et al. 2012b). The carcinogenic potential of chromium VI compounds is well documented in humans and animals. The mechanism of tumor formation in response to exposure to heavy metals consists in an increase in DNA damages, increased production of highly reactive oxygen species, and interference in the process of DNA repair (Kasprzak 1991; Zocche et al. 2010). The lipid bilayer is the main permeability barrier in the membrane, and structural disturbances caused by chromium affect this permeability. Chromium may also impair the function of ion channels, enzymes, and receptors submerged in the lipid layer (Suwalsky et al. 2008). Ingestion of large doses of Cr (VI) may be lethal for people and animals (Zayed and Terry 2003; ATSDR 2012). Intake of Cr(VI) with drinking water is carcinogenic to both sexes of mice and rats (National Toxicology Program 2008; Zhitkovich 2011).

Although much attention is being focused on Cr(VI), information on the toxicity of Cr(III) is also available (Vasylkiv et al. 2010). Chromium(III) may reduce the activity of the immune system and contribute to formation of necroses, but its compounds are not classified as carcinogens, since there is no sufficient evidence to it (Speranza et al. 2007; Suwalsky et al. 2008; ATSDR 2012). Animal and epidemiological studies indicate that the inorganic form of Cr(III) is nontoxic and has no carcinogenic properties (IARC 1990; ATSDR 2000). The lack of toxic effects of Cr(III) compounds results from their poor ability to penetrate into cells, lack of their intracellular accumulation, and good stability of their bonds with ligands, which prevents binding cellular macromolecules (Zhitkovich 2011).

Concentrations of heavy metals, including chromium, were evaluated in the liver of three insectivorous bat species in the Catarinense coal basin, southern Brazil (Table 3.6). The waters, soil, animals, and vegetation over an area of 2000–6000 hectares were directly compromised by heavy metals. Coal mining residues contain large quantities of heavy metals (O'Shea et al. 2001; Sampaio, 2002; Zocche et al. 2010). Exposure to metals or their uptake by aquatic and terrestrial animals may vary and depend on the local status of the environment quality (Zocche et al. 2010). Open-pit mines may fill with water and become lakes with possibly toxic levels of heavy metals and, in consequence, may pose a threat for animals, either through drinking their water or via a contaminated trophic chain (O'Shea et al. 2001;

Table 3.6 Chromium concentration (mg kg^{-1}) in soft tissues of birds and mammals

Species	Place and years	*n*	Liver	Kidney	Muscle	Brain	Other	References and additional data
Birds								
Aquatic birds								
Anas platyrhynchos Mallard	Russia, SW, 1993–1995	4					Bone: 2.90	Lebedeva (1997)
Anas platyrhynchos	Poland			0				Bojar and Bojar (2009) ww
Mallard	Czestoborowice reservoir, 2002	24	0.07	1.53	0.03			
			0.05–0.13	0.28–3.63	<DL–0.06			
	Przytoczno,	19	0.02	0.03	0.02			
	ref. group 2002		0.02–0.03	0.02–0.04	0.01–0.03			
Anas platyrhynchos Mallard	USA, New Jersey, 1980–1981	7	1.22 ± 0.55				Salt gland: 165.5 ± 18.5	Burger and Gochfeld (1985) AM ± SE, ww
Anas platyrhynchos Mallard	Japan, Izumi coast, 2003	13	0.26 ± 0.09 (0.182)	0.15 ± 0.04 (0.1125)	0.15 ± 0.08 (0.105)			Nam et al. (2005b) AM ± SD; dw, (ww)
Anas poecilorhyncha Spot-billed duck	Japan, Izumi coast, 2003	1	0.23 (0.161)	0.59 (0.4425)	0.056 (0.0392)			Nam et al. (2005b) AM ± SD; dw, (ww)
Anas acuta Pintail	Japan, Izumi coast, 2003	2	0.27 (0.189)	0.16 (0.12)	0.091 (0.064)			Nam et al. (2005b) AM ± SD; dw, (ww)
Anas crecca Common teal	Japan, Izumi coast, 2003	2	0.45 (0.315)	0.16 (0.12)	0.086 (0.060)			Nam et al. (2005b) AM ± SD; dw, (ww)

(continued)

Table 3.6 (continued)

Species	Place and years	*n*	Liver	Kidney	Muscle	Brain	Other	References and additional data
Aythya affinis Lesser scaup	Canada, Lower Great Lakes, 1999–2000							Petrie et al. (2007) GM; dw, (ww)
	Fall	64	0.88 (0.616) 0.77–1.02					
	Spring	56	ND					
Aythya marila Greater scaup	Canada, Lower Great Lakes, 1999–2000							Petrie et al. (2007) GM; dw, (ww)
	Fall	41	1.02 (0.714) 0.91–1.28					
	Spring	28	ND					
Aythya marila Greater scaup	USA, Connecticut, Branford, 1996–1997	9 W 11 S	3.07 (2.149) 1.26 (0.882)	1.80 (1.35) 0.98 (0.735)	2.37 (1.66) 1.91 (1.34)			Cohen et al. (2000) dw; (ww) W, winter S, spring
Aythya marila Greater scaup	USA, New Jersey, 1980–1981	16	1.53 ± 0.44				Salt gland 3.54 ± 1.17	Burger and Gochfeld (1985) ww; AM ± SE
Anas rubripes Black duck	USA, New Jersey, 1980–1981	14	2.05 ± 0.43				Salt gland 18.90 ± 4.81	Burger and Gochfeld (1985) AM ± SE, ww
Branta canadensis Canada goose	USA, New Jersey, 2007	26	0.16 ± 0.04		0.07 ± 0.02			Tsipoura et al. (2011) ww
Cygnus olor Mute swan	USA, Watson Creek Marsh, 1997	13	0.24 ± 0.14 (0.17)					Beyer and Day (2004) dw; (ww)
Egretta gularis Western reef heron	Iran, Hara Biosphere Reserve, 2010	15	1.05 ± 0.11 (0.735) 0.37–1.82	0.96 ± 0.08 (0.72) 0.35–1.63	0.56 ± 0.04 (0.392) 0.34–0.04			Mansouri et al. (2012) GM, dw; (ww)

Larus heuglini Siberian gull	Iran, Hara Biosphere Reserve, 2010	15	2.75 ± 0.28 (1.925) 1.63–4.51	2.32 ± 0.25 (1.74) 1.22–4.35	1.02 ± 0.04 (0.714) 0.78–1.30			Mansouri et al. (2012) GM, dw; (ww)
Larus atricilla Laughing gull	USA, New Jersey, 1992	20M 20F	0.37 ± 0.03 0.42 ± 0.06	0.21 ± 0.09 0.18 ± 0.03	0.22 ± 0.02 0.28 ± 0.03			Gochfeld et al. (1996) AM ± SE, ww
Haliaeetus leucocephalus Bald eagle	USA, Great Lakes, 2002–2010	46	1.28 ± 0.18 (0.896)			1.47 ± 0.30 (1.18)		Nam et al. (2012) dw; (ww)
Haliaeetus leucocephalus Bald eagle	USA, Alaska, Adak Island, 1993–1998	26	0.73 (0.51) <0.61–18.7 50% of samples	0.93 (0.6975) <0.61–58.9 54% of samples				Stout and Trust (2002) dw; (ww)
Pandion haliaetus Osprey	USA, 1975–1982	21	17 > DL 0.33 0.09–1.70					Wiemeyer et al. (1987) AM, ww
Haliaeetus albicilla White-tailed eagle	Poland, 1991–1995		$n = 3$ 0.09 ± 0.10 (0.063)	$n = 6$ 0.06 ± 0.08 (0.04)				Falandysz et al. (2000) AM ± SD; dw, (ww)
Phalacrocorax carbo Great cormorant	Spain, Murcia, 2009–2010	8 juv	0.41 ± 0.24 (0.287) 0.13–0.78	0.49 ± 0.42 (0.37) 0.05–1.27	0.48 ± 0.31 (0.34) 0.18–1.13		Bone: 0.21 ± 0.15 0.03–0.40	Navarro et al. (2010) AM ± SD; dw, (ww)
Phalacrocorax carbo Great cormorant	Japan, 2003							Nam et al. (2005a) AM ± SD; dw, (ww)
	Lake Biwa	11	0.37 ± 0.26[a]	0.47 ± 0.66[a]	0.13 ± 0.04			
			(0.259)	(0.35)	(0.09)			
			0.18–1.1	0.10–2.3	0.10–0.21			
	Mie	19	0.22 ± 0.10 (0.154) 0.13–0.53	0.17 ± 0.09 (0.1275) 0.06–0.37	0.14 ± 0.03 (0.098) 0.10–0.18			

(continued)

Table 3.6 (continued)

Species	Place and years	*n*	Liver	Kidney	Muscle	Brain	Other	References and additional data
Pelecanus occidentalis Brown pelican	USA, Florida, 1969–1972	5	0.92 (0.644) 0.80–1.20	4.01 (3.07) 2.65–4.71			Bone: 15.40 8.82–22.89	Connors et al. (1972) dw, (ww)
Pelecanus occidentalis Brown pelican	USA, California, 1969–1971	3	1.37 (0.959) 0.70–1.80	3.57 (2.68) 1.45–6.27			Bone: 6.03 4.65–8.68	Connors et al. (1972) dw, (ww)
Pelecanus erythrorhynchos White pelican	USA, California, 1969–1971	1	0.70 (0.49)	1.19 (0.89)			Bone: 3.83	Connors et al. (1972) dw, (ww)
Passerine								
Parus major Great tit	Belgium, Antwerp, 2000	10F	0.034 (0.024) 0.007–0.051	0.049 (0.037) 0.027–0.17	0.014 (0.01) 0.003–0.050	0.020 (0.016) 0.005–0.052	Lung: 0.014 1 nd–0.077	Dauwe et al. (2005) dw; median; (ww)
Parus major Great tit	China, Western Mountains of Beijing, 2004	25	1.86 ± 0.33 (1.302)	6.26 ± 1.08 (4.69)	1.14 ± 1.20 (0.798)	1.65 ± 0.26 (1.32)	2.22 ± 0.13 Lung: 8.90 ± 1.99	Deng et al. (2007) dw; (ww)
Carduelis sinica Greenfinch	China, Western Mountains of Beijing, 2004	20	0.96 ± 0.34 (0.672)	2.61 ± 0.47 (1.96)	1.07 ± 0.54 (0.749)	1.12 ± 0.28 (0.90)	1.54 ± 0.12 Lung: 1.10 ± 0.11	Deng et al. (2007) dw; (ww)
Pycnonotus xanthopygos White-spectacled bulbul	Turkey, 2002–2003	21M	0.13 ± 0.03	6.22 ± 1.22	1.19 ± 0.21	Lung M:	Bone M:	Aslan et al. (2006) dw; (ww)
			(0.091)	(4.66)	(0.83)	2.07 ± 0.44	2.09 ± 0.17	
		21F	0.21 ± 0.04 (0.147)	6.58 ± 1.33 (4.93)	1.25 ± 0.22 (0.875)	Lung F: 2.15 ± 0.45	Bone F: 2.16 ± 0.17	
Sayornis nigricans Black phoebe	USA, Texas, 1997	8					Carcass: 1.69 1.0–3.6	Mora et al. (2002) dw; AM

Petrochelidon pyrrhonota Cliff swallow	USA, Texas, 1997	8					Carcass: 1.58 1.3–2.0	Mora et al. (2002) dw; AM
Other								
Centrocercus urophasianus Greater sage-grouse	USA, Wyoming and Montana, 2003–2006	70	0.50 ± 0.02 0.17–0.80					Dailey et al. (2008) ww
Mammals								
Ungulata								
Cervus elaphus Red deer	Slovakia	22	0.138 0.030–0.368	0.139 0.010–4.130	0.246 0.040–0.584			Gasparik et al. (2004) ww, median
Cervus elaphus Red deer	Croatia, Sedico						Bone (teeth) 5.489 ± 0.218 4.214–6.338	Zaccaroni et al. (2008a) AM ± SE, dw
Capreolus capreolus Roe deer	Croatia, Sedico						Bone (teeth) 4.595 ± 0.255 0.954–6.678	Zaccaroni et al. (2008a) AM ± SE, dw
Capreolus capreolus Roe deer	Poland, 2009	13			0.61 ± 0.75 0.04–2.35			Długaszek and Kopczyński (2013) AM ± SD, ww
Capreolus capreolus Roe deer	Poland, 2009	14	0.04 ± 0.01 0.03–0.07					Długaszek and Kopczynski (2011) AM ± SD, ww
Odocoileus virginianus White-tailed deer	USA, Texas, 2005	20	<0.5–1.0 20% of samples		<0.5–1.5 50% of samples			Bruckwicki et al. (2006) dw

(continued)

Table 3.6 (continued)

Species	Place and years	*n*	Liver	Kidney	Muscle	Brain	Other	References and additional data
Alces alces Moose	Yukon, Canada, 1994–2001		$n = 56$ 0.52 ± 0.24	$n = 384$ 0.22 ± 0.15	$n = 37$ 0.26 ± 0.09			Gamberg et al. (2005), ww
Porcupine caribou Caribou	Canadian Arctic, 1994–2003	331		0.28 ± 1.18				Gamberg et al. (2005), ww
Rangifer tarandus Reindeer (semi-domesticated)	Northern Norway, 2004–2005	29	0.028 <0.028–0.095		0.038 0.028–1.56			Hassan et al. (2013), Med, ww
Rangifer tarandus Reindeer	Norwegian-Russian border areas, 1990–1991							Sivertsen et al. (1995), Med, ww
	Jarfjord	31	0.07					
			<0.01–0.09					
	Pasvik	30	<0.01					
			<0.01–0.02					
	Finnmark	40	<0.01					
			<0.01–0.03					
Alces alces Moose	Norwegian-Russian border areas, 1990–1991							Sivertsen et al. (1995), Med, ww
	Jarfjord	31	<0.01					
			<0.01–0.04					
	Pasvik	30	<0.01					
			<0.01–0.09					
	Finnmark	40	<0.01					
			<0.01–0.06					

Sus scrofa Wild boar	Poland, 2009	11			0.12 ± 0.06 0.04–0.27			Dlugaszek and Kopczynski (2013) AM ± SD, ww
Sus scrofa Wild boar	Poland, 2009	10	0.14 ± 0.21 0.03–0.72					Dlugaszek and Kopczynski (2011) AM ± SD, ww
Sus scrofa Wild boar	Slovak Republic, 1998–1999 Polluted area	15	0.15 ± 0.12 0.02–0.36	0.19 ± 0.11 0.09–0.48	0.29 ± 0.42 0.10–1.80			Piskorova et al. (2003) AM ± SD, ww
Sus scrofa Wild boar	Italy, Lazio Region, 2005–2006	54	0.15 ± 0.11 <DL–0.63		0.13 ± 0.08 0.07–0.69			Danieli et al. (2012) ww
Sus scrofa Wild boar	Italy, Lazio Region		$n = 75$ 0.141 ± 0.110 0.003–0.626	$n = 65$ 0.097 ± 0.075 0.035–0.590	$n = 78$ 0.139 ± 0.082 0.069–0.692			Amici et al. (2012) ww
Equus ferus caballus Horse	Germany	21	0.116 0.022–0.427	Cortex 0.085 0.016–0.051 Medulla 0.091 0.028–0.348				Paßlack et al. (2014) ww
Bos taurus Cattle	India, 1991 Polluted area		10.95 0.54–21.37	1.09 0.65–1.52				Dogra et al. (1996) In ash
Carnivora								
Neovison vison	Poland, 2009–2011							Brzezinski et al. (2014) dw, AM ± SD; (ww)
American mink	Drawa N. Park							
		26	0.25 ± 0.50	0.62 ± 0.34				
			(0.175)	(0.465)				
	Narew N. Park		<DL–2.34	0.25–1.65				
		26	0.48 ± 0.67	0.79 ± 0.47				
			(0.336)	(0.593)				
			<DL–3.17	0.26–2.39				

(continued)

Table 3.6 (continued)

Species	Place and years	*n*	Liver	Kidney	Muscle	Brain	Other	References and additional data
Neovison vison American mink	Canada, British Columbia, 1990–1996							Harding et al. (1998) AM ± SE, dw; (ww)
	Kootenay River	4		0.98 ± 0.34 (0.735)				
	L. Fraser River	8	1.16 ± 0.28 (0.812)	1.68 ± 0.33 (1.26)				
Neovison vison American mink	USA, South Carolina, 1987–1988	55	0.156 0.01–5.08					Carmichael and Baker (1989) GM, ww
Neovison vison American mink	USA, Illinois, 1984–1989	29	12/29 (41%) 1.72 0.60–2.63	15/29 (52%) 2.16 0.66–3.29	12/29 (41%) 1.80 0.66–3.10			Halbrook et al. (1996) AM, ww
Lontra canadensis River otter	Canada, British Columbia, 1990–1996							Harding et al. (1998) AM ± SD, dw; (ww)
	Kootenay River	12	1.44 ± 0.30 (1.008)					
	L. Fraser River	3	1.40 ± 0.12 (0.98)					
	U Fraser River	6	1.42 ± 0.22 (0.994)					
Lontra canadensis River otter	USA, Illinois, 1984–1989	8	1/8 (12%) 0.52		8/8 (100%) 2.20 ± 4.61 0.21–11.6			Halbrook et al. (1996) AM ± SD, ww
Lutra lutra Eurasian otter	England and Wales, 2009	50	0.219 (0.153) 0.155–0.306					Walker et al. (2011) Med., dw; (ww)

Lutra lutra Eurasian otter	England and Wales, 2007	48	0.164 (0.115)					Walker et al. (2010) Med., dw; (ww)
			0.097–0.266					
			0.302 (0.211)					
	2008	57	0.214–0.370					
Lutra lutra Eurasian otter	France	21	0.63 (0.441) 0.07–4.90					Ruiz-Olmo et al. (2000) GM, dw; (ww)
Gulo luscus Wolverine	Canada, British Columbia, 1997	11	0.50 ± 0.16 (0.35)					Harding (2004) AM ± SD, dw; (ww)
Martes americana Marten	Canada, British Columbia, 1997	5	<0.40					Harding (2004) AM ± SD, dw
Procyon lotor Raccoon	USA, South Carolina, SRS 1996–1997							Burger et al. (2002) SRS, Savannah River Site AM ± SE, ww
	On-site area	46	0.36 ± 0.02	0.31 ± 0.02				
			0.19–1.08	0.14–1.00				
	Off-site area	25	0.32 ± 0.02	0.25 ± 0.01				
Vulpes vulpes Red fox	Slovak Republic, 1998–1999	18	0.26 ± 0.19 0.12–0.58	0.29 ± 0.16 0.14–0.52	0.33 ± 0.20 0.18–0.62			Piskorova et al. (2003) AM ± SD, ww
	Polluted area							
Herpestes javanicus Javan mongoose	Japan, Amami Oshima Islands, 2004–2005		$n = 53$ 0.039 ± 0.027 0.006–0.135	$n = 47$ 0.033 ± 0.021 0.06–0.158			Brain: $n = 10$ 0.047 ± 0.055 0.14–0.197	Horai et al. (2007) AM ± SD, ww
Vulpes vulpes Red fox	Poland, 2009	14			0.34 ± 0.23 0.07–0.65			Dlugaszek and Kopczynski (2012) AM ± SD, ww
Other species								
Lepus europaeus Brown hare	Poland, 2009	11	0.04 ± 0.03 0.01–0.12					Dlugaszek and Kopczynski (2011) AM ± SD, ww

(continued)

Table 3.6 (continued)

Species	Place and years	*n*	Liver	Kidney	Muscle	Brain	Other	References and additional data
Lepus europaeus Brown hare	Poland, 2009	11			0.09 ± 0.13 0.02–0.44			Dlugaszek and Kopczynski (2013) AM ± SD, ww
Lepus europaeus Brown hare	Germany, E part	25	0.807 ± 0.185				Bone (rib): 7.652 ± 1.343	Anke et al. (2005)
Rattus rattus Wild rat	Portugal						Spleen: TG ($n = 4$) 1.231 ± 0.332	Pereira et al. (2006) AM ± SE, dw; (ww)
	TG, Tapada	4	0.513 ± 0.221	0.345 ± 0.051				
	Grande		(0.359)	(0.259)				
	M4, Sulfur mill	5	0.117 ± 0.029	0.072 ± 0.012				
			(0.082)	(0.054)				
Mus spretus Algerian mouse	Portugal						Spleen: TG ($n = 7$) 14.921 ± 6.127 M4 ($n = 5$) 8.357 ± 2.961	Pereira et al. (2006) AM ± SE, dw; (ww)
	TG, Tapada	7	0.361 ± 0.068	1.441 ± 0.343				
	Grande		(0.253)	(1.01)				
	M4, Sulfur mill	8	0.651 ± 0.238 (0.456)	0.985 ± 0.361 (0.739)				
Crocidura russula White-toothed shrew	Spain, Donana Reserve, 1999							Sánchez-Chardi et al. (2009) dw, AM ± SE; (ww)
	Polluted site		$n = 19$	$n = 19$				
			1.74 ± 0.60	1.91 ± 0.19				
			(1.218)	(1.433)				
	Reference site		$n = 10$	$n = 9$				
			3.00 ± 0.48	2.07 ± 0.27				
			(2.1)	(1.553)				

ww wet weight, *dw* dry weight, *AM* arithmetic mean, *SD* standard deviation, *SE* standard error, *GM* geometric mean, *ND* not detected, *DL* detection limit, *M* male, *F* female

[a]Significant differences between Biwa and Mie

Zocche et al. 2010). Liver Cr content in *Molossus molossus* bats in the mining area was highest (5.7 mg kg^{-1} dw), while in the other two species, the values were below the limit of detection. There were also no significant differences in the comet assay results in this species in relation to the control. The authors speculate that the accumulation of metals in bats is probably a reflection of the degradation of habitats within the mining area, the availability of food exposed to contamination, as well as the foraging behavior, the use of habitat, physiological differences, and, as indicated by Walker et al. (2007), interspecific variability in adaptation to the environment.

7 Toxicokinetics and Effects of Chromium in Wildlife

The distribution of chromium in the body of a homeothermic vertebrate is determined by several factors: the form of Cr; its concentration in the water, air, and food; as well as the route it penetrates the body. Biological membranes are less permeable to Cr(III) compared to Cr(VI) (Upreti et al. 2004; ATSDR 2008; EFSA 2009). Form Cr(VI) does not react with macromolecules like DNA, RNA, proteins, and lipids, but it is metabolically reduced to Cr(III) and the reductional intermediate Cr(V) inside the cell, where they are capable of coordinate and covalent interactions with macromolecules (Upreti et al. 2004).

Hexavalent chromium in the body is quickly reduced by glutathione, ascorbic acid, or cysteine to kinetically much more stable Cr(III), which is bound intracellularly (Miksche and Lewalter 1997; Gagelli et al. 2002; Suwalsky et al. 2008). The cellular metabolism of Cr(VI) may result in both oxidative and non-oxidative DNA damage (Sugden and Stearns 2000; Salnikow and Zhitkovich 2008). Chromium (VI) displays no ability of damaging DNA directly; instead, it must be reduced to gain its genotoxic property. Intracellular reduction is an activation process, which produces oxidation-reduction intermediates Cr(V/IV) and stable Cr(III), forming mutagenic Cr-DNA adducts. Cellular Cr(VI) reduction in vivo is primarily driven by ascorbate (Asc), whereas glutathione (GSH) is the most obvious reducing agent in cultured cells due to the lack of Asc (Zhitkovich 2011). Extracellular reduction of Cr(VI) is a detoxification process, which produces nontoxic Cr(III), poorly permeable through cell membranes (Zhitkovich 2011). Studies on the reductive activity in tissue homogenates and biological fluids have shown that Asc is the key biological reducing agent of Cr(VI), accounting for 80–95% of its metabolism (Suzuki and Fukuda 1990; Standeven and Wetterhahn 1992). Jointly, the activity of Asc, GSH, and Cys is responsible for more than 95% of in vivo Cr(VI) reduction. Asc and GSH concentrations in tissues are usually not very different, and the dominant role of Asc is due to the very high degree of Cr(VI) reduction (Zhitkovich 2011).

Tandon et al. (1979) showed in the study on rats the greater concentration of Cr in the nuclear fraction of liver cell than in the mitochondrial fraction, but they also revealed that it was dose dependent. The increase in the dose of chromium from 1 mg kg^{-1} to 2 or 3 mg kg^{-1} has increased uptake of the metal by the mitochondrial fraction. Feng et al. (1999) using $^{50}Cr(III)$ confirmed that the nucleic fraction has the

highest Cr concentration in the liver cell of both normal and diabetic rats. They concluded also that diabetic rats retain more Cr in the mitochondrial and lysosomal fractions of the liver and have lower Cr concentration in the subcellular fractions of the pancreas, testes, and kidney, which can indicate Cr participating in the glucose or lipid metabolism to compensate the low level of insulin in the body of diabetic rats.

On average in mammals, depending on the species, absorption of Cr(III) remains in the range from 0.4% to 5.0% (Dowling et al. 1989; Krejpcio 2001; Pechova and Pavlata 2007; Wang et al. 2012a; Kirman et al. 2013). In an organic form, Cr is absorbed better than the inorganic form, which promotes Cr concentration in the tissues (Ohh and Lee 2005). The highest tissue accumulation of Cr was demonstrated after administration of Cr in the form of nanoparticles (Zha et al. 2007; Wang et al. 2009; Lewicki et al. 2014).

Chromium absorption is low, ranging between 0.4 and 2.0% for inorganic compounds, while the availability of organic Cr is more than ten times higher (Cefalu and Hu 2004; Pechova and Pavlata 2007). Although Anderson et al. (1996) showed in rats fed diets supplemented with Cr-chloride, chromium an apparent absorption rate of up to 0.9 %, while that for organic Cr sources, such as Cr-nicotinate, Cr-picolinate, Cr complex of dinicotinic acid-diglycine-cysteine-glutamic acid: 1.3, 1.1 and 0.6 %, respectively. Absorption of Cr depends on its diet content, chemical form, and other dietary components. Higher phytate, calcium, manganese, titanium, zinc, vanadium, and iron can inhibit Cr absorption (EFSA 2009). A study on rats revealed that Cr(VI) was reduced in gastric juice, whereas chromium picolinate complex was stable (Gammelgaard et al. 1999).

After intestinal absorption, Cr(III) is released to blood and bound by proteins involved in iron metabolism, mainly transferrin, as shown by in vitro and in vivo studies on rats (Feng et al. 2003). In this form, Cr is transported to cells, and the cells' transmembrane transfer efficiency depends on insulin concentration (Clodfelder and Vincent 2005). The common transport mechanism of chromium and iron makes these metals compete for transferrin-binding sites. Rats intraperitoneally administered with Cr ions showed a decrease of Fe bioavailability in the body, and initial symptom characteristics to anemia were observed (Ani and Moshtaghie 1992; Lewicki et al. 2014).

Absorbed chromium distributes to nearly all tissues, with the highest concentrations noted in the kidney and liver, while the bone may contribute to long-term retention kinetics of chromium (Outridge and Scheuhammer 1993; ATSDR 2008). Mouse and human pharmacokinetic data support that even low, environmentally relevant doses of Cr(VI) are likely to escape reduction in the stomach, due to the ability of absorption and gastric emptying to successfully compete with reduction (Collins et al. 2010; Casalegno et al. 2015).

According to Nam et al. (2005a), chromium in the great cormorant (*Phalacrocorax carbo*) is not evenly distributed among the particular parts of the body. The highest percentage of chromium in its body (see Fig. 3.3) was found in the muscle which is ~37%, followed by the feather 20%, skin 16%, and bone 10%. Much lower amount was located in the liver (5%). The highest concentration of Cr (mean ± SD, mg kg^{-1} dw) was recorded in the lung (0.67 ± 0.63) and spleen

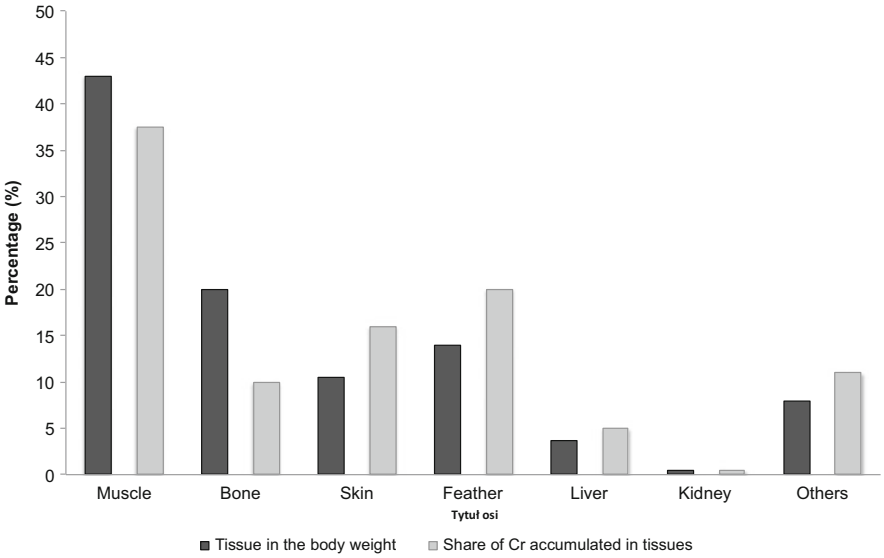

Fig. 3.3 Percentage share of tissues in the body of the great cormorant and percentage of Cr bioaccumulated in various tissues (source of data Nam et al. 2005a)

(0.51 ± 0.03), whereas the lowest in the bone (0.07 ± 0.01), uropygial gland (0.11 ± 0.02), eyeball (0.12 ± 0.01), pancreas (0.13 ± 0.01), and gonads (0.11–-0.14 mg kg^{-1} dw).

ATSDR (2008) informs that toxicokinetic data for chromium in humans, dogs, rats, mice, rabbits, and hamsters, generally correlate well among species however, exposures to chromium(VI) resulted in different organ distribution patterns between rats and mice. Cr accumulates to a greater extent in the blood of rats *vs* mice after short-term exposure by injection; after oral exposure, liver concentrations of chromium were three to four times higher in mice than rats, whereas kidney concentrations were about 50% lower (Kargacin et al. 1993).

Exposure of wild animals to chromium present in the air is poorly known. Outridge and Scheuhammer (1993) suggested that Cr concentrations in fur or feathers can be extremely variable even among individuals within the same habitat, and, at best, it might be used to indicate relative levels of airborne Cr contamination. People working in the environment with chromium-contaminated air exhibit its elevated levels in the lungs. In unexposed people, this level usually remains within 0.07–1 mg kg^{-1} ww; however, chromium concentrations in lung cancer-affected workers are usually higher, from 0.5 to 192 mg kg^{-1} ww (Mancuso 1997; Wise et al. 2008). Birds of urban areas and places with heavily polluted air can accumulate large amounts of Cr in the lungs. For example, the resident great tit *Parus major*, which inhabits a park in the capital of China being confronted with extremely heavily polluted air, had chromium at a level of 8.9 mg kg^{-1} dw (Deng et al. 2007). On the other hand, a great tit living in the capital of Belgium, a European country concerned

with the air quality and the environment protection, had lung Cr concentrations lower by two orders of magnitude (0.014 mg kg^{-1} dw) (Dauwe et al. 2005). Compared to these great tits, another passerine species, the white-spectacled bulbul (*Pycnonotus xanthopygos*) inhabiting the Turkish Mediterranean coast, including Antalya, where chromite ore is mined, showed Cr concentrations of 2.1 mg kg^{-1} dw (USGS 2015; Aslan et al. 2006). This is four times lower compared to that measured in the great tit in China and even several hundred times higher than in the same species in Belgium. In birds, especially small passerines (characterized by high metabolism rates and very active respiratory function), the air contaminated with heavy metals, including inhaled Cr, probably promotes accumulation in the lungs. A small number of data in this area do not allow drawing more general conclusions though. Nevertheless, high concentrations of Cr observed in avian lungs in polluted areas, similar to those observed in the lungs of people occupationally exposed to dust contaminated with the metal, may indicate equivalence of food and air as sources of Cr intoxication in passerines.

Deng et al. (2007) examined the concentrations of Cr in tissues of great tits and greenfinches (*Carduelis sinica*) collected at Badachu Park in the Western Mountains of Beijing (China) and concluded that the highest concentrations of Cr were found in their kidneys (6.26 ± 1.08 and 2.61 ± 0.47 mg kg^{-1} dw, respectively). They also noted higher Cr level in tissues of most body parts in great tits which are primarily insectivorous than in greenfinches which feed mainly on seeds and fruits, for example, 1.86 ± 0.33 and 0.96 ± 0.34 for the liver, 4.66 ± 0.95 and 0.69 ± 0.06 for the heart, and 1.65 ± 0.26 and 1.12 ± 0.28 for the brain.

For most wild birds and mammals, their food is the main source of chromium. Animals feeding on aquatic organisms may be dangerously exposed to Cr present in fish, shellfish, molluscs, and plants. Chromium accumulates in the tissues of aquatic animals and thus can have toxic effects also on the consumers of fish (Govind and Madhuri 2014).

On being absorbed in the intestine and/or lungs, Cr is bounded by the blood, and chromium transport depends on its valence. Chromium(VI) easily penetrates to red blood cells and, after reduction to Cr(III), binds to hemoglobin. Chromium(III) is not capable of passing through cell membranes; however, to some extent it may penetrate into erythrocytes (Suwalsky et al. 2008). More than 99% of Cr(III) absorbed in the blood appears in plasma (EFSA 2009). Absorbed chromium can circulate in a free state, may bind to transferrin or plasma proteins, or circulate as GTF complex (Ducros 1992; Piva et al. 2003). According to results of in vitro and in vivo studies on rats receiving Cr-chloride, approximately 90% of Cr(III) in the serum was associated with β-globulin fraction and 80% of all Cr was bounded to transferrin (EFSA 2009). Apart from chromates, all chromium compounds are quickly removed from blood (Stern and Mansdorf 1998). Soluble chromates show similar kinetics of distribution and excretion, despite significant differences in their solubility (Collins et al. 2010). The rapid uptake of Cr(VI) from the gastrointestinal tract appears to result from the transport of anionic chromate and dichromate complexes across cell membranes by the SO_4^{2-} and PO_4^{3-} anion transport system, and Cr(III) crosses cell membranes only by passive diffusion (Collins et al. 2010; Casalegno et al. 2015).

Mertz et al. (1965) proposed body retention of chromium (after administration of $^{51}CrCl_3$ to rats) in terms of three compartment models with three half-lives of 0.5, 5.9, and 83.4 days. Subsequent studies reported similar results in man and rat (EFSA 2009). It has been demonstrated that within 3 h, hens absorb approximately 11.8% of trivalent ^{51}Cr administered into the crop. The absorption rate of ^{51}Cr was highest within 6 h after administration, representing about 15% of the dose. In rats, orally administered with ^{51}Cr, the absorption ranged from 14 to 17% (Anke et al. 2005). The respiratory tract is the primary target organ for inhaled chromium, including its water-insoluble forms (Gad 1989).

Chromium absorbed by blood in the lungs or intestines is transported to various tissues and organs and deposited there in varying degrees. Most chromium (>95%) present in the food eaten and water drunk remains unabsorbed, and endothermic vertebrates excrete it with feces; on the other hand, a major part of the absorbed chromium is removed with urine (Gad 1989; Outridge and Scheuhammer 1993; Gammelgaard et al. 1999; ATSDR 2012; Kler et al. 2014). According to Ducros (1992), mammals are able to get rid of about 80% of absorbed chromium with urine and the rest with bile and sweat. Urinary chromium excretion process begins within an hour after oral ingestion and reaches its peak intensity within 12–24 h. Fecal chromium excretion starts within 6–12 h after ruminal administration, reaching its maximum after 24 h and lasting for more than 4 days. Biliary and urinary excretion of absorbed chromium takes more than 4 days (Anke et al. 2005).

It is suggested that, apart from the kidney, aquatic birds may use the salt glands to remove Cr that penetrates the bloodstream (Burger and Gochfeld 1985). The kidney, which is able to accumulate high levels of Cr, is probably the target organ for systemically absorbed chromates (Gad 1989; De Flora 2000). However, a high level of Cr accumulation is sometimes observed not only in the kidney and liver but also in other soft parts of a mammal and avian body (spleen, pancreas, brain, bone marrow) and also in highly mineralized keratin (hair, feathers) and bone growths (Jenkins 1979; Eisler 1986; Burger et al. 1993; Outridge and Scheuhammer 1993; Lebedeva 1997; Piva et al. 2003; Pereira et al. 2006; Deng et al. 2007; Manjula et al. 2015). According to Anke et al. (2005), the largest part of Cr in mammals is accumulated in the skeleton (45%). For example, in the mouflon, *Ovis aries musimon*, wild boar *Sus scrofa*, roe deer *Capreolus capreolus*, and European hare *Lepus europaeus*, living in Thuringia, Germany, the bone Cr concentrations ranged between 4.5 and 7.7 mg kg dw. Some percentage of Cr is found in the skin and hair of mammals (16%), muscle (13%), and more than 5% in the blood, kidney, and liver (7.4%, 5.7%, 5.3%, respectively). Monitoring of Cr content in erythrocytes can be a marker of chromium(VI) exposure (IARC 1990, 1999; Sobański et al. 2007).

8 Bioaccumulation of Chromium

Huffman and Allaway (1973) propose that Cr(III) is beneficial for plants in low concentrations. A level of 0.05 to 1 mg Cr L^{-1} was found to promote growth and increase yield, yet it is not considered essential to plants (Oliveira 2012). Zou et al.

(2006) indicate that high concentrations of Cr have been found harmful to plants and—if increasing—adversely affect several biological parameters. Plants tend to absorb Cr(VI) and reduce it to less toxic Cr(III) in roots (Mei et al. 2002), but there is also another suggestion that dissolved Cr(VI) is taken up by plants without reduction (Oliveira 2012). The subcellular localization of Cr as found by electron energy loss spectroscopy and electron spectroscopic imaging suggested that Cr is accumulated mainly in the cell wall and vacuoles (Zou et al. 2006). Cr content in the plants grown on uncontaminated soils is in the range 0.02–1.0 mg kg^{-1}, whereas those from contaminated or serpentine-derived soils can accumulate Cr within the range 10–-190 mg kg^{-1}, depending upon the soil concentration and the plant species (Hood 2010). Oliveira (2012) indicate that under normal conditions, concentration of Cr in plants is less than 1 mg kg^{-1}. Hood (2010) showed distribution of accumulation in different parts of plant, root > leaves or shoot > grain, which indicates restricted translocation of Cr. The high accumulation of Cr in root is likely due to its immobilization in the vacuoles of root cells. Chromium compounds used in dyeing and tanning processes are often found in the soil and groundwater in industrial areas, which need environmental cleanup and phytoremediation (Zayed and Terry 2003; Lytle et al. 1998). Chromium enters the food chain with the plant material (Zou et al. 2006), but there is no indication of biomagnification of chromium along the terrestrial food chain (WHO/IPCS 2013).

Chromium is also not expected to biomagnify in the aquatic food chain (WHO/IPCS 2013). Metal bioconcentration processes depend on the fish species and their trophic level and also on the kind of food, the kind of absorption carried out by the organism, or the phase in which the metal or particulate is dissolved (Voigt et al. 2015). Aquatic animals are more sensitive to metals than are aquatic plants, for example, 62 μg kg^{-1} inhibits growth in algae and 16 μg kg^{-1} inhibits growth in Chinook salmon (Solomon 2008).

Chromium is present in all animal tissues in a concentration ranging from a few to several tens of micrograms per kg, rarely exceeding 100 μg kg^{-1} (NRC 2005). The highest concentration of this element was found in the liver, kidney, and spleen, slightly lower in the heart, muscle, pancreas, lungs, bones, and brain (Feng et al. 2007; Uyanik et al. 2005). It has been demonstrated that some tissues, such as bone, testes, and epididymides, are capable of long-time Cr storing, as compared with the heart, pancreas, and brain (Lewicki et al. 2014).

In ecotoxicological studies, concentration of Cr in endothermic vertebrates is determined mainly in the liver and kidneys and less often in the muscles, lungs, brain, bones, and other samples (Tables 3.6 and 3.7). In the liver of wild herbivorous mammals, Cr concentration normally remains in the range 0.022–0.427 mg kg^{-1} ww (Table 3.6), and the values are within those specified for cattle by the WVDL (2015). In European ungulates, such as roe deer and red deer inhabiting areas either totally uncontaminated or slightly contaminated with heavy metals, hepatic Cr concentrations do not exceed an average of 0.52 mg kg^{-1} ww, like in the moose living in the Arctic area of Canada (Table 3.6). The range of the median concentrations of Cr in the liver of roe deer, hare, and wild boar from central Poland ranged between 0.03 and 0.07 mg kg^{-1} ww (Długaszek and Kopczyński 2011). In turn, the average

Table 3.7 Chromium in feathers, bone, and mammalian hair

Species	Place and years	*n*	Mean (mg kg^{-1} dw)	References
Avian feathers				
Aquatic birds				
Anas platyrhynchos Mallard	Iran, Fereydoonkenar International Wetland, 2012	10	2.92 ± 0.83	Aghdasi et al. (2013)
Ardea alba Great egret	USA, New Jersey, Barnegat Bay, 1989–2011	271	0.447 ± 0.376 (own calculation)	Burger (2013)
Aythya ferina Pochard	Iran, Fereydoonkenar International Wetland, 2012	10	3.05 ± 0.87	Aghdasi et al. (2013)
Somateria mollissima Common eider	USA, Aleutian Islands, 2007	30	1.78 ± 0.11	Burger et al. (2009)
Branta canadensis Canada goose	USA, New Jersey, 2007 USA, New Jersey, Mill Creek, 2007	26 5	1.360 ± 0.241 2.740 ± 0.545	Tsipoura et al. (2011)
Cygnus olor Mute swan	Hungary, Balaton Lake	17	82%<DL 1.02 ± 0.09	Grúz et al. (2015)
Bubulcus ibis Cattle egret 4–6-day chicks	Pakistan, Rawal Lake Reservoir Chenab River Ravi River, 2007	10 10 10	6.6 ± 2.6 7.1 ± 2.2 5.38 ± 1.0	Malik and Zeb (2009)
Phalacrocorax carbo Great cormorant	Spain, Murcia, 2009–2010	8 juv	4.88 ± 1.83 2.55–8.59	Navarro et al. (2010)
Phalacrocorax carbo Great cormorant	Serbia, 2010	21	<DL	Skoric et al. (2012)
Phalacrocorax carbo Great cormorant	Japan, 2003			Nam et al. (2005a)
	Lake Biwa	11	0.32 ± 0.35	
			0.12–1.3	
	Mie	19	0.23 ± 0.08	
			0.16–0.45	
Calidris canutus Red knot	USA, NJ, Delaware Bay			Burger et al. (2015)
	1991–1992	16	0.291 ± 0.042	
	2011–2012	30	0.578 ± 0.083	
Calidris alba Sanderling	1991–1992	12	0.764 ± 0.260	Burger et al. (2015)
	2011–2012	20	0.463 ± 0.062	
Calidris pusilla Semipalmated sandpiper	1991–1992	12	1.149 ± 0.294	Burger et al. (2015)
	2011–2012	30	0.523 ± 0.064	
Calidris canutus Red knot	USA, NJ, Delaware Bay, 1991	16	24.10 ± 2.58	Burger et al. (1993)

(continued)

Table 3.7 (continued)

Species	Place and years	*n*	Mean (mg kg^{-1} dw)	References
Calidris alba Sanderling	USA, NJ, Delaware Bay, 1991	13	16.52 ± 2.46	Burger et al. 1993
Calidris pusilla Semipalmated sandpiper	USA, NJ, Delaware Bay, 1991	11	26.29 ± 4.37	Burger et al. (1993)
Larus atricilla Laughing gull	USA, New Jersey, 1992	20M 20F	0.76 ± 0.15 0.68 ± 0.12	Gochfeld et al. (1996)
Ciconia ciconia White stork	Poland, 2005	32	0.0031 ± 0.0003 0.0012–0.0084	Orłowski et al. (2006)
Nycticorax nycticorax Black-crowned night heron nestlings	USA, Chesapeake and Delaware Bays, 1998			Golden et al. (2003)
	Pea Patch Island	12	2.49	
	Baltimore Harbor	12	3.28	
	Holland Island	9	3.17	
Passerine				
Corvus splendens House crow	India, Tiruchirappalli, 2013			Manjula et al. (2015)
	Urban area		76.47 ± 3.88	
	Rural area		60.13 ± 8.80	
Agelaius phoeniceus Red-winged blackbird	USA, New Jersey, Meadowlands District, 2006	29	0.607 ± 0.0532	Tsipoura et al. (2008)
Cistothorus palustris Marsh wren	USA, New Jersey, Meadowlands District, 2006	15	1.040 ± 0.109	Tsipoura et al. (2008)
Tachycineta bicolor Tree swallow	USA, New Jersey, Meadowlands District, 2006	5	0.659 ± 0.219	Tsipoura et al. (2008)
Other birds				
Centropus phasianinus Pheasant coucal	India, Tiruchirappalli, 2013			Manjula et al. (2015)
	Urban area		36.96 ± 5.72	
	Rural area		53.12 ± 5.39	
Agapornis roseicollis Rosy-faced lovebird (pet bird)	India, Tiruchirappalli, 2013			Manjula et al. (2015)
	Urban area		6.11 ± 1.01	
	Rural area		6.00 ± 3.20	
All species ($n = 11$)—free-living birds	India, Tiruchirappalli, 2013			Manjula et al. (2015)
	Urban area		55.48	
	Rural area		51.43	
Falco biarmicus jugger Laggar falcon	Pakistan, 1996			Movalli (2000)
	Bahawalnagar	8	1.72	
	Bahawalpur	8	1.67	
	Karachi	11	2.31	

(continued)

Table 3.7 (continued)

Species	Place and years	*n*	Mean (mg kg^{-1} dw)	References
Avian bone				
Waterbirds				
Anas platyrhynchos Mallard	Russia, SW, 1993–1995	4	2.90	Lebedeva (1997)
Aythya fuligula Tufted duck	Russia, SW, 1993–1995	2	1.5	Lebedeva (1997)
Ardea cinerea *Grey heron*	Russia, SW, 1993–1995	2	0.99	Lebedeva (1997)
Phalacrocorax carbo Great cormorant	Russia, SW, 1993–1995	1	0.31	Lebedeva (1997)
Falconiformes and owls				
Buteo buteo Common buzzard	Russia, SW, 1993–1995	2	7.59	Lebedeva (1997)
Falco tinnunculus Common kestrel	Russia, SW, 1993–1995	1	14.70	Lebedeva (1997)
Passerine				
Parus major Great tit	Belgium, Antwerp, 2000	10F	0.26 0.23–0.43	Dauwe et al. (2005) dw, Med
Parus major Great tit	Russia, SW, 1993–1995	4	0.38	Lebedeva (1997)
Passer montanus Tree sparrow	Russia, SW, 1993–1995	1	14.70	Lebedeva (1997)
Passer domesticus House sparrow	Russia, SW, 1993–1995	4	0.41	Lebedeva (1997)
Mammalian hair				
Homo sapiens Man	USA		Normal range: 0.0–4.0 Reported range: 0.0–6.43	Jenkins (1979)
Homo sapiens Man, children 6–9 years	Spain, 2001	117	0.64 0.33–1.00	Pena-Fernández et al. (2014)
Ungulates				
Equus ferus caballus Horse	Poland	20	0.324 ± 0.221 0.029–1.037	Topczewska (2012)
Equus ferus caballus Horse	Japan	24	0.22 ± 0.16	Asano et al. (2002)
Equus ferus caballus Horse			1.5–3.3	Puls (1994)
Rangifer tarandus Reindeer	Norway, 1988 Spitsbergen	11	1.03	Drbal et al. (1992)

(continued)

Table 3.7 (continued)

Species	Place and years	*n*	Mean (mg kg^{-1} dw)	References
Bos taurus Cattle	Poland	33	0.075 ± 0.050	Gabryszuk et al. (2010)
Capreolus capreolus Roe deer	Poland, 2009	13	0.20 ± 0.23 Med 0.10	Długaszek and Kopczyński (2014)
Carnivores				
Felis bengalensis Leopard cat	India, Assam and Meghalaya	10–15	72.3 ± 7	Dey et al. (1999) AM ± SD
Panthera pardus Leopard	India, Assam and Meghalaya	10–15	<DL	Dey et al. (1999) AM ± SD
Viverra zibetha Civet cat	India, Assam and Meghalaya	10–15	<DL	Dey et al. (1999) AM ± SD
Vulpes vulpes Red fox	Poland, 2009	14	0.20 ± 0.23 Med 0.10	Długaszek and Kopczyński (2014)
Vulpes vulpes Red fox (farmed)	Poland, rural region and urbanized region	8 8	0.268 ± 0.137 0.145 ± 0.033	Filistowicz et al. (2012)
Vulpes lagopus Arctic fox (farmed)	Poland, rural region and urbanized region	8 8	0.193 ± 0.079 0.147 ± 0.032	Filistowicz et al. (2012)
Vulpes vulpes Red fox (farmed)	Poland			Cholewa et al. (2014)
Fire morph		15F	0.431 ± 0.020	
Silver		11F	4.251 ± 0.063	
Canis familiaris Dog	Italy, Campania			Zaccaroni et al. (2014)
	A, triangle of death	30	0.14 ± 0.03	
	B, urban	30	0.16 ± 0.03	
	C, rural	30	0.38 ± 0.66	
Canis familiaris Dog	Korea, urban areas	204	2.41 ± 0.28	Park et al. (2005)
Other species				
Lepus europaeus European hare	Poland, 2009	11	0.27 ± 0.45 Med 0.14	Długaszek and Kopczyński (2014)
Erinaceus europaeus Hedgehogs	Belgium, 2002			D'Havé et al. (2006)
	Hoboken, metal-polluted area	12	1.57 ± 0.33	
	Zoersel, control area	10	1.46 ± 0.09	
Erinaceus europaeus Hedgehogs	Belgium, Flanders, 2002/2003	43	5.4 ± 0.7	D'Havé et al. (2006)
Rattus rattus Wild rat	Portugal, 2000			Pereira et al. (2006) TG, the mine pit
	TG, Tapada	4	1.309 ± 0.197	
	Grande			
	M4, Sulfur mill	5	0.232 ± 0.066	

(continued)

Table 3.7 (continued)

Species	Place and years	*n*	Mean (mg kg^{-1} dw)	References
Mus spretus Algerian mouse	Portugal, 2000			Pereira et al. (2006) TG, the mine pit
	TG, Tapada	7	1.673 ± 0.618	
	Grande			
	M4, Sulfur mill	8	0.579 ± 0.165	
Spermophilus beecheyi Ground squirrel	USA, California, 2001–2002	181	0.45 ± 0.57	Hubbart (2012)
Rattus norvegicus Rat (lab)	Germany,			Ambeskovic et al. (2013)
	Young, 6 months	7	0.599	
	Adult, 18 months	7	0.612	
Callithrix jacchus Common marmoset	Germany, Gottingen, German Primate Center			Ambeskovic et al. (2013)
	Young, 1–2 years	8	1.269	
	Middle-aged, 4 years of age, 6–8 years	8	1.523	
		8	1.454	
Macaca mulatta Rhesus	China SW, animal farm	28	11.33 ± 4.26	Lee et al. (2012)
Apodemus sylvaticus Wood mice	Italy, Modena, 2004	26	~1	Marcheselli et al. (2010)
Petaurista magnificus Flying squirrel	India, Assam and Meghalaya	10–15	<DL	Dey et al. (1999)
Didelphis virginiana Opossum	USA, Costa Rica	12M 12F	1.57 ± 0.19 3.56 ± 0.64	Burger et al. (1994)
Zapus princeps Western jumping mouse	USA, Wyoming	3	23–45	Jenkins (1979)
Microtus montanus Mountain vole	USA, Wyoming	16	4.7–180	Jenkins (1979)
Antilocapra americana Pronghorn	USA, Idaho Wyoming	30 7	1.9–640 0.3–130	Jenkins (1979)
Canis latrans Coyote	USA, Wyoming	15/19	0.7–12.0	Jenkins (1979)
Cervus canadensis Elk	USA, Idaho	15	1.9–570	Jenkins (1979)
Odocoileus hemionus Mule deer	USA, Idaho	9/11	13–630	Jenkins (1979)

Feather Cr threshold, 2.8 mg kg^{-1} dw
DL detection limit, *F* female, *M* male

hepatic content of Cr in animals caught in the eastern states of Germany was much higher, in the range 0.495 (0.347) in red deer, 0.581 (0.407) in wild boar, 0.628 (0.44) in roe deer, 0.728 (0.51) in mouflon, and 0.807 (0.565) mg kg^{-1} dw (ww) in hare (Anke et al. 2005). Amici et al. (2012) evaluated the content of Cr in the organs of wild boar living in the area of Central Italy. The concentrations of Cr in the liver (Table 3.6) are comparable to those reported by Piskorová et al. (2003). Similar Cr content in the muscle (Table 3.6) was measured by Długaszek and Kopczyński (2013). The renal Cr concentration was different compared to data published by Piskorová et al. (2003). Długaszek and Kopczyński (2013) determined the content of Cr also in the muscles of roe deer and hare (Table 3.6). The results showed strong variability; in roe deer muscle, these values ranged from 0.04 to 2.35 mg kg^{-1} ww. The concentration of Cr in the liver of the reindeer ranged from 0.01 to 0.09 mg kg^{-1} ww (Table 3.6). One reindeer only had a muscle Cr concentration of 1.56 mg kg^{-1} ww (Hassan et al. 2013). Daily adequate intakes of 25 μg for adult female and 35 μg for male were established by the Food and Nutrition Board at the Institute of Medicine of the National Academies (Hassan et al. 2013).

Among the carnivores Cr concentrations were analyzed in tissues of piscivorous otters (European otter *Lutra lutra* and North American river otter *Lontra canadensis*) as well as in tissues of the American mink *Neovison vison*, which is native to North America and is an invasive species in Eurasia. Moreover, Cr was analyzed in Europe in the red fox and in North America in raccoon *Procyon lotor* and wolverine *Gulo gulo* (Table 3.6). Mason and Stephenson (2001) compared the concentration of Cr in the liver of European otters from Denmark, Great Britain, and Ireland. No chromium was detected in the livers of a part of the animals, although in some others the concentration exceeded 4 mg kg^{-1} dw. The highest average (geometric mean) concentration of the metal was measured in the liver of otter living in Britain (0.270 mg kg^{-1} dw), whereas Cr levels in the specimens from Denmark and Ireland were an order of magnitude lower. The relatively high level of Cr in the otters from Great Britain may be a consequence of high water concentrations of chromium, leached from the Cr-rich bedrock.

Both feral and ranch American mink from Poland and the wild mink from Illinois (USA) revealed higher Cr concentrations in the kidney compared to the liver (Table 3.6) (Halbrook et al. 1996; Brzezinski et al. 2014). In raccoon tissues (heart, kidney, muscle, spleen, and liver) from Steel Creek, which was within the watershed of a former reactor effluent stream, the highest Cr concentration was noted in muscle (0.95 ± 0.13 μg kg^{-1} ww) and spleen (0.98 ± 0.18), which differed significantly compared to territory outside of the Department of Energy's Savannah River Site (SRS-South Carolina, USA) (0.24 ± 0.02 μg kg^{-1} ww). Higher ($p < 0.001$) Cr concentration was found also in the kidney of raccoons from SRS (0.31 ± 0.02) in relation to out-site of SRS (0.25 ± 0.01 μg kg^{-1} ww) (Burger et al. 2002). The mean concentration of Cr in the wild canids was 99 times higher than in the fox *Vulpes vulpes* from a contaminated site in Italy (Alleva et al. 2006). Foxes from Slovakia also showed low levels of Cr content (Piskorová et al. 2003) (see details in Table 3.6).

Analysis of Cr content in various species of herbivorous mice and voles have shown that, despite the differences in diets of these two groups, there were no significant differences in the Cr content in their bodies, which ranged from 1.064 to 1.779 mg kg^{-1} dw. Living in the same area, insectivorous shrews (*Sorex* sp.) had twice that level of Cr which is 3.447 mg kg^{-1} dw (Anke et al. 2005).

The issue of Cr concentration in the organs of livestock animals and their diet chromium supplementation has been widely discussed and investigated. Pigs' diet supplementation with 0.2 mg Cr kg^{-1} resulted in deposition of the element in the liver and kidneys, without a significant impact on the muscles. Cr supplementation of cattle diet remained without detectable changes (Spears et al. 2004). In chickens, Cr was administered in various forms (yeast, chromium picolinate, or chloride), which accumulated in the liver, kidneys, and muscles, without affecting the Cr content in eggs (Dębski et al. 2001; Uyanik et al. 2005; Lewicki et al. 2014). It was found that application of $CrCl_3$ in amounts 25, 100, and 200 μg kg^{-1} increased the accumulation of the metal in the liver and kidney, but did not alter its levels in eggs and meat (Anderson et al. 1989). Laying hens fed with high doses (500, 1000, 2000 mg kg^{-1}) of inorganic $CrCl_3$ for 75 days transported a very small part (0.0026%) of the daily intake to the edible parts of the egg (Piva et al. 2003).

Table 3.6 presents the data divided by aquatic birds, passerines, and others. The average hepatic Cr content in these groups ranged between 0.1 and 2.75, in aquatic birds, and between 0.13 and 1.86 mg kg^{-1} dw, in passerines. According to WVDL (2015), the normal range of Cr in the liver of an avian is 0.05–0.40 mg kg^{-1} ww. The great tit inhabiting the Western Mountains of Beijing in China had 50 times more Cr in the liver than birds of the same species in Belgium (Table 3.6), not high enough though to be referred to as toxic, which—according to WVDL (2015)—is 13–-150 mg kg^{-1} ww. Renal content of Cr in the great tit was 6.26 mg kg^{-1} dw, whereas the level considered as toxic is in the range 19–170 mg kg^{-1} ww (WVDL 2015). The data presented in Table 3.6 concerning aquatic birds does not show that plant or animal diet raises the level of Cr in avian organs. Ducks of the genera *Anas* and *Aythya* are characterized by variable hepatic level of Cr as the species of *Haliaeetus* sp., *Pandion* sp. and *Larus* sp., or *Parus* and *Carduelis* sp.

Table 3.7 presents data on the concentration of Cr in the feathers, hair, and bone of various animals. Chromium content in the feathers of white stork in Poland was several thousands lower than those measured in the feathers of seagulls and terns (5.5–12.87 mg kg^{-1}) in North America (Burger 1996; Orłowski et al. 2006). Burger (2013) studied Cr in the feather of young great egrets *Ardea alba* from Barnegat Bay (New Jersey, USA) and observed that these varied in the range 0.09–1.47 mg kg^{-1} dw in 1989–2011 (Table 3.7), and no significant reductions in Cr levels were observed over the years. Burger et al. (2014) investigated Cr levels in various tissues of the semipalmated sandpiper *Calidris pusilla* during its migratory stopover in Delaware Bay (New Jersey, USA). The highest Cr level was found in feathers (Table 3.7). Tsipoura et al. (2008) measured feather Cr contents in three passerine species feeding in the highly urbanized area of Meadowlands of New Jersey. It ranged between 0.6 and 1.0 mg kg^{-1} dw and was nearly 80 times lower as compared

to another passerine species inhabiting a polluted area in India (Table 3.7). Golden et al. (2003) determined the Cr content in feathers of *Nycticorax nycticorax* chicks from Chesapeake and Delaware Bays (USA). They suggested that wading birds may be exposed to industrial and agricultural contaminants; hence, it is necessary to monitor the environmental pollution (Table 3.7). D'Havé et al. (2006) measured Cr concentration (all values in mg kg^{-1} dw) in the hair (5.4), spikes (4.3), liver (3.9), kidneys (3.4), and muscle (4.6) in European hedgehog *Erinaceus europaeus*. It should be noted that the concentration of Cr in the hair and spikes was higher than in the liver and kidney.

9 Ecological Effects of Chromium

Chromium belongs to the group of heavy metals that raise serious concerns in terms of increasing environmental pollution resulting from human activity. Few researchers have focused on the analysis of Cr levels in organisms representing various trophic levels, to bring new knowledge on the possible biomagnification of this metal. Inland ecosystems, both aquatic and terrestrial, have been studied in this respect by, e.g., Outridge and Scheuhammer (1993), Zaccaroni et al. (2003), Alhashemi et al. (2011), Sample et al. (2014), and Zojaji et al. (2014). Sample et al. (2014) conducted soil-screening studies in order to find out the reference values, which could be used to evaluate the toxicity of soil in relation to wild animals. Ecological soil screening is a simplified method assuming that the soil contaminant concentration is at the level of toxicity reference value (TRV), without adverse effects. The analyses involved six mammalian and avian species: the meadow vole (*Microtus pennsylvanicus*), northern short-tailed shrew (*Blarina brevicauda*), long-tailed weasel (*Mustela frenata*), American woodcock (*Scolopax minor*), and red-tailed hawk (*Buteo jamaicensis*). The analyses showed that food and soil have the strongest effect on wildlife exposure to chromium. In the soil-plant system, most chromium is retained in roots, and only a small portion of this is transported to the upper parts of the plant (the stem and leaves). Therefore, the authors assume that the risk of Cr intoxication from plants eaten by herbivorous mammals is low.

For example, Cr was last in the sequence of eight metals studied by Ma (1982) in earthworms, with a geometric mean of 0.06. According to other authors (van Gestel et al. 1993), BAF (bioaccumulation factor) for earthworms depend on the concentration in the soil. Beyer et al. (1990), however, did not find a correlation between Cr concentration in the soil and the biota. These authors considered it unlikely for chromium to accumulate in the trophic chain. According to Outridge and Scheuhammer (1993), there is no evidence of chromium biomagnification. On the contrary, with an increase in the trophic level, the concentration of Cr considerably decreases, which is referred to as "biominification." The literature cited by Outridge and Scheuhammer (1993) brings many examples of decreasing Cr concentrations at a higher trophic level. Biominification exists in the wildlife (mammals), both within

land and marine trophic chains. In some organs of predators (seals, porpoises, and dolphins), the level of Cr was lower than in the fish they preyed on. A similar situation was found in birds: seagulls had a lower concentration of Cr in their tissues compared to organisms they ate, such as clams, snails, crabs, or finfish. An example of biominification in a terrestrial trophic chain is domestic cattle fed with a *Festuca* sp. grass on a pasture contaminated with chromium-containing wastes. Also in the case of Cr-rich wastewater discharged to a forest, mammals living there, such as voles, mice, or even red deer, demonstrated the effect of biominification. The authors explained this with the fact of low absorption of Cr in the alimentary tract (Outridge and Scheuhammer 1993). Zukal et al. (2015) proposed Cr as one of the heavy metals of concern in terms of wildlife conservation. They reviewed the literature for the use of bats as bioindicators of environmental pollution and pointed out that a major challenge is to create standardized programs to monitor the concentration of elements in the tissues of bats of different species and coming from different countries and continents, using modern analytical techniques.

According to Appendix H of the Technical Support Document for Exposure Assessment and Stochastic Analysis (OEHHA 2000), the bioconcentration factor (BCF) for Cr in fish has been established in the range 1–3.4. The arithmetic mean of these values, which is 2, is recommended as the default BCF for Cr. Bioconcentration of Cr in piscine tissues may lead to impaired respiratory functions and osmotic regulation due to damages in the gill epithelium. Chromium levels measured in fish (0.02–0.75 mg kg^{-1}) in most samples exceeded the limits established by the WHO (2000) and FEPA for fish as seafood (0.15 mg kg^{-1}). Consumption of fish with such a high content of Cr may lead to health hazards.

For invertebrates, Outridge and Scheuhammer (1993) recommend the BAF 0.6, whereas for small mammalian species, after Beyer et al. (1990), the BAF 0.2. According to Alhashemi et al. (2011), the trend in Cr allocation in plants was roots > stem > leaves. The translocation factor (TF) from stem to leaves was higher than from roots to stem. Chromium bioaccumulation was studied in relation to diet in the white-spectacled bulbul *Pycnonotus xanthopygos* in various tissues (kidney, rib, muscle, lung, liver, heart) and eggs (yolk and shell). Significant differences were found in Cr bioaccumulation; the levels in kidneys and ribs were higher compared to those in other tissues (Aslan et al. 2006). The results of studies show that an excess beyond the reducing capacity of the environment leads to bioaccumulation of Cr(IV) in the environment and to an increase in its pollution (Vajpayee et al. 1999; Jianlong et al. 2004). Zojaji et al. (2014), who irrigated an experimental plantation of maize (*Zea mays*) using wastewater with a high content of Cr (12 μg kg^{-1}), demonstrated a high level of Cr accumulation in the soil, roots, stems, and leaves of the plants, with the highest levels found in roots. The results presented by Imam Khasim et al. (1989) indicate a dangerous level of Cr bioaccumulation in tissues of animals representing various levels of the trophic chain, as well as in agricultural produce, due to penetration of Cr from soil and water.

10 Bioindicators and Biomarkers of Chromium in Ecotoxicological Studies

Typical Cr levels, considered as physiological, have been established only for a small group of birds and mammals (see Table 3.6, WVDL 2015). Data on Cr concentrations in tissues and hair of livestock animals have been collected by Puls (1994). For man, Yoo et al. (2000) determined in Korean human organs the following Cr concentrations: liver 0.21, kidneys 1.6, heart 0.56, lungs 0.80, spleen 3.4, brain 0.42, bone 0.27, blood 0.24, hair 0.57, and nail 0.54 mg kg^{-1} ww.

The most useful samples in ecotoxicological studies determining Cr concentration in animals tissues seem to be liver, kidneys, (Harding et al. 1998; Piskorova et al. 2003; Pereira et al. 2006), bone and lungs (Dauwe et al. 2005; Horai et al. 2007; Aslan et al. 2006), and in birds also salt glands (Burger and Gochfeld 1985). However, existing empirical records do not suffice to allow drawing definitive conclusions. Further research is needed to collect new data and to monitor Cr concentrations in the environment.

Hair and feathers are promising materials, which can be sampled from living animals (Burger et al. 2015; Manjula et al. 2015). Cr analysis in birds, however, based on feather samples has its limitations. Orlowski et al. (2006), basing on their own research and that by other authors, have shown that feathers are a good indicator of the concentration of Cr in the environment; however, feathers of similar length and collected from corresponding parts of the body, preferably the breast, should be used for analyses. Of the ungulates, wild boars and deer (game animals, widespread across the world) can be used to indirectly assess the impact, which heavy metals, including Cr, have on the environment. Otters are at the top of the trophic chain in aquatic environments and appear to be a useful bioindicator of contaminant metals, including Cr (Harding et al. 1998; Mason and Stephenson 2001; Walker et al. 2010). Mink may also provide data on changes in the environment in terms of chromium levels (Harding et al. 1998; Brzezinski et al. 2014). Also the hair and spikes of the European hedgehog seem to represent suitable biological material to assess environmental pollution with heavy metals, including Cr, since:

- The hedgehog lives in suburban areas and, due to a relatively small foraging territory (1-10-30 hectares) and a low migration index, reflects well the level of local pollution.
- Its long average life span (Reeve 1994) may suggest long-term exposure to contaminants, which may lead to chronic toxic effects (D'Havé et al. 2006).

From among birds, many authors propose passerines, the most numerous avian order, widely distributed, as good bioindicators of Cr pollution (Deng et al. 2007; Tsipoura et al. 2008; Aslan et al. 2006).

Domesticated animals can also be used for environmental pollution assessment, provided they are fed exclusively with feeds from the areas close to their habitat. Studies on livestock animals also show how the diet affects Cr absorption and accumulation (Spears et al. 2004; Dębski et al. 2001).

It is essential to simultaneously obtain information on the geochemical background of the analyzed area and possible anthropogenic sources of Cr and to establish reference values for the content of chromium in various tissues, in order to read the results correctly.

11 Conclusions

- Chromium is an essential trace element for both animals and humans.
- In the natural environment, the effects of hexavalent and trivalent chromium compounds differ fundamentally.
- Trivalent Cr is essential for humans and animals; it underlies the normal glucose metabolism by participating in the glucose tolerance factor (GTF) and plays a role in the glucose-signaling pathway.
- Chromium activates insulin activity.
- In homeothermic vertebrates chromium takes part in the metabolism of hydrocarbons, proteins, and lipids.
- In animals chromium deficiency leads to reduced glucose tolerance, impaired insulin function, changes in protein metabolism, general weakness, and damage to the cardiovascular system.
- Chromium deficiency in mammals leads to growth disorders and low sperm motility in the semen.
- Hexavalent chromium is highly toxic for both plants and animals.
- Anthropogenic Cr pollution of air, water, and soil is a result of combustion of coal and other fossil fuels, smelting of iron and nonferrous metals, and discharges of wastes from paint factories and tanneries, from wastewater treatment plants, and from scrap piles of chrome steel.
- In animal cells, hexavalent Cr is reduced to trivalent Cr, which produces free radicals.
- Hexavalent Cr is carcinogenic, mutagenic, and teratogenic in endothermic animals.
- Excess of Cr, like its deficiency, in males deteriorates sperm quality, damages testicles, and reduces libido.
- It was found that a higher level in the trophic chain does not cause biomagnification of chromium; on the contrary, the higher the trophic level, the lower the tissue Cr content, which is referred to as “biominification.”

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Chapter 4
Copper, Cu

Natalia Łanocha-Arendarczyk and Danuta I. Kosik-Bogacka

Abstract Copper (Cu) is an essential micronutrient for human and animal organisms, playing a structural and enzymatic role in endothermic animals. The profile of Cu emission to the environment has changed significantly in the past decades, with Asia responsible for 50% of global anthropogenic copper emission. This review of reports on the presence of Cu in different avian and mammalian species, usually evaluated in soft tissues including the liver and kidney, shows that it is mainly influenced by the type of diet and anthropogenic environmental contamination with Cu fungicides and with the high natural soil Cu levels resulting from volcanic activity. The good bioindicators of environmental Cu concentration are birds associated with wetland areas, e.g., herbivores such as the mute swan, ducks from the genera *Anas* and *Aythya*, terrestrial passerines (house sparrow, great tit, and blue tit), and birds of prey including the common buzzard, white-tailed eagle, and bald eagle. In terrestrial mammals, a measurable response to pollution with Cu is exhibited by canids common in natural and seminatural habitats, e.g., the Arctic fox, red fox, raccoon dog, American mink, otters, and ungulates, such as the wild boar and red deer. In Europe, Cu levels may now be tested in increasingly popular alien species, e.g., mink, raccoon, and raccoon dog, which allows wider intercontinental comparative studies. Biomarkers for identification of copper status are still being defined, and still the best solution to evaluate the exposure is to measure Cu concentrations in wildlife and the environment.

1 Introduction

Emissions of copper into the environment are from similar volumes of both natural sources (mainly from dust carried by winds, forest fires, and volcanic particles) and anthropogenic sources (e.g., storage of ash, fungicides, Cu nanomaterials, mining,

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and smelting) (AMAP 2002; Kabata-Pendias and Szteke 2015). About 90% of world copper reserves are sulfide ores, ~9% copper oxides, and the remaining 1% pure copper. The twentieth century saw an unprecedented growth in demand and production of this element, and although annual global production of mined copper has stabilized at about 10 million tonnes, consumption is still very high. World reserves of economically viable copper deposits are currently estimated at 300 million tonnes (USGS 2016).

Copper is an essential trace element involved in the formation and metabolism of bone tissue but most importantly in oxidation-reduction processes where it acts as a coenzyme (Angelova et al. 2011). The persistent presence of Cu compounds in the environment results in exposure to its toxic effects to many aqueous and terrestrial organisms (including invertebrates, birds, and mammals) (Eisler 1998; Hernandez et al. 1999; Millan et al. 2008). The negative effects to wild animals from the various Cu compounds in the environment have been well documented in multifaceted field studies in North America, Canada (mainly trans-Arctic animals), and Europe (mainly herbivores, carnivores, and omnivores) (Clausen and Wolstrup 1978; Beyer et al. 1998; Eisler 1998; Rush et al. 2008; Bilandžić et al. 2012).

Birds and mammals with the highest accumulation of Cu include both herbivores and carnivores (Reglero et al. 2008; Schummer et al. 2011; Bilandžić et al. 2012). Wetland birds are reported to accumulate much higher levels of Cu than terrestrial birds, with many ecotoxicological studies showing their potential usefulness in biomonitoring of inland water ecosystems in North America and Europe (Kalisińska et al. 2004; Taggart et al. 2009; Schummer et al. 2011; Komosa et al. 2012). Importantly, there is a lack of biomonitoring studies on Cu levels in Europe using alien species originating from North America and southeastern Asia, e.g., mink, raccoon, or raccoon dog, namely, animals which in the ecotoxicological studies carried out in North America have given a measurable response to Cu contamination in aqueous environments (Brzezinski et al. 2014; Souza et al. 2013).

Available literature lacks data on background Cu levels for avian and mammalian species. Moreover, there are no threshold levels of copper toxicity for terrestrial animals (birds and mammals), with the proposed physiological Cu ranges in organs and tissues often very different (Eisler 1998; AMAP 2013). Reports also relatively rarely identify a threat of Cu intoxication (many wild animals demonstrate high Cu tolerance). Nonetheless, Cu intoxication has been reported in swans (*Cygnus olor*), geese (*Branta canadensis*), and also red foxes (*Vulpes vulpes*) from highly polluted areas (Millan et al. 2008). In addition to acute Cu poisoning, there are also reports of Cu deficiencies in various wild cervid populations, e.g., in white-tailed deer (*Odocoileus virginianus*), red deer (*Cervus elaphus*), and moose (*Alces alces*) (Skibniewski et al. 2016; Handeland et al. 2017).

Given the important role of Cu in vertebrate organisms, and the reported northern hemisphere cases of health risks associated with a deficiency or excess of Cu in the consumed diet, it seems justified to perform ecotoxicological studies (including comparative research) of this important micronutrient in the tissues of wild birds and mammals in Europe, especially alien species studied in North America.

2 General Properties

Copper (Cu) is a metallic element in Group 11 of the periodic table (previously group IB) (atomic number 29, atomic weight 63.546) that occurs naturally as a free metal or more commonly associated with other elements in compounds comprising a variety of minerals (Kabata-Pendias 2011). Almost all copper found in nature exists as one of two stable isotopes, ^{63}Cu (69.09%) and ^{65}Cu (30.91%). Its specific gravity is 8.96 at 20 °C, melting point at 1083 °C, and boiling point at 2927 °C (Rudnick and Gao 2003). Copper has very high electrical and thermal conductivity and is resistant to corrosion. Moreover, it is a lightweight and malleable metal (ICSG 2014). Most Cu compounds occur in Cu (I) and Cu (II) valence states, with oxidation states from 0 to +4 (Cotton and Wilkinson 1980). Copper is naturally present in the Earth's crust (lithosphere) at a concentration of about 50–70 mg kg^{-1} (0.0068%); the highest concentrations are found in volcanic and basic igneous rock, with the lowest in lime and sandstone. Copper levels in major rock types can be placed in the following decreasing order (mg kg^{-1}): basic igneous (100) > shales and clay (40) > acid igneous (10). The concentration of copper in the core of the Earth is estimated to be 125 ppm, while in the bulk of the mantle and crust, it is estimated at 30 ppm (Rudnick and Gao 2003). Copper is generally present in low levels in coal (17 mg kg^{-1}), in oil at 0.2–1 mg kg^{-1}, and gasoline at <3 mg kg^{-1} (average values) (Rauch and Pacyna 2009; Georgopoulos et al. 2001).

3 Copper Minerals, Production, and Uses

Cu occurs very rarely in nature as native copper, being found mostly in the form of sulfide minerals, particularly chalcopyrite ($CuFeS_2$), chalcocite (Cu_2S), bornite (Cu_5FeS_4), and tetrahedrite $(CuFe)_{12}Sb_4S_{13}$ (British Geological Survey 2013; Kabata-Pendias and Szteke 2015). As a result of chemical weathering of these primary copper sulfide minerals, secondary minerals may be formed, including the oxide mineral cuprite (Cu_2O), the carbonate minerals malachite ($Cu_2(CO_3)(OH)_2$) and azurite ($Cu_3(CO_3)_2(OH)_2$), and the sulfate minerals brochantite ($Cu_4SO_4(OH)_6$) and antlerite ($Cu_3SO_4(OH)_4$) (CCME 1999). There are many copper alloys, e.g., brass (Cu + Zn), bronze (Cu + Sn), cupronickel (Cu + Ni), and Ti-Cu alloys, which exhibit strong antibacterial ability (Zhang et al. 2016). Copper is widely used in a variety of industries, e.g., in pipes, sheets, strips, and cables in electrical engineering. It is an important component of brass and bronze. Copper sheets are used as roofing and in the chemical industry, e.g., in the production of coolers, chemical instruments, and heat exchangers. Copper is a component of dental amalgams. Cu is also the primary component of electrical and data communication wiring such as the windings of stators and generator rotors and most electronic circuit boards. It is also still used to produce copper coins, ammunition, and as a catalyst in chemical processes (Bharti et al. 2010; ICSG 2014). Nanocolloidal copper is a powerful disinfectant and

fungicide. The Bordeaux mixture ($Ca(OH)_2 + CuSO_4$) is used in medicine, cosmetics, and food industries. Cu compounds are also used as animal feed additives (Brun et al. 2001; Kabata-Pendias and Szteke 2015). Copper oxide nanoparticles (CuO NPs) are used as additives in lubricants, polymers, plastics, metallic coatings, inks, photocatalysts, gas sensors, and an antimicrobial agent (Midander et al. 2009; Hou et al. 2017). It is possible that a new composite containing Cu and graphene (allotropic variety of carbon) will contribute to the development of the electricity industry with a variety of applications in the electronics, machinery, automotive and food industries, as well as in the construction industry and medicine (Nam and Lee 2016). In the USA, in 2015, Cu has been used in building construction (43%), in electric and electronic products (19%), transportation equipment (19%), consumer and general products (12%), industrial machinery and equipment (7%), and for wiring, plumbing, and waterproofing (USGS 2016). Between 1992 and 2003, there was a more than twofold increase in the use of Cu in the construction industry, from 21% to 46%. Moreover, in the twenty-first century, a downward trend was observed in copper use in electrical and electronic products by ~50% compared to the 1990s (USGS 2014). Copper is one of the few materials than can be recycled. Globally, it is estimated that 2/3 of the 550 million tonnes of copper produced since 1900 is still in productive use, of which 70% has been used for electrical applications and 30% for non-electrical. Around 55% of this usage is in buildings, 15% in infrastructure, 10% in manufacturing, 10% in transport, and 10% in equipment manufacture (Glöser et al. 2013; ECI 2014). Countries with the largest natural resources of Cu range downward from Chile > Peru > Australia > Mexico > USA > China > Indonesia > Russia > Poland, at 150, 90, 80, 38, 35, 30, and 26 Mt, respectively (ISGS 2011). About two thirds of global resources are located in the western hemisphere, with the largest natural deposits of copper in the world in the Atacama desert in the northern part of Chile, with an estimated 200 million tonnes (Kabata-Pendias and Szteke 2015). From 1960 to 2013, copper consumption has shown some interesting trends. From less than 750,000 tonnes in 1960, copper mine production in Latin America surged to over 7.5 million tonnes in 2013, representing 42% of the global total. Asia has also exhibited a significant growth, probably caused by the rapid industrialization of the continent (USGS 2014). China's copper consumption has expanded markedly over the past decade. Between 2001 and 2011, China's copper usage increased by 5.1 million tonnes (million mt), or by 215% (ISGS 2011).

4 Copper in Nature (Soil, Water, and Air)

The average Cu content in different types of soil in the world ranges from 13 to 30 mg kg^{-1} dw and usually does not exceed 50 mg kg^{-1} dw (Kovačič et al. 2013; Kabata-Pendias and Szteke 2015). Copper concentrations from four remote locations in Greenland soils were <12–37 mg kg^{-1} dw, probably representing background levels (AMAP 1998). Copper levels in various types of soils can be placed in the

following decreasing order: heavy clay soils > cambisols > histosols > rendzina > arenosols. The lowest Cu concentrations (70 mg kg^{-1} dw) were found in arenosols and calcisols and the highest (140 mg kg^{-1} dw) in heavy clay soils, from which copper can be easily extracted (Kabata-Pendias 2011; Kabata-Pendias and Szteke 2015). The mean concentrations of Cu in soils in North America (USA) and in agricultural soils in China range from 5–70 to 5.8–66.1 mg kg^{-1} dw, respectively (Kabata-Pendias 2011; Li et al. 2014). Copper-deficient soils do occur across large areas of Europe (including Poland, northeastern Germany, Sweden, Central France, Spain), while potentially toxic levels are rarely reached (in Italy, Croatia, Greece) (Reimann et al. 2013). A large difference is observed in the concentration of Cu between the soils from northern and southern Europe. In northern Europe, young soils have 2–3 times lower Cu concentrations than the older and more weathered southern European soils (Reimann et al. 2013). Mean levels of Cu < 5 mg kg^{-1} dw have been observed in some European countries, e.g., the UK, Croatia, Finland, Greece, Norway, Sweden, and Belgium (Kovačič et al. 2013). However, levels higher than 100 mg kg^{-1} dw also occur in Italy (probably because of the volcanic origin of these soils), Norway, Spain, and the UK (Mantovi et al. 2003; Heijerick et al. 2006). Cu contamination in the surface layers of soil, mostly in the area of mines and smelters (especially copper smelters), can exceed several thousand mg kg^{-1} dw (e.g., in Canada, Japan, and Bulgaria) (Kabata-Pendias and Szteke 2015). Some soils close to the Russian Severonickel copper smelter (e.g., Kola Peninsula, one of the most polluted ecocatastrophe areas of the former Soviet Union) have Cu concentrations 50–80 times higher than the background level (AMAP/UNEP 2013). Significant sources of soil Cu contamination are copper fungicides, fertilizers, and waste used to fertilize soils. In some regions of Europe, e.g., in Switzerland, soil Cu may exceed 6000 mg kg^{-1} dw on military training grounds (Kabata-Pendias and Szteke 2015).

Copper content in waterway sediment, especially in polluted water reservoirs and rivers, can be as high as 2000 mg kg^{-1} dw (Kabata-Pendias 2011; Kabata-Pendias and Szteke 2015). Cu levels in surface waters range from 0.5 to 1000 μg l^{-1}, with a median of 10 μg l^{-1}. Seawater contains from <1 to 5 μg l^{-1} (Martin et al. 1993; EPA 2007; AMAP/UNEP 2013). In uncontaminated natural waters, Cu compounds are relatively rare, with water from wetlands or peat containing trace amounts of Cu, up to about 0.01 mg dm^{-3}. Small amounts of Cu may leak into the groundwater; in areas of temperate climate, these waters contain on average 5.0 μg l^{-1} (Zhang et al. 2011). Cu concentrations in groundwater can be classified as permissible (20 μg l^{-1}), requiring monitoring (50 μg l^{-1}) and requiring treatment (500 μg l^{-1}) (Dutch Pollutant Standards 2011). The world average concentration of Cu in rivers has been estimated as 23.6 nM Cu dissolved load and 100 ppm Cu suspended particulate load (Martin et al. 1993). Dissolved ambient Cu concentrations in European surface waters typically range from 0.5 in Denmark to 4.7 μg l^{-1} in Ireland (EPA 2007).

The concentrations of copper in the air depend on the proximity of the site to major particulate sources such as smelters, power plants, and incinerators (IPCS 1998; ATSDR 2004). In the air, Cu occurs most frequently in the form of oxides which combine with particulates and are readily soluble in rainwater, especially

acidified rainwater (containing sulfur compounds) (Kabata-Pendias and Szteke 2015). Over 90% of copper in the atmosphere falls to the surface of the soil and plants via precipitation (e.g., fog, clouds, and rain) as a result of global cycling (AMAP/UNEP 2013). Copper in the atmosphere occurs in very different concentrations, from 0.03 ng m^{-3} over the South Pole to 5000 ng m^{-3} in industrial areas of Germany. The average amount of natural Cu in the air is 4 ng m^{-3} (Kabata-Pendias and Szteke 2015) and in nonindustrial and urban locations from 2.5–4.0 to 30–200 ng m^{-3}, respectively (IPCS 1998). The average annual value of Cu in precipitation has been evaluated at 34.0 g ha^{-1} $year^{-1}$, with the least in Finland (5) and the most in Austria (100) (Nicholson et al. 2003).

4.1 Geogenic and Anthropogenic Sources of Copper

Cu has entered the environment via both natural and anthropogenic sources, with both emissions appearing comparable (Table 4.1). The average annual global emissions of Cu (thousand tones) from various natural sources include dust carried by winds (0.9–15), forest fires (0.2–7.5), volcanic particles (0.9–10), biogenic transformation (0.1–6.4), and spraying seawater (0.2–6.9) (AMAP 2002; ATSDR 2004; Kabata-Pendias and Szteke 2015). The mean natural emission rates for copper are 2.6×10^6 kg $year^{-1}$ for Canada, 5.0×10^7 kg $year^{-1}$ for North America, and 2.0×10^9 kg $year^{-1}$ globally (Richardson et al. 2001; AMAP/UNEP 2013). Emissions of Cu into the atmosphere are mainly from nonferrous metal smelting and

Table 4.1 Global emissions of copper from natural and anthropogenic sources ($\times 10^6$ kg $year^{-1}$)

Natural sources		
Wind-borne particulates	8.0	0.9–15
Marine-sprayed sea salt and surface organic microlayers	4.0	0.25–7.7
Volcanoes	9.4	0.9–18
Forest fires	3.8	0.1–7.5
Biogenic-continental particulates and volatiles	2.9	0.11–5.6
Total emission	28	2.3–54
Anthropogenic sources		
Coal combustion	5.15	2.3–8.0
Oil combustion	1.86	0.42–3.3
Pyrometallurgical	23.5	15–32
Secondary nonferrous metal production	0.115	0.06–0.17
Steel and iron manufacturing	1.47	0.14–2.8
Refuse incineration	1.5	1.0–2.0
Phosphate fertilizers	0.415	0.14–0.69
Wood combustion	0.9	0.60–1.2
Total emission	35	20–50

Nriagu and Pacyna (1988), AMAP (2002), and ATSDR (2004)

refining (~70%), with concentrations well in excess of 1 μg m^{-3} frequently recorded near Cu smelters (AMAP 2002), as well as from burning coal for power generation and from municipal waste incinerators. Asia and South America were responsible for 50% and 21%, respectively, of global anthropogenic copper emissions (AMAP 2002; AMAP/UNEP 2008). In 2010, 3.3 kt of copper was emitted to the atmosphere in Europe (AMEC 2014). Between 1990 and 2012, Cu emissions in European countries dropped by 1.3%, and between 2011 and 2012, emissions decreased by a further 1.9%, mainly from reduced emissions in Germany, Italy, and Romania (EEA 2014).

5 Copper in Living Organisms

5.1 Plants

Copper is an essential nutrient for plant growth and development, as a component of many enzymes involved in photosynthesis. It has protective properties against plant diseases and affects the metabolism of nitrogen compounds and DNA and RNA synthesis (Mahmood and Islam 2006; Nagajyoti et al. 2010; Szatnik-Kloc 2014). Copper may become phytotoxic and cause metabolic disorders at high concentrations and so lead to a potential threat to animal health through the food chain (Chang and Page 2000; Xu et al. 2013). Cu accumulation in leaves is between 15 and 25 mg kg^{-1} dw (Hladun et al. 2015), with Cu content in plants in contaminated regions usually elevated and exceeding concentrations considered toxic (Kabata-Pendias 2011). A critical Cu deficiency level in vegetative plant parts is generally 3–5 mg kg^{-1} dw (Robson and Reuther 1981). Cu levels in plants are influenced by soil pH; Cu mobility in soils increases only at pH < 5.0. It has also been demonstrated that soil liming reduces the accumulation of Cu (Kabata-Pendias 2011; Kabata-Pendias and Szteke 2015). Nitrogen and phosphorus fertilization adversely affects Cu uptake due to elevated levels of phosphorus, nitrogen, or zinc in the soil. Cu content in plants varies depending on the parts: fruit (3–8 mg kg^{-1} dw), nuts (0.2–24 mg kg^{-1} dw), grasses (2–10 mg kg^{-1} dw), and clover (7–15 mg kg^{-1} dw). Plants growing on Cu-polluted sites tend to accumulate increased amounts of this metal, especially near industrial areas and in soils treated with Cu-bearing herbicides (Eisler 1998). Some plants from the *mint* family (e.g., *Aeollanthus biformifolius*) are useful indicators of Cu levels in soils, with samples growing on mineralized land containing 13,700 mg Cu kg^{-1} dw (Kabata-Pendias 2011).

5.2 Biological Effects, Metabolism, and Toxicity of Cu in Homeothermic Animals

Copper is an essential trace element involved in the formation and metabolism of bone tissue. However, its primary function is its participation in oxidation-reduction

reactions as a coenzyme, a regulator of iron metabolism and transport, as well as collagen metabolism (Honda et al. 1997; Angelova et al. 2011; AMAP/UNEP 2013; Cornu et al. 2017). Cu metabolism disorders can lead to hereditary diseases, e.g., Menkes disease (steely hair syndrome) and Wilson's disease (Roberts and Schilsky, 2008; Ojha and Prasad 2016). These diseases are characterized by deposition of Cu in the internal organs, leading to their damage. In the blood, Cu occurs in complexes with histidine, threonine, and glutamic acid. In complexes with amino acids (e.g., Cu-lysine) and albumin, Cu is transported to the liver, kidney, intestines, and other tissues. From the ingested food (mainly from plants), about 50%–70% of Cu is absorbed in the digestive tract, particularly in the small intestine, with small quantities being absorbed in the stomach, and then transported via albumins, then hepatocytes and hepatic ceruloplasmin (Cp) (IPCS 1998). Cu absorbed into the intestinal endothelium may be sequestered by metallothionein (MT), or it may migrate to the portal circulation. Most Cu is transported across the mucous membrane involving copper translocation, while intestinal metallothionein may participate in the detoxification of excess copper (Kabata-Pendias and Szteke 2015). In the bodies of some animals, e.g., in sheep, a much smaller proportion of copper in the liver is bound to MT, as sheep have a limited ability to increase metallothionein synthesis in response to increased liver copper. In mammals, the liver is the main organ responsible for the accumulation of Cu (Osredkar and Sustar 2011). Outside the liver, this element is associated mainly with enzymatic proteins: SOD (superoxide dismutase), tyrosinase, cytochrome c oxidase, and lysyl oxidase (IPCS 1998; WHO 2004). Copper is present in all tissues at levels ranging from 0.7 to 7.8 mg kg^{-1} body weight and varies between animal species.

Antagonistic interactions occur between Cu and Zn, Mo, Cd; a high level of zinc in the diet reduces the absorption and bioavailability of Cu. Copper deficiency in animals results in anemia, loss of appetite, damage to internal organs, bone deformities, reduced reproductive capacity, changes in coat, myocardial fibrosis, and chronic debilitating diarrhea. Copper deficiency may be primary, i.e., associated with a low Cu intake, or secondary, when Cu absorption or metabolism is adversely affected due to high levels of molybdenum, iron, sulfur, or zinc in the diet (Vengust et al. 2015). Among domesticated species, signs of Cu deficiency are observed mainly in cattle, with sheep showing a high sensitivity to even low concentrations of Cu in the diet (Puls 1994). Copper deficiency has been reported in various wild cervid populations (O'Hara et al. 2001; Handeland et al. 2017). Subclinical Cu deficiency may produce marginal signs of poor health and result in morbidity and mortality from other opportunistic factors, such as secondary infections, predation, and weather events (O'Hara et al. 2001). In addition, white-tailed deer (*Odocoileus virginianus*) from Texas, USA, with mean liver Cu levels of 16.7 mg kg^{-1} ww, had stunted and twisted antlers (King et al. 1984). In moose, Frank (1998) regarded a Cu concentration of >5 mg kg^{-1} ww in the liver as an indication of severe Cu deficiency. In addition, in red foxes, Cu deficiencies are usually observed in offspring; puppies are born weak, poorly developed, and with high mortality rates. Cu deficiency-related anemia results in a pale skin and mucous membranes, discoloration, and loss of elasticity and silkiness of hair (Frank 1998).

Excess copper is harmful to wildlife, but it occurs rarely. Mammals and birds are at least 100 times more resistant to Cu than other organisms. An excessive dietary intake of Cu by 20- to 50-fold over normal levels may, however, have serious adverse effects on birds and mammals. No data are available on the toxicity of copper to avian wildlife (Eisler 1998). Research on the adverse effects of higher concentrations concern only domestic waterfowl fed with extremely high doses of copper (diet containing up to 500 mg Cu per 1 kg of feedstuff). The more common effects of high copper concentrations in the environment on birds can be seen through the tropic chain where the prey of some avian species is eliminated by pollution (which limits the nutrition sources) (Eisler 1998). In mammals, the mechanism of copper toxicity is complex. Copper can increase cell permeability in erythrocytes leading to lysis and inhibition of intracellular enzymes. Thus, copper poisoning can lead to oxidative stress in erythrocytes and to accelerated loss of intracellular glutathione. In addition, copper ions can cause mitochondrial swelling and inhibit oxygen consumption, which leads to cell degeneration (EPA 2007). Scientific literature describes cases of acute and chronic toxicity in laboratory and farm animals, although there is little data on contamination with Cu compounds in wildlife.

Acute responses to copper vary with the species and copper compound. Ferrets, sheep, dogs and cats are more sensitive to copper than rodents, pigs, and poultry (WHO 2004). Acute poisoning from the ingestion of excessive Cu can cause temporary gastrointestinal distress with symptoms such as nausea, vomiting, and abdominal pain. Liver toxicity was seen in doses high enough to result in death. High levels of exposure to copper can cause the destruction of red blood cells, possibly resulting in anemia. An oral LD_{50} (median lethal dose) of 300 mg cupric sulfate/kg in rats has been reported (Siegel and Sisler 1977). Acute copper poisoning can occur at copper intakes of 20–100 mg kg^{-1} in sheep and young calves and 200–800 mg kg^{-1} in adult cattle. The chronic LOAEL (*lowest-observed-adverse-effect level*) in bobwhite quail (*Colinus virginianus*) was 289 mg kg^{-1} dw Cu as metallic copper. An acute oral LD_{50} for this bird exposed to copper sulfate was also reported as 616 mg kg^{-1} dw (ATSDR 2004). Luo et al. (2005) fed 450 mg kg^{-1} dw of copper sulfate to male chicks for 21 days and noted reduced feeding and less weight gain in the exposed birds. Liver Cu residue is a commonly used and reliable index of exposure in cases of acute Cu toxicosis. Reported liver Cu levels in wild adult mallard ducks ranged from 35 to 585 mg kg^{-1} dw (Eisler 1998). Mute swans diagnosed as having Cu poisoning in the north American Mamaroneck Harbor had a mean Cu concentration in the liver of ~3900 mg kg^{-1} dw. Significantly, some mute swans tolerated liver Cu residues at levels up to 1000 mg kg^{-1} dw. In wild birds with symptoms of inanition, anemia, and generalized weakness, concentrations of Cu in the liver and kidney were 3000 and 50 mg kg^{-1} dw, respectively.

Mammals have efficient mechanisms to regulate Cu stores in the body such that they are generally protected from excess dietary copper levels. In chronic poisonings, sheep and cattle are the most affected species, with copper exerting a hepatotoxic effect (Oruc et al. 2009). Fuentealba and Aburto (2003) established a normal copper content in the liver at between 10 and 50 mg kg^{-1} ww. Buck and

Sharma (1969) observed sheep liver Cu concentrations ranging from 160 to 550 mg kg^{-1} ww in animals diagnosed with chronic copper poisoning and kidney concentrations between 12 and 220 mg kg^{-1} ww. Chronic copper intoxication in calves could only be seen at levels higher than 200 mg kg^{-1} ww (Croubels et al. 2001), while Hadrich (1996) reported liver Cu content between 500 and 800 mg kg^{-1} dw in cases of poisoning. Grobler and Swan (1999) observed liver Cu concentrations above 150 mg kg^{-1} (for chronic copper poisoning in domestic sheep) in impala (*Aepyceros melampus*) within a high risk zone (near a copper smelter of a mine). Gilbert et al. (1996) fed copper sulfate at concentrations of 78 and 1437 mg kg^{-1} bw to laying hens for 2 weeks. At the highest concentration, hens produced fewer eggs, consumed less feed, and developed ulcers in the gizzard and oral cavity (Gilbert et al. 1996; Boone et al. 2012). Other studies on chickens that were fed copper sulfate reported oral lesions proportional to the dose of Cu and conflicting effects on feeding rate and weight gain (Boone et al. 2012). Scientific literature lacks data on toxic thresholds of Cu indicating subclinical or clinical poisoning in wild birds and mammals (AMAP/UNEP 2013). There are reports describing a wildlife toxicity reference value (TRV) and a no effect hazard concentration (NEHC) for the American bald eagle (*Haliaeetus leucocephalus*), at 4.05 and 40.5 mg kg^{-1} dw, respectively. The same parameters were established for ranch mink at 5.60 and 41.2 mg kg^{-1} dw, respectively (EPA 2007).

Cu compounds can have a mutagenic effect on the cells of mammals. Copper is currently categorized by the EPA as a Group D carcinogen (inadequate evidence to classify) and has not yet been reviewed for placement into any of the new cancer classification categories (WHO 2004). Cu may affect cancer growth and cell proliferation and stimulate blood vessel formation (Boone et al. 2012). Developmental effects have been observed in only a few studies giving animals high doses of copper, such as delayed growth and development, delayed bone formation, and reduced litter size and body weights (ATSDR 2004).

5.3 Copper in Biological Samples from Birds and Mammals

Ecotoxicological studies on Cu in birds usually determine levels in the feathers, eggs, blood, the liver and kidneys and much less frequently in the muscles, brain, and bones (Kalisińska et al. 2004, 2007; Schummer et al. 2011; Binkowski and Meissner 2013). In mammals, the concentration of Cu is commonly determined in parenchymal organs (liver and kidney), which are essential for detoxification. There is a lack of publications on Cu in the brain, muscle, or bone fragments, with the latter preferred in assessing long-term changes in the accumulation of elements, including Cu (Kalisińska et al. 2004, 2006; Lanocha et al. 2012). In mammals, apart from blood levels that reflect short-term exposure, Cu is increasingly often determined in the hair, which consists of keratin with cysteine sulfhydryl groups capable of binding metals. In birds, Cu is also determined in the feces and urine, which have been

suggested as useful nondestructive indicators of Cu contamination in the diet and environment (Berglund et al. 2015).

Cu concentrations in biological material from birds usually can be placed in the following descending order: liver > kidney > feathers > muscle > brain > blood > eggs > bone (Ek et al. 2004; Lucia et al. 2010). The muscles and feathers typically contain the highest levels of total Cu (up to 53% and 34%, respectively); sometimes in birds associated with water ecosystems, e.g., the great cormorant (*Phalacrocorax carbo*), muscle tissues had the highest total Cu levels at ~70% (Honda et al. 1986; Nam et al. 2005), ~11% in the liver, 7% in feathers, and 2% in bone tissues (Nam et al. 2005). In birds, the concentrations of Cu in feathers are higher than in the eggs and blood due to the affinity of Cu to keratin (the principal structural protein in building a feather, rich in sulfhydryl groups (SH)), although >20% of the total content of Cu is incorporated into newly formed feathers (Honda et al. 1986; Ek et al. 2004; Costa et al. 2013). As shown in environmental monitoring, Cu concentrations in bird feathers occur over a wide range, from ~0.5 to 88 mg kg^{-1} dw, with generally higher concentrations detected in birds living in contaminated environments (Dauwe et al. 2002). St Clair et al. (2015) have suggested that a toxicity threshold has not been established for Cu in feathers. Lester and van Riper (2014) stated in southwestern song sparrows (*Melospiza melodia fallax*) that the concentration of Cu in the feathers, ranging from ~10 to ~15 mg kg^{-1} dw, did exceed background levels.

In terrestrial mammals, Cu concentrations in biological materials can usually be arranged in the following descending order: liver > kidney > heart > brain > lung > muscle > bone, with variations in mineral content not only from organ to organ but also between animal species (Hanusova et al. 2007). Han et al. (2002) described the distribution of Cu in the European otter (*Lutra lutra*), where 30% of total Cu found was in the liver, 30% in hair, 20% in kidneys, and 10% each in muscle and bone tissues. It is estimated that 30% of total Cu in mammals is in the hair, as the process of normal hair and wool pigmentation requires Cu (Brzezinski et al. 2014).

5.3.1 Bioaccumulation of Copper in Avian Liver, Kidney, and Muscle

Although most of the data on Cu concentrations in birds concern the liver, scientific literature does not present values indicative of elevated concentrations of Cu against the geochemical background. The no-effect level of Cu in bird livers has been stated at <60 mg kg^{-1} dw, with the toxicity threshold >540 mg kg^{-1} dw (U.S. Department of the Interior 1998). It has been found that a concentration ~50 mg kg^{-1} dw in the kidney may cause a nephrotoxic effect in the mute swan (Frank and Borg 1979). However, in scientific literature we have only found information on a so-called typical range for Cu in the liver for wild birds, e.g., the wild Canadian goose and mute swan: ranging from 6 to 30 mg kg^{-1} ww (~20–100 mg kg^{-1} dw) and 120 to 360 mg kg^{-1} dw, respectively (Puls 1994; Isanhart et al. 2011).

The concentrations of Cu in internal tissues represent the available levels of this metal in the diet, which in turn can reflect the degree of contamination of the

ecosystem (Carneiro et al. 2016). Taking into account the trophic groups of birds associated with northern hemisphere terrestrial ecosystems, the concentrations of Cu in the parenchymal organs (liver and kidney) in each group trophic can be arranged in the following descending order: herbivores > omnivores > piscivores > birds of prey (Fig. 4.1). In omnivorous birds, the mean concentrations of Cu in the liver are not as high as in herbivores (although in some cases they can reach >200 mg kg^{-1} dw) (Hernandez et al. 1999; Taggart et al. 2006). Omnivorous avian species have high average concentrations of Cu in the kidneys (~45 mg kg^{-1} dw), although these levels may differ significantly between studies (Frank and Borg 1979; Schummer et al. 2011; Komosa et al. 2012). Jackson et al. (1979) found a concentration of Cu in the kidneys between ~11 and 29 mg kg^{-1} dw in dunlin (*Calidris alpina*) that could be associated with toxicity in other avian species, where Cu levels in the kidneys can remain stable even with toxic doses in the diet (St Clair et al. 2015).

Studies on Cu in wild birds from the northern hemisphere published after 1980 usually concern wetland birds and rarely discuss the concentration of Cu in the kidney. Only a few species of terrestrial birds have average Cu concentrations in the kidney above the avian nephrotoxic level, ~60 mg kg^{-1} dw, including Eurasian wigeon (*Anas penelope*), mute swan, mallard (*Anas platyrhynchos*), spectacled eider

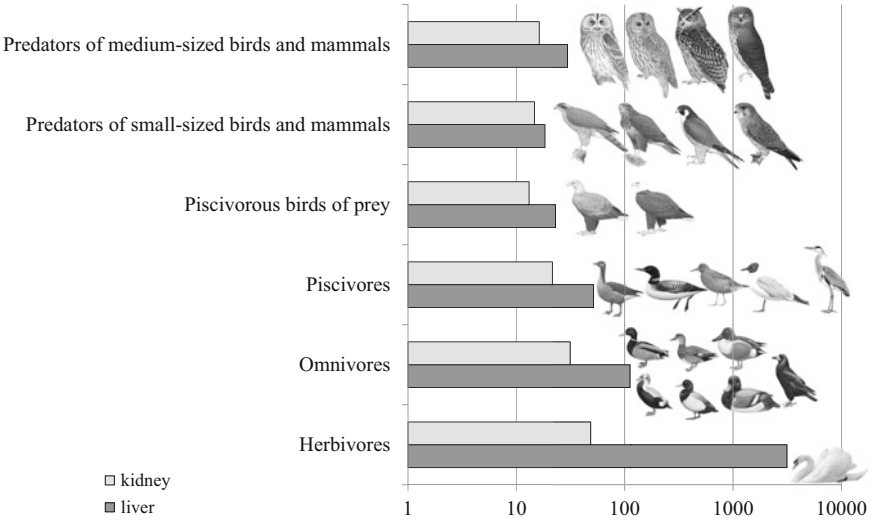

Fig. 4.1 The concentration of Cu (mg kg^{-1} dw) in the livers and kidneys of birds with different diets; logarithmic scale based on herbivores (Beyer et al. 1998; Frank and Borg 1979; Schummer et al. 2011), omnivores (Hernandez et al. 2017; Kalisińska et al. 2004; Kim and Oh 2012; Lucia et al. 2008; Orlowski et al. 2007; Taggart et al. 2006; Trust et al. 2000), *piscivores* (Kim and Oh 2015; Lucia et al. 2008; Lucia et al. 2010; Mateo and Guitart 2003; Orlowski et al. 2007; Schummer et al. 2011), *fish eaters* (Falandysz et al. 2001; Falandysz et al. 1988; Falandysz and Szefer 1983; Kalisińska et al. 2006; Kim and Oh 2012; Mierzykowski and Todd 2012; Stout and Trust 2002), small-sized bird and mammal eaters (Ek et al. 2004; Hontelez et al. 1992; Jager et al. 1996; Kalisińska et al. 2008; Komosa et al. 2012; Licata et al. 2012; Naccari et al. 2009), and medium-sized bird and mammal eaters (Kalisińska et al. 2009a; Komosa et al. 2012)

(*Somateria fischeri*), and brown hawk-owl (*Ninox scutulata*) (Clausen and Wolstrup 1978; Trust et al. 2000; Lucia et al. 2008; Kim and Oh 2012). One of the highest mean kidney Cu concentrations was found by Kim and Oh (2012) in the Korean brown hawk-owl, at ~67 mg kg^{-1} dw, and the authors suggest that as this bird is a summer visitor, the pollutant levels may reflect both Korean and wintering site levels. Furthermore, in the American spectacled eider, the concentrations of Cu in the kidney and liver exceeded levels that can cause nephro- and hepatotoxic effects in birds: means were ~67.5 and ~559 mg kg^{-1} dw, respectively (Trust et al. 2000).

The highest concentrations of Cu in the liver, indicative of poisoning, have been reported in herbivorous birds related to freshwater ecosystems, at times reaching 5000 mg kg^{-1} dw in North American and 3820 mg kg^{-1} dw in European specimens (Frank and Borg 1979; Beyer et al. 1998). High levels of hepatic copper observed in the mute swan can be explained by the fact that the swans consume daily up to 35%–43% of their body mass in aquatic vegetation (Komosa et al. 2012). Copper is an essential micronutrient for all higher plants and is easily absorbed by aquatic vegetation (Xue et al. 2010). Such a high consumption of water plant biomass may contribute to the high levels of Cu in the livers of the mute swans. Schummer et al. (2011) found concentrations of Cu in the liver >2000 mg kg^{-1} dw in swans residing in the lower Great Lakes in Canada (Fig. 4.1). Toxicological thresholds for Cu in mute swans are unknown, and mortality rates noted in studies from Sweden, New York, and northeastern America may have resulted from contaminants other than Cu or a lethal combination of contaminants (Frank and Borg 1979; Schummer et al. 2011). In the livers of grey heron (*Ardea cinerea*) and intermediate egret (*Mesophoyx intermedia*), Horai et al. (2007) found concentrations of Cu as high as 4970 and 2420 mg kg^{-1} dw, respectively.

Many scientific publications document the usefulness of ducks (genera *Anas* and *Aythya*) in biomonitoring studies, and it has been reported that wetland birds can accumulate much larger amounts of Cu than terrestrial birds, with the largest concentrations recorded in contaminated areas (Hernandez et al. 1999; Horai et al. 2007; Schummer et al. 2011). Hernandez et al. (1999) analyzed the concentration of Cu in omnivorous wetland birds in a polluted area of the Doñana National Park (NDP) in Spain and showed that liver Cu levels were lower before the ecological catastrophe in 1998, when waste water heavily contaminated with heavy metals (including Cu) leaked from a damaged mine tank into groundwaters. Concentrations of Cu in the liver of birds surveyed before the disaster were below 35 mg kg^{-1} dw, and after 1998 ranged from ~52 to 1300 mg kg^{-1} dw, and at almost 480 mg kg^{-1} dw in the common pochard (Hernandez et al. 1999).

The accumulation of Cu in the liver may differ significantly between bird species. Within the *Anatidae*, the mute swan can accumulate more Cu in the liver than other species even in the absence of environmental contamination (Beyer et al. 1998). Parslow et al. (1982) detected the highest and the lowest Cu concentrations in common pochard and common snipe (*Gallinago gallinago*): 603 and 33 mg kg^{-1} dw, respectively. Moreover, comparisons between species living in the same areas indicate that *Aythya* and *Netta* genera, closely related but with different feeding habits, may also accumulate more Cu in the liver than other waterfowl

species (Figuerola and Green 2000). In El Hondo, Spain, a wetland by a river heavily polluted by agricultural pollution, samples analyzed from marbled teal (*Marmaronetta angustirostris*) and white-headed ducks (*Oxyura leucocephala*) showed that ~40% of the animals had liver Cu levels above 100 mg kg^{-1} ww (~350 mg kg^{-1} dw) (Taggart et al. 2009), these being above the level indicating acute Cu poisoning in a study of Canadian geese (Henderson and Winterfield 1975). The authors suggest that such a large concentration of Cu in the liver of the birds, indicating intoxication, probably depended on several polluting factors, e.g., geological, agricultural (including plant Cu fungicide), or industrial sources near El Hondo, or key invertebrate food bioaccumulating Cu at unusual levels (Taggart et al. 2009). The interpretation of biomonitoring results obtained from terrestrial birds and waterfowl is thus very difficult, and Pillatzki et al. (2011) suggest that many factors can influence the interpretation of hepatic Cu levels, including various interspecies sensitivities, differences in hepatic accumulation by species and age, interaction of copper with other elements, and seasonal variation (Eisler 1998; Pillatzki et al. 2011).

Birds of prey are particularly susceptible to the effects of heavy metals as they occupy the uppermost positions in the food pyramid, and their diet can accumulate a significant amount of particularly toxic trace elements (Jager et al. 1996; Ek et al. 2004; Kalisińska et al. 2008; Zaccaroni et al. 2008; Naccari et al. 2009; Licata et al. 2012). Based on an analysis of scientific papers, it was found that the average concentration of Cu in the liver and kidney in wild birds is ~17 and 14 mg kg^{-1} dw, respectively (Fig. 4.1) (Hontelez et al. 1992; Zaccaroni et al. 2008; Komosa et al. 2012). In the liver and kidney of the common buzzard (*Buteo buteo*) and common kestrel (*Falco tinnunculus*), birds with a similar diet sourced from Poland and the Czech Republic, Kalisińska et al. (2009a) determined Cu levels and noted significant differences in kidney Cu levels between these two species of birds: Cu was significantly lower in the common buzzard than in the common kestrel (~16.0 and 10.0 mg kg^{-1} dw, respectively). In the livers of both species, the concentration of Cu was below 17.2 mg kg^{-1} dw.

Ecotoxicological analysis on Cu in the common buzzard in the Netherlands was conducted by Jager et al. (1996) and Hontelez et al. (1992), with concentrations of Cu in the livers in both studies similar, ranging from 13 to 16 mg kg^{-1} dw. In the case of birds from the south of Europe, e.g., Sicily in Italy, we noticed larger concentrations of Cu in the liver, at >39 mg kg^{-1} dw, i.e., more than two times higher than in the buzzards from the Netherlands, Poland, and Czech Republic, which may be associated with the higher natural level of Cu in the soils in Italy and a higher affinity of this element to the volcanic rocks (Naccari et al. 2009; Licata et al. 2012).

In European literature we found several publications on Cu in owls (Fig. 4.1). In different areas of the Calabria region in Italy, Zaccaroni et al. (2008) observed that Cu concentrations were generally higher in the liver of the marsh harrier (*Circus spilonotus*) and tawny owl (*Strix aluco*), at 14.6 and 49.4 mg kg^{-1} dw, respectively, while in the marsh harrier and barn owl (*Tyto alba*), the kidney Cu concentration did not exceed 17.5 mg kg^{-1} dw, suggesting that the values of Cu in the parenchymal

organs of the analyzed birds of prey are within the range for physiological values and do not show the presence of any deficiency or excess. Komosa et al. (2012) in the long-eared owl (*Asio otus*) from eastern Poland and Kim and Oh (2012) in eagle owls (*Bubo bubo*) and brown hawk-owls from eastern Asia detected Cu levels similar to those observed in birds of prey from Italy, with concentrations of Cu in the liver not exceeding 17 mg kg^{-1} dw. Data on Cu in wild birds obtained from the northern hemisphere are in many cases difficult to interpret, especially given the small number of examined specimens. Cu concentrations in the liver and kidney of various birds of prey are generally lowest in piscivorous species and highest in medium-size birds and carnivorous species (Fig. 4.1). In comparison of piscivorous bird species, e.g., European white-tailed eagle (*Haliaeetus albicilla*) and North American bald eagle sometimes show substantial differences. The highest concentration of Cu in the muscle tissues of white-tailed eagle was found by Falandysz et al. (1988) at ~30 mg kg^{-1} dw (range, 15–320 mg kg^{-1} dw) and in key parenchymal organs ~20 mg kg^{-1} dw. In white-tailed eagle specimens collected in northwestern Poland in 1991–1995, Falandysz et al. (2001) observed hepatic and nephric Cu levels ranging from ~6–36 to ~7–40 mg kg^{-1} dw, respectively. Six years later in the same Polish region, Kalisińska et al. (2006) observed even lower concentrations of Cu in the liver and kidney in white-tailed eagles, with the average concentration of Cu below 8 mg kg^{-1} dw in either organ. Much higher concentrations of Cu in the liver and the kidney have been reported in bald eagle in North America; the average levels in both organs ~33 mg kg^{-1} dw range between 9 and 395 mg kg^{-1} dw (Stout and Trust 2002; Mierzykowski and Todd 2012). In Cu-contaminated sites, high Cu levels in kidneys and muscles have been reported in omnivorous and herbivorous bird species such as the common pochard and Eurasian coot (*Fulica atra*), at ~48 and 44 mg kg^{-1} dw, respectively (Gomez et al. 2004). Lower concentrations in these organs have been detected in crab- and fish-eating predators such as the black-headed gull (*Chroicocephalus ridibundus*) at <12 and <17 mg kg^{-1} dw, respectively (Hernandez et al. 1999; Gomez et al. 2004; Orlowski et al. 2007). Muscle tissues of birds are tested only occasionally for Cu, even though it is a muscle (representing 30%–40% of the weight of the bird) that can be the source of this metal for predatory species. Available scientific literature presents a certain tendency where the highest Cu muscle levels are recorded in piscivorous birds from freshwater ecosystems, such as the grey plover (*Pluvialis squatarola*), greylag goose, and red knot, 51, 43, and ~30 mg kg^{-1} dw, respectively. Lower concentrations of Cu have been found in the muscle of birds of prey and omnivorous birds (Lucia et al. 2008, 2010; Kalisińska et al. 2004, 2008; Bojar and Bojar 2009; Licata et al. 2012). In birds of prey, e.g., white-tailed eagle and Eurasian buzzard, the average concentration of Cu in the muscle is similar at below 32 mg kg^{-1} dw (Falandysz et al. 1988; Licata et al. 2012). The biggest difference in this respect was noted in the case of a highly emaciated female peregrine falcon, in which the concentration of Cu in the muscle was more than two times higher (~67 mg kg^{-1} dw) (Kalisińska et al. 2008). The lowest muscle Cu levels are observed in birds with varied diets, including mallard and tufted ducks (*Aythya fuligula*) from Polish territories (~1.6–6 and ~6 mg kg^{-1} dw, respectively) (Szymczyk and Zalewski 2003; Kalisińska et al. 2004).

Binkowski et al. (2013) suggested that Cu levels in bird tissues may significantly differ between waterfowl, where the concentration of Cu in the pectoral muscle (~40 mg kg^{-1} dw) of coot from the Zator area (fishing farms), southern Poland, was almost 7 times higher than in mallard from northwestern Poland as determined by Kalisińska et al. (2004). In some water ponds, some Cu compounds are used as algaecides to control the growth of phytoplankton and filamentous algae and to control certain fish diseases. Their possible transfer into the food chain may cause a significant increase in the concentration of Cu in the muscles of birds.

Passerines such as the house sparrow (*Passer domesticus*) and great and blue tit (*Parus major* and *Cyanistes caeruleus*) play an important role in biomonitoring in terrestrial ecosystems and have been studied in Finland, Belgium, Serbia, Portugal, Turkey, and China. In these birds, Cu concentrations are most often analyzed in the feathers and eggs and much less frequently in the liver, kidneys, and muscles (Dauwe et al. 2002; Nam et al. 2005; Gong et al. 2012; Costa et al. 2013). In Finland, Kekkonen et al. (2012) found that concentrations of Cu in the liver of house sparrows sampled in the 1980s were higher in urban than in rural areas, at 4.03 and 3.7 mg kg^{-1} dw, respectively. More than 30 years later, Millaku et al. (2015) studied the same species from a polluted area in Serbia and observed an order of magnitude higher concentration of Cu in the liver (20.2 mg kg^{-1} dw) and kidney (28.4 mg kg^{-1} dw) and considered the species a good bioindicator of the terrestrial environment. The authors of many studies suggest that the accumulation of Cu in the respective tissues depends on the degree of exposure (Kekkonen et al. 2012; Millaku et al. 2015). In China, Gong et al. (2012) showed that hepatic Cu in the tree sparrow (*Passer montanus*) differed depending on the area of foraging, mining area (MA), urban district (UD), or reference site (RS), where hepatic Cu could be arranged in the following descending order: UD > MA > RS (~25.6, 22.7, and 12.2 mg kg^{-1} dw, respectively). In addition to anthropogenic pollution, higher Cu concentrations in the livers in these insectivorous birds may be associated with the local use of copper-based agricultural fungicides and diet. Some terrestrial songbirds fed mainly on spiders, which contain high levels of Cu in their hemocyanin (Eeva et al. 2005, Belskii and Belskaya 2013). The concentration of Cu in the muscles of passerine species sometimes varies between contaminated sites, e.g., in China and Turkey, respectively; muscle Cu levels were <7 and 25 mg kg^{-1} dw (Albayrak and Mor 2011; Gong et al. 2012).

5.3.2 Relationship Between Cu Levels and Age and Sex of Terrestrial Birds

Studies on the relationship between the age of wild birds and the concentration of Cu in their organs do not allow firm conclusions to be drawn. Sometimes, liver Cu levels show a significant correlation with age and sex, e.g., in coots and mallards, while there are discrepancies in others. Taggart et al. (2006) in Spain did not note an increase in Cu concentration with age as reported in the greylag goose by Mateo and Guitart (2003), in the barn owl by Esselink et al. (1995), in the bald eagle by Stout

and Trust (2002), in the white-tailed eagle by Kalisińska et al. (2006), or in passerine bird species by Berglund et al. (2015). In the black duck (*Anas rubripes*), Gochfeld and Burger (1987) observed significantly higher liver Cu concentration in males than in females. Similarly, Schummer et al. (2011) showed differences in liver Cu between females and males, suggesting that the differences reflected the different feeding areas of the males and females. Moreover, Barjaktarovic et al. (2002) and Kalisińska et al. (2004) observed that for scoter (*Melanitta* sp.) from Canada and Mallard from Poland, sex was not a factor correlating to kidney Cu.

The aforementioned test results indicate that copper impurities are present in the environment for a long time, during which both typically aqueous and terrestrial birds are exposed. There is only fragmentary data on Cu in the organs and tissues of typically terrestrial species in Asia, including China. More comprehensive studies are recommended in this regard, especially in light of the rapid industrialization in Asia in recent decades and the greatest share of this continent in global anthropogenic atmospheric Cu emission.

5.4 *Bioaccumulation of Copper in Mammalian Liver, Kidney, and Muscle Tissues*

Cu concentrations in the organs crucial for detoxification in wild mammal taxa from the northern hemisphere can be arranged in the following ascending order: piscivorous < omnivorous < carnivorous < herbivorous (Arnhold et al. 2002). Herbivores accumulate the highest amount of Cu and are the subject of intense and multifaceted research in the USA, Canada, and Europe, despite the fact that Cu deficiencies are often reported in herbivorous and omnivorous mammals (Skibniewski et al. 2016). There are also many signs that predatory mammals, acting as the final link in the trophic chain, tend to accumulate Cu in tissues and organs. It seems that this observation is strongly pronounced in Europe, especially in southern parts, e.g., in Spain, where the environment has been exposed to a lot of anthropogenic deposition of Cu (Millan et al. 2008). In mammals associated with freshwater ecosystems, Cu levels are not so high; in this group the highest concentrations have been found in piscivores. Copper poisoning in terrestrial mammals appears to be rare, thanks to their efficient mechanisms to regulate Cu stores, so they are generally protected from excess dietary Cu levels.

5.4.1 Piscivorous Mammals (Fish-Eating Mammals)

Piscivorous mammals play an important role in biomonitoring, e.g., American mink (*Neovison vison*) and European otter (*Lutra lutra*), which have been studied in the USA, Canada, and various European countries (Fig. 4.2). In the 1980s, Stejskal et al. (1989) determined reference ranges for Cu concentrations in the liver and kidney of

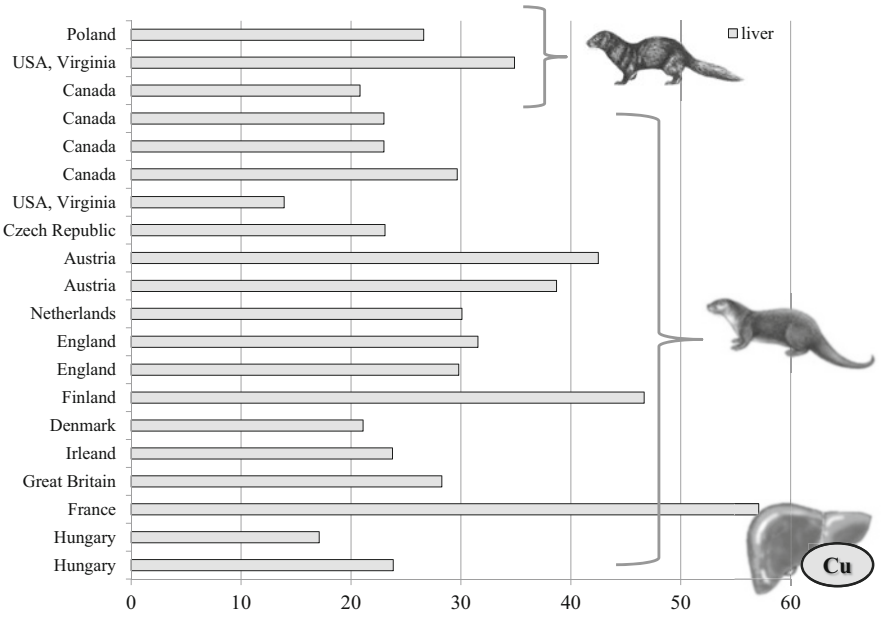

Fig. 4.2 The concentration of Cu (mg kg^{-1} dw) in livers of American mink and otter from Europe and North America based on data by American minks (Brzezinski et al. 2014; Harding et al. 1998; Ogle et al. 1985; Wren 1984) and otters (Anderson-Bledsoe and Scanlon 1983; Broekhuizen 1987; Gutleb 1992; Gutleb et al. 1998; Lanszki et al. 2009; Lemarchand et al. 2010; Lodenius et al. 2014; Mason and Stephenson 2001)

mink at ~15–250 and ~10–33 mg kg^{-1} dw, respectively. A review of scientific literature shows that the concentrations of Cu in the liver and kidney of North American mink are usually slightly lower than the corresponding specimens in the Central Europe, not exceeding 35 mg kg^{-1} dw (Ogle et al. 1985; Harding et al. 1998; Brzezinski et al. 2014). Sometimes individual specimens of these piscivorous mammals have liver Cu > 190 mg kg^{-1} dw, albeit this value is considered normal for these mink (Ogle et al. 1985; Stejskal et al. 1989). We have found only one European work, Brzezinski et al. (2014), on the concentrations of Cu in feral and ranch minks, observing that liver Cu concentrations in ranch mink were almost two times higher than in feral mink from Polish National Parks, i.e., 42.8 vs. 22.4–28.1 mg kg^{-1} dw, respectively. The authors suggest that this is associated with the high Cu level in feed additives given to ranch mink to maintain normal hair pigmentation (Brzezinski et al. 2014).

Ecotoxicological studies conducted in European countries, including Denmark, Czech Republic, France, Hungary, Finland, Ireland, and Austria, have shown that the concentrations of Cu in the liver of the Eurasian otter, a top predator in aquatic food chains, range from ~23 to 57 mg kg^{-1} dw, while kidney levels do not exceed 20 mg kg^{-1} dw (Gutleb et al. 1998; Mason and Stephenson 2001; Lanszki et al. 2009; Lemarchand et al. 2010; Walker et al. 2010, 2011; Lodenius et al. 2014)

(Fig. 4.2). Kang et al. (2015) showed that hepatic copper concentrations in Eurasian otter (*Lutra lutra*) from South Korea did not exceed 30 mg kg^{-1} dw, similar to levels reported in England, Hungary, and Austria (Gutleb et al. 1998; Lanszki et al. 2009; Walker et al. 2010, 2011), but lower than those reported in Finland and France where hepatic copper levels were >46 mg kg^{-1} dw (Lemarchand et al. 2010; Lodenius et al. 2014) (Fig. 4.2). In North American river otter (*Lontra canadensis*), concentrations of Cu in the liver and kidney appear to be consistent with the results obtained in individuals from Europe, at <35 and 6 mg kg^{-1} dw (Fig. 4.2). There is very little data on the concentration of Cu in muscle tissues in piscivorous species. Lodenius et al. (2014) showed that the concentration of Cu in the muscle of otters from Finland was below 6.5 mg kg^{-1} dw, an order of magnitude lower than those reported for the liver and kidney.

5.4.2 Carnivores and Omnivores (Mustelidae)

In scientific literature we found no data on toxic thresholds for Cu in wild predatory mammals. It is known that in the domestic dog (*Canis lupus familiaris*), natural Cu concentrations in the liver are from 200 to 400 mg kg^{-1} dw (Skibniewska et al. 2012). Meanwhile, Puls (1994) had shown that a concentration of 20 mg kg^{-1} ww (~67 mg kg^{-1} dw) could cause potential nephrotoxic effects. In the kidney of wild carnivores and omnivores, Cu concentrations typically range from 11 to 77 mg kg^{-1} dw (Fig. 4.3) and in the muscle from 2 to ~41 mg kg^{-1} dw (Millan et al. 2008; Bilandžić et al. 2012). Most of the ecotoxicological works mentioning concentrations of copper in the tissues and organs of carnivores and omnivores concern European countries, while the few papers mentioning North American predatory mammals were in relation to trans-Arctic mammals such as polar bears (*Ursus maritimus*) and polar foxes (*Alopex lagopus*) (Hoekstra et al. 2003; Rush et al. 2008; Routti et al. 2011).

Mean Cu concentrations in the liver of wild carnivores vary widely among species. In mammalian predators from the northern hemisphere, the average concentration of Cu in the liver ranged from ~5.2 to 230 mg kg^{-1} dw, with only sporadically levels >400 mg kg^{-1} dw reported, e.g., indicating subclinical hepatitis in European red foxes from Spain (between 205 and 950 mg kg^{-1} dw) (Millan et al. 2008). Recent ingestion of contaminated water or food is likely to be responsible for these single cases of increased Cu. The highest obtained Cu concentrations in terrestrial top carnivores and omnivores measured in the liver can be placed in the following descending order: Arctic wolf (*Lupus canis*) > polar bear > stone marten and pine marten (*Martes foina* and *Martens martens*) > Eurasian badger (*Meles meles*) > wolverine (*Gulo gulo*) > brown bear (*Ursus arctos*) > red fox > Iberian lynx (*Lynx pardinus*) > raccoon dog (*Nyctereutes procyonoides*) (Fig. 4.3) (Medvedev 1999; Gamberg and Braune 1999; Kannan et al. 2007; Millan et al. 2008; Bilandžić et al. 2010; Routti et al. 2011; Bilandžić et al. 2012). The highest concentrations of Cu in the liver of the Canadian Arctic wolf ranged from ~157 to 230 mg kg^{-1} dw (Gamberg and Braune 1999). Much lower concentrations of Cu

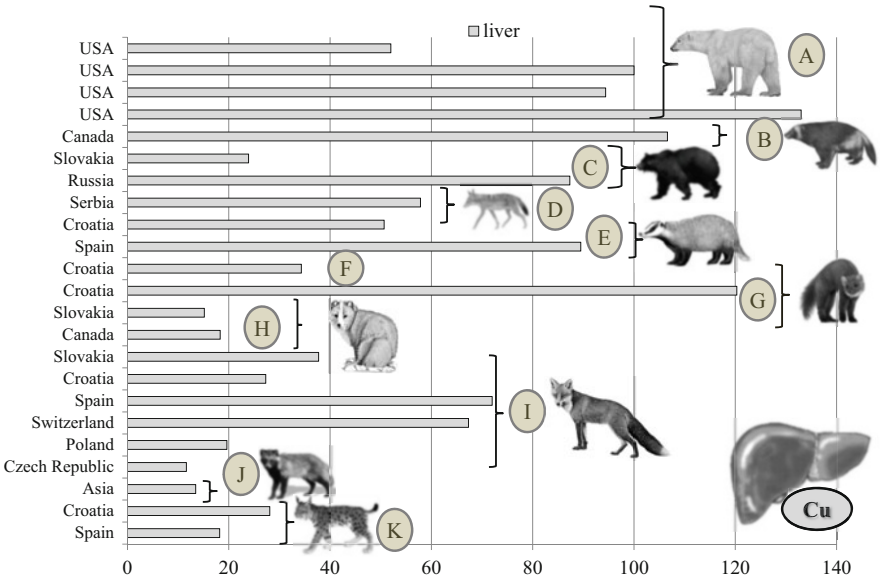

Fig. 4.3 The concentration of Cu (mg kg^{-1} dw, after conversion from wet weight to dry weight; we assumed that the liver contain 70% of water) in livers of carnivores and omnivores from North America, Europe, and Asia: A. polar bear (Kannan et al. 2007; Routti et al. 2011; Rush et al. 2008; Woshner et al. 2001), B. wolverine (Hoekstra et al. 2003), C. brown bear (Čelechovská et al. 2006; Medvedev 1999), D. golden jackal (Ćirović et al. 2015), E. Eurasian badger (Bilandžić et al. 2012; Millan et al. 2008), F. European pine marten (Bilandžić et al. 2012), G. stone marten (Bilandžić et al. 2010), H. polar fox (Hanusova et al. 2007; Hoekstra et al. 2003), I. red fox (Bilandžić et al. 2010; Dip et al. 2001; Hanusova et al. 2007; Jankovská et al. 2010; Millan et al. 2008), J. raccoon dog (Hou et al. 2017), K. Eurasian lynx and Iberian lynx (Bilandžić et al. 2012; Millan et al. 2008)

were found in individuals of the European gray wolf from Croatia, an order of magnitude smaller at <22 mg kg^{-1} dw (Bilandžić et al. 2012). Hoffmann et al. (2010) suggested that the differences in metal levels (including Cu) between organs are consistent with the variability observed in other studies on metal levels in Arctic and sub-Arctic wolf prey, including the moose (*Alces alces*) and caribou (*Rangifer tarandus*) (Aastrup et al. 2000). Only in some predatory mammals did the average concentration of Cu in the liver exceed 100 mg kg^{-1} dw, including the wolverine, stone marten, and polar bear (Fig. 4.3). Occasionally, in some omnivores from the Mustelidae family, e.g., a stone marten from suburban area in Croatia, concentrations of Cu in the liver exceeded ~120 mg g^{-1} dw (~36.1 mg kg^{-1} ww) albeit not approaching the toxic level for domestic dog (Bilandžić et al. 2010). In polar bears the Cu concentrations were comparable to those reported for other marine mammals, including sea otters (*Enhydra lutris*) from coastal California (Kannan et al. 2007).

In Europe, ecotoxicological studies most commonly use the red fox, which meets a number of the established criteria for bioindication (Dip et al. 2001; Naccari et al. 2013; Binkowski et al. 2016), and studies involving these mammals have been carried out in various countries, e.g., Czech Republic, Slovakia, Switzerland,

Spain, Italy, Croatia, Hungary, and Poland. It has been shown that the concentrations of Cu in the liver, kidney, and muscles of this species ranged from ~12 to 90, 6 to 60, and 9 to 27 mg kg^{-1} dw, respectively (Millan et al. 2008; Bilandžić et al. 2010; Naccari et al. 2013; Binkowski et al. 2016). In North American polar foxes, the average concentration of Cu in the liver did not exceed ~20 mg kg^{-1} dw (Hoekstra et al. 2003). Only in one case of a gray wolf from Canada did the average concentration of Cu in the kidney exceed ~67 mg kg^{-1} dw, a level deemed likely to cause nephrotoxic effects in mammals (Puls 1994; Gamberg and Braune 1999). A concentration of Cu in the kidney >25 mg kg^{-1} dw (~9 mg kg^{-1} ww) was recorded in a Croatian stone marten, higher than the levels observed in the polar and brown bears, red foxes, and badgers from the northern hemisphere (Fig. 4.4).

Little is known about muscle Cu levels in carnivores and omnivores. Concentrations of ~12 mg kg^{-1} dw have been found in Mustelidae and the European badger (Millan et al. 2008; Bilandžić et al. 2010, 2012). In addition, muscle Cu concentrations <9 mg kg^{-1} dw have been reported in canines, such as raccoon dogs, red foxes, polar foxes, the Egyptian mongoose (*Herpestes ichneumon*), and common

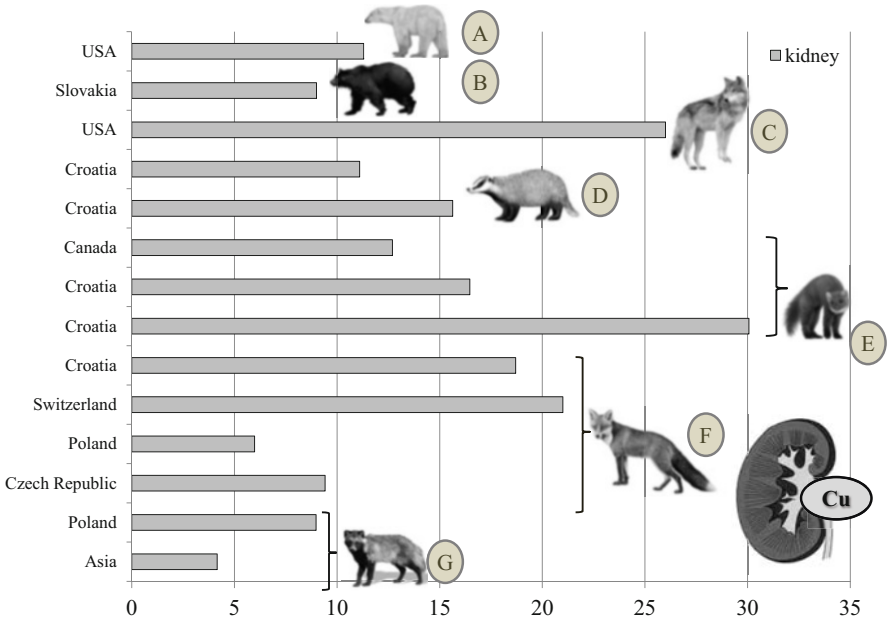

Fig. 4.4 The concentration of Cu (mg kg^{-1} dw, after conversion from wet weight to dry weight; we assumed that the kidney contain 75% of water) in the kidney of carnivores and omnivores from Europe, North America, and Asia. Based on data: A. polar bear (Woshner et al. 2001); B. brown bear (Čelechovská et al. 2006); C. grey wolf (Hoffmann et al. 2010); D. Eurasian badger (Bilandžić et al. 2012); E. American marten (Harding et al. 1998), pine marten (Bilandžić et al. 2012), stone marten (Bilandžić et al. 2010); F. red fox (Bilandžić et al. 2010; Dip et al. 2001; Jankovská et al. 2010; Kopczewski and Kopczewska 1996); G. raccoon dog (Hou et al. 2012; Mertin et al. 2006)

genet (*Genetta genetta*) from Spain (Mertin et al. 2006; Hanusova et al. 2007; Millan et al. 2008; Bilandžić et al. 2010). The lowest concentration of Cu in the muscle, at <2 mg kg^{-1} dw, has been detected, for example, in felines in southern Europe, including Iberian and Eurasian lynxes (Millan et al. 2008; Bilandžić et al. 2012). However, the greatest concentration of Cu in the muscles, >41 mg kg^{-1} dw, was observed by Horai et al. (2006) in the Javan mongoose (*Herpestes javanicus*) in Japan. Differences in diet are likely to provide the main explanation for resultant differences in Cu levels in the tissue of wild mammals. The mongoose family prefers to eat lizards, snakes, small mammals and birds, as well as invertebrates, mainly spiders associated with a soil habitat (Kalisińska et al. 2009b). Similarly, badgers feed mainly on earthworms and insects, where the known application of agricultural chemicals can lead to higher accumulation of Cu. The lynx showed the lowest levels of Cu in muscles than other carnivores; the diet of this mammal comprises 85%–90% rabbits. Canidae and Mustelidae have more varied feeding habits, including small birds, reptiles, and eggs (Millan et al. 2008).

5.4.3 Omnivorous Mammals (Raccoon and Wild Boar)

The raccoon (*Procyon lotor*) is a predator with a diet similar to the wild boar (*Sus scrofa*). Raccoons come from North America and are an invasive species in Europe (Lanocha et al. 2014). In European biomonitoring studies, the extent of environmental pollution with trace elements is assessed in the omnivorous wild boar; however, we have not found any publications about Cu concentration in raccoons from Europe (Amici et al. 2012; Roslewska et al. 2016). Comparing the North American raccoon to the European wild boar, the concentration of Cu in the raccoon liver is greater than in wild boar, at <47 and <26 mg kg^{-1} dw, respectively (Fig. 4.5) (Burger et al. 2000, 2002; Levengood 2001; Zaccaroni et al. 2003; Gasparik et al. 2012; Souza et al. 2013; Hernandez et al. 2017). Sometimes concentrations of Cu in the liver are found an order of magnitude higher, e.g., in wild boar from Italy, at ~154 mg kg^{-1} dw (Fig. 4.5) (Amici et al. 2012). In many areas of Italy, soils are volcanic. Cu that occurs in the soil and vegetables is tightly linked to the volcanic origin, and the high hepatic Cu in the wild boar may likely be due to such high dietary exposure (Amici et al. 2012).

In the case of the kidney, an opposite trend can be observed, with the concentration of Cu in the kidney of the North American raccoon not exceeding 20 mg kg^{-1} dw and in the European wild boar ~30 mg kg^{-1} dw (Fig. 4.5) (Wren 1984; Burger et al. 2000, 2002; Levengood 2001; Długaszek and Kopczynski 2011; Gasparik et al. 2012; Souza et al. 2013). Concentrations of hepatic Cu detected in raccoon from polluted areas in North America (including those exposed to coal ash dust) ranged from ~26 to ~47 mg kg^{-1} dw, and the kidney Cu did not exceed ~17 mg kg^{-1} dw, well below the reference values for the liver and kidneys in unexposed piscivorous minks (<250 and <33 mg kg^{-1} dw, respectively) (Stejskal et al.1989; Burger et al. 2002; Souza et al. 2013). Little is known about the concentrations of Cu in the muscles of North American raccoon, with studies sometimes significantly different

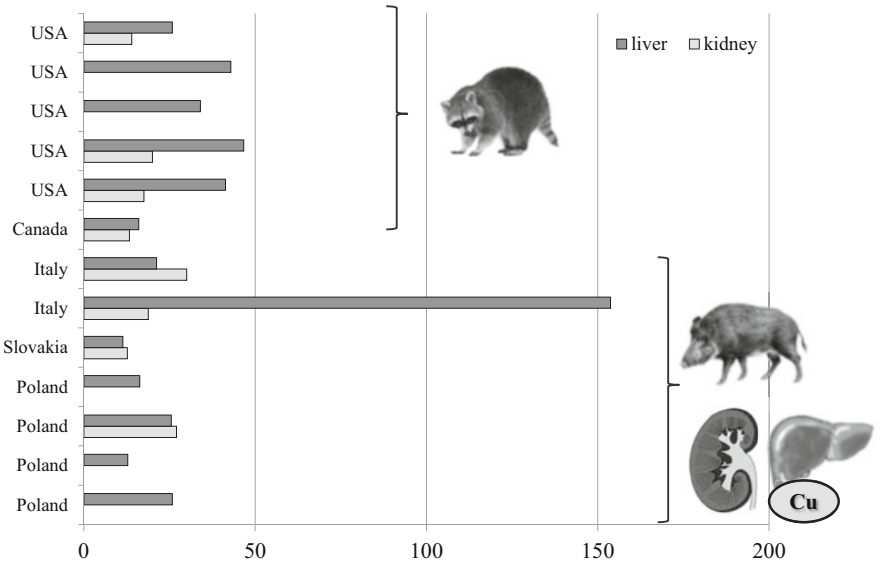

Fig. 4.5 The concentration of Cu (mg kg^{-1} dw, after conversion from wet weight to dry weight; we assumed that the kidneys contain 80% of water and the liver as well as muscles 70% of water) in the kidney and liver of omnivores from North hemisphere. Based on data: raccoon, North America (Burger et al. 2002; Hernandez et al. 2017; Levengood 2001; Souza et al. 2013); wild boar, Europe (Amici et al. 2012; Bakowska 2014; Burger et al. 2002; Długaszek and Kopczynski 2011; Gasparik et al. 2012; Krynski et al. 1991; Mazurek et al. 1991; Wren 1984; Zaccaroni et al. 2008)

from each other, but in contaminated sites, levels range from >6 to <38 mg kg^{-1} dw (Burger et al. 2002; Souza et al. 2013).

Publications after 1990 on Cu in wild boar have concerned only European countries. Pollock (2005) proposed a biochemical criteria for determining the concentration of Cu in the liver, which indicated the following levels: deficiency (<35 mg kg^{-1} dw), marginal (35–87.5 mg kg^{-1} dw), and optimal (>87.5 mg kg^{-1} dw). The concentration of Cu in the liver of European wild boar ranged from ~3.4 mg kg^{-1} ww (11.4 mg kg^{-1} dw) in Slovakia to ~25.5 mg kg^{-1} dw in Poland (Gasparik et al. 2012; Bakowska 2014). Given the above, we can conclude that wild boars from Poland and Slovakia were deficient in Cu. The kidneys of these mammals had similar values of Cu in the liver, at 3.8 mg kg^{-1} ww (12.7 mg kg^{-1} dw) to ~27.0 mg kg^{-1} dw (Gasparik et al. 2012; Bakowska 2014). The concentration of Cu in European wild boar muscle, especially in the areas of Cu-rich soil, appears to be greater than has been reported for the North American raccoon, ranging between ~1.6 mg kg^{-1} ww (5.5 mg kg^{-1} dw) in Hungary, ~7.5 mg kg^{-1} ww (25 mg kg^{-1} dw) in Poland, and ~12.2 mg kg^{-1} ww (40.7 mg kg^{-1} dw) in Italy (Skobrak et al. 2010; Amici et al. 2012; Roslewska et al. 2016). The greatest levels (~90 mg kg^{-1} dw) were recorded in the muscle of wild boar in Italy, although those high values do

not appear to cause particular concern when compared with exposure in humans (Gupta and Gupta 1998; Amici et al. 2012).

5.4.4 Herbivorous Mammals

Differences in the concentrations of the hepatic, kidney, and muscle Cu in between examined wild mammals likely result from the varied diets. Herbivorous animals take in fiber from vegetable food, a component consisting of poly- and oligosaccharides, which increase the absorption and retention of Cu and other elements. In addition, the absorption and metabolism of Cu are significantly affected by elements such as sulfur (S) and molybdenum (Mo). The presence of S and Mo contribute to Cu deficiency, with lower than normal concentrations of these elements in the diet of animals conducive to the bioaccumulation of Cu. The antagonistic relationship between Cu, Mo, and S in ruminants lowers Cu bioavailability and has a negative impact on Cu absorption (Kabata-Pendias and Szteke 2015). In red deer and roe deer (*Capreolus capreolus*) as well as other herbivorous species including moose and European hare (*Lepus europaeus*), the highest concentrations of Cu are recorded in the liver (Gasparik et al. 2004; Reglero et al. 2008; Jarzyńska and Falandysz 2011; Skibniewski et al. 2016). In a study by Ivan (1993), the normal level of Cu in the liver of ruminants ranges from 100 to 400 mg kg^{-1} dw, and a value <25 mg kg^{-1} dw indicates a possible Cu deficiency. It seems that the capacity of the liver to accumulate Cu differs between ruminants. Lazarus et al. (2008) showed that hepatic copper levels in Croatian deer ranged from ~1.6 to 54 mg kg^{-1} ww (~5.3–180 mg kg^{-1} dw). Concentrations of Cu in the liver were comparable with levels reported for red deer in Spain (51.7 mg kg^{-1} dw), Slovak Republic (44.3 mg kg^{-1} dw), Poland (59 mg kg^{-1} dw), and Norway (86.7 mg kg^{-1} dw) (Gasparik et al. 2004; Vikøren et al. 2005; Reglero et al. 2008; Jarzyńska and Falandysz 2011). At the same time, in some specimens from Poland and Germany (areas with copper-deficient soils), the concentration of Cu in the liver was ~3.0 mg kg^{-1} ww (10 mg kg^{-1} dw), which may suggest a deficiency of this element; these low levels imply that red deer have the ability to adapt to low nutritional levels of Cu (Hecht 1996; Skibniewski et al. 2015). In addition, a possible Cu deficiency has been reported in free-ranging moose from Alaska, Northwest Minnesota, and Sweden. Ecotoxicological studies on herbivores were carried out by Vikøren et al. (2011) in Norway, who observed that moose had a significantly higher Cu concentration in the liver (222 mg kg^{-1} dw) than roe deer (112 mg kg^{-1} dw) and reindeer (105 mg kg^{-1} dw). Moreover, the Cu status of moose and roe deer in Norway are among the highest reported in Europe. Cu content in the liver of Alaskan elks reported by Gamberg et al. (2005) was definitely higher than that observed in Poland: ~43.5 vs. 23.1 mg kg^{-1} ww, respectively (145.1 and 76.9 mg kg^{-1} dw) (Skibniewski et al. 2016). Importantly, red deer from European countries did not seem to accumulate and retain Cu amounts that would cause a harmful effect. Much higher mean concentrations of Cu in the liver have been recorded in some North American white-tailed deer, at ~27.4–122 mg kg^{-1} ww (91.3–406.7 mg kg^{-1} dw); still, these concentrations did not exceed ~150 mg kg^{-1}

ww (500 mg kg^{-1} dw), i.e., a level associated with Cu poisoning (Sleeman et al. 2010). In the kidneys of Canadian porcupine caribou (*Rangifer tarandus granti*), red deer from Croatia and Slovakia, and in moose from Canada and Russia, concentrations of Cu did not exceed ~19.0 mg kg^{-1} dw (Gasparik et al. 2004; Gamberg et al. 2005; Lazarus et al. 2005, 2008). Data obtained from various studies may sometimes differ, i.e., in the case of porcupine caribou from Canada and red deer from Poland, with the concentrations of Cu in the kidney in both studies >66.0 mg kg^{-1} dw (Jarzyńska and Falandysz 2011). The concentration of Cu in the muscles of herbivores usually does not exceed ~12 mg kg^{-1} dw, e.g., in red deer from Poland (~10 mg kg^{-1} dw), Croatia (~12 mg kg^{-1} dw), and Slovakia (~8 mg kg^{-1} dw), in roe deer from Poland (~11 mg kg^{-1} dw), and moose from Russia (~13 mg kg^{-1} dw) (Medvedev 1999; Karpinski 1999; Gasparik et al. 2004; Lazarus et al. 2008; Skibniewski et al. 2015).

5.4.5 Copper Levels in Relation to Age and Sex of Mammals

In addition to diet, trophic level, and environmental pollution, the level of Cu bioaccumulation depends on biological factors including age and sex. The results of research on the relationship between Cu content and the age and gender of wild mammals are in many cases markedly varied and difficult to interpret. Among predatory mammals, the relationship between the concentration of Cu in the liver and kidney compared to age has been analyzed in the mink, otter, red fox, polar fox, gray wolf, and polar bear, and no significant relationship has been found between these levels (Ogle et al. 1985; Dip et al. 2001; Kannan et al. 2007; Hoffmann et al. 2010; Kang et al. 2015; Binkowski et al. 2016). In contrast to the abovementioned examples, Skobrak et al. (2010) observed significant age-related differences in the concentration of Cu in the muscle of wild boar from Hungary. In ungulates, Vikøren et al. (2011) observed that Cu concentration increased significantly with age for moose, but no age relationship was found for reindeer. In predatory mammals, e.g., mink from North America, otter, red fox, polar fox, polar bear, wolverine, golden jackal, and gray wolf, no significant differences were found between females and males and the concentration of Cu (Ogle et al. 1985; Hoekstra et al. 2003; Kannan et al. 2007; Rush et al. 2008; Hoffmann et al. 2010; Ćirović et al. 2015; Kang et al. 2015; Binkowski et al. 2016). In contrast to the cited papers, Brzezinski et al. (2014) detected a statistically significant difference in the concentration of Cu in the kidney between male and female mink, similar to Mertin et al. (2006), who observed such a relationship in raccoon dog muscles. In addition, differences in the concentrations of Cu between sexes have been observed in ungulates, for example, in wild boar, but in the case of red deer from Norway, such gender-related differences have not been observed (Roslewska et al. 2016).

6 Biomarkers of Cu in Ecotoxicological Studies

Good biomarkers of Cu levels in humans and domestic animals seem to be found in serum, urine, hair, and the liver. Little is known about wild animals, e.g., due to the difficulty in obtaining biological samples (ATSDR 2004). Some researchers suggest that liver analysis is the gold standard for evaluating Cu reserves in ungulates, but liver samples can only be collected from dead animals. For live ruminants, serum ceruloplasmin can be used as a nonlethal biomarker of liver Cu in species such as muskoxen, sheep, and cattle, but it must be validated by age, sex, and species (Barboza and Blake 2001). Burger et al. (2000) indicated that sometimes the induction of metallothionein levels in raccoon tissues may be a more rapid and cost-effective method for screening metals, including Cu.

7 Conclusions

1. Proper interpretation of results requires knowledge of physiological concentrations of Cu in the tissues and organs, values reflecting the geochemical background, and consideration of the specificity of the animal species and diet.
2. Characteristics of useful bioindicators of terrestrial environmental pollution with Cu can be found among birds (birds associated with wetland areas, e.g., herbivores such as the mute swan, ducks from the genera *Anas* and *Aythya*, including the mallard, shoveler, pochard) and terrestrial passerines (house sparrow, great tit, and blue tit). Birds of prey are important for biomonitoring studies, as are rare species threatened with extinction and protected by law. Good bioindicators include the common buzzard, Eurasian kestrel, Eurasian eagle-owl, tawny owl, northern goshawk, peregrine falcon, white-tailed eagle, and bald eagle. In ecotoxicological studies on terrestrial mammals, a measurable response to pollution with Cu is exhibited by canids common in natural and seminatural habitats, e.g., the Arctic fox, red fox, raccoon, American mink, otters, and ungulates, such as the wild boar and red deer. It should be noted that in Europe, there is now the possibility of testing the concentration of Cu in increasingly popular alien species, e.g., mink, raccoon, and raccoon dog, which allows wider intercontinental comparative studies. In addition to information on common terrestrial species, there is a widely felt need for collection of comparative ecotoxicological data on Cu concentrations in other less abundant species (including mongoose, marten, and badger).
3. In biomonitoring studies on wild birds, it is advisable to perform noninvasive sampling of eggs and feathers and of hair from mammals. Internal tissues and organs (mainly liver, kidney, muscles, and bones for analyses of long-term impact) may be collected from dead specimens (hunting and/or roadkills). The deliberate killing of animals for research should be avoided for ethical reasons. In

field studies on wild mammals, Cu is analyzed in the liver, kidneys, muscles and much less frequently in the brain, bones, and hair.
4. The ecotoxicological effects of nano-Cu may be expected to be closely linked with aquatic environments and affect species inhabiting water ecosystems, mainly piscivores. Moreover, in the immediate future, the continued and increased reliance on coal combustion for electricity and heat production will result in an increased diffuse contamination of soils and waters with various elements, including Cu.
5. No efficient and good biomarkers for Cu exposure have been found, and still the best solution to evaluate the exposure is to measure Cu concentrations in wildlife and the environment.

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Chapter 5
Iodine, I

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Abstract Iodine is not a common element in nature, so many regions of the world suffer rather from a deficiency than an overabundance. The northern part of North America, most of South America, Africa, Asia (Himalaya), and Europe are classified as endemic regions with low iodine content.

Iodine plays a crucial role in the thyroid for hormone synthesis, which in turn regulates the regularity of most of metabolic pathways in mammalian cells. An iodine deficiency in animals causes malformation, growth retardation, decreased fertility, increased perinatal mortality, and lowered animal performance and productivity, e.g., reduced growth of wool, egg, and milk production. Moreover it has been shown that in roe deer, iodine-containing hormones play a role in the complex neurohormonal regulation of antler development. Antler weight increases with increasing iodine concentration.

The content of iodine in wild range animals is subject to evaluation only occasionally. For most wild-ranging species of mammals and birds, there is no information about iodine requirements. As more than 90% of dietary iodine is expelled by the kidneys, urine is found to be a good study material to assess recent iodine intake.

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1 Introduction

Iodine (I, in Latin iodum) is an element that was discovered in 1811 by Bernard Courtois (Baumann 1896). Its name comes from the characteristic violet color of its fumes (in Greek iodes). It is an uncommon element in nature, present in only trace amounts.

In the animal organism, iodine plays several important biological functions. As a main component of the thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4), every single molecule of T_3 and T_4 contains three atoms of iodine. According to the World Health Organization (WHO), this element is considered to be one of the factors with a direct effect on the health of the human population. In men, thyroid swelling (endemic goiter) and impaired intellectual development are the main symptoms of iodine deficiency. Iodine-deficiency disorders (IDD) include the increased risk of spontaneous miscarriages, stillbirths and deformations, increased mortality in infants in the perinatal period, irreversible brain damage in the fetus and infants, as well as thyroid tumors. The evident consequences of iodine deficiency are a decreased rate of metabolism, which then causes body weight gain, feeling cold, overstrain, and depressive disorders. Deficiencies of selenium, iron, and vitamin A exacerbate the effects of an iodine deficiency (American Thyroid Association 2003). In animals, a deficiency of iodine causes malformations, growth retardation, decreased fertility, increased perinatal mortality, and reduced animal performance and productivity, e.g., reduced growth of wool, egg, and milk production. Calves born to iodine-deficient dams may be stillborn, with goiter and areas of alopecia and subcutaneous edema (Potter et al. 1980, 1981). In roe deer the iodine-containing hormones produced by the thyroid gland play a role in the complex neurohormonal regulation of antler development. Antler weight increases with increasing iodine concentration (Lehoczki et al. 2011).

The thyroid gland in birds is located in the thoracic inlet. In this group of vertebrates, the clinical symptom of goiter is the effect of the pressure placed on organs adjacent to the gland. A loud wheezing respiration with the neck extended may occur if there is pressure against the trachea (Tollefson 1982).

It is estimated that about 1 million years ago, the distribution of iodine across the Earth was rather uniform, but subsequent Ice Ages caused a disturbance in that balance. Changes in the shape of the Earth's surface lead to iodine impoverishment in some regions and to enrichment in another (Merke 1965). This process is still in progress due to constant movements in the tectonic plates, earthquakes, and volcanic eruptions. The formation of iodine-deficient regions is observed particularly in areas with heavy precipitation (mountain areas) and repeated floods.

Globally, it is estimated that about 2 billion individuals have an insufficient iodine intake, with South Asia and sub-Saharan Africa particularly affected (Zimmermann 2009). In Europe, around 60% of the population consumes too little iodine (Delange et al. 2001). The rate of iodine deficiency is lowest in North and South America, at 10.1%. Populations settling in mountainous areas are most exposed to lack of iodine. As reported by Lee (2002), endemic low iodine areas include the northern part of

North America (the Great Lakes region, northwestern Pacific coast, surroundings of Mississippi, and Quebec province in Canada), most of South America, Africa, Asia (Himalaya), and Europe (Alps, Balkan Peninsula, Scandinavia, Carpathian and Sudety mountains, Germany particularly surrounding Munich, and Scotland).

2 General Properties

Iodine is a chemical element with ordinal 53 and atomic weight 126.9045, not common in the Earth's crust. Iodine is slightly soluble in water (Przewłocki and Śliwowski 2007).

Chemically separated iodine at room temperature forms gray-black crystals with a metallic gloss and characteristic smell (boiling point +184.35 °C). It sublimes easily, forming violet fumes. Its density is 4940 kg m^{-3}. Iodine is located in main group VII of the periodic table within the group of halogens (Przewłocki and Śliwowski 2007). The main valence of halogens is −1, but in special conditions (e.g., in photolysis), halogens may have a positive valence: +1, +3, +5, and +7. There are 36 isotopes of iodine, and 14 of these yield significant radiation. The only naturally occurring isotopes of iodine are the stable isotope ^{127}I and the radioactive isotope ^{129}I.

Binary compounds with other elements called halides form salts belonging to fluorides, chlorides, bromides, and iodides. Also, compounds of halogens with nonmetallic elements are known, as well as halogenated organic compounds with carbohydrates and carboxyl acids.

Iodine is a widespread trace element in the hydrosphere, lithosphere, atmosphere, and biosphere, although it usually only occurs in low concentrations. Iodine occurs in the Earth's crust at an average level of 0.45 mg kg^{-1} (Muramatsu and Wedepohl 1998; Wong 1991). The concentration of iodine in bedrock varies between 0.5 and 380 mg kg^{-1}, depending on whether the rock is igneous or sedimentary (ATSDR 2004).

3 Iodine Minerals, Production, and Uses

The primary source of iodine is rocks rich in this element, such as oil shales, which release iodine into the seas and oceans following erosion, making these and the creatures within (e.g., algae, shellfish, and fish) the most iodine abundant (Manz 1992). The concentration of iodine in seawater is about 50 μg L^{-1} and is 10 times higher than in freshwater (Manz 1992). The average iodine content in deep water carbonate rocks is about 0.03 ppm (or 30 ppb). Most of the iodine (>70%) in the Earth's surfaces exists in the oceans, at 45–60 μg L^{-1} (Wong 1991; Muramatsu and Wedepohl 1998). The continental crust, the oceanic crust (including seawater), and the remainder of the Earth's crust contains 119, 777, and 300 ppb of iodine,

respectively. Nearly 70% of total iodine is estimated to exist in ocean sediments (Muramatsu and Wedepohl 1998).

In the seas, iodine is usually present as IO^- and in a much smaller amount as iodides (I^-). Under solar light both forms decompose to elementary iodine, which evaporates into the atmosphere and is transferred back into land via winds and precipitation. The concentration of iodine in river water ranges between 0.1 and 18 μg L^{-1}, in rainwater from 0.1 to 15 μg L^{-1}, and in underground water 1 μg L^{-1}. The concentration of iodine in river water from urban areas often increases due to the discharge of municipal waste into refining installations (Kabata-Pendias and Pendias 2000).

With the increase in distance inland from the coast, the content of iodine in the air decreases (usually it is about 0.7 μg m^{-3}) (Hetzel and Marberly 1986). The content of iodine in the air depends on the vicinity of salt waters, wind direction (the lowest concentration is noted in continental winds), and environmental pollution (compounds of sulfur, mercury, lead).

Iodine (as iodide) is present in soils. The content may fluctuate widely within regions and between regions as a result of a number of factors (e.g., differences that occurred during geological formation, impact of glaciation, flooding, and soil erosion) (Rohner et al. 2014).

Areas with a low iodine content in the soil include Asia (including parts of China, India, Bangladesh, the Himalayan hillsides, Indonesia), Africa (mountain regions of Morocco and Algeria; large part of Western and Central Africa: Nigeria, Cameroon, the Central African Republic, Democratic Republic of Congo, and some regions of Eastern Africa like Uganda, Ethiopia), Europe (regions of the Alps and Pyrenees, inland areas of England and Wales, Greece, and the Netherlands), South America (including the Andes and inland Brazil), North America (Midwestern United States), Southern Australia, and the New Guinea Highlands (WHO 1999; Kabata-Pendias and Pendias 2000; Eastman and Zimmermann 2009; Zimmermann 2010). Additionally, postglacial areas, high mountains (Alps, Andes, Himalayas), are a great distance from the sea coast and floodplains (surroundings of the Ganges river in Southeastern Asia). One exception is Japan, as most Japanese soils (excluding paddy soils) are rich in iodine, at 14.2 mg kg^{-1} (Yuita and Kihou 2005), which is an effect of the mild climate, the oceans that surround this insular country, and the volcanic nature of the geology (Yuita 1994; Johnson 2003). By comparison, the mean content of iodine in soils in Great Britain is 8 mg kg^{-1} (Johnson 2003), in Germany and Austria 2.2 mg kg^{-1} (Schnell and Aumann 1999; Gerzabek et al. 1999), in Russia 3.8 mg kg^{-1}, and in India 3.65–12.59 mg kg^{-1} (Ghose et al. 2003). The primary source of iodine in the Earth's crust is volcanic rock: granite, basalt, diorites, and tonalites. The mean content of iodine in such rocks is from 4 to 9 ppb (Johnson 2003) (Table 5.1).

Iodine occurs as iodides and iodates in seawater, most mineral waters, and in some marine algae. Moreover it is an additive (sodium iodide) in Chilean saltpeter (nitratine). For industrial needs, large amounts of iodine are obtained from mineral deposits found in Chile (as a coproduct of surface mineral deposits used to produce nitrate fertilizers) and from brines in the USA (Colorado, Nevada, New Mexico).

Table 5.1 Concentrations of iodine in various rocks

Material	Concentration (mg kg^{-1})	References
Igneous rocks	5–200	Fuge and Johnson (1986)
Granite	0.25	Fuge and Ander (1998)
All other intrusives	0.22	Fuge and Ander (1998)
Basalts	0.22	Fuge and Ander (1998)
All other volcanics	0.24	Fuge and Ander (1998)
Volcanic glasses	0.52	Fuge and Ander (1998)
Sedimentary rocks		
Shales	2.3	Fuge and Johnson (1986)
Sandstones	0.8	Fuge and Johnson (1986)
Limestones	2.7	Fuge and Ander (1998)
Organic-rich shales	16.7	Fuge and Ander (1998)
Carbonates	2.7	Fuge and Johnson (1986)

However, this element is mostly obtained from marine algae (sometimes containing up to 14% of iodine in dry matter) (Szymańska and Bruchajzer 2010). World iodine production in 2012 was about 28,400 Mt (USGS 2013). For years, the main iodine producers in the world have been Chile (~66%) and Japan (~33%), where in 2012 17,000 and 9400 Mt, respectively, were obtained (USGS 2013). In recent years (2000–2013) no significant changes in the production of this element have been noted (Table 5.2).

Iodine and its compounds are used in photography (for the production of light-colored material), the printing industry, laboratory diagnostics, dye production (erythrosine, cyanine – Bengali red), pharmacology as a disinfecting agent (alcohol solutions of iodine and sodium iodide), and also for iodination of salt and disinfection of water (Backer and Hollowell 2000).

The highest occupational exposures are found in employees of chemical industries (e.g., during the synthesis of dyes), pharmacy, printing industry, and those using iodine-containing disinfection agents (in medicine, veterinary, and water purification), as well as in agriculture and the food industry (food and fodder supplementation) (Szymańska and Bruchajzer 2010).

The release of iodine into the environment occurs from both natural sources and human activity. Sources of iodine from human activities include effluents from municipal plants and the combustion of waste and fossil fuels (ATSDR 2004). After the experimental nuclear tests during World War II, and as a result of leakages from nuclear power plants, the environment has been burdened with anthropogenic-origin iodine as a product of uranium and plutonium fission (Likhtarev et al. 1993; Moore and Groszko 1999; Rao and Fehn 1999; Johnson 2003). Radioactive iodines from fuel reprocessing plants enter the environment primarily in a gaseous state and are incorporated into the food chain by deposition onto vegetation or via inhalation. Iodine-129 can also be incorporated into food chains via deposition onto soil surfaces and subsequent uptake by plant roots (Price et al. 1981; Johnson 2003).

Table 5.2 Production of iodine 2000–2013 (metric tons)

	Year													
Country	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Chile	10,474	11,355	11,648	13,916	14,931	15,346	16,494	15,473	15,503	17,399	15,793	16,000	17,494	20,656
Japan	6157	6643	6548	6524	7264	8095	8724	9282	9500	8232	9216	9277	9315	9400
USA	1470	1290	1420	1090	1130	1570	1220	1200	1200	1250	1250	1270	1270	1270
China	500	500	500	500	550	550	560	570	570	580	590	590	600	600
Turkmenistan	200	200	200	200	250	270	270	270	500	270	270	270	270	270
Azerbaijan	2	–	–	–	–	–	–	21	116	149	191	200	240	249
Russia	24	46	58	58	105	105	105	105	105	105	105	105	105	105
Indonesia	75	75	75	75	75	75	75	75	75	75	75	75	75	75
World	18,902	20,109	20,449	22,363	24,305	26,011	27,448	269,96	27,569	28,060	27,490	27,787	29,369	32,625

Source: British Geological Survey (2006) World Mineral Production 2000–2004; British Geological Survey (2010) World Mineral Production 2004–2008; British Geological Survey (2015) World Mineral Production 2009–2013

4 Iodine in Nature: Geogenic and Anthropogenic Sources (Global Iodine Budgets)

Once released into the atmosphere, iodine may be present in different physicochemical forms: elementary iodine (I and I_2) and organic iodine (methyl iodide, CH_3I; hypoiodous acid, HOI). It is estimated that global emissions of CH_3I types are as follows: oceanic 130–1300 Gg year^{-1} (Rasmussen et al. 1982; Nightingale 1991; Reifenhauser and Heumann 1992; Campos et al. 1996; Moore and Groszko 1999), terrestrial biomass burning <10 Gg year^{-1} (Andreae et al. 1996), plant-soil systems (rice paddies) 20–71 Gg year^{-1} (Muramatsu and Yoshida 1995; Redeker et al. 2000), peatland ecosystems 1.4 Gg year^{-1} (Dimmer et al. 2000), and wetlands 7.3 Gg year^{-1} (Dimmer et al. 2000).

5 Biological Status of Iodine

The content of iodine in surface and groundwaters, from where it is absorbed by plants, depends on the content in precipitation and the soil. The content of iodine in precipitation is higher than in the air. Iodine can penetrate into plants by direct deposition on overground parts of plants or from the soil by the root system (soil-accumulated iodine). The concentration of iodine in plants depends on their absorptive potential and the content in the soil. Plants show a low ability to bind iodine from the soil and air, which—with a simultaneous deficiency in selenium—would exacerbate the problem. Iodine absorbed by a plant is in 60% accumulated in leaves, with the remainder in the stalks and roots. Iodine ions penetrate through trichomes and together with plant enzymes are transported to the rhizosphere. Enzyme-rich substances secreted by trichomes activate particular morphological types of soil microorganisms (Strzetelski 2005). The content of iodine in land plants is on average about 1 mg kg^{-1} dw (Hetzel and Marberly 1986). The plants richest in iodine are those residing in alluvial riverside soils and on clays and sands that have been deposited by water flow (Hetzel and Marberly 1986).

In homoeothermic vertebrates, the rate of absorption of iodine via the alimentary tract varies and depends on both the form of iodine and the species of mammal (Akiba and Matsumoto 1976; Thrall and Bull 1990; Johnson 2003; ATSDR 2004). It is estimated that in dogs, it is about 80–92% (Alexander et al. 1967; Nath et al. 1992; Flachowsky 2007; Ghazvinian et al. 2012). In cattle, between 70% and 90% of dietary iodine is absorbed directly via the bovine rumen, reticulum, and omasum. In turn in humans, gastrointestinal absorption of iodine (taken as water-soluble iodide salts) is almost 100% (ATSDR 2004). Fisher et al. (1965) say that fecal excretion of ^{131}I was <1% of the dose in seven euthyroid adult subjects who received a single tracer dose of ^{131}I and that daily urinary iodine excretion was approximately 80–90% of the estimated daily intake, which unambiguously indicates the near-complete absorption of the ingested radioiodine. Similar results were

obtained in an acute ingestion study of nine healthy subjects (Ramsden et al. 1967—quoted from ATSDR 2004). Urinary radioiodine accounted for 97% (±5, SD) of a single ingested tracer dose of radioiodine (^{131}I or ^{132}I).

Thrall and Bull (1990), in studies on the effect of a chemical form on the uptake and distribution of radioiodine in fed and fasted rats, showed that the initial distribution of ^{125}I to the thyroid depended sharply on the chemical form, being greater when iodide rather than iodine was administered, irrespectively of whether the animals were fed or fasted. The authors have also found that after oral administration of $^{125}I_2$ or $^{125}I^-$, the concentration of ^{125}I in the blood reached a maximum after 2 h and was comparable between the group of feed animals supplemented with $^{125}I^-$ and the fasting group supplemented either with $^{125}I_2$ or $^{125}I^-$.

Available scientific data indicate that there are large differences in the transfer of iodine from feed to animal tissues and products such as eggs or milk. For example, the transfer of iodine from feed to pork and beef was only 0.3% and <1%, whereas in milk and eggs, it was 30–40% and 10–20%, respectively (Richter 1995; Yalcin et al. 2004).

Only 10% of iodine demand in humans comes from drinking water (Ziemlański et al. 2001). Inorganic iodine compounds (e.g., potassium iodide) are absorbed very quickly and almost entirely, while the absorption of organic compounds is limited (Bobek 1998; Nath et al. 1992; Ziemlański et al. 2001). Other vectors of iodine penetration are the pulmonary system and the skin. These tracts for most mammals and birds are less relevant (excluding the littoral areas, where the air is rich in this element). After being absorbed by an organism, inorganic iodine is transformed into organic compounds, which are vital for the functioning of the thyroid, which produces tetraiodothyronine (T_4) and triiodothyronine (T_3). The thyroid gland is the critical target organ in vertebrates, including humans, following excessive repeated oral intake of stable iodine. As said by Nath et al. (1992), an organism accumulates iodine mostly in the thyroid gland (70–80%). The other stores are the salivary glands, skeletal muscles, mammary glands, gastric mucosa, and in females the ovaries. Moreover iodine also accumulates in the epidermis and hair follicles in rats and probably in other mammals as well (Brown–Grant 1961; Ziemlański et al. 2001). Absorbed iodine is excreted primarily in the urine and feces but can also be excreted in breast milk, exhaled air, sweat, and tears. Urinary excretion normally accounts for >97% of the elimination of absorbed iodine, while fecal excretion accounts for approximately 1–2% (ATSDR 2004).

5.1 Toxicity of Various Iodine Forms in Homoeothermic Animals

A large excess of iodine can be harmful to the thyroid, inhibiting the process of synthesis and release of thyroid hormones, the Wolff-Chaikoff effect (WHO 2004). The mechanism of iodine toxicity is related to its strongly caustic activity, affecting

protein degradation and cellular dilapidation, while the basic symptom of iodine toxicity in low doses or small concentrations is the irritation of mucosal membranes. In countries where the consumption of seafood is high, for instance, in Japan, iodine intoxication is more likely (Kostogrys et al. 1999).

In available literature no reports have been found that consider the mutagenic effects of nonradioactive iodine. No mutagenic activity by iodine was shown in mouse L5178Y lymphocytes or colonies of Balb/c mice 3T3 cells (iodine concentration 0.1 ÷ 10 μg mL^{-1}) (Merkle and Zeller 1970; Kessler et al. 1980) nor in a study performed with *Saccharomyces cerevisiae* yeast (Mehta and Borstel 1982). Still, genotoxic activity has been proven in the case of ^{131}I (Joseph et al. 2009). Also, Wlodkowski et al. (1975) noted that Povidone-iodine, used as a disinfectant, is capable of specifically altering DNA and the induction of base-substitution mutations, which potentially may lead to the development of cancers.

Although no unambiguous data about the carcinogenic activity of iodine is available in present literature, the results of some studies suggest that an elevated iodide intake may be a risk factor for thyroid cancer in certain populations, particularly in populations in iodine-deficient regions with endemic goiter (Zimmermann and Galetti 2015).

5.2 Toxicokinetics and Effects of Iodine

As reported by Szymańska and Bruchajzer (2010) and RTECS (2006), based on medial lethal doses for laboratory animals, iodine is unranked in acute toxicity (DL_{50} for rats after an intragastric administration is 14,000 mg kg^{-1} body weight, bw). No changes were found in hamsters (*Cavia porcellus*) and rats after a single exposure (inhalation) to iodine at 5 mg m^{-3}. To a small extent, exposure of rats to 8.6 mg m^{-3} and dogs to 10 mg m^{-3} of iodine produced an effect in the pulmonary system (Casarett 1975). At 73–100 mg m^{-3} of iodine, an irritating effect was observed, with an adverse effect on lung function. At an inhaled concentration of 4.7 mg m^{-3} for 3–4 months in rats, some changes in the structure of mucosal membranes of the mouth, eyes, and tooth enamel were observed. As reported by Biegishev (1975), the exposure of hamsters and rats to iodine at 0.5 or 3.1 mg m^{-3} (at an increased temperature) resulted in temporal disorders of smell, slight kidney damage, and decreases in body weight and oxygen uptake.

An oral LD_{50} of 3320 mg I kg^{-1} bw has been reported in rats for both sodium iodide and for potassium iodide, and an oral LD_{100} of 1425 mg I kg^{-1} bw has been reported for mice (Clayton and Clayton 1981; EFSA 2006). According to Clayton and Clayton (1981), an acute oral LD_{50} value for potassium iodide in rats was 3320 mg I kg^{-1} bw, and the lowest oral lethal dose in mice was 1425 mg I kg^{-1} bw. Amounts at 200–500 mg kg^{-1} bw can cause death in experimental animals (SCOGS 1975).

Humans seem to be less sensitive to iodine than rodents, concerning thyroid disturbances, even though the basic hypothalamic-pituitary-thyroid axis functions in

a similar way in animals and humans. Animal data are therefore of limited value in relation to human toxicity (Nielsen et al. 2014).

A toxic level in total diet for ruminants is 50 ppm (excluding goats, 8 ppm); pigs, 800 ppm; horses, 4.8 ppm; and poultry, 625 ppm (NRC).

5.3 *Bioaccumulation of Iodine*

The collocation of iodine in the environment is very varied, as shown in Fig. 5.1. The content of iodine in water plants is different and mostly depends on the type of water (fresh, sea). Freshwater algae contain 10^{-5}% by weight of iodine, whereas marine algae contain 10^{-3}% by weight. In freshwater fish, iodine concentrations in tissues ranged from 0.003 to 0.81 mg kg^{-1} ww, while in marine fish, they ranged between 0.023 and 0.11 ppm ww (ATSDR 2004). The average iodine concentration in terrestrial plants was 0.42 mg kg^{-1} dw (Moiseyev et al. 1984).

The content of iodine in vertebrate tissues depends mostly on the species of the animal and the environment in which it remains. Kaňa et al. (2015) found a highest content of iodine in the skeletal muscles of sea fish, especially in Atlantic cod (*Gadus morhua*), 1.484 mg kg^{-1} ww, and a lower concentration in blue shark (*Prionace glauca*), at 0.0506 mg kg^{-1} ww. According to Kaňa et al. (2015), the levels of iodine in the tissues of farm animals are much lower than in fish, where in pigs in the thyroid gland, the level of iodine was 0.513 mg kg^{-1} ww and in the kidney, liver,

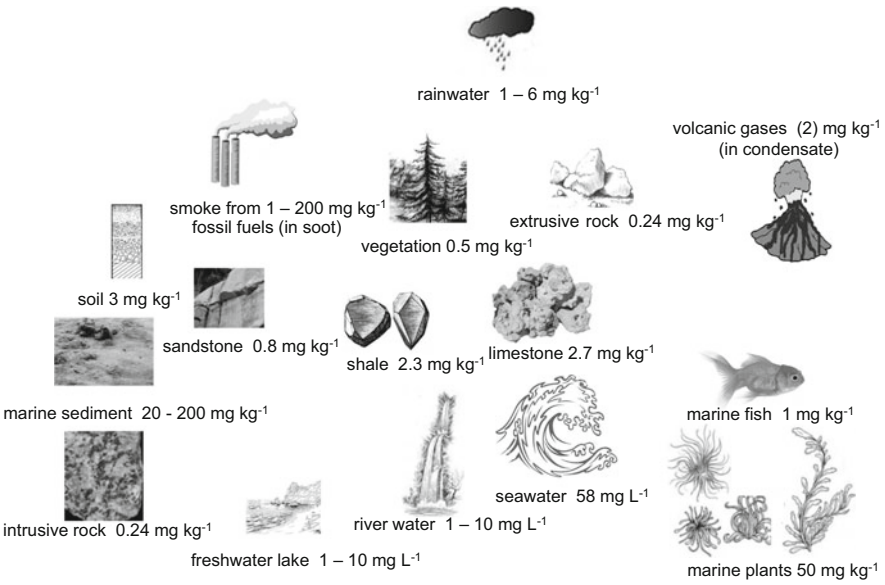

Fig. 5.1 Collocation of iodine in the environment (based on Johnson 1980)

and muscle 0.103, 0.051, and 0.034 mg kg^{-1} ww, respectively. In chickens, relatively more iodine is present in the gut (0.123 mg kg^{-1} ww), with the levels in the liver and muscle (0.068 and 0.029 mg kg^{-1} ww) similar to that observed in pigs. A higher content of iodine was found in turkey livers than in chickens and pigs (0.105 mg kg^{-1} ww).

In plants growing in iodine-deficient soils, concentrations may be as low as 10 mg kg^{-1} dw, compared with approximately 1 mg kg^{-1} in iodine-sufficient soils (Zimmermann 2009), with average iodine concentrations in fleshy fungi at 6.2 mg kg^{-1} dw, ferns 5.7 mg kg^{-1} dw, coniferous trees 3.9 mg kg^{-1} dw, monocotyledons 5.9 mg kg^{-1} dw, dicotyledonous trees 2.7 mg kg^{-1} dw, and dicotyledonous vegetables 6.9 mg kg^{-1} dw (Shacklette and Cuthbert 1967).

Studies in goats and sheep have revealed that in temperate climate (Iran), seasons affected the content of iodine in animal organisms. The highest concentration of iodine was noted in autumn with the lowest in spring (Gharahveysi et al. 2012). Also Topczewska (2012) showed significant differences between seasons in the concentrations of iodine in horse hair in Poland. The author observed the highest level of iodine in hair in winter and the lowest in spring.

5.4 *Ecological Effects of Iodine*

The content of iodine in free ranging animals is measured only occasionally. For the most wild mammals and birds, no iodine requirements have been suggested.

Due to the suitability of meat for consumption from different animals, including game, muscle tissue is usually considered to be an appropriate tissue for studies in both food quality and ecotoxicology. However, literature data does not indicate the suitability of muscles in the evaluation of environmental levels of iodine (Rambeck et al. 1997; Schone et al. 1986; Schone 1999). Admittedly, German scientists introduced additional iodine supplementation (potassium iodide) to the diet of porkers and observed an increased level in muscle tissues and internal organs (liver, kidneys) of animals, yet the results were not satisfactory (Schone et al. 1986; Rambeck et al. 1997; Schone 1999). The skeletal muscles of farm and game animals living without supplemental sources of iodine contain 0.10–0.30 mg kg^{-1} ww (Anke 2007). Most likely studies on the concentration of this element in the thyroid or other organs that are known to be sensitive to a deficiency of iodine would provide a better view on the relationship between the presence of iodine in the environment and its content in homoeothermic animals, yet the availability of data in this field is very scarce.

The iodine-containing hormones produced by the thyroid gland play a role in the complex neurohormonal regulation of antler development (Lehoczki et al. 2011). This study revealed that the level of iodine in the environment has a determinant effect on roe deer (*Capreolus capreolus*) antler weight and that iodine deficiency (ID) can be an additional limiting factor constraining optimal deer performance for antler weight. Bubenik et al. (1987) studied white-tailed deer (*Odocoileus*

virginianus) and showed that the T3 utilization rate in the growing antler correlated with the intensity of antler growth. Iodine levels may so influence roe deer performance (antler development) through the mechanisms of thyroid function. As reported by Watkins et al. (1983), the iodine requirements of white-tailed deer can be met by feed (dry matter) containing 0.26 ppm of iodine. This recommended iodine content in feed is required to cover the average iodine needs of domestic ruminants (generally 0.1–0.25 mg kg^{-1} of consumed fodder and 0.5–0.6 ppm for lactating animals) (Schöne and Rajendram 2009).

Problems with iodine deficiency may also occur in birds, especially those feeding on seeds, as observed in individuals of different species kept in captivity or nesting in human neighborhoods. This element is particularly important for the budgerigar (*Melopsittacus undulatus*) and pigeons, which appear to be particularly susceptible to thyroid problems. In these species, iodine deficiency may lead to goiter (enlargement of the thyroid glands), while such an affliction is not common in other groups of birds (Tollefson 1982).

5.5 *Bioindicators and Biomarkers of Iodine in Ecotoxicological Studies*

In humans a reliable method of evaluating iodine supply is population studies in which iodine urinal excretion, frequency of goiter occurrence, and concentrations of TSH (thyroid-stimulating hormone) and thyroglobulins are considered.

Because more than 90% of dietary iodine eventually appears in the urine, the amount of iodine excreted with the urine is a very good indicator of recent iodine intake (Nicola et al. 2009; WHO 2007). In humans, based on this, the degree of iodine deficiency can be defined for further development of prophylactic programs.

It is assumed that the content of iodine in the urine translates into the supply of this element in recent days, the concentration of thyroglobulins for weeks and months, and the presence of goiter for years (Zimmermann 2008; Erdman et al. 2012).

Detection of an enlarged thyroid gland and a ratio of thyroid weight to body weight greater than 0.4 g kg^{-1} provides an indication of goiter in lambs and kids. Iodine concentrations in doe milk less than 0.8 μmol L^{-1} indicate an inadequate iodine intake (Caple et al. 1983). A concentration of thyroxine in blood serum of neonatal lambs lower than 50 μmol L^{-1} indicate hypothyroidism (Caple and Nugent 1982).

Typical biomarkers of hyperthyroidism are an elevation in the circulating levels of T_4 and/or T_3 above their normal ranges, which is always accompanied by a depression of TSH below the normal range. The clinical manifestation of abnormally elevated circulating levels of T_4 and/or T_3 is often referred to as thyrotoxicosis or Graves' disease or Basedows' disease. Serum thyroglobulin represents a very sensitive index of the state of thyroid hyperstimulation in humans (Karasek and

Lewiński 2003). In domestic ruminants, an assessment of iodine status is done by measurement of serum I, protein-bound I, thyroxine (T4), or the presence of goiter (McDowell 1992). Also, to diagnose iodine deficiencies, female milk can be used. As reported by Caple et al. (1983), iodine concentrations in cow milk less than 0.2 μmol L^{-1} indicate inadequate iodine intake. Unfortunately, in the wild, obtaining urine or milk is a difficult problem, and practically such studies are no longer performed.

In wild ruminants, including cervids, the content of iodine depends on the concentration of this element in their plant food (Watkins and Ullrey 1983; Whitehead 1984; Anke et al. 1995). However, Ceacero et al. (2009) suggest that deer were able to modulate mineral intake to meet requirements and that, on the other hand, relative ID can occur if goitrogenic compounds were present in the food (Whitehead 2000; Tripathi and Mishra 2007). In the case of evaluation of anthropogenic iodine in the environment, probably the thyroid glands of cervids may turn out to be good bioindicators of this element, as was shown in the studies by Price et al. (1981). The authors established the current levels of ^{129}I in the environs of the Hanford Site (USA) prior to the proposed restart of fuel reprocessing at the PUREX plant (nuclear production complex on the Columbia River in the US state of Washington). The results of this study clearly demonstrated the longevity of ^{129}I in the biosphere, following an earlier gaseous release from the nuclear facility. Price et al. (1981) demonstrated that the thyroid glands of deer living within 160 km (Wooten Game Range) of Hanford had elevated levels of ^{129}I when compared to distant Pacific Northwest locations (Centralia or Bend). Levels of ^{129}I in deer thyroid from Bend or Centralia (15 fCi g^{-1} wet weight) were about five times higher than those reported in the Central United States, with Hanford samples about 2700 times higher. The average concentration of ^{129}I in deer thyroids collected at Hanford in 1978 was similar to samples collected 14 years earlier (Price et al. 1981).

It also cannot be excluded that bird eggs may turn out to be good indicators of environmental iodine levels, as was shown in farm birds where they can easily accumulate this element. After weeks of feeding hens with iodine-supplemented fodder, an increased content was observed in the eggs, reaching a maximal value during the eighth week (Ryś et al. 1995).

6 Conclusions

Literature data on iodine in wildlife is very scarce, while problems with health or the environmental effects of a possible iodine deficiency or surplus are not yet sufficiently well understood. In land habitats we usually observe the problem of a deficiency rather than an overabundance. For this reason, regarding the possible indirect effect of this element on the animal reproductive potential, we can suppose that iodine clearly may affect the size and condition of populations in some species of animals and can also play a role in shaping the structure of particular ecosystems, especially in isolated groups of animals in mountain areas.

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Chapter 6
Iron, Fe

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Abstract Iron (Fe) is an essential micronutrient for human and animal organisms, playing an important role in the metabolic process in endothermic animals. This metal is one of the most abundant elements in the Earth. In this review the recent studies on Fe existence in environment and terrestrial ecosystems and their organisms are presented. The reports show that Fe concentration in tissues of different avian and mammalian species can be influenced by the type of diet and biological parameters. Owing to the wide range of Fe concentration in animal tissues of different taxonomic groups and between individuals of the same species, it is hard to indicate the bioindicator of environmental Fe concentration.

1 Introduction

Iron (Fe) is the second most abundant metal in the Earth's crust, and it is known to be biologically essential element of every living organism (Soetan et al. 2010; Kabata-Pendias and Szteke 2012). Despite its common occurrence in water, soils, and plants, iron bioavailability is very low due to the fact that in contact with oxygen Fe forms insoluble oxides (Abbaspour et al. 2014; Kabata-Pendias and Szteke 2012). Iron is essential in transport of oxygen in the body, and it is involved in many enzymatic reactions. Its deficient or excessive amount in the body can cause disease symptoms

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(Soetan et al. 2010; MacKenzie et al. 2008). Iron deficiency is manifested by a decrease in hemoglobin in the blood, which leads to anemia. Excess accumulation of Fe in the body can lead to iron overload disease (Soetan et al. 2010; Abbaspour et al. 2014; Powell et al. 2016).

The research on the Fe concentration, usually evaluated in the liver, are conducted both in domesticated and wild avian and mammalian species. The ranges of Fe concentration in mammals and birds of different taxonomic groups and between individuals of the same species from North America and Europe vary greatly, and the scientists from such studies deter from interpretation. Nonetheless, Fe deficiency and iron storage disease have been reported in farm and wild animals (Underwood 1977; Dierenfeld et al. 1994; Andrews 1999; Cork 2000; Clauss and Paglia 2012).

Given the important role of Fe in human and animal organisms and the reported cases of health risks associated with a deficiency or excess of Fe, it seems worthwhile to monitor the Fe concentration in the environment and tissues of wild birds and mammals.

2 General Properties

Iron (Latin: ferrum, Fe) is a metallic chemical element belonging to group 8 in the periodic table. Its atomic number is 26, atomic weight 55.847, specific gravity 7.874, melting point 2795 °F (1535 °C), and boiling point 4982 °F (2750 °C).

Pure iron is a glossy, pliable, and ductile metal, which undergoes oxidation (passivation). One of the most characteristic features of iron is its ferromagnetism or ability to become strongly and permanently magnetized in a magnetic field. In its pure form, iron is relatively soft and slightly magnetic, but its magnetism increases after hardening. There are four stable allotropic iron species, alpha iron (α), beta iron (β), gamma iron (γ), and delta iron (δ), and one high-pressure form: epsilon iron (ε). Iron allotropes differ from one another in their durability, crystalline lattice structure, and magnetism (Boehler 2000). Iron has many isotopes, of which only four occur naturally in the environment. These are durable isotopes with atomic weights of 54 (5.8%), 56 (91.7%), 57 (2.2%), and 58 (0.3%). The other isotopes of iron are artificial and radioactive (Audi et al. 2004).

Iron creates compounds at the second and third stages of oxidation. In an abiotic environment with a pH of 4.0–4.5, Fe occurs at the second stage of oxidation, while at pH $>$ 4.5, the element is oxidized to Fe^{3+}. In aluminosilicate minerals, iron easily substitutes magnesium and aluminum. Its circulation in the environment is closely linked to the cycling of O, S, and C. Iron is one of the most common elements on Earth. Its content in the Earth's crust is about 5%. The highest levels of Fe are found in ultra-alkaline and alkaline igneous rocks ($<$10%). In contrast, in acidic igneous rocks, iron content does not exceed 3%. In sedimentary rocks, the Fe content is very different (0.4–4.8%), while iron-rich sedimentary rocks can contain up to 15% Fe. The smallest amount of Fe is found in limestones and dolomites (Kabata-Pendias and Pendias 2001).

3 Ferrous Minerals and the Production and Uses of Iron

A high concentration of iron is found in metamorphic limonite deposits. Fe is also found in at least 25 minerals. The most important iron ores in terms of industrial significance are magnetite (72% Fe), hematite (70% Fe), goethite (63% Fe), and siderite (48% Fe). As an element, iron is easily oxidized, reduced, or hydrolyzed (depending on the prevailing environmental conditions) and is quickly released from minerals such as aluminosilicates, silicates, and carbonates. Only a small amount of Fe is contained in minerals which are resistant to weathering processes. Iron is the least expensive and the most widely used metal. Iron must be processed before use, in order to improve its qualities. More than 90% of mined iron ore is used for the production of steel and metal alloys. Global production of pig iron in 2014 and 2015 was 1170 and 1180 million tons, respectively. The production of raw steel in 2014 and 2015 was at a similar level, amounting to 1650 million tons (USGS 2016).

Iron ores are distributed widely around the earth. Currently, it is mainly ores containing a high level of pure iron which are mined. The level of iron ore mining around the world has risen from 2283 million tons to 3328 million tons over the years 2009–2015. Today, China is the largest iron ore producer in the world (1381 million tons in 2015), having increased its production fourfold in the last 10 years. A substantial growth in iron ore production in China occurred between 2009 and 2014, from 880 million tons to 1514 million tons, while in 2015 production fell to 1381 million tons. Major mining areas in China include the provinces of Liaoning (especially around the city of Anshan), Hebei (NE China), Inner Mongolia (N China), and Sichuan on Hainan Island (S China). Australia is the second largest producer of iron ore. Its mining output has increased from 394 million tons in 2009 to 816.7 million tons. Its main iron ore mining areas include Hamersley (NW - Australia) and the area northwest of Adelaide. Australia exports 90% of its mined iron ore. In Asia, India is an important producer of iron ore (over 155 million tons in 2015). Iron ore deposits in India are very rich and of high quality. The main deposits of magnetite and hematite occur in the central states of the country (Maharashtra, Goa, Andhra Pradesh, Odisha, and Bihar). North America has a much smaller share of iron ore production and has seen a 3% decline due to lower production in the USA (42.5 million tons). Brazil and Australia account for half of the world's exports of iron ore. In Europe, the most important iron ore deposits are located in northern Sweden (in the Kiruna and Gallivare basins). Japan is the largest importer of iron ore in the world (O'Brien 2009; Indian Bureau of Mine 2014; British Geological Survey 2015).

Iron is rarely used in its chemically pure form due to its poor mechanical properties, with industry using alloys produced by alloying metals and nonmetals. Steel is an alloy of iron and processed carbon (about 0.8%). In addition, steel contains about 2% of an admixture of chromium and nickel. It is estimated that steel is four times stronger than pure iron and, due to its properties, is used for manufacturing springs and parts of machines which are exposed to heavy loads. Another type of steel is stainless steel, which is made up of iron, 0.2% carbon and

13% chromium, and is used for manufacturing equipment for the food industry, as well as measuring devices and surgical instruments. Cast iron is another example of an iron alloy, with a carbon content of up to 6%. This alloy can be cast very effectively and, due to its properties, is used for casting complex shapes such as engine hulls and lathes. Between 2009 and 2015, world production of crude steel increased by an average of 2–3% annually. Asian countries, whose share of global steel production is about 70%, contributed to this increase the most significantly. In contrast, European Union (EU) countries' share of world steel production, which at present is about 10%, has been steadily decreasing. The apparent consumption of steel in the EU amounted to 187 million tons in 2008 and 149 million tons in 2015. The largest users of steel in the EU are the construction (35%) and automotive (18%) industries. The apparent use of steel products globally increased by over 70% between 1997 and 2007. Between 2009 and 2015, this accounted for an increase in steel production from 1232 million to 1620 million tons. The countries with the highest apparent per capita use of steel are South Korea (1057 kg per head), Taiwan (793 kg), the Czech Republic (547 kg), Japan (516 kg), and China (515 kg) (British Geological Survey 2015).

4 Iron in Nature

In the soil, iron occurs in the form of silicates, sulfates, and carbonates, as well as oxides and hydroxides. The latter may form crystalline or amorphous structures. Iron oxides include hematite (αFe_2O_3), maghemite (γFe_2O_3), magnetite (Fe_3O_4), ferrihydrite ($Fe_2O_3 \cdot H_2OFe_2O_3 \cdot H_2O$), goethite ($\alpha FeOOH$), lepidocrocite ($\alpha FeOOH$), ilmenite ($FeTiO_3$), and pyrite ($FeS_2$) (Cornell and Schwertmann 2003). All Fe (II) compounds are mobile, and their solubility increases proportionally to the degree of soil acidity. In addition, they exhibit low stability, as opposed to Fe (III) compounds, which are durable. Fe content in soils can vary to a considerable degree, ranging between 0.1% and 5% (Kabata-Pendias and Pendias 2001). Cornell and Schwertmann (2003) found that Fe concentration in arable soils varied between 20 and 40 g kg^{-1} dry weight (dw). Szymański et al. (2017) observed that Fe content was significantly lower in topsoil and eluvial horizons (5.22 g kg^{-1} dw) than in the lower horizons (7.87 g kg^{-1} dw), indicating translocation of Fe with clay minerals further down the soil profile. The natural causes of Fe in bodies of water are the processes of weathering and soil migration. Iron in the form of fine and colloidal hydroxides is subjected to sorption on the surface of solid particles that form a suspension and are transported over long distances, while Fe in minerals which are hardly subject to weathering (e.g., silicates, magnetite) is rapidly sedimented. In addition, the presence of Fe in bodies of water results from urban and industrial effluents (Park et al. 2006; Stopić et al. 2007).

Fe content in freshwaters usually ranges from 1 to 28 μmol L^{-1} and in marine waters from <0.2 to 0.8 nmol L^{-1} (Johnson et al. 1997; Kritzberg and Ekström 2012). Because Fe occurs predominantly in surface water in the form of insoluble

trivalent compounds that precipitate as a sediment, the concentration of Fe in soluble form is usually small. Schönfelder et al. (2002) reported that Fe concentration in freshwaters (69 lakes and 15 rivers) ranged from 11 to 318 μg L^{-1}, with an average of 59.9 μg L^{-1}. However, it has been noted that during floods the concentration of this form of Fe in water is three times greater (Baixing et al. 2016).

In river bottom sediments, Fe content is generally >10%. However, Kanbar et al. (2017) demonstrated that if a river runs through a location affected by mining or metallurgical activities, iron content can reach 29%. In lake bottom sediments, the concentration of Fe is 8–47 g kg^{-1} (Czaplicka et al. 2016; Rajkowska and Protasowicki 2011); the organic fraction of the sediments contains about ten times more Fe than the mineral fraction (Rajkowska and Protasowicki 2011). Estuary sediments can contain an amount of Fe 5 up to 25 times greater than the levels of background metals (Carral et al. 1995). In river or lake bottom sediments, as with soils, Fe concentration increases with depth (Kanbar et al. 2017).

The source of Fe in atmospheric air is crustal and industrial dust. Depending on the degree of industrialization, iron content may range from 50 to 14,000 ng m^{-3} (Reimann and Caritat 1998). Iron in atmospheric dust is mainly found in the largest fractions: as shown in a study carried out by Rogula-Kozłowska et al. (2015), in dust fraction $PM_{0.03–0.17}$, no Fe was found to be present, whereas in fractions $PM_{0.26–0.4}$ and $PM_{0.4–0.65}$, Fe contents of 0.4 and 7.5 ng m^{-3}, respectively, were found. It is estimated that the annual fall of Fe on urban areas is between 16.8 and 43.2 kg ha^{-1} (Kabata-Pendias and Mukherjee 2007).

5 Biological Functions of Iron

Iron is essential for the growth and development of all living organisms. It plays a significant role in many different biological processes, including oxygen transport and storage, oxidative phosphorylation, regulation of cell growth and differentiation, detoxification, cellular respiration, the activity of many enzymes, and the promotion of apoptosis (MacKenzie et al. 2008). Iron participates in DNA and RNA synthesis, gene regulation, and catalysis of many metabolic redox reactions (Thelander et al. 1983; Coffey and Ganz 2017). It is also responsible for the generation of reactive oxygen species (ROS), which induce oxidative stress and lipid and DNA damage (Zhang 2014). It participates in erythropoiesis, formation of leukocytes, and immune reactions, influencing the humoral and cellular immunity of the body (Beard 2001; Zhang 2014).

In endothermic animals Fe is necessary for cytochrome c production and is the core of molecules such as hemoglobin and myoglobin (Li and Ginzburg 2010), compounds that in mammals contain about 70% and 5–10% of Fe in the body, respectively (Albretsen 2006). Iron is also found in iron-binding proteins, including ferritin, hemosiderin, transferrin, ovotransferrin, and lactoferrin (Ganz 2013). Ovotransferrin is found in bird egg white, while lactoferrin in the colostrum and milk of mammals and in the secretions of glandular cells and neutrophils (Adlerova

et al. 2008). In mammals, ferritin, hemosiderin, and transferrin in the liver, spleen, and bone marrow contain up to 25% of Fe (as Fe^{3+}) (Kohgo et al. 2008).

Ferritin is the main cytoplasmic protein regulating the labile iron pool. Its serum level is a sensitive indicator of Fe status in cattle (Puls 1994). Produced in the liver, and also in Sertoli cells, and oligodendroglia, this alpha globulin has a very high affinity to Fe^{3+} (Espinosa de los Monteros et al. 1990; Lécureuil et al. 2004). It occurs in the blood, lymph, cerebrospinal fluid, bile, amniotic fluid, and milk. It transports Fe from the duodenum and mononuclear phagocyte system to cells, especially the bone marrow and rapidly dividing cells. Transferrin transports Fe to the inside of cells via the transferrin receptor (TfR). The iron transport to a cell is based on endocytosis of the transferrin complex saturated with iron together with TfR (Luck and Mason 2012). In cytoplasm, trivalent iron (III) is reduced to the divalent form (II). Formed in a vesicle, the complex of apotransferrin and receptor is transported onto the cell surface, and apotransferrin dissociates from TfR (Bakker and Boyer 1986; Brock 1989).

Iron metabolism is a semi-closed system without natural mechanisms that could remove any excess of iron. Iron homeostasis in mammals includes cells for transport to other cells and organs (Pantopoulos et al. 2012). Systemic Fe regulatory processes occur in the following order: (1) intestinal iron absorption, (2) cell transport (into cells), (3) ion transport across cell membranes, (4) participation in metabolic process, (5) iron recycling from erythrocytes, and (6) Fe storage (Duck and Connor 2016). Gastrointestinal iron absorption occurs primarily in duodenum and constitutes 5–10% Fe from the diet. The amount of iron absorbed from the gastrointestinal tracts is equivalent to the amount of iron excreted from the body. Among other things, the absorption of Fe depends on (1) age, (2) Fe status and state of health of the animal, (3) conditions within the gastrointestinal tract, (4) the amount and chemical form of the Fe ingested, (5) the diet, and (6) season of the year. Demand for Fe is lower in adult animals than in young animals, which need it for maintaining a correct concentration of hemoglobin and rate of tissue growth (Underwood 1977).

Rapidly proliferating cells have a much higher demand for iron than cells with a small proliferative potential. High iron concentrations in food may result in the development of iron-dependent microorganisms (including *Yersinia* bacteria, such as *Yersinia pseudotuberculosis*, causing cecal abscesses in birds (Stovel 1963; Czernomysy-Furowicz and Furowicz 1999)). On the other hand, Fe serum levels have been observed to be reduced down to 40% during infectious diseases with a fever (Puls 1994).

Low serum Fe levels and low saturation of transferrin with iron result in a release of stored iron and transport to the bone marrow. High Fe concentrations in serum and high saturation of transferrin with iron cause an increase in iron storage, e.g., in hepatocytes (Williams et al. 1982). In physiological conditions, high transferrin levels in serum accompany elevated iron concentrations in the blood. During pregnancy the concentration of free transferrin, e.g., in mares, increases due to the elevated demand for iron in the developing fetus. Serum Fe concentration decreases in the 8th–9th months of pregnancy until the 1st month of lactation (Puls 1994).

Transferrin does not undergo filtration in the glomeruli, which protects a healthy body against a loss of iron (Czernomysy-Furowicz 2007).

Iron accumulates in various tissues and organs of endothermic vertebrates, becoming toxic above 100 mg kg^{-1} body weight (bw) and causing anemia below 1 mg kg^{-1} bw. High Fe concentration may indicate inflammation and rapid immune response (Ganz and Nemeth 2015). Excessive Fe accumulation in the liver can lead to high hepatic load, with hepatic Fe reaching thousands of mg kg^{-1} dry weight (dw), a pathological phenomenon known as hemosiderosis (Cork 2000). In cases where Fe concentration exceeds the binding ability of apoferritin, it undergoes additional accumulation as insoluble hemosiderin.

In humans, Fe deficiency is associated with malnutrition and parasitic and neoplastic diseases and accompanies chronic inflammatory diseases, including intestinal and gastrointestinal bleeding (Abbaspour et al. 2014). This leads to severe anemia, immune and cognitive disorders, and growth impairment.

The symptoms of Fe deficiency are observed quite often in farm animals, which is associated with the low level of assimilable forms of Fe in feed or with problems with Fe absorption. Deficiency symptoms manifest themselves in generic symptoms of anemia, which are tiredness, lassitude and general feelings of a lack of energy, poor immunity, and retarded growth. Iron is much more common than other trace elements, and iron excess can lead to poor absorption of copper and manganese (Underwood 1977). In a study by Puls (1994), the normal level of Fe in the liver of cattle ranged from 45 to 300 mg kg^{-1} wet weight (ww), and a value <30 mg kg^{-1} ww indicates a possible Fe deficiency. Moreover, Fe deficiency in the liver of domestic dogs (*Canis lupus familiaris*) was observed at concentrations less than 25 mg kg^{-1} ww (Puls 1994). In young pigs (*Sus scrofa f. domestica*), Fe deficiency was found if the diet was not supplemented with Fe. Hepatic deficient Fe concentrations in adult and day 3 weaning pigs usually ranged from 30–40 and 10–-15 mg kg^{-1} ww, respectively (Puls 1994).

Free Fe ions (Fe^{2+}) are toxic to cells and tissues (Goyer 1996). The exact biochemical basis for Fe toxicosis is not well known, although it is suggested that free radicals form when free iron is present (Bacon and Britton 1990). Excess Fe in the cell leads to the formation of hydrogen peroxide in the cytosol during iron-catalyzed dissociation, followed by a diffusion of hydrogen peroxide through the nuclear membrane, DNA strand breaks, and purine purification (Yamazaki and Piette 1990). In order to protect the cell against Fe toxicity, Fe is incorporated into ferritin present in each cell (Piperno 1998).

Acute and subacute Fe poisonings in animals are mainly found in dogs, foals, piglets, and occasionally in other species. The causes of acute poisoning in animals may include the use of preparations used to destroy moss on lawns. No toxic dose has been established to date, with an oral dose of 20–60 mg kg^{-1} bw considered to cause mild to moderate poisoning and 100–200 mg kg^{-1} bw lethal for all animal species (Albretsen 2006).

Excess of Fe induces damage in the liver, heart, pancreas, thyroid, and the central nervous system, due to the overproduction of ROS in the presence of excess iron. This is followed by cell death, fibrosis, and carcinogenesis. Iron

toxicosis causes coagulation disturbances that are related to thrombocytopenia, hypoprothrombinemia, and impaired clotting factor synthesis (Greentree and Hall 1995; Hillman 1995). In addition to iron deposition in the liver and heart, pancreatic beta cells are another important target of iron toxicity, which causes glucose intolerance and diabetes mellitus (Kohgo et al. 2008).

Iron toxicosis in mammals manifests clinically in four stages. The first stage (6 h after the overdose) is manifest by gastrointestinal symptoms, including vomiting, diarrhea, and gastrointestinal bleeding (Osweiler et al. 1985; Greentree and Hall 1995; Hillman 1995; Liebelt 1998). Then 6–24 h after the overdose, a latent period is observed (Greentree and Hall 1995). The third stage of iron toxicosis occurs about 12–96 h after the initial clinical signs: it is characterized by lethargy, a recurrence of gastrointestinal signs, metabolic acidosis, shock, hypotension, tachycardia, cardiovascular collapse, coagulation deficits, hepatic necrosis, and possibly death (Greentree and Hall 1995; Hillman 1995; Liebelt 1998). The last stage, which may occur 2–6 weeks after the iron overdose, is when the animals that survived gastrointestinal ulceration are healing.

5.1 Iron Storage Disease (ISD)

The pathogenesis of ISD (iron storage disease) is poorly understood. It is characterized by the accumulation of Fe in the liver until heart failure, hypoalbuminemia, and death (Cork 2000). To date, ISD has been described in wild birds, including toucans (Rhamphastidae), mynahs (Sturnidae), birds-of-paradise (Paradisaeidae), curassows (Cracidae), quetzals (*Pharomachrus* species), tanagers, and hornbills, and in *Turdus* species (Crissey et al. 2000; Dierenfeld et al. 1994; Turner 1994; Pavone et al. 2014). Excess iron stores in the body are classified as hemochromatosis or hemosiderosis (Pietrangelo 2010; Powell et al. 2016). Hemochromatosis is characterized by the accumulation of ferritin and hemosiderin in hepatocytes, Kupffer cells, bile duct epithelium, heart, pancreas, joints, and fibroblasts in the dermis. In humans, hereditary hemochromatosis is autosomal recessive and characterized by normal iron-driven erythropoiesis and toxic accumulation of iron in parenchymal cells of vital organs that can be caused by mutations in any gene that limits iron entry into the blood (Pietrangelo 2010). Patients with hemochromatosis may develop liver failure and may die of cardiac arrhythmias; this condition usually develops in men after 40 years of age (Nichols and Bacon 1989).

Hemosiderosis is characterized by storage of increased amounts of iron in Kupffer cells of the liver with no apparent hepatocellular damage. It can be caused by high concentrations of iron in the diet, transfusions, or thalassemias, which are diseases with defective hemoglobin metabolism (Halliday and Searle 1996). Hemosiderosis has been reported in a wide range of species in zoo and private collections (Randell et al. 1981; Gosselin and Kramer 1983; Spelman et al. 1989; Crawshaw et al. 1995; Lowenstine and Munson 1999; Paglia and Dennis 1999). In wild mammals and birds, hemosiderosis is very poorly investigated. In mammals,

hemosiderosis in the liver may be associated with inflammations in the intestine due to bacterial and parasitic infections (Andrews 1999). This pathological Fe storage has been described in lemurs, hyraxes, and some carnivores, including procyonids and pinnipeds (Clauss and Paglia 2012).

In birds, hemosiderosis is characterized by the accumulation of iron in body tissues, especially the liver. Based on a retrospective study of 180 necropsy cases representing 40 different species of birds, Cork et al. (1995) showed that hepatic hemosiderosis is a common histological finding in most avian species. Although not necessarily associated with overt liver disease, it is often associated with concurrent malignant and infectious diseases. The authors observed that the presence of excess stainable iron in the liver is probably a reflection of an altered iron metabolism associated with an increased turnover of tissue iron and may be caused by conditions such as starvation or trauma. In the liver of Falconiformes, Kalisinska et al. (2008) observed Fe liver concentrations over 6000 mg kg^{-1} dw, where usually in this group of birds, the physiological level ranges from ~430 to 2300 mg kg^{-1} dw (Jager et al. 1996; Kalisinska et al. 2006). In some cases ISD or hemosiderosis in birds is associated with elevated levels of lead (Pb) in tissues (Lewis et al. 2001). Hemosiderosis has also been described in a trematode infection of the liver and spleen of the mute swan (*Cygnus olor*) (van Bolhuis et al. 2004). Fruit-eating and insect-eating birds have a predisposition to develop hemosiderosis (Dierenfeld et al. 1994; Cork et al. 1995).

6 Iron Bioaccumulation in Mammals and Birds

Wild animals are affected by a variety of environmental factors, which, to a large extent, determine the process of accumulation of heavy metals, both toxic ones and those essential to life. Analysis of heavy metal concentrations in animal tissues and organs usually provides indirect information about the quality of the environment. However, Fe concentration in animal tissues generally does not reflect its content in the environment. This probably results from effective homeostatic regulation within mammals and birds, the low food chain transfer of this element, and the forms in which iron is found in the environment, which determine its bioavailability (Wren et al. 1988; Cork et al. 1995; Miret et al. 2002; Soetan et al. 2010). The percentage of Fe absorbed from food (its bioavailability) varies but can range from 1% to 50%. Intestinal absorption of the metal can be affected by the form of ingested Fe and other food compounds including ascorbic acid, phytates, and proteins (Finch and Cook 1984; Miret et al. 2002; Hurrell and Egli 2010). Moreover, biological parameters such as age, physiological stage, genetic factors, and diet have a substantial influence on the content of Fe in endothermic vertebrates (Borch-Iohnsen et al. 1991; Puls 1994; Borch-Iohnsen and Thorstensen 2009; Olias et al. 2011). Animals with an active life, which run a lot and are in good shape, for example, horses and hares, contain more myoglobin, which is an iron-rich protein, and so the Fe concentration in their tissues is higher than in weak organisms of the same species (Mendel and

Wiechetek 2006; Myslek and Kalisinska 2006). Excessive storage of Fe (iron storage disease) in mammals and birds, especially in the liver, can occur as a result of genetically determined diseases, seasonal changes in their diet, and/or periodic starvation (Borch-Iohnsen et al. 1991; Dierenfeld et al. 1994; Clauss et al. 2002; Borch-Iohnsen and Thorstensen 2009; Clauss and Paglia 2012). At the same time, it should be noted that iron stimulates pathogenic bacteria to produce toxins. That is why, in response to inflammation, animal organisms retain iron in the cells of the reticuloendothelium system, intestinal epithelium, and other parts of the body, which may contribute to its increased concentration in different tissues (Puls 1994; Czernomysy-Furowicz and Furowicz 1999; Filipczyk et al. 2010; Pantopoulos et al. 2012).

6.1 Iron Concentration in Mammals

The average Fe content in the fresh tissue of adult mammals is about 0.005% (Hanusová et al. 2007). The main areas in which Fe is accumulated in mammals are the liver and spleen and, to a lesser degree, the kidneys, skeletal muscles, and bone marrow. In wild mammals, iron concentration is most frequently tested in their edible parts, such as the muscles, liver, and kidneys of ungulate game animals, and more rarely of omnivores and predators (Clauss and Paglia 2012). However, few studies offer information on physiological concentrations of Fe in wild herbivorous, omnivorous, or carnivorous mammals. Herbivores accumulate the lowest amount of Fe. This is probably because the Fe form present in plants is non-heme (inorganic) and hard to assimilate. The hemolytic form of readily assimilable iron occurs in foods of animal origin, which may explain the higher content of this element in piscivorous and carnivorous animals than in herbivores (Soetan et al. 2010).

Ranges of Fe concentration obtained during ecotoxicological studies from vertebrates of different taxonomic groups and between individuals of the same species vary greatly, making it difficult to interpret the results, which, in turn, deters many scientists from such studies, and so they are rarely undertaken.

6.1.1 Bioaccumulation of Fe in Herbivorous Mammals

In the diet of herbivorous mammals, iron interferes with many other elements. Cobalt (Co), manganese (Mn), and nickel (Ni) inhibit the uptake and transport of Fe, whereas zinc (Zn), phosphorus (P), potassium (K), sulfur (S), and calcium (Ca) decrease its bioavailability and disturb its metabolism (Kabata-Pendias and Szteke 2012; Sears 2013). Iron deficiency is not normally observed in ruminants (Doyle and Spaulding 1978). Mean hepatic Fe concentrations in large and medium wild herbivorous mammals range from 100 to 2800 mg kg^{-1} dw (Table 6.1). According to Puls (1994), a typical Fe concentration in the liver of domesticated ruminants changes between 100 and 200 mg kg^{-1} ww (or 330–670 mg kg^{-1} dw).

Table 6.1 The iron concentration in selected tissues of herbivorous mammals

Species	Location	Fe concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Ruminants					
Red deer *Cervus elaphus*	Poland, central part	147.8[a]	345.0[a]	109.2[a]	Michalska and Zmudzki (1992)
	Poland, S part	213	105	91	Swiergosz et al. (1993)
	Poland, NW part	102.5	66.98		Wieczorek-Dabrowska et al. (2013)
	Poland, NW part	126.7[a]	330[a]	101.7[a]	Falandysz (1994)
	Sweden			110[a]	Wilkund et al. (2014)
	Croatia	228.3[a]	505[a]	247.7[a]	Lazarus et al. (2008)
	Croatia		605[a]		Lazarus et al. (2005)
Fallow deer *Dama dama*	Slovenia	470[a]			Vengušt and Vengušt (2004)
White-tailed deer *Odocoileus virginianus*	USA, Georgia	320[a]			Lewis et al. (2001)
	USA, Virginia	S: 620[a]			Sleeman et al. (2010)
		H: 485.7[a]			
	USA, Dakota	537.8[a]			Zimmerman et al. (2008)
Mule deer *Odocoileus hemionus*	USA, California	600[a]			Roug et al. (2015)
	USA, South Dakota	514.6[a]			Zimmerman et al. (2008)
Roe deer *Capreolus capreolus*	Poland, central part	684.0[a]			Dlugaszek and Kopczynski (2011)
	Poland, NW part			127[a]	Dlugaszek and Kopczynski (2013)
	Poland, NW part	240.2[a]	304.0[a]	117.3[a]	Michalska and Zmudzki (1992)
	Poland, NW part	1007[a]			Chudzinska-Popek and Majdecka (2010)
	Poland, NW part	201.4	106.3		Wieczorek-Dabrowska et al. (2013)
	Poland, northern part	150[a]	422.5[a]	91[a]	Falandysz (1994)
Elk/moose *Alces alces*	Russia, NW part, Karelia	578.1[a]	161.4[a]	170.5[a]	Medvedev (1999)
	Poland, NW part			90[a]	Falandysz (1994)
	Canada, NW part	693	171	232	McDonald et al. (2005)
	USA, Minnesota	848.5			Custer et al. (2004)
	Canada, Ontario	368.4	236.1	145.7	Parker and Hamr (2001)
Caribou *Rangifer tarandus*	USA, Alaska, northern part	2797[a]	892.5[a]	316.7[a]	O'Hara et al. (2003)
Reindeer *Rangifer tarandus*	Sweden	467[a]		98[a]	Odsjö et al. (2007)
	Sweden			113[a]	Wilkund et al. (2014)
	Russia, NW part, Karelia			179.9[a]	Medvedev (1999)

(continued)

Table 6.1 (continued)

Species	Location	Fe concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Lagomorphs					
European hare *Lepus europaeus*	Poland, central part	758[a]			Dlugaszek and Kopczynski (2011)
	Poland, central part			95.3[a]	Dlugaszek and Kopczynski (2013)
	Poland, NW part	730[a]	600.0[a]	138.7[a]	Myslek and Kalisinska (2006)
	Slovakia	163.3	159.0		Czajkowska et al. (2011)

We assumed that the kidneys contain 80% of water, liver and muscles 70% of water
H healthy, *S* sick with diarrhea
[a]Values converted from wet weight to the dry weight, dw

Medvedev (1999) showed that hepatic levels of Fe in the elk *Alces alces* (known as the moose in North America), which is a cervid species from the ruminant group, inhabiting the northern parts of Russia (Karelia) ranged from 115 to 273 mg kg^{-1} ww (385–910 mg kg^{-1} dw), and these were considered normal physiological levels. These values are similar to those determined by Puls (1994). Compared to the studies by Puls (1994) and Medvedev (1999), the values of Fe concentration proposed as physiological in the cervid liver by the Wisconsin Veterinary Diagnostic Laboratory (WVDL 2015) are lower (40–90 mg kg^{-1} ww or 130–300 mg kg^{-1} dw). The data on hepatic Fe in cervid species (elk/moose *Alces alces*, red deer *Cervus elaphus*, roe deer *Capreolus capreolus*, mule deer *Odocoileus virginianus*, fallow deer *Dama dama*, and reindeer/caribou *Rangifer tarandus*) as presented in Table 6.1 show that the mean values of Fe concentration are never lower than 100 mg Fe kg^{-1} dw. They usually range from 100 to 600 mg kg^{-1} dw, while the range is significantly higher in red deer from Poland and Croatia (Central and Southern Europe, respectively) (100–230 mg kg^{-1} dw) and similar to that defined by WVDL (2015). A significant Fe concentration in the liver, exceeding 600 mg kg^{-1} dw, was observed in moose and caribou from North America (O'Hara et al. 2003; Custer et al. 2004; McDonald et al. 2005) and in roe deer from Poland (Chudzinska-Popek and Majdecka 2010; Dlugaszek and Kopczynski 2011) as well as in the European hare *Lepus europaeus* from Poland (Myslek and Kalisinska 2006).

Although iron toxicity is rare in ruminants, it does occur (Doyle and Spaulding 1978; Clauss and Paglia 2012). In reindeer from Svalbard (Norway), whose diet varies during the year with respect to Fe content and who starve during winter, a loss of body mass is observed, including the liver (about 40% and 65%, respectively). In this species so-called seasonal liver siderosis was described. In late winter, the liver of reindeer foraging on iron-rich plants or plants with a normal iron level can contain 2910 and 1650 mg kg^{-1} ww (or 9700 and 5500 mg kg^{-1} dw), respectively (Borch-Iohnsen and Nilssen 1987). Another example of cervids with iron overload affecting the liver is the red deer from Germany. Iron storage disease was diagnosed in a few

2-year-old males of the same herd, and on top of that, cachexia and weight loss were observed. Hepatic Fe concentrations were very high in these animals (1108–-2275 mg kg^{-1} ww or 3690–7580 mg kg^{-1} dw). A possible genetic basis connected with the cervid hemochromatosis gene (HFE) was identified and compared between diseased and healthy red deer, but the results did not reveal any differences in HFE sequences (Olias et al. 2011). The authors found significantly increased Fe concentration in the water used by the animals and suggested that polymorphisms in other non-HFE genes involved in iron metabolism may have led to a higher sensitivity to iron in some members of the investigated herd. Probably an emaciation of diseased red deer and the loss of liver weight connected with this resulted in a simultaneous increase of iron concentrations in hepatic cells. The work by Borch-Iohnsen and Nilssen (1987) and Olias et al. (2011) indicates that in comparative studies related to hepatic Fe concentration in wild animals, greater emphasis should be paid to the condition of the animals and to seasonal changes in the quality of their food.

Ecotoxicological studies in Central Europe related to hepatic concentration of Fe in the European hare have shown that specimens from Poland contained over four times more of this metal than hares from neighboring Slovakia (~740 and 160 mg kg^{-1} dw, respectively). Also in roe deer from various parts of Poland, average Fe concentration in the liver ranged widely – from 150 to >1000 mg kg^{-1} dw. Thus, even in populations of the same species of mammal living at relatively short distances from one another, hepatic Fe concentrations can reach significantly different values (Table 6.1). This may be related to the effects of other heavy metals present in the environment and/or to the condition of the tested animals (Dlugaszek and Kopczynki 2011; Wieczorek-Dabrowska et al. 2013).

Iron is more rarely assayed in the kidneys than the liver of wildlife. Average Fe concentration in the kidneys of herbivorous mammals changes within the range of 70–1500 mg kg^{-1} dw and is smaller when compared to the liver range. On the whole, hepatic Fe level is higher than the nephric one (Table 6.1). According to Puls (1994), adequate nephric Fe level in ruminants ranged from 30 to 150 mg kg^{-1} ww (150–750 mg kg^{-1} dw), but in cervids this range is probably narrower: 45–90 mg kg^{-1} ww or 225–450 mg kg^{-1} dw (WVDL 2015). However, as indicated in Table 6.1, mean nephric Fe concentration in cervids usually remains within the range of 100–500 mg kg^{-1} dw, in which the lower threshold is lower than that in the studies cited here. The levels of Fe in the kidneys of herbivores are rarely higher than 600 mg kg^{-1} dw, for example, in caribou from Alaska, USA, and in the European hare from Poland (O'Hara et al. 2003; Myslek and Kalisinska 2006).

Mean Fe concentrations in the muscle of wild herbivores range from 90 to 320 mg kg^{-1} dw and usually remain within the range of 90–150 mg kg^{-1} dw (Table 6.1). Doyle and Spaulding (1978) as well as Puls (1994) describe a somewhat narrower range for the meat of domesticated ruminants: 64–130 and 45–54 mg Fe kg^{-1} dw, respectively. Generally speaking, Fe content in the flesh of domesticated animals is lower than in wild ruminants (Wilkund et al. 2014).

On the basis of the analyzed studies, average concentrations of Fe in the liver, kidneys, and muscles of large- and medium-sized herbivorous mammals generally remain within the range of 100–600, 100–500, and 90–150 mg kg^{-1} dw, respectively.

6.1.2 Bioaccumulation of Fe in Omnivorous Mammals

From the ecological point of view, the raccoon *Procyon lotor* (native to North America) and wild boar *Sus scrofa* (indigenous to Eurasia) can be ranked as omnivorous mammals. However, they belong to separate taxonomic orders (carnivore Carnivora and even-toed ungulates Artiodactyla, respectively). Both species are widespread as invasive species outside the area of their natural distribution (Genovesi et al. 2009; Snow et al. 2017). The raccoon is an opportunistic carnivore that relies on both aquatic and terrestrial habitats for foraging and may accumulate heavy metals present in either or both habitats (Souza et al. 2013). The wild boar is a typical terrestrial species, and its diet is dominated by plant material (Ballari and Barrios-García 2014). Assaying the content of elements in the tissues and organs of raccoons and wild boars is one way of evaluating their nutritional status and the partial environmental exposure of these animals, which is important for potential game consumers (Souza et al. 2013; Dlugaszek and Kopczynski 2011). Although, as an invasive species, the wild boar inhabits North America, and the raccoon Europe, there are no studies on Fe in these animals living outside their natural range. So far, no physiological Fe concentrations have been established either for the wild boar or the raccoon. In the case of wild boar, it can be assumed that they are close to the adequate values given for porcine and swine by Puls (1994) and WVDL (2015). Both of these reports of hepatic concentrations were given as normal levels of 100–200 mg Fe kg^{-1} ww (330–670 mg Fe kg^{-1} dw). In the livers of wild boar from various parts of Poland, mean Fe concentration ranges between 100 and 870 mg kg^{-1} dw, but does not usually exceed 300 mg kg^{-1} dw (Michalska and Zmudzki 1992; Swiergosz et al. 1993; Dlugaszek and Kopczynski 2011). In Italy the hepatic Fe level of the species was found to be ~420 mg kg^{-1} dw (Zaccaroni et al. 2003). These data indicate that mean Fe concentration in the liver of wild boar oscillated around the lower values given for swine. Michalska and Zmudzki (1992) noticed that in good nourished wild boar, hepatic Fe concentration was significantly higher in autumn than in spring (290 and 240 mg kg^{-1} dw, respectively). This observation also applies to the kidneys and muscles of wild boar obtained in autumn. In spring their nephric Fe and muscular concentrations were about 560 and 420 and 163 and 76 mg kg^{-1} dw, respectively. In comparison with data from Michalska and Zmudzki (1992) concerning Fe levels in the kidneys of wild boar from South Poland, Swiergosz et al. (1993) found that concentration of this metal in animals from the central part of that country was twice as low (55 mg kg^{-1} dw). There are significantly more reports on muscle Fe than offal Fe of the species because its meat has the highest value for consumers. Iron content in meat depends on the amount of fat and blood (Strazdina et al. 2013). Therefore, mean muscle Fe concentration in European wild boar can vary from 60 (in Romania) to 170 (in Poland) mg kg^{-1} dw (Crăciunescu et al. 2014; Roslewska et al. 2016), while the values usually fall within the range of 80–120 mg kg^{-1} dw (Swiergosz et al. 1993; Dlugaszek and Kopczynski 2013; Strazdina et al. 2013).

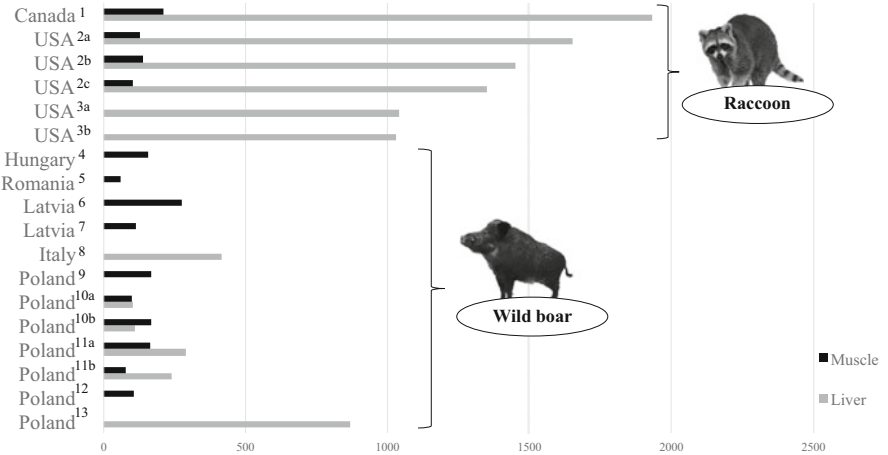

Fig. 6.1 Hepatic and muscle iron concentrations (mg kg^{-1} dw) in raccoons from North America and wild boar from Europe (raccoon: 1. Wren 1984; 2. Souza et al. 2013: 2a polluted area in 2009, 2b polluted area in 2010, 2c unpolluted area; 3. Lewis et al. 2001: 3a studied group, 3b control group), wild boar (4. Skobrák et al. 2011; 5. Crăciunescu et al. 2014; 6. Strazdina et al. 2014; 7. Strazdina et al. 2013; 8. Zaccaroni et al. 2003; 9. Roslewska et al. 2016; 10. Swiergosz et al. 1993: 10a Niepolomicka Forest, 10b Beskid Sadecki; 11. Michalska and Zmudzki 1992: 11a in autumn, 11b in spring; 12. Dlugaszek and Kopczynki 2013; 13. Dlugaszek and Kopczynki 2011)

In North America raccoon is classified as a game species, and its meat is used for human consumption and for bioindicative purposes yet more rarely than that of wild boar in Europe (Fig. 6.1). Raccoon is solely opportunistic in its feeding habits. Fruits, insects, acorns, and crayfish are normally the main elements of its diet (Wilhide et al. 1992). Average concentration of Fe in the liver and kidneys of raccoon ranges from 1030 to 1940 and 458 to 1970 mg kg^{-1} dw, respectively (Wren 1984; Lewis et al. 2001; Souza et al. 2013).

Souza et al. (2013) determined Fe concentration in the liver, kidney, and muscle of raccoons originating from areas unexposed and exposed to coal fly ash. Only muscle Fe concentration was significantly higher in raccoons from the polluted areas (~130 mg kg^{-1} dw) than the unpolluted areas (~100 mg kg^{-1} dw). When comparing Fe concentration in the livers of two omnivorous species from Europe and North America, it may be noticed that wild boar livers contain 2–3 times less Fe than those of raccoons, which may result in a higher percentage of animal material in the diet of raccoons than in the diet of wild boar, for whom plants contribute to even 90% of their food (Ballari and Barrios-García 2014).

In the case of muscle Fe, such clear interspecies differences are not observed (Fig. 6.1). What is more, as far as Fe concentrations in raccoon are concerned, there is clear and strong differentiation between tissues (liver > kidney > muscle), but no such trend has been observed in wild boar. Sometimes the concentration of Fe in the kidney was higher than in the liver (Michalska and Zmudzki 1992), or Fe concentrations in the liver and muscle were similar (~100 mg kg^{-1} dw) and lower in the kidneys by half (Swiergosz et al. 1993).

6.1.3 Bioaccumulation of Fe in Carnivorous Mammals

With respect to their diet, carnivores dwelling on land can be divided into piscivores, which are associated with aquatic habitats (including river otter *Lontra canadensis* and American mink *Neovison vison*), typical terrestrial predators (mainly canids such as gray wolf *Canis lupus*, red fox *Vulpes vulpes*, arctic fox *V. lagopus*, and raccoon dog *Nyctereutes procyonoides*), and opportunistic predators, which feed on small- and medium-sized endothermic animals and, to a lesser degree, on fruit and other plant material. This last group includes, for example, representatives of the genus *Martes*. The species most commonly used in ecotoxicological studies of Fe include American mink, otters, and canids, but the number of such studies is not large. Most data on normal metal concentrations found in the literature pertain to American mink and dog, because they are domestic or partially domestic mammals (Stejskal et al. 1989; Puls 1994). American mink, as a fur-bearing species, is farmed in North America, Europe, and on other continents, but the animals sometimes escape from farms and live as feral (Bowman et al. 2017). Stejskal et al. (1989) determined mean Fe concentrations in the liver and kidneys of the adults of natural dark ranch mink to be as high as 392 and 206 mg kg^{-1} ww (or 1310 and 1030 mg kg^{-1} dw, respectively). In wild minks from Canada (British Columbia and Ontario), the mean values of hepatic Fe concentrations were similar to those described by Stejskal et al. (1989) (Fig. 6.2). However, nephric Fe levels in mink from Ontario (Wren et al. 1988) and British Columbia (Harding et al. 1998) were lower than those reported by Stejskal et al. (1989) by about 17% and 43%,

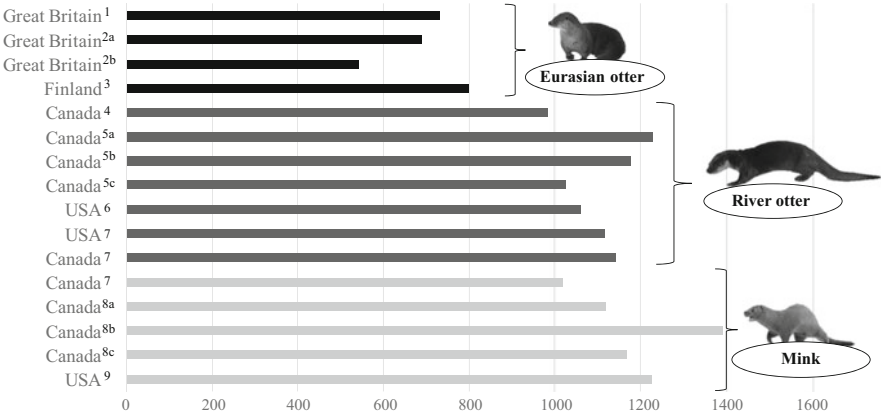

Fig. 6.2 Hepatic iron concentration (mg kg^{-1} dw) in piscivorous mammals (from Europe – Eurasian otter: 1. Walker et al. 2011; 2. Walker et al. 2010: 2a year 2007, 2b year 2008; 3. Lodenius et al. 2014; from North America: river otter; 4. Wren 1984; 5. Wren et al. 1988: 5a Muskoka, 5b Sudbury, 5c Turkey Lake; 6. Grove and Henny 2008; 7. Harding et al. 1998; wild American mink: 7. Harding et al. 1998; 8. Wren et al. 1988: 8a Muskoka, 8b Sudbury, 8c Turkey Lake; ranch mink: 9. Stejskal et al. 1989)

respectively. Although the concentrations of different metals were investigated in feral American mink living in Europe, they did not concern iron (Brzezinski et al. 2014; Ljungvall et al. 2017).

As indicated in Fig. 6.2 in river otters from Canada and the USA, hepatic Fe concentrations change within a small range (980–1230 mg kg^{-1} dw). Only in young specimens can it be significantly lower (~830 mg kg^{-1} dw) than in adults, as indicated by Grove and Henry (2008). Usually mean Fe concentrations in the liver of the river otter are similar to those of wild and ranch mink. Similarly to the wild mink, kidney Fe levels in river otters are generally lower than liver Fe levels. River otters had mean values of nephric Fe concentration within the range of 130–195 mg kg^{-1} ww or 650–970 mg kg^{-1} dw (Wren 1984; Wren et al. 1988). In Eurasian otters from Great Britain and Finland, only hepatic Fe concentrations were measured, and their average values were within the range of 540–800 mg kg^{-1} dw (Fig. 6.2). It appears therefore that in comparison with North American otters, mean Fe concentration in the liver was lower by a few hundred mg kg^{-1} dw. These differences in hepatic Fe concentrations between river and Eurasian otters may result from the biological parameters of the studied animals and be affected by local environmental factors, including the presence of other heavy metals in the otters' food (Wren et al. 1988; Grove and Henny 2008; Walker et al. 2010, 2011; Lodenius et al. 2014).

Mean values of Fe concentration in the kidneys of wild piscivores from North America ranged from ~460 to 960 mg kg^{-1} dw and were lower than those in their livers (Wren 1984; Wren et al. 1988; Harding et al. 1998). It seems that nephric Fe concentration in wild mink is lower in comparison with ranch animals: 456–880 versus 1030 mg kg^{-1} dw (Wren et al. 1988; Stejskal et al. 1989; Harding et al. 1998). In other North American mustelid species, like marten (*Martes americana*), Fe levels in the kidney were similar to those in wild mink and reached 777 mg kg^{-1} dw (Harding 2004).

In ecotoxicological studies of heavy metals, different canid species are utilized. Natural hepatic Fe concentration in the domestic dog is 400–1200 mg kg^{-1} dw (Puls 1994). According to WVDL (2015), normal, deficient, and toxic hepatic Fe concentration in canines ranges from 100 to 300 mg kg^{-1} ww (330–1000 mg kg^{-1} dw), 20 to 60mg kg^{-1} ww (70–200 mg kg^{-1} dw), and above 500 mg kg^{-1} ww (>1700 mg kg^{-1} dw), respectively. Normal nephric levels remain within the range 66–150 mg kg^{-1} ww or 330–750 mg kg^{-1} dw (WVDL 2015). Schultheiss et al. (2002) determined liver Fe concentration and analyzed pathological symptoms in the organs of dogs. They found hepatic Fe levels between 177 and 7680 mg kg^{-1} dw. Dogs with concentrations >2400 mg kg^{-1} dw had severe inflammation and fibrosis, but they did not appear to have hemochromatosis. Some pathological changes (mainly mild periportal inflammation) also occurred in some dogs whose Fe concentration in the liver ranged between 1200 and 2400 mg kg^{-1} dw. In the progenitor of the dog, namely, the wolf (in individuals from four parts of North America), nephric Fe concentrations were assayed, and the mean values ranged between 102 and 172 mg kg^{-1} ww, but usually did not exceed 120 mg kg^{-1} ww or 600 mg kg^{-1} dw (Hoffman et al. 2010). It is only in wolves from Alaska, USA, that increased Fe levels were observed in the kidneys when compared to the normal

values determined for dogs (WVDL 2015). In wild Arctic foxes in North America (Canada) and Europe (Norway) and in red fox in Poland, the mean Fe concentration in the liver remains in the range between 110 and 344 mg kg^{-1} ww (370–1147 mg kg^{-1} dw) and generally does not deviate from the values determined for the house dog (Prestrud et al. 1994; Hoekstra et al. 2003; Binkowski et al. 2016).

However, in different canid species (silver fox, Arctic fox, and raccoon dog) kept at fur farms, mean hepatic concentration of Fe generally ranged between 1300 and 1500 mg kg^{-1} dw, which may indicate the occurrence of some pathological changes (Hanusová et al. 2007; WVDL 2015). Hepatic, nephric, and muscle Fe concentrations were investigated in farm raccoon dogs in Europe and Asia. In a European study, Hanusová et al. (2007) detected in the livers of males and females about 1300 and 1470 mg Fe kg^{-1} dw, respectively, but in an Asian analysis, the hepatic Fe concentration was at least 3.5 times lower in the control raccoon dog group in comparison with the cited report (Hou et al. 2012). For that reason using data obtained from farm animals to interpret Fe concentration in the livers of wild animals may have a rather limited significance. It is also worth noting that Fe concentration in the kidneys of farm raccoon dogs from Europe and Asia, as well as in wild red fox from Poland, was similar and ranged from 180 to 270 mg kg^{-1} dw (Hanusová et al. 2007; Hou et al. 2012; Binkowski et al. 2016).

Iron concentration in the muscles of carnivores is rarely studied. In wild animals, the highest value of Fe concentration was found in the river otter, an animal which swims and dives a lot throughout its life (158 mg kg^{-1} ww or 527 mg kg^{-1} dw), and values were much lower in red fox and brown bear: 103 and 218 mg kg^{-1} dw, respectively (Wren 1984; Medvedev 1999; Binkowski et al. 2016). In farm canids Fe concentrations in the muscle were within the range of 180–390 mg kg^{-1} dw (Hanusová et al. 2007; Hou et al. 2012).

6.1.4 Bioaccumulation of Fe in Micromammals

Fe concentration in the livers of micromammals followed a descending order: insectivorous shrew *Crocidura russula* > plant-eating rodents (bank vole *Clethrionomys glareolus*, Algerian mice *Mus spretus*, wood mice *Apodemus sylvaticus*, and yellow-necked mice *Apodemus flavicollis*). Mean hepatic Fe concentrations of insectivores and other micromammals are in the ranges ~730–3300 and 100–1080 mg kg^{-1} dw, respectively (Damek-Poprawa and Sawicka-Kapusta 2003; Sanchez-Chardi et al. 2007, 2009a, b; Marques et al. 2008). On the whole, Fe levels in the liver and kidneys of rodents are within 400–650 and 300–500 mg kg^{-1} dw (Damek-Poprawa and Sawicka-Kapusta 2003; Topolska et al. 2004; Martiniaková et al. 2010). Such a wide range of Fe concentration in the organs of micromammals can be most likely explained by differences in metabolism rates, altered feeding patterns, seasonal food availability, habitat suitability, and connectivity, as well as life-stage-related food (Martiniaková et al. 2010).

Most data related to medium and large wild mammals concern Fe concentration in the liver. As far as Fe concentration is concerned, they can be arranged in the

following order of magnitude: piscivorous > carnivorous > omnivorous > herbivorous. These data indicate that Fe concentrations in the liver, kidneys, and muscles of mammals vary not only among different tissues, are dependent on the species and may differ depending on the age of an animal and its trophic level. Sleeman et al. (2010), Grove and Henny (2008), and Puls (1994) observed significantly higher Fe concentration in the liver of juvenile white-tailed deer, river otters, and dogs than in adults. Moreover, Lazarus et al. (2008) found that Fe concentration was higher in the kidneys and muscles of juvenile red deer than in adults of the species. However, although the relationship between Fe levels in the liver, kidneys, and muscles and the age of an animal have been analyzed in roe deer, fallow deer, reindeer, raccoon dog, red fox, gray wolf, shrew, and otter, no significant relationship has been found (Prestrud et al. 1994; Medvedev 1999; Hoekstra et al. 2003; Vengušt and Vengušt 2004; Hanusová et al. 2007; Sanchez-Chardi et al. 2007; Dlugaszek and Kopczynski 2011, 2013; Walker et al. 2011; Binkowski et al. 2016).

Generally, there were no significant differences in Fe concentration in the tissues of many wild mammalian species related to their sex (Prestrud et al. 1994; Medvedev 1999; Hoekstra et al. 2003; Zaccaroni et al. 2003; Skobrak et al. 2011; Sleeman et al. 2010; Walker et al. 2011; Binkowski et al. 2016; Roslewska et al. 2016). In contrast to the papers cited above, Vengušt and Vengušt (2004) found significantly higher Fe concentration in the liver of female fallow deer when compared to that of males.

6.2 Bioaccumulation of Fe in Birds

Concentrations of trace elements, including Fe, in birds depend on a number of factors, including their position in the trophic chain, feeding and dietary habits, health condition, physiological state, and age, as well as the susceptibility of a given species to absorption of different elements (Kim et al. 1996; Kalisinska et al. 2009). Iron is accumulated in differing concentrations in the tissues and organs of birds. It becomes toxic above 100 mg kg body weight (bw), while at 1 mg kg bw, it results in anemia. High concentrations of Fe in the liver may indicate inflammatory processes in the body and immune response (Cook et al. 1974). Many factors affect the pathological deposition of Fe in birds' livers. It has been suggested, however, that parenchymal siderosis can hardly be explained by liver weight loss (Borch-Iohnsen et al. 1991; Dierenfeld et al. 1994; Sheppard and Dierenfeld 2002). It may well be related to diseases that the birds had previously suffered from and/or be a result of inflammatory processes in the body (Kalisinska et al. 2008). Saiz et al. (1990) suggested that excess Fe is stored in nontoxic form as ferritin molecules, mainly in the liver. It is therefore not unusual to find high hepatic Fe concentrations, which may reflect physiological variations in Fe levels related to the egg-laying process. High levels of Fe in the liver can be related to lead and zinc poisoning (Carpene et al. 1995).

Studies of Fe concentration in the organs of birds are not very common. In birds, Fe concentration is commonly determined in the liver, kidneys, muscles, feathers,

blood, brain, and bones. Even though Fe concentrations in wild birds are most often studied in the liver, the scientific literature has not proposed normal Fe values for different avian species. The Wisconsin Veterinary Diagnostic Laboratory determined normal, deficient, high, and toxic hepatic Fe concentrations in poultry, which ranged from 60–300mg kg^{-1} ww (200–1000 mg kg^{-1} dw), 30–35mg kg^{-1} ww (100–120 mg kg^{-1} dw), 300–2000 mg kg^{-1} ww (1000–6600 mg kg^{-1} dw), and above 8000 mg kg^{-1} ww (>26,000 mg kg^{-1} dw), respectively. Normal concentration in the kidneys of poultry ranges from 45 to 100 mg kg^{-1} ww (225–500 mg kg^{-1} dw), while the toxic level begins above 200 mg kg^{-1} ww (>1000 mg kg^{-1} dw) (WVDL 2015).

6.2.1 Bioaccumulation of Fe in Avian Liver, Kidney, Muscles, and Feathers

Among the various bird species, Fe concentration in different organs and tissues is most commonly analyzed in ducks, including genera *Anas* and *Aythya*. Because of their wide geographical ranges, long life, the fact that the species and the sex of those birds are easily recognizable, as well as the large sizes of their populations, this group of birds is considered a good biomonitor (Onderscheka et al. 1985; Furness and Greewood 1993; Kalisinska et al. 2004).

In adult ducks the highest iron concentrations were found in liver < kidneys < muscle (Kozulin and Pavluschick 1993; Kalisinska et al. 2004). Physiological concentration not exceeding 1000 mg kg^{-1} dw (WVDL 2015) was determined in mallards (*Anas platyrhynchos*) from Iran (Sinka-Karimi et al. 2015) and Korea (Kim and Oh 2012b), in pochards (*Aythya ferina*) from Iran (Sinka-Karimi et al. 2015), and spot-billed ducks (*Anas poecilorhyncha*) from Korea (Kim and Oh 2012a). Iron concentration exceeding 1000 mg kg^{-1} dw (ranging between about 1200 and 2800 mg kg^{-1} dw), indicating high Fe accumulation in the liver (WVDL 2015), was observed in common eider (*Somateria mollissima*) from Finland (Franson et al. 2000), mallards from central Poland (Kalisinska et al. 2004), and lesser scaup (*Aythya affinis*) and redhead (*Aythya americana*) from North America (Michot et al. 1994; Custer et al. 2003; Pillatzki et al. 2011). The highest average Fe concentration in the liver of Anseriformes was observed in great scaup (*Aythya marila*) from Alaska and in mallard from a polluted area in Russia, ranging from around ~4500 to 5900 mg kg^{-1} dw, respectively (Kozulin and Pavluschick 1993; Badzinski et al. 2009). However, these concentrations did not exceed 26,000 mg kg^{-1} dw, which would indicate toxic Fe concentration (WVDL 2015). In some cases, including the mynah bird (*Gracula religiosa*), which is one of the species most commonly reported to be susceptible to iron overload, hepatic Fe concentration ranged from ~6700 to 23,000 mg kg^{-1} dw (Mete et al. 2003).

In the kidneys, normal Fe concentration not exceeding 500 mg kg^{-1} dw was assayed in mallard and pochard from Iran (Sinka-Karimi et al. 2015). Higher Fe concentration was observed in the kidneys of mallard from Poland and Russia and ranged around 800 mg kg^{-1} dw (Kozulin and Pavluschick 1993; Kalisinska et al.

2004). Taking into consideration their habitat, nephric Fe concentrations in ducks from Asia were at physiological levels, but they reached high levels in the same species of birds from Europe (WVDL 2015).

Based on the data available in the literature, it was found that Fe concentration in the muscle of Anseriformes ranged from ~140 to ~370 mg kg^{-1} dw, which reflected physiological iron levels in the tissues (Proske et al. 1993; Kalisinska et al. 2004; Sinka-Karimi et al. 2015).

Passerines play an important role in the biomonitoring of terrestrial ecosystems. Some of the studied species include the house sparrow (*Passer domesticus*), the great tit (*Parus major*), and the blue tit (*Cyanistes caeruleus*), which have been studied in China, Finland, Poland, and Spain. However, there are only a few studies reporting on Fe concentrations in the organs of those birds, and they usually pertain to hepatic concentrations of this element. In the livers of great tit from Europe, Fe concentration ranged around ~1500 mg kg^{-1} dw (Ingervo et al. 1995; Llacuna et al. 1995; Sawicka-Kapusta et al. 1986). In house sparrow (*Passer domesticus*), hepatic Fe concentration did not exceed 570 mg kg^{-1} dw (Kekkonen et al. 2012). Twofold higher Fe levels were observed in the liver of the tree sparrow (*Passer montanus*) from industrial areas in China. In its muscles Fe level ranged from ~170 to ~270 mg kg^{-1} dw (Chao et al. 2003).

High Fe concentrations of several, sometimes even a few tens of thousands of mg kg^{-1} dw, were found in dead birds of prey, which had died in various circumstances and been found in the field. In the liver of these birds, which originated from Europe and Asia, Fe concentrations ranged from ~1030 to ~2500 mg kg^{-1} dw (Hontelez et al. 1992; Jager et al. 1996; Falandysz et al. 1988; Kalisinska et al. 2009; Kim and Oh 2015; Kitowski et al. 2017a, b). A significantly higher Fe concentration was reported, among others, in a severely emaciated female peregrine falcon (*Falco peregrinus*) from Poland, and amounted to over 6000 mg kg^{-1} dw (Kalisinska et al. 2008).

Even higher concentrations were reported by Kitowski et al. (2017a) in a few specimen of buzzard (*Buteo buteo*). In the liver of these birds, Fe concentration exceeded 18,000 mg kg^{-1} dw, which could indicate Fe hyper-accumulation. A high Fe level in the liver could be associated with serious bacterial and helminthological infections as well as cadmium (Cd), lead (Pb), or zinc (Zn) poisoning (Lewis et al. 2001).

Nephric Fe concentration in birds of prey ranged from ~530 to ~820 mg kg^{-1} dw (Jager et al. 1996; Falandysz et al. 1988; Kalisinska et al. 2006, 2008, 2009). Higher levels of nephric Fe of ~1200 mg kg^{-1} dw were reported by Hontelez et al. (1992) and Falandysz et al. (2000) in buzzard from the Netherlands and white-tailed eagle from Poland (*Haliaeetus albicilla*), respectively. Mean concentration of Fe in the muscles of white-tailed eagle did not exceed 400 mg kg^{-1} dw (Falandysz et al. 1988, 2000; Kalisinska et al. 2006; Mihaljev et al. 2012).

In birds associated with aquatic ecosystems, including the gray heron (*Ardea cinerea*) and black-crowned night heron (*Nycticorax nycticorax*), Fe concentrations were mainly assayed in the liver. The average Fe concentration in the liver of those birds varied from ~600 to ~820 mg kg^{-1} dw (Kim and Oh 2015). Higher

concentrations were, however, found in the gray heron from Serbia (Mihaljev et al. 2012) and in the bald eagle (*Haliaeetus leucocephalus*) from Alaska (Stout and Trust 2002). Such wide ranges of Fe concentration in a specimen of the same species and the same trophic group make it difficult to interpret the results. The average nephric Fe concentrations in the intermediate egret (*Egretta intermedia*) and in little egret (*Egretta garzetta*) were similar and ranged between 350 and 450 mg kg^{-1} dw (Kim et al. 2010; Kim and Oh 2015). Much lower Fe concentrations in the kidney were noted in the western reef egret (*Egretta gularis schistacea*), and they did not exceed 40 mg kg^{-1} dw (Mansouri et al. 2012).

Ecotoxicological studies researching Fe concentration in the tissues and organs of herbivorous birds were carried out in Korea, Russia, and the USA. Fe concentration in the liver of these birds depended, among other factors, on their habitat. In the mute swan (*Cygnus olor*) from Lake Erie, USA, hepatic Fe ranged from ~600 to ~12,000 mg kg^{-1} dw, and in birds of the same species from St. Clair, USA, it ranged between ~700 and 6000 mg kg^{-1} dw (Schummer et al. 2011). The concentration of Fe in the liver of the southern subpopulation of the lesser snow goose (*Anser caerulescens*) ranged between ~400 and ~4600 mg kg^{-1} dw and, in the liver of the northern subpopulation, from ~1200 to ~4200 mg kg^{-1} dw (Hui et al. 1998). The authors suggested that geese from the northern subpopulation feed in pastures and on coastal marshes and migrate along the coast, while those from the southern subpopulation feed predominantly in rice fields and migrate over farmland. Increased concentrations of various elements, including the organic forms of Hg, in rice paddy fields may possibly lead to changes in liver function, thus increasing, inter alia, hepatic Fe levels (Strickman and Mitchell 2017).

Rose and Parker (1982) determined that grouse's feathers act as a natural indicator of iron levels present in the environment – not, however, through endogenous incorporation of iron into growing plumage but through exogenous adsorption of iron onto plumage surfaces during the plumage year. There is little research pertaining to Fe concentration in bird feathers. There are just a few studies concerning birds associated with land and wetland ecosystems, including the cattle egret (*Bubulcus ibis*) and the black-crowned night heron (Abdullah et al. 2015; Kim and Koo 2007; Malik and Zeb 2009; Manjula et al. 2015; Ullah et al. 2014). The average Fe concentration in the feathers of these birds ranged from ~100 to ~340 mg kg^{-1} dw. The highest Fe concentrations were found in birds from highly urbanized areas (Abdullah et al. 2015; Manjula et al. 2015). High Fe concentrations in feathers may reflect diet and the mobilization quantities stored during the period of feather growth (Dauwe et al. 2000; Rattner et al. 2008). Fe concentration in the feathers of birds of prey, including ospreys (*Pandion haliaetus*) originating from the heavily polluted coastal waters of Chesapeake Bay (USA), differed significantly in the years 2000 and 2001 and amounted to ~170 mg kg^{-1} dw and ~80 mg kg^{-1} dw, respectively (Rattner et al. 2008). The authors suggest that Fe concentrations in feathers may be affected, among other factors, by extensive metal-working and petroleum refinery activities in this area.

Generally, there were no significant differences in Fe concentration in the tissues of various birds with respect to sex and age (Custer et al. 2003; Jager et al. 1996;

Janiga et al. 1990; Kekkonen et al. 2012; Malinga et al. 2010; Mansouri et al. 2012; Michot et al. 1994; Stout and Trust 2002). However, Sinka-Karni et al. (2015) observed that sex affected Fe levels in mallards, as females had a higher Fe hepatic concentration than males. This could result from differences in the production of metalloprotein, which plays a fundamental role in the transport, storage, and excretion of metals. Ingervo et al. (1995) observed that Fe concentrations in the livers of female great and blue tits were lower than in the males. Schummer et al. (2011) observed significantly higher hepatic Fe concentration in female mute swans than in males. Borch-Iohnsen et al. (1991) attributed high iron content in the livers of female birds partly to catabolism of lean body tissue during incubation. Moreover, Proske et al. (1993) studied ducklings hatched in captivity, aged 1 day to 22 weeks, and found that the liver iron content increased between the ages of 1 and 16 weeks. Mallards from the two areas in northwestern Poland studied by Kalisinska et al. (2004) showed positive and significant correlations between muscle iron content and age. Greater Fe content in the muscles of adult ducks most likely results from physiological differences in muscle structure. Adult ducks protect young birds during flight and thus carry out more work.

Generally, hepatic Fe concentration in birds can be ranked in the following order: carnivores > herbivores > omnivores > piscivores (Fig. 6.3). Differences in Fe

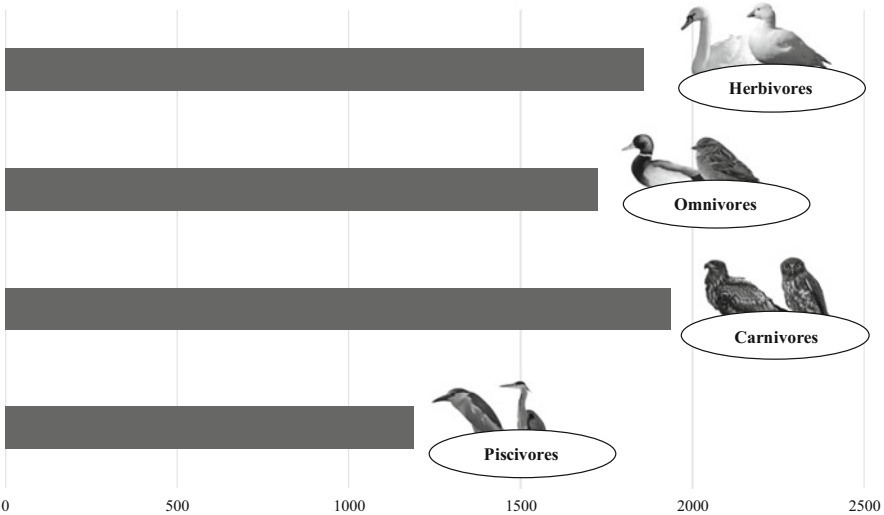

Fig. 6.3 The concentration of Fe (mg kg^{-1} dw) in the livers of birds with different diets based on herbivores (Hui et al. 1998; Schummer et al. 2011; Kim and Oh 2013b), omnivores (Sawicka-Kapusta et al. 1986; Michot et al. 1994; Ingervo et al. 1995; Franson et al. 2000; Chao et al. 2003; Custer et al. 2003; Kalisinska et al. 2004; Badzinski et al. 2009; Pillatzki et al. 2011; Kekkonen et al. 2012; Kim and Oh 2012b; Sinka-Karimi et al. 2015), carnivores (Falandysz et al. 1988, 2000; Hontelez et al. 1992; Esselink et al. 1995; Jager et al. 1996; Kalisinska et al. 2006, 2008, 2009; Kim et al. 2008; Kim and Oh 2012a, 2015; Mihaljev et al. 2012), piscivorous (Carpene et al. 1995; Stout and Trust 2002; Kim et al. 2010; Mansouri et al. 2012; Mihaljev et al. 2012; Kim and Oh 2013a, 2015)

content in bird tissues may be due to different physiological demands for this element at different times of life and the intensity of enzyme reactions in the cells. Despite various studies focusing on iron content in wild birds, our understanding of the concentration of this element in the parenchyma is only fragmentary, and further studies are needed. Such research should take into account various factors affecting Fe concentration in bird organs and tissues, including age, sex, diet, health condition, seasonal changes, and migrations. A multivariate analysis of this kind would certainly facilitate the interpretation of results.

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Chapter 7
Manganese, Mn

Elżbieta Kalisińska and Halina Budis

Abstract Manganese is considered an important essential trace element, and there is extensive literature concerning its accumulation in ecosystems. This metal is continuously released into the biosphere by volcanoes and the natural weathering of rocks, but also by numerous anthropogenic activities such as mining, fossil fuel combustion and industrial and urban waste. In this review, recent studies on manganese presence in soil, freshwater and terrestrial ecosystems and their organisms are presented. Metal speciation, natural and anthropogenic sources and level of bioaccumulation in biota, as well as abiotic and biotic factors affecting their bioavailability are reviewed, in addition to the use of bioindicator organisms for the biomonitoring of this metal in the environment and the related toxicity mechanisms and ecological effects of manganese pollution.

1 Introduction

Manganese (Mn) is an essential metal for humans, animals and plants. It is one of the most commonly used metals, especially in metallurgic and chemical industries; hence, its elevated levels in the environment cause excessive Mn exposure to terrestrial animals. Manganese plays an important role in the biochemical reactions of several enzymes, but its excessive amount in the body can cause both acute and chronic diseases (ATSDR 2012; O'Neal and Zheng 2015; Prashanth et al. 2015). Generally, Mn is found in low levels in all types of animal diet. Ingestion is the principal route by which animals are exposed to this metal, although toxicologically

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significant inhalation exposures also occur in humans and laboratory animals as it has been demonstrated (ATSDR 2012; Zeman et al. 2015; Wang et al. 2015).

The gastrointestinal and hepatobiliary systems play crucial role in regulating and maintaining Mn tissue levels within a relatively narrow physiologic range (Aschner and Aschner 2005; Foster et al. 2015; Zeman et al. 2015). It was observed that, in mammals, a moderate increase of Mn levels in the diet causes a compensatory decrease of Mn absorption in the gut and an increased Mn concentration in the liver. In such a condition, an elevated biliary excretion of Mn helps to maintain normal Mn level in the brain and other tissues (Aschner and Aschner 2005; Foster et al. 2015). Excessive exposure to Mn and/or results in disturbances in liver functioning can overwhelm normal homeostatic controls, which, in turn, results in elevated or toxic Mn levels in different tissues, especially in the central nervous system (O'Neal and Zheng 2015). The research on the role of Mn and its normal, deficient and excessive concentrations predominantly focuses on studying the tissues of domesticated and laboratory animals. Much fewer reports describe wild mammals and birds in which Mn uptake from the environment occurs mainly through food and water. Taking into consideration that the amount of anthropogenic Mn in nature has been steadily increasing, including increasing number of nanoparticles containing Mn that are ever more often released into aquatic and terrestrial ecosystems, it would seem worthwhile to monitor its concentration not only in air, water and soil but also in biotas (Karmakar et al. 2014; Pinsino et al. 2012).

In such biomonitoring, careful attention should be paid selecting species of animals representing different trophic groups and using appropriate types of samples. Systematic research conducted in different areas would allow for a better indirect assessment of Mn pollution in the environment and potential hazards to human health as well as for a direct assessment of health status of the analysed animals.

2 General Properties

Manganese (Lat. manganum, Mn) is a chemical element; it has an atomic number of 25 and an atomic weight of 54.94. It belongs to group 7 in the periodic table, next to iron (Fe). These metals have similar chemical properties and often coexist in different minerals and ores. The melting and boiling points of manganese are 1244 °C and 1962 °C, respectively, and its density is 7470 kg m^{-3}. Manganese compounds occur at oxidation states I, II, III, IV, VI and VII. The higher the level of oxidation, the greater the acidic character of manganese. At oxidation state II, Mn forms stable Mn^{2+} cations and, at oxidation state VII, MnO^{4-} permanganate anions. Manganese is a silvery metal, harder than iron, but more brittle. It reacts to diluted acids and water with hydrogen separation. This element is ubiquitous in the earth's crust and accounts for about 0.095% of its composition (Lide 2005; Yaroshevsky 2006). In nature, Mn most commonly occurs in the form of oxides, carbonates and silicates. Minerals in which Mn is most abundant include pyrolusite (MnO_2), of

which it constitutes 60–63% of its composition. Other important minerals containing Mn include rhodochrosite ($MnCO_3$), manganite ($Mn_2O_2•H_2O$), hausmannite (Mn_3O_4), braunite ($3Mn_2O_3•MnSiO_3$) and rhodonite ($MnSiO_3$). Minerals rich in Mn usually also contain other heavy metals: iron, cobalt, zinc or nickel (Adriano 2001).

3 Production and Uses of Manganese

The most valuable manganese ores are those containing more than 20% of this metal, but in some regions of the world, deposits with less than 5% of Mn are also mined (USGS 2017a). USGS (2017a, b) estimated world manganese ore production in 2015 to be 17,500 thousand metric tons (Mt). The largest producers of this metal are South Africa, Australia and China, which account for 34%, 17% and 14% of world production, respectively. More than 90% of land-based manganese resources belong to six countries: South Africa, Ukraine, Brazil, Australia, India and China (USGS 2017b).

Manganese is mainly used in ferroalloy production (about 90% of total Mn) and as an oxidizer in other metallurgical processes. In addition, it is used in the chemical, textile, ceramic and electrochemical industries (welding electrodes) and in the manufacturing of dyes, plant protection agents and fertilizers (Howe et al. 2004; USGS 2016). Manganese is an indispensable ingredient in the production of steel because it removes sulphur from molten pig iron, causes the deoxidation of steel and acts as a fusing agent. It also helps to increase the hardness and elasticity of steel, as well as its resistance to stress.

Manganese oxide is commonly used as a cathode in zinc manganese batteries. In the USA, such alkaline cells are commonly used in households, mainly in wireless electrical appliances and torches (Aschner et al. 2006). In the course of the development of the automotive industry, so-called leaded and highly toxic fuels have gradually been replaced by unleaded fuels, and a compound containing Mn—methylcyclopentadienyl manganese tricarbonyl, or MMT—was used as an antiknock agent to improve the work of car engines. This fuel additive was developed in the 1950s to increase the octane level of gasoline. As MMT is combusted in gasoline engines, manganese oxide, the main product of combustion, is released into the atmosphere. In urban environments with heavy traffic, the concentration of manganese in the air is many times greater than in suburban areas (Loranger and Zayed 1997; Zayed et al. 1999; Vezer et al. 2005). Over the course of time, due to the negative impact of MMT on human health and the environment, the use of this substance has been restricted or prohibited in many countries. Recent data suggest that MMT is rarely used in developed countries, including Canada and the USA, nowadays (ATSDR 2012).

4 Manganese in Nature: Geogenic and Anthropogenic Sources

Manganese is a trace element present in rocks, soils, waters, air and food (Reimer 1999). In soils, this metal is found in mineral and organic compounds, and its concentration is estimated at 500–900 mg kg^{-1} dry weight, dw (WHO 1999, 2004). In the air, manganese is a constituent of dust, the transport of which depends on the size and density of the particles forming it and the speed and direction of the wind. Weathering rocks and soil are the main sources of atmospheric Mn. Other important sources include ocean evaporation, forest fires, plant vegetation and volcanic activity (Schroeder et al. 1987). At the end of the 1980s, it was estimated that 2/3 of Mn present in the atmosphere came from natural sources (Stokes et al. 1988). However, since the beginning of the 1990s, there has been a dramatic increase in the content of this metal in the environment, especially in the air, as the result of human economic activity. In 1995, emissions of Mn compounds into the atmosphere were 30% higher than in 1983, most of which came from the industrialized countries of Asia, following those in the North America and Europe (Pacyna and Pacyna 2001).

Nearly 80% of industrial emissions of Mn are related to the production of iron and steel (EPA 2003). Concentration of this metal near industrial centres ranges from 0.22 to 0.30 μg Mn m^{-3} (WHO 2004), while in areas remote from them, it does not exceed 0.01 μg Mn m^{-3} (Sweet et al. 1993).

The dust, containing Mn compounds, which migrates to the atmosphere in the process of manganese ore mining, metal melting and fuel production, is particularly dangerous to human health as it can cause various respiratory and nervous system diseases (Williams-Johnson 1999). Neurological symptoms occur in people exposed to Mn levels of about 2000 μg m^{-3}.

Manganese migrates into the water from soil, dead plant parts and industrial pollutants dumped into surface waters where it can undergo oxidation or adsorption to sediment particles, depending on factors such as pH, presence of anions and oxidation potential (ATSDR 2000). Groundwater with poor oxygen content, or entirely depleted of it, often shows elevated concentrations of dissolved manganese. Bivalent manganese (Mn^{2+}) is prevalent in most waters with pH values between 4 and 7. Manganese can occur at higher oxidation states if the pH value of water is higher, but its higher valency may also be due to microbial oxidation. Generally, mean concentrations of Mn are 16 and 5 μg Mn L^{-1} for surface and groundwater, respectively. Natural Mn concentrations in seawater range from 0.4 to 10 μg Mn L^{-1}. In some groundwaters, lakes and reservoirs, Mn concentrations can reach up to 1300 μg L^{-1} in neutral conditions and 9600 μg L^{-1} in acidic environments (ATSDR 2012). The presence of Mn in groundwater is often detected as the result of its ubiquity in soils and rocks. Similarly, Mn is also found in surface waters, but its concentrations are generally too low to cause any adverse health effects. Manganese is commonly found in sediments, plant and animal tissues, and the process of manganese accumulation in aquatic ecosystems is much more intense than in

terrestrial ones (US EPA 2003; WHO 2011). Concentrations of Mn found in some water organisms (phytoplankton, algae, molluscs and some fish) suggest only slight bioaccumulation, while in higher organisms, bioaccumulation does not occur (ATSDR 2000; US EPA 2003; Niemiec and Wisniowska-Kielan 2015). Biomagnification of this element in the food chain appears to be of little importance (ATSDR 2000). Nriagu and Pacyna (1988) estimated that in 1983, between 109,000 and 414,000 tons of Mn of anthropogenic origin found its way into the water environment, mainly from municipal sewage and landfills. At the same time, it should be noted that potassium permanganate ($KMnO_4$), which has strong oxidizing, bactericidal and fungicidal properties, is commonly used in many countries for water purification. It is also used to reduce and eliminate unpleasant odours and as air freshener, especially in paint factories and processing plants (ATSDR 2012).

Manganese is a naturally occurring component of almost all soils, and its concentration (ATSDR 2000) ranges from <2 to 7000 mg kg^{-1} (or ppm) dw and an average of 550 ppm dw (Shacklette and Boerngen 1984; ATSDR 2000). Mn accumulation takes place in the substrate rather than on the surface of the soil (ATSDR 2000). It is estimated that 60–90% of Mn in the soil is bonded with a fraction of sand (WHO 1981).

5 The Biological Role of Manganese

Manganese is an essential element for plants because it plays an important role in many processes, including chlorophyll production. It works as an activating factor in more than 35 different plant enzymes. The uptake and transfer of manganese in plants occurs in the form of Mn^{2+}. Younger plant organs are richer in Mn than older ones (Mousavi et al. 2011). A wide range of Mn concentrations were found in plants (10–600 mg kg^{-1} dw mean is about 50 mg kg^{-1} dw). However, high Mn levels may be toxic for plants and induce iron deficiency (Lohry 2007). Manganese is also essential for the proper development and functioning of invertebrates and endothermic vertebrates. It is included in many enzymes and is involved in reproduction and growth processes, the metabolism of carbohydrates and fats, the functioning of the immune system and the processes of cartilage and bone formation (Erikson and Aschner 2003; Erikson et al. 2005; Baden and Eriksson 2006). In freshwater crustaceans from pristine areas, the highest Mn concentrations (~100 or more mg kg^{-1} dw) are found in midgut glands, exoskeletons and gills. Mn concentration in the muscles is usually several and rarely several dozen, mg Mn kg^{-1} dw (Baden and Eriksson 2006). Benthic organisms are especially sensitive to the accumulation of Mn, which is much higher in water sediments. In these organisms, average concentration of this metal is about 25 mg kg^{-1} dw (Niemiec and Wisniowska-Kielan 2015). In fish, depending on the species, the highest Mn levels are observed in the skin and gills (6–8 and 2–9 mg kg^{-1} ww, respectively) and are significantly lower in the liver

(~0.8 mg kg^{-1} ww) and muscles (~0.2 mg kg^{-1} ww). In benthic fish, such as bream *Abramis brama*, a much higher Mn concentration was found in the skin and gills than in the analogous parts of predatory pike *Esox lucius* (Rajkowska and Protasowicki 2013).

In mammals, manganese is found in every kind of tissue, mainly in the form of metalloenzymes, sometimes in combination with pyruvate carboxylase, superoxide dismutase and glycosyltransferases. Its concentration ranges from 0.3 to 2.9 mg kg^{-1} ww, while tissues rich in mitochondria and pigments (including retina and dark skin) tend to have high Mn concentrations (Prashanth et al. 2015). Metalloenzymes containing Mn play an important role in the metabolism of amino acids, cholesterol and carbohydrates (Reynolds et al. 1998). Manganese is also involved in the processes of ossification and synthesis of cartilage and mucopolysaccharides, i.e. in the processes of formation of chondrocytic tissues, which is especially intensive in young organisms (Schroeder et al. 1966; Hurley and Keen 1987; Levander 1988; Freeland-Graves and Llanes 1994; Wedler 1994; Reynolds et al. 1998; Smrcka 2005).

The uptake of Mn in mammals and birds occurs through the digestive and respiratory tracts. Manganese absorption through the airways is poorly understood. It is known, however, that grains of Mn dust (especially in the form of oxides: MnO_2 i Mn_3O_4) with a diameter of less than a few tenths of a micrometre are absorbed into the bloodstream from the lungs, which, in cases of chronic exposure, may trigger respiratory disease. Mn molecules of small enough size enter the bloodstream, where they are found in compounds with transferrin and α-macroglobulin (ATSDR 2008). The main source of Mn in animals is food. The highest concentrations of this metal (expressed dw) are found in nuts (up to 47 mg kg^{-1}), legumes (up to 7 mg kg^{-1}) and cereal grains (up to 41 mg kg^{-1}) and the smallest in meat, fish and eggs (0.10–3.99 mg kg^{-1}) and fruit (0.20–10.38 mg kg^{-1}) (WHO 2011). In fields and grasslands treated with fertilizers containing Mn, leaves and roots may reach hundreds or even thousands of mg kg^{-1} dw. Such high Mn concentrations in plants may be toxic for them and also become a cause of excessive Mn accumulation in herbivorous animals (Millaleo et al. 2010; Reis et al. 2010).

Only 3–7% of absorbed Mn from food remains in the body. It is most effectively deposited in the liver, pancreas, kidneys and bones, in which over 40% of all Mn in the body is found (O'Neal and Zheng 2015). Mn is transformed in the liver from its Mn^{2+} form into Mn^{3+}, which is associated with transferrins and transported to cells. In this transformation Mn can be replaced by other metals, including magnesium (Scheuhammer and Cherian 1983). Manganese absorption from the gastrointestinal tract occurs mainly through the mucous membrane, in duodenum and ileum. This process is influenced by many factors, including the presence and concentration of other metals in food and the body (iron, calcium), the age of the organism and environmental exposure (CICAD 1999).

Manganese is metabolized in the liver. Inorganic and organic Mn compounds are mainly excreted in faeces (40–70%). Small amounts are also expelled in urine, perspiration and milk (Newland 1999).

5.1 Manganese Deficiency and Excess

Manganese deficiency in various organisms may cause growth disorders, skeletal deformities and glucose intolerance problems (Erikson et al. 2005). Deformities in the bone structure caused by this deficiency are the result of enzymatic defects in the synthesis of glycosaminoglycans, which are part of the sugar part of glycoproteins forming the organic framework of connective tissue, including cartilage and bone. Cartilage tissue makes up a large share of the skeleton in the early postnatal period.

Therefore, most abnormalities in the skeletal structure are related to morphological changes in the epiphyseal cartilage and epiphyseal plate, within which the growth of long bones occurs (Mills et al. 1976; Watts 1990). Manganese deficiency has been demonstrated in several animal species, including laboratory animals, swine, cattle and poultry. Symptoms of Mn deficiency in animals include skeletal deformities, inhibited growth and neurological disorders, such as problems with motor coordination (Gehrke 1997; Takeda 2003; Spears 2011). As a result of experimental insufficient Mn supply in the diet of laboratory and farm animals, their bones became shorter and more fragile than normal (Ellis et al. 1947; Spears 2011). Moreover, it was found that the complete absence of Mn in food causes dysfunction in milk production in mammals, and the atrophy of certain organs, as well as a decrease in bone density, and infertility in cattle (ATSDR 2012). In birds, Mn deficiency results in *perosis* (or slipped tendon), skeletal deformities, impaired growth and eggshell formation and, in young chicks, cartilage dystrophy (Underwood 1981; Soetan et al. 2010).

Not only Mn deficiency but also its excess can be harmful to animals because it can cause metabolic disturbances in other elements, such as iron. Manganese introduced into mammalian organisms in too large quantities acts as a neurotoxin and osteotoxin and disrupts the physiology of many other tissues and organs (Mergler and Baldwin 1997). Manganese penetrates through the blood-brain barrier, and therefore with large Mn accumulation in the body, symptoms of brain damage appear, especially extrapyramidal symptoms, including those related to the corpus striatum and globus pallidus. Muscle stiffness and dystonia, motor slowdown, spasmodic movements and tremors may also occur (Davis 1999; Newland 1999; O'Neal and Zheng 2015).

In humans, exposure to excessive amounts of Mn results in clinical signs and symptoms resembling Parkinson's disease (O'Neal and Zheng 2015). With smaller Mn exposure, mammals experience neurobehavioral disorders, especially in cognitive functioning (Levy and Nassetta 2003; Knauer et al. 2017). Schneider et al. (2006) observed the influence of Mn on the behaviour of monkeys. Long-tailed macaque (*Macaca fascicularis*), which suffered from chronic exposure to this metal, exhibited abnormal behaviours, including uncontrolled reactions, decreased motor activity and problems with executing movements.

The adverse effects of Mn excess on the bones and the symptoms accompanying it have been relatively well documented in laboratory animals. Komura and Sakamoto (1992) reported damage to the central nervous system and growth

inhibition in mice. It has also been shown that an excess of Mn causes a decrease in proteoglycan levels, inhibiting DNA and collagen synthesis in chondrocytes (Litchfield et al. 1998). It was observed that toxic levels of Mn in mice caused poor rib development in their foetuses, with reduction or complete lack of ossification in segments of the sternum, as well as the parietal and occipital bones (Sanchez et al. 1993; Torrente et al. 2000). In addition, Doyle and Kapron (2002) demonstrated the adverse effect of excessive Mn concentration on the calcification process of growth plate in murine chondrocyte cell cultures. These researchers believe that excessive levels of Mn in the mother's body, which occurs in the embryo at the chondrogenesis stage, might result in skeletal deformities of the foetus.

Little information can be found in the literature regarding the effects of Mn overload on the skeletal and nervous systems of wild endothermic vertebrates. The existing data are scarce and pertain mostly to birds and few species of mammals, especially herbivores. Even less information in that respect can be found on predators.

5.2 Bioindicators and Biomarkers of Manganese in Ecotoxicological Studies

Evaluation of the quality of the natural environment can be carried out based on indicator organisms, i.e. bioindicators. Vertebrates, especially birds and mammals, have been increasingly used as bioindicators. Based on analysis of the mineral composition of various tissues and organs of endothermic vertebrates, attempts are made to indirectly assess the state of the environment.

Different taxonomic and trophic groups of endothermic vertebrates, originating most commonly from Europe and North America, underwent comparative analysis. For most wild mammals and birds, normal, marginal and toxic ranges of manganese concentration in different tissues were not defined. The normal values assumed by Puls (1994) and Wisconsin Veterinary Diagnostic Laboratory (WVDL 2015) for some species and/or taxonomic groups (bovine, cervid, lapine, porcine, canine, poultry, birds) may serve as a certain frame of reference in relation to wild animals. The data available in the literature, mainly pertaining to domesticated animals, are shown in Tables 7.1 and 7.2. In ecotoxicology, trace elements are primarily assayed in the liver and kidneys, which are responsible for detoxification of the organism and at the same time are places of accumulation of high concentrations of various substances. Considerable attention is paid to the muscles of game animals (because of their usefulness as food), and data on other parts of the body (including the brain, bone, lung, hair and feathers) are significantly fewer. Tables 7.1 and 7.2 show various data pertaining to Mn concentrations in biological materials obtained from mammals and birds associated with land as well as inland aquatic ecosystems.

Table 7.1 Manganese mean concentrations in selected tissues of mammals

Species or animal group	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Domestic and ranch animals					
Cattle *Bos taurus*	Canada				Puls (1994)
	Adequate, ww	2.5–6.0	1.2–2.0		
	dw	8.3–20[a]	6.0–10.0	2.0–3.8	
	Marginal, ww	1.5–3.0	0.93–1.2		
	dw	5.0–10[a]	04.6–6.0[a]		
Swine *Sus scrofa*	Canada				Puls (1994)
	Adequate, ww	2.0–4.0	1.3–2.0		
		6.7–13.3[a]	6.5–10[a]		
	Marginal, ww	2.8–3.1	0.75–1.13		
		9.3–10.3[a]	3.75–5.65[a]		
Dog *Canis lupus*	Canada				Puls (1994)
	Adequate, ww	3.0–5.0	1.2–1.8		
		10.0–16.7[a]	6.0–9.0[a]		
Raccoon dog *Nyctereutes procyonoides*	Poland, ranch	F: 5.89 M: 3.62	F: 2.46 M: 2.05	F: 1.07 M: 1.04	Mertin et al. (2006)
Bovine	Normal, ww	2.5–6.0	1.2–2.0		WVDL (2015)
	dw	8.3–20.0[a]	6.0–10.0[a]		
Cervid	Normal, ww	2.5–8.0	1.0–4.0		
	dw	8.3–26.7[a]	5.0–20.0[a]		
Lapine	Normal, ww	1.0–2.0	2.0–3.0		
	dw	3.3–6.7[a]	10.0–15.0[a]		
Porcine	Normal, ww	2.3–4.0	1.3–2.0		
	dw	7.7–13.3[a]	6.5–10.0[a]		
Canine	Normal, ww	3.0–5.0	1.2–1.8		
	dw	10–16.7[a]	6.0–9.0		
American mink *Neovison vison*	Ranch (dark)	5.97[a]	4.15[a]		Stejskal et al. (1989)
Wild animals					
Herbivorous ungulates					
Red deer *Cervus elaphus*	Poland, central part				Michalska and Żmudzki (1992)
	Autumn	10.4[a]	10.0[a]	1.30[a]	
	Spring	7.4[a]	6.90[a]	1.07[a]	
	Poland, N part (1987)	14.3[a]	27.5[a]	2.4[a]	Falandysz (1994)
	Poland, NE part	12.0	6.6	2.3	Jarzynska and Falandysz (2011)
	Poland, S part	19.8	4.2	28.0	Świergosz et al. (1993)
	Romania			2.04	Craciunescu et al. (2014)

(continued)

Table 7.1 (continued)

Species or animal group	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
	Austria			0.50	Ertl et al. (2016)
	Scotland, NW part				French et al. (2017)
	M	9.29			
	F	14.6			
	Slovakia, W part	11.6[a]	6.7[a]	6.8[a]	Gasparik et al. (2004)
Roe deer *Capreolus capreolus*	Austria			0.81[a]	Ertl et al. (2016)
	Poland, central part				Michalska and Żmudzki (1992)
	Autumn	10.9[a]	14.5[a]	1.50[a]	
	Spring	7.6[a]	5.7[a]	0.90[a]	
	Poland, central part	7.5[a]		1.2[a]	Dlugaszek and Kopczynski et al. (2013)
	Poland, N part (1987)	16.7[a]	27.5[a]	2.8[a]	Falandysz (1994)
	Poland, N part				Chudzinska-Popek and Majdecka (2010)
	Male	22.3[a]			
	Female	19.0[a]			
Reindeer *Rangifer tarandus*	Norway, Svalbard	8.7[a]	6.5[a]		Borch-Iohnsen et al. (1996)
	Sweden, Lapland	8.5[a]		0.49[a]	Odsjo et al. (2007)
Moose (elk) *Alces alces*	USA, Minnesota				Custer et al. (2004)
	Agriculture and prairie	7.9			
	Bog and forest	8.0			
	Canada, Nova Scotia	9.2	13.0		Pollock and Roger (2007)
	Canada, Nova Scotia	10.1[a]	14.0[a]		Frank et al. (2004)
	Sweden, NW part				Frank et al. (2000)
	Healthy	14.4[a]	21.9[a]		
	Affected	13.6[a]	15.8[a]		
White-tailed deer *Odocoileus virginianus*	Canada, Nova Scotia	11.6			Pollock and Roger (2007)
	USA, Texas	13.7		0.67	Bruckwicki (2006)
	USA, South Dakota	13.2[a]			Zimmerman et al. (2008)
Mule deer *Odocoileus hemionus*	USA, South Dakota	12.4[a]			Zimmerman et al. (2008)
	USA,				Wolfe et al. (2010)
	Colorado				
	Infected	8.5			
	Uninfected	9.5			
	USA, California	11.7			Roug et al. (2015)

(continued)

Table 7.1 (continued)

Species or animal group	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Japanese serow *Capricornis crispus*	Japan	14.4[a]	27.6[a]	0.87[a]	Honda et al. (1987)
Lagomorphs					
European hare *Lepus europaeus*	Austria			0.69[a]	Ertl et al. (2016)
	Slovakia			1.5[a]	Strmiskova and Strmiska (1992)
	Poland, N part	11.7[a]	10.5[a]	7.16[a]	Myslek and Kalisinska (2006)
	Poland, central part	6.0[a]		0.33[a]	Dlugaszek and Kopczynski et al. (2013)
Rodents					
Canadian beaver *Castor canadensis*	Canada, Ontario	12.3[a]	17.0[a]	2.0[a]	Wren (1984)
Omnivores					
Wild boar *Sus scrofa*	Poland, central part				Michalska and Zmudzki (1992)
	Autumn	10.5[a]	11.7[a]	1.6[a]	
	Spring	7.4[a]	6.9[a]	0.97[a]	
	Poland, S part	2.2	1.0	3.4	Świergosz et al. (1993)
	Poland, N part, 1987	4.7[a]	5.0[a]	0.93[a]	Falandysz (1994)
	Poland, central part	4.2[a]		1.0[a]	Dlugaszek and Kopczynski et al. (2013)
	Austria			0.33[a]	Ertl et al. (2016)
	Slovakia			2.1[a]	Strmiskova and Strmiska (1992)
	Romania			0.28	Craciunescu et al. (2014)
Carnivores					
Gray fox *Urocyon cinereoargenteus*	USA, California (Zoo)	8.4	4.7		Arnhold et al. (2002)
Arctic fox *Vulpes lagopus*	Norway, Svalbard	8.0[a]			Prestrud et al. (1994)
	Canada, Nunavut	12.8[a]			Hoekstra et al. (2003)
Red fox *Vulpes vulpes*	Czech Republic	6.45	3.84		Jankovska et al. (2010)
	Romania	15.9			Farkas et al. (2017)

(continued)

Table 7.1 (continued)

Species or animal group	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Golden jackal *Canis aureus*	Romania	13.8			Farkas et al. (2017)
Marten *Martes americana*	Canada, Northwest Territories		2.16		Poole et al. (1998)
	Canada, British Columbia		4.32		Harding (2004)
Wolverine *Gulo gulo*	Canada, British Columbia	9.43			Harding (2004)
	Canada, Nunavut	9.7[a]			Hoekstra et al. (2003)
Javan mongoose *Herpestes javanicus*	Japan, Amami Oshima Island	14.6[a]	4.0[a]		Horai et al. (2006)
Raccoon *Procyon lotor*	Canada, Ontario	10.3[a]	6.5[a]	1.3[a]	Wren (1984)
	USA, South Carolina	17.0[a]	7.5[a]	1.2[a]	Burger et al. (2002)
	USA, Tennessee				Souza et al. (2013)
	Polluted area				
	2009	9.3[a]	6.0[a]	0.62[a]	
	2010	9.5[a]	5.5[a]	0.60[a]	
	Unpolluted area	7.3[a]	6.2[a]	0.65[a]	
River otter *Lontra canadensis*	Canada, Ontario	9.7[a]	3.0[a]	1.7[a]	Wren (1984)
	Canada, Ontario, Sudbury	9.3[a]	3.5[a]		Wren et al. (1988)
	Canada, British Columbia, Fraser River	11.5			Harding (2004)
	USA, Illinois	10.1[a]		1.3[a]	Halbrook et al. (1996)
	USA, SW Washington	10.7			Grove and Henny (2008)
Eurasian otter *Lutra lutra*	Finland	11.4[a]			Skaren (1992)
	Finland	10.7[a]			Lodenius et al. (2014)
	Denmark Great Britain Ireland	3.53 7.37 4.91			Mason and Stephenson (2001)
	England and Wales				Walker et al. (2010)
	2007	8.30			
	2008	8.98			
	South Korea	9.18	2.92		Kang et al. (2015)

(continued)

Table 7.1 (continued)

Species or animal group	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
American mink *Neovison vison*	Canada, Ontario, Sudbury	14.1[a]	5.3[a]		Wren et al. (1988)
	Canada, NT, Inuvik		2.88		Poole et al. (1998)
	Canada, British Columbia, Fraser River	8.98	3.56		Harding (2004)
	USA, Illinois	21.8[a]	16.2[a]	4.9[a]	Halbrook et al. (1996)
	Poland				Brzezinski et al. (2014)
	Feral: WMNP	6.87	2.90		
	Feral: NNP	7.13	3.34		
	Ranch	5.02	2.83		
Insectivores					
White-tooted shrew *Crocidura russula*	Spain				Sanchez-Chardi et al. (2009)
	Polluted site	38.27	20.02		
	Reference site	36.78	17.81		
European hedgehog *Erinaceus europaeus*	Finland	6.33	2.38		Rautio et al. (2010)

im immature, *ad* adult *M* male, *F* female, *WMNP* Warta Mouth National Park, *NNP* Narew National Park

[a]Values converted from wet weight to dry weight according to the author's data, or we assume that the kidneys consist of 80% water and the liver and muscle 70%

5.2.1 Mammals

There are not many studies in which Mn concentration be assayed in different tissues and organs of specimen belonging to the same species. One such study is a report by MacDonald et al. (2005) on one moose *Alces alces* from the area of an abandoned gold mine (Colomac Mine, Northwest Territories, Canada). The highest Mn concentration (expressed in dw) was found in various parts of its stomach and intestines (from 177 to 948 and from 101 to 154 mg kg^{-1} dw, respectively). Manganese concentration ranging between 11.9 and 13.6 mg Mn kg^{-1} dw was detected in the cranial part of the lung, kidney and liver, while skeletal muscle contained 2.0 mg Mn kg^{-1}. External tissues, such as skin and antlers, contained 9.8 and 18.6 mg Mn kg^{-1} dw, respectively. The data on Mn concentrations that can be found in the available literature mostly relate to herbivores (mainly ruminants) and carnivorous mammals.

Table 7.2 Manganese mean concentrations in selected avian tissues

Species	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Domesticated animals					
Poultry	Deficient				Puls (1994)
	ww	1.5–4.0			
	dw	5–13.3[a]			
	Adequate ww				
	dw	2.0–4.0	1.5–2.5		
	High	6.7–13.3[a]	6.0–10[a]		
	ww				
	dw	4.0–6.0	2.5–6.0		
		13.3–20.0[a]	10–24[a]		
Wild birds					
Galliformes					
Pheasant *Phasianus colchicus*	Slovakia			0.53[a]	Strmiskova and Strmiska (1992)
	Austria			0.70[a]	Ertl et al. (2016)
	Italy			<1.1[a]	Roselli et al. (2016)
Quail *Coturnix coturnix*	Romania			3.5[a]	Roselli et al. (2016)
Columbiformes					
Wood pigeon *Columba palumbus*	Italy			1.2[a]	Roselli et al. (2016)
Turtle dove *Streptopelia turtur*	Italy			1.8[a]	Roselli et al. (2016)
Feral pigeon *Columba livia*	Japan, Kanto	7.12	20.4	1.32	Horai et al. (2007)
Mourning dove *Zenaida macroura*	USA, South Carolina				Burger et al. (1997)
	1992	15.40[a]		2.18[a]	
	1993	18.64[a]		1.83[a]	
Anseriformes					
Swans and geese					
Mute swan *Cygnus olor*	Poland, E part	7.92			Komosa et al. (2012)
	Canada, Ontario	F: 10.59 M: 7.85			Schummer et al. (2011)
Whooper swan *Cygnus cygnus*	Japan	8.6[a]	10.0[a]	1.43[a]	Honda et al. (1990)
Bewick's swan *Cygnus columbianus*	Japan	15.4[a]	12.2[a]	1.40[a]	Honda et al. (1990)

(continued)

Table 7.2 (continued)

Species	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
White-fronted goose *Anser albifrons*	Korea	28.1	40.6	3.29	Kim and Oh (2013)
Lesser snow goose *Anser caerulescens*	Russia	SP: 10.3 NP: 9.9			Hui et al. (1998)
Ducks					
Lesser scaup *Aythya affinis*	USA, Mississippi flyway	17.9			Custer et al. (2003)
	USA	F: 21.1[a] M: 21.2[a]			Pillatzki et al. (2011)
Spot-billed duck *Anas poecilorhyncha*	Korea	17.7	12.5	9.46	Kim and Oh (2013)
Mallard *Anas platyrhynchos*	Japan	13.7	10.6	1.79	Nam et al. (2005b)
	USA, New Jersey	10.5[a]			Burger and Gochfeld (1985)
	Poland, NW part, Szczecin	ad: 21.8[a] im: 17.0[a]	ad: 33.3[a] im: 46.8[a]	ad: 2.19[a] im: 2.00[a]	Kalisinska et al. (2004)
Black duck *Anas rubripes*	USA, New Jersey	6.2[a]			Burger and Gochfeld (1985)
Eurasian wigeon *Anas penelope*	Spain, NE part	8.7			Mateo and Guitard (2003)
Common teal *Anas crecca*		8.6			
Gadwall *Anas strepera*		12.0			
Northern pintail *Anas acuta*		9.0			
Northern shoveler *Anas clypeata*		13.0			
Red-crested pochard *Netta rufina*		11.0			
Common pochard *Aythya ferina*		8.1			
Redhead *Aythya americana*	USA, Texas and Louisiana	7.27			Michot et al. (1994)
Gruiformes					
Moorhen *Gallinula chloropus*	Japan, Kanto	9.67	13.1	1.10	Horai et al. (2007)

(continued)

Table 7.2 (continued)

Species	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Falconiformes					
Bald eagle *Haliaeetus leucocephalus*	USA, Alaska	9.94	5.57		Stout and Trust (2002)
	USA, Maine	11.35			Mierzykowski et al. (2011)
	USA, Michigan, Minnesota	14.5			Nam et al. (2012)
White-tailed eagle *Haliaeetus albicilla*	Poland, NW part	12.13[a]	7.64[a]	2.06[a]	Kalisinska et al. (2006)
	Poland, NW part	8.5	4.6		Falandysz et al. (2001)
Common buzzard *Buteo buteo*	Poland, E part	5.30			Komosa et al. (2012)
	Italy, Sicily	9.0	1.41	0.90	Licata et al. (2010)
	Netherlands	11.35	5.52		Jager et al. (1996)
Black kite *Milvus migrans*	Japan, Kanto	9.39	4.02	1.32	Horai et al. (2007)
Northern goshawk *Accipiter gentilis*	Japan, Kanto	13.4	5.74	2.07	Horai et al. (2007)
Strigiformes					
Barn owl *Tyto alba guttata*	Netherlands	9.8	6.7		Esselink et al. (1995)
Ural owl *Strix uralensis*	Japan, Kanto	12.4	9.19	0.88	Horai et al. (2007)
Brown hawk-owl *Ninox scutulata*	Japan, Kanto	12.0	5.27	1.59	Horai et al. (2007)
Passeriformes					
Greenfinch *Chloris chloris*	China	4.28	6.08	1.87	Deng et al. (2007)
Great tit *Parus major*	China	5.14	6.58	1.82	Deng et al. (2007)
	Belgium	2.71	4.85	0.94	Dauwe et al. (2005)
	Spain	P: 5.98 NP: 8.72	P: 8.26 NP: 8.19	P: 2.10 NP: 2.21	Llacuna et al. (1995)
Rock bunting *Emberiza cia*	Spain	P: 7.90 NP: 6.18	P: 10.34 NP: 9.91	P: 1.56 NP: 1.97	Llacuna et al. (1995)
Blackbird *Turdus merula*	Spain	P: 4.84 NP: 3.90	P: 11.97 NP: 8.56	P: 1.59 NP: 1.31	Llacuna et al. (1995)
Rook *Corvus frugilegus*	Poland, E part	2.53			Komosa et al. (2012)
Jungle crows *Corvus macrorhynchos*	Japan, Kanto	4.23	8.35	1.36	Horai et al. (2007)

(continued)

Table 7.2 (continued)

Species	Location	Mn concentration (mg kg^{-1} dw)			References
		Liver	Kidney	Muscle	
Carrion crow *Corvus corone*	Japan, Kanto	4.07	9.39	1.32	Horai et al. (2007)
Pelecaniformes					
Great cormorant *Phalacrocorax carbo*	Spain, Murcia	9.41	4.67	1.79	Navarro et al. (2010)
	Serbia	9.38			Skoric et al. (2012)
	Japan	19.0	11.0	1.95	Nam et al. (2005a)
	Japan	16.6	8.64	1.98	Nam et al. (2005b)
	Japan, Kanto	15.7	7.74	1.57	Horai et al. (2007)
Great white egret *Egretta alba*	Japan			2.29	Honda et al. (1985)
Great white egret *Egretta alba*	Japan, Kanto	9.85	5.46	1.83	Horai et al. (2007)
Intermediate egret *Egretta intermedia*	Japan, Kanto	12.0	8.0	1.52	Horai et al. (2007)
Grey heron *Ardea cinerea*	Poland, E part	6.43			Komosa et al. (2012)
	Poland, NE part	5.3[a]			Babinska et al. (2008)
	Japan	13.4	8.43	1.71	Horai et al. (2007)

ad adult, *im* immature, *M* male, *F* female, *SP* southern population, *NP* northern population
[a]Value converted from wet weight to the dry weight according to author's data, or we assumed that the kidney contains 75% of water, liver and muscle 70% of water

5.2.1.1 Hepatic Manganese

In ruminants such as bovines and cervids, normal Mn hepatic concentrations remain within the following ranges: 2.5–6.0 and 2.5–8.0 mg kg^{-1} ww or 8.3–20.0 and 8.3–26.7 mg kg^{-1} dw, respectively (Puls 1994; WVDL 2015). The overwhelming majority of the data related to mean Mn levels in the livers of wild cervids (expressed in dw), shown in Table 7.1, stays within the aforementioned range or is slightly lower than 8 mg kg^{-1} dw. Average Mn concentrations most commonly range between 8.5 and 14.5 mg kg^{-1} dw. Only in two studies were hepatic Mn levels in red deer *Cervus elaphus* and roe deer *Capreolus capreolus* (from N and S Poland, respectively) ≥19 mg Mn kg^{-1} dw (Falandysz 1994; Chudzinska-Popek and Majdecka 2010). Significant differences were noted between Mn hepatic concentrations in autumn and spring of both these species, living in Poland, while the spring value was lower by ~3 mg kg^{-1} dw than the autumn value (Michalska and Zmudzki 1992). Zimmerman et al. (2008) also detected inter-seasonal differences in Mn concentration in the same organs of white-tailed deer females *Odocoileus virginianus* from South Dakota, USA. What is more, different diseases can contribute to lowering Mn concentration in the liver of the moose *Alces alces* from Sweden, as demonstrated by Frank et al. (2000).

In the omnivorous ungulate wild boar *Sus scrofa*, average hepatic Mn levels change from 2.2 to 10.5 mg kg^{-1} dw (Table 7.1). For farm swine, Mn concentrations ranging from 9.3 to 10.3 mg kg^{-1} dw (or 2.8–3.1 mg kg^{-1} ww) indicate marginal levels of this element (Puls 1994). Probably, the natural demand for Mn is lower in the house pig's ancestor than in intensively fattened farm animals.

Mean Mn concentration in the liver has a somewhat wider range in carnivores compared to ruminants: from 3.5 (in the Eurasian otter from Denmark) to 21.8 mg kg^{-1} dw (in the American mink from Illinois, USA). Usually, in the livers of wild and feral American mink and otters from North America and Europe, mean Mn levels stay in the range between 7 and 14 mg kg^{-1} dw. The cited values are higher for wild/feral animals than for ranch minks, 5–6 mg kg^{-1} dw (Table 7.1), as had been previously observed by Halbrook et al. (1996) in their research on Illinois minks. A similar tendency can be observed in canids. For the domesticated dog *Canis lupus*, the analogous range falls between 10 and 16.7 mg kg^{-1} dw (Puls 1994), but it is slightly wider in wild canids: 6.4–15.9 mg kg^{-1} dw (Table 7.1). In comparison with herbivorous, omnivorous and carnivorous species, the highest mean Mn concentrations in the liver were found in the small insectivorous white-tailed shrew *Crocidura russula* from Spain. In the livers of animals from polluted and reference sites, similar concentrations (~38 mg Mn kg^{-1} dw) were detected (Sanchez-Chardi et al. 2009). This might be related to fast metabolism in that species. With the exception of the aforementioned species, hepatic mean levels of Mn in other wild terrestrial mammals usually range between 6 and 16 mg kg^{-1} dw.

5.2.1.2 Nephric Manganese

The highest mean Mn concentration in the kidneys has been observed in three cervid species: Japanese serow *Capricornis crispus* from Japan and red deer and roe deer from Poland (27.5–27.6 mg kg^{-1} dw), while it was lowest in wild boar (1.0 mg kg^{-1} dw) from a southern part of Poland polluted by heavy metals (Table 7.1). For cervids and swines, normal levels of Mn in the kidneys are as follows: 5–20 and 6.5–-10 mg kg^{-1} dw, respectively (WVDL 2015). In wild cervids and other herbivorous species (European hare *Lepus europaeus*, Canadian beaver *Castor canadensis*), nephric Mn levels usually range between 6 and 17 mg kg^{-1} dw. In wild boar from Poland, Mn levels varied between 1 and 12 mg kg^{-1} dw, whereas in different carnivorous species, Mn nephric levels were clearly lower than in herbivores and did not exceed 6 mg kg^{-1} dw. The exception here is the raccoon *Procyon lotor*, whose mean Mn concentration values in the kidneys ranged from 5.5 to 7.5 mg Mn kg^{-1} dw (Table 7.1), but its diet contains substantial amounts of plant material. Normal Mn concentration in the kidneys of wild animals is lower than in the liver, but in some cases, the opposite is true (Table 7.1). For example, higher nephric than hepatic values were observed in moose from Canada and Sweden (Frank et al. 2000, 2004; Pollock and Roger 2007). Moreover, in moose from NW Sweden, nephric Mn levels were about 28% higher in healthy individuals than in diseased animals (Frank et al. 2000).

Similarly to the liver, variations in nephric Mn concentrations are observed both between herbivorous species and individuals of the same species occurring in the same area. There was a spectacular case of a moose affected by a disease with an unknown aetiology and healthy animals from NW Sweden. In the affected moose, nephric Mn level was almost 30% lower than in healthy individuals (Table 7.1). Additionally, concentration of molybdenum was 36% higher in the livers of the diseased animals, and the concentration of copper was about 60% lower than in animals from the control group. The changes in these and other trace element concentrations in the kidney and liver, as well as some clinical biochemical parameters observed in these animals, corresponded to molybdenosis and secondary copper deficiency in domesticated ruminants (Frank et al. 2000). These studies indicate the existence of complex and still poorly understood relationships between concentrations of various elements in mammalian detoxification organs.

5.2.1.3 Manganese in Skeletal Muscle and Other Tissues

Manganese concentration in the muscles is mainly assayed in game animals, which are obtained for food. They are mostly cervids, wild boars, hares and raccoons (mainly in North America). In these mammals, Mn concentration in the skeletal muscles ranges from <0.30 to >7.0 mg kg^{-1} dw, but sporadically can exceed 25 mg Mn kg^{-1} dw as was the case in red deer from a southern area of Poland polluted with heavy metals. Generally, in wild herbivores and boars, the values of mean Mn muscle levels change around 1 mg kg^{-1} dw (Table 7.1). Analogical values for herbivorous cattle and sheep, but not for omnivorous swine (<0.5 mg Mn kg^{-1} dw), were described by Doyle and Spaulding (1978). Puls (1994) found that the adequate Mn levels in sheep and cattle muscle tissues changed in ranges 0.24–0.40 and 2.0–3.8 mg kg^{-1} dw, respectively, which clearly diverges from the value of 1 mg Mn kg^{-1} dw usually observed in game mammals. It appears that Mn concentration in the muscles of animals whose diet predominantly includes plants with various concentrations of this metal can differ to a considerable degree. Seasonal changeability observed in Mn concentrations in the muscle (also in liver and kidneys) in red deer, roe deer and wild boar seems to support this point of view (Michalska and Zmudzki 1992). These researchers demonstrated that in the autumn, i.e. after the abundance of readily available young plants, the muscles of these animals contained more Mn than in the early spring, preceded by a long and difficult winter season. In temperate climates, during winter, especially when there is a lot of snow, vegetation is more difficult to access, and the older parts surviving above ground contain significantly less Mn than young shoots and leaves (Millaleo et al. 2010; Mousavi et al. 2011).

The data on Mn concentrations in the muscle of piscivorous mammals are scarce (Table 7.1). It appears that the average Mn concentration exceeds 1 mg Mn kg^{-1} dw, but its range does not vary much (1.2–4.9 mg kg^{-1} dw) compared to the muscle of omnivorous boar/swine and herbivorous ruminants (0.3–28 mg Mn kg^{-1} dw). This

may be the result of a fish diet (which has a lower and more constant Mn content than a plant-based diet) and the high degree of physical activity of piscivorous animals.

Manganese crosses the blood-brain barrier and is accumulated in varying concentrations in different parts and structures of mammalian brains. In mammals, one of the most important target tissues in Mn toxicity is the brain (Zheng et al. 2010). Increased brain Mn concentration is a critical step in the pathogenesis of manganese-induced neurotoxicity (Aschner et al. 2006, 2009). Accumulation of Mn occurs mainly in the basal ganglia and leads to a syndrome called manganism, whose symptoms, including cognitive dysfunction and motor impairment, resemble Parkinson's disease. In this structure, which is a group of subcortical nuclei, and in the cortex, intra- and interspecies differences are observed. For example, in primates such as humans, rhesus macaque *Macaca mulatta* and marmoset *Callithrix jacchus*, mean Mn concentrations were, in the basal ganglia, 2.0–2.5, 0.34–0.48 and 0.21 mg kg^{-1} ww, respectively, and in the cortex as follows: 1.0–1.2, 0.25 and 0.20 mg kg^{-1} ww (Dorman et al. 2006; Ramos et al. 2014; Knauer et al. 2017). In fact, studies designed to explain the effects of Mn concentration on the central nervous system functioning due to manganese-induced neurotoxicity as seen in humans, primarily occupationally and/or environmentally exposed to elevated concentrations of this metal in air, water and food, have been carried out only on humans, laboratory rodents and primates (Takeda et al. 1998; Dorman et al. 2006; Erikson et al. 2005; Fitsanakis et al. 2008; Ramos et al. 2014; Knauer et al. 2017).

Only two studies in which brain Mn levels in wild mammals were assayed were found in the available literature. They concerned a small marsupial living in North America—the northern opossum *Didelphis virginiana* and raccoon. The brains of immature and adult opossums contained 3.8 and 2.2 mg Mn kg^{-1} dw, respectively (Arnhold et al. 2002). This observation is analogous to the human brain because children accumulate higher levels of Mn than adults (O'Neal and Zheng 2015). In the whole brains of raccoons, mean values ranged from 0.33 to 0.37 mg Mn kg^{-1} ww, depending on the year and site of collection, but such differences were insignificant (Souza et al. 2013). Assuming that the brain of a medium-sized mammal consists of 77% water (Kalisinska et al. 2016), Mn levels in the brain of the adult opossums were ~0.51 mg kg^{-1} ww. Similarly, to the aforementioned raccoons and opossums, the brain Mn levels (in the cortex/cerebrum) assayed in dogs (aged 1–7 years old), cats and lambs were 0.33, 0.41 and 0.44–0.61 mg kg^{-1} ww, respectively (Michalska et al. 1991; Soltysiak et al. 1997; Bakirdere et al. 2011).

Hesketh et al. (2007) and White et al. (2010) compared Mn concentrations in different parts of the central nervous system of ruminants suffering from animal prion diseases such as bovine spongiform encephalopathy (BSE), scrapie of sheep and chronic wasting disease (CWD) of cervids. In sheep and cattle from control groups, Mn concentrations in the frontal cortex were 0.26 and 0.33 mg kg^{-1} ww, respectively (Hesketh et al. 2007). Those values were similar to Mn concentration in the parietal/optic lobes of healthy Rocky Mountain elks (*Cervus elaphus nelsoni*): 1.32 mg kg^{-1} dw (White et al. 2010) or 0.26 mg kg^{-1} ww. Since the brain of large ruminants consists of ~80% water (Jung et al. 2015), considering the aforementioned values, it can be assumed that Mn concentration in the cerebrum and/or cortex parts

of mammals differs across various species, but it changes only slightly, i.e. from 0.20 to 0.65 mg kg^{-1}. It should be stressed that substantial differences in Mn concentration in the central nervous system occur naturally, and in the case of some diseases (BSE, scrapie), a significant increase in the concentration of this metal has been documented, compared to controls, in the brain stem, spinal cord and cerebellum, but not in the frontal cortex (Hesketh et al. 2007).

Analysis of the research presented here reveals that in farm mammals, and especially in wild animals, the concentration of Mn in the brain is very rarely assayed. This is the case for several reasons. Firstly, the brain is enclosed in the skull, which makes obtaining samples of nervous tissue a more difficult task. Secondly, the distribution of Mn in the brain is heterogeneous, which in the case of samples taken from different parts of the brain may complicate the performance of comparative ecotoxicological studies. Finally, the value of the brain of pigs, cattle, sheep, cervids and wild boar as food is negligible, and so the mineral composition of their brains is only sporadically analysed.

However, given the local environmental Mn pollution found in dust and food, especially in food originating from plants, its increased penetration into the mammalian brain cannot be excluded, and to determine this would require extensive further field studies.

About 100 years ago, Mn was recognized as an essential nutrient for proper bone formation (Erikson et al. 2005). It is believed that the mammalian skeletal contains up to 40–43% of all Mn accumulated in an organism (O'Neal et al. 2014). The bone is one of the major organs for long-term storage of Mn in the body, and Mn half-life there is much longer than in soft tissues such as liver and kidney or body fluids. In adult mammals, the main function of the skeleton is bone remodelling, which involves both bone formation and resorption. Metals incorporated into the skeleton are subject to bone turnover and remodelling processes that occur at approximately 10% per year in adult individuals. For these reasons, bone tissue is considered to be a suitable long-term bioindicator of environmental metal exposure (Martiniakova et al. 2012; O'Neal et al. 2014). O'Neal et al. (2014) and O'Neal and Zheng (2015) suggested that the bone reflects the Mn body burden much better than body fluids or keratinized tissues such as nails and hair. Additionally, bone Mn level correlates with Mn concentrations in some brain structures. All of these features indicate that bone tissue is a useful biomarker in epidemiological and ecotoxicological studies of Mn.

Despite the many advantages of the bone as a long-term bioindicator in the environmental investigation of the Mn body burden, surprisingly little data have been published on its concentrations in the bones of wildlife, with the exception of cervid antlers, which are produced annually by males (Arnhold et al. 2002; Dobrowolska 2002; McDonald et al. 2005; Sanchez-Chardi and Lopez-Fuster 2009; Budis et al. 2013; Ceacero et al. 2015; Cappelli et al. 2017). Recently Buddhachat et al. (2016) conducted an elemental analysis of the humerus bone of 14 species representing carnivores, ungulates, primates, elephants and dolphins, which originated from the collection of Chiang Mai University in Thailand. They have shown that Mn occurred in all the studied bones and found interspecies differences. Distribution of many elements (including Mn) was determined using a

handheld X-ray fluorescence device. Each element was expressed as a percentage obtained from the area under the peak of each element divided by the total area for all the elements recorded in the scan. Elemental values represented a relative amount (elemental fingerprint), but not the actual concentrations of each element in a tested sample. In humerus bone, the highest Mn percentage values were detected in the Asian elephant *Elephas maximus* and dog (0.068% and 0.059%) and moderate values in the lion *Panthera leo* and Assam macaque *Macaca assamensis* (0.035% and 0.032%). In other analysed animals, the values of the analysed parameter did not exceed 0.015% (ranging between 0.008 and 0.015%). An important feature of this report is the comparative analysis of the same bone (humerus bone), because Mn concentrations can vary greatly between different bones from the same individual (e.g. rib, carpal bone, thigh bone and lower jaw). This has been demonstrated in experimental studies, among others, on sheep and other domestic ruminants (Hidiroglou 1980). Buddhachat et al. (2016) observed this kind of difference between the antlers and frontal bones of cervids (0.028% vs. 0.006%). It was also observed that Mn concentrations vary in different fragments of the same bone (layers of cartilage, compact bone and spongy bone coming from the femur head of the hip joint). Significantly higher Mn concentrations were found in samples of canid cartilage and cartilage/compact bone than in spongy bone (Budis et al. 2013, 2015). Moreover, experimental research on Mn in rat bones showed that the shortest half-lives of this metal were related to weight-bearing bones such as the femur and tibia, while the longest half-lives were related to parietal bones that form part of the skull (O'Neal et al. 2014).

In wild mammals, relatively high Mn levels in large bones were found in insectivorous white-toothed shrews from Spain. The animals from the Ebro Delta, which is contaminated by heavy metals, differed significantly from those originating from the reference area (Medas Islands). Their mean Mn bone levels were 7.80 vs. 4.58 mg kg^{-1} dw. Adult individuals from the contaminated site were characterized by higher Mn bone concentrations in comparison with juveniles and seniles: 10.81, 7.45 and 7.02 mg kg^{-1} dw, respectively. However, in insectivores from the Medes Islands, the values in analogous age groups were similar and ranged between 4.06 and 4.89 mg kg^{-1} dw (Sanchez-Chardi and Lopez-Fuster 2009). In the ribs of immature and adult northern opossums (from San Diego, USA), which are scavenger omnivores, values of 11.0 and 3.1 mg Mn kg^{-1} dw were found (Arnhold et al. 2002). In comparison with the white-toothed shrew and the northern opossum, Mn concentration a few times lower (~1.0 mg kg^{-1} dw) was found in the femur head of the red fox, whereas in the samples from cartilage and compact bone, it was significantly higher than in spongy bone: 1.14 vs. 0.92 mg kg^{-1} dw (Budis et al. 2013). In two other canids, dog and ranch raccoon dog (studied by Budis et al. 2015 and Mertin et al. 2006, respectively), mean bone Mn levels were as follows: ~0.60 mg kg^{-1} dw in dog and 2.60 and 1.40 mg kg^{-1} dw in male and female raccoon dogs. The cited values were, respectively, lower and higher than in the wild red fox, but all of them remained in a rather narrow range (0.6–2.6 mg Mn kg^{-1} dw). These differences may be related to the different composition of the diets of canids, their biology and types of bone. A much wider range of mean Mn concentrations

(1.0–10 mg kg^{-1} dw) was found in the bones of domestic ruminants in a number of nutritional experiments in which different doses of Mn were administered to animals of various ages (Hidiroglou 1979, 1980; Bellof et al. 2007). An even greater range of Mn concentrations (0.30–18.0 mg kg^{-1} dw) was observed in the antlers of cervids from Eurasia and North America (Dobrowolska 2002; McDonald et al. 2005; Ceacero et al. 2015; Capelli et al. 2015, 2017). This is probably due to interspecies differences, Mn content in the diet and/or sample collection sites: for example, Mn concentration observed in the outer rim of the antlers was 200 times higher than in the adjacent bone tissue (Turyanskaya et al. 2016). It can be surmised from the above data that Mn concentrations in mammalian skeletons vary slightly, from a few decimals to 10 mg kg^{-1} dw. The highest Mn concentration in the bones occurs in small insectivorous mammals with very high metabolisms, followed by herbivores, and is the lowest in carnivores. In all these animal groups, the concentration of Mn in bones was significantly influenced by the contents of their diet. However, it should be kept in mind that Mn concentrations may vary within the same organism, in different bones, which have various structures and functions. Therefore, in ecotoxicological comparative studies, not only should the same bones be chosen but also the same parts, such as the head of a femur, in the case of large- and medium-sized mammals, or the whole femur of micromammals. In addition, ecological retrospective studies of the bones and antlers of museum specimens can provide valuable insights into the dynamics of Mn levels in the environment over the past decades and centuries.

5.2.2 Birds

Of nine different soft tissues and bones in which Dauwe et al. (2005) assayed Mn concentration in the great tit *Parus major*, the highest mean values were found in the intestine, bone and kidney (10.7, 5.08, 4.85 mg kg^{-1} dw) followed by the ovary, stomach and liver (4.14, 3.86 and 2.71 mg kg^{-1} dw). Based on the research by Nam et al. (2005a), it can be assumed that most of the Mn accumulated in avian organisms is found in the feathers, bones, muscles and liver (28.8, 25.1, 20.5 and 16.7%, respectively). Manganese contained in the skin and kidneys amounts to 2.8% and 1.4% and in all other body parts to 4.7%. Manganese penetrates into feathers only during their growth and later on is permanently bound in them and does not participate in biological changes. It has been shown that concentration of Mn bound in plumage is affected by its colour. Feathers containing large quantities of melanin, including black, brown and greenish ones, have a higher concentration of Mn than white feathers, which are devoid of this dye (Niecke et al. 1999; Burger and Gochfeld 2009). For that reason, feathers are rarely used in ecotoxicological studies pertaining to Mn, though about 30% of Mn in the organism is found in plumage. In that respect, the liver is considered to be a better biomarker; however, the kidneys, muscles and bones are also important for various reasons. Although the brain is an important organ and in endothermic vertebrates excess Mn there leads to severe

dysfunction of the whole body, Mn concentrations in avian nerve tissue are rarely examined.

5.2.2.1 Manganese in Avian Liver, Kidney and Muscle

In wild birds, mean hepatic Mn concentrations range from 2.5 to 28.1 mg kg^{-1} dw. Taking into account the adequate values of hepatic Mn in poultry suggested by Puls (1994) (2.0–4.0 mg kg^{-1} ww or 7–14 mg kg^{-1} dw), it can be noted that 56.2% out of 64 hepatic Mn concentrations in wild birds (shown in Table 7.2) remain between 7 and 14 mg kg^{-1} dw. Only in 21.9% of cases did Mn concentrations fall below 7 or above 14 mg Mn kg^{-1} dw. The lowest Mn concentrations (<5 mg kg^{-1} dw) were observed only in passerines from Europe and Asia (Llacuna et al. 1995; Deng et al. 2007; Dauwe et al. 2005; Horai et al. 2007; Komosa et al. 2012), which may indicate naturally lower hepatic Mn levels in this bird group. A tendency to accumulate higher hepatic Mn levels (>15 mg kg^{-1} dw) is observed mainly in herbivorous birds (mourning dove *Zenaida macroura*, Bewick's swan *Cygnus columbianus* and white-fronted goose *Anser albifrons*) and in some omnivorous ducks whose diet contains large quantities of plant material (lesser scaup *Aythya affinis*, mallard *Anas platyrhynchos* and spot-billed duck *A. poecilorhyncha*), particularly in areas treated with Mn for agricultural and/or industrial purposes (Table 7.2). The mean Mn concentration in the kidneys of wild birds ranges between 1.4 and 46.8 mg kg^{-1} dw, which is wider than the respective hepatic range. This metal is more rarely assayed in avian kidneys than in livers. According to Puls (1994), adequate nephric Mn concentration ranges between 1.5 and 2.5 mg kg^{-1} ww (or 6.0–10 mg kg^{-1} dw). Of the 37 cases summarized in Table 7.2, almost 43.3% lie within the range of adequate values, while 29.7% and 27.0% remain, respectively, above or below the limit values set for poultry. Much higher Mn concentration (>20 mg Mn kg^{-1} dw) was found in the kidneys of the feral pigeon *Columba livia*, the white-fronted goose and the mallard whose diets are mainly composed of plants, which are generally much richer in Mn than animal tissues.

Nephric Mn levels were a little above or below 5 mg kg^{-1} dw in some diurnal and nocturnal predators (black kite *Milvus migrans*, common buzzard *Buteo buteo*, white-tailed eagle *Haliaeetus albicilla*, bald eagle *H. leucocephalus*, northern goshawk *Accipiter gentilis*, brown hawk-owl *Ninox scutulata*), in piscivores (great cormorant *Phalacrocorax carbo* and great white egret *Egretta alba*) and sporadically in passerines (Table 7.2). On the whole, hepatic Mn concentrations in birds are higher than their nephric values (22 out of 37 cases, ~60%, presented in Table 7.2), but sometimes the opposite is true, especially among passerines.

Avian skeletal muscles and bones are the major internal body pools of Mn. Unlike the liver and kidneys, mean concentrations of Mn in the muscles of wild birds change within a very narrow range, from 0.5 to 3.5 mg kg^{-1} dw (Table 7.2). Only exceptionally does Mn muscle concentration reach a higher level (~9.5 mg kg^{-1} dw), such as in the spot-billed duck *Anas poecilorhyncha*, which prefers plant food (Kim and Oh 2013). With regard to potential consumers Mn content, along with that

of other metals, is most often studied in the muscles of game birds, such as pigeons, galliforms, geese and ducks. Their meat generally contain low concentration of Mn, most commonly ranging between 0.7 and 2.0 mg kg^{-1} dw (Table 7.2).

5.2.2.2 Manganese in Avian Brain and Bones

In the brains of wild birds, average Mn concentrations remain in a very narrow range, between 0.22 and 0.44 mg kg^{-1} dw or 1.10–2.20 mg kg^{-1} ww. The highest average concentrations of this metal (>1.80 mg kg^{-1} dw) were found in herbivorous and omnivorous anseriforms (whooper swan *Cygnus cygnus*, white-fronted goose, bean goose *Anser fabalis* and mallard) as well as in some piscivorous birds such as the bald eagle and grey heron *Ardea cinerea* (Honda et al. 1990; Kalisinska 2000; Kalisinska et al. 2004; Horai et al. 2007; Nam et al. 2012). In other piscivorous species, the average brain Mn concentration is ~1.7 mg kg^{-1} dw, including the white-tailed eagle, great white egret *Egretta alba* and intermediate egret *E. intermedia*. In birds foraging on land, such as the feral pigeon *Columba livia*, blackbird *Turdus merula* and black kite *Milvus migrans*, Mn concentration in the brain usually does not exceed 1.60 mg kg^{-1} dw, while in some passerines (carrion crow *Corvus corone*, jungle crow *C. macrorhynchos* and great tit) markedly lower values, ranging from 1.1 to 1.2 mg kg^{-1} dw, were observed (Llacuna et al. 1995; Dauwe et al. 2005; Horai et al. 2007). There are no rules for this however. For example, large amounts of Mn penetrated from food and air into the organisms of the great tit and greenfinch *Chloris chloris* from the polluted city of Beijing, China, and Mn concentrations in their brains were 1.91 and 1.68 mg kg^{-1} dw, respectively (Deng et al. 2007). Kalisinska (2000), investigating migrating geese, who, during their flights, stop in large numbers at the floodplains of Warta and Odra River (W Poland), has also shown that Mn concentration in their brains is affected by the environment. Immature and adult bean geese flying from their breeding grounds (located in NE Europe and even beyond the Ural) have lower Mn concentrations in the brain (~0.30 mg kg^{-1} ww or 1.50 mg kg^{-1} dw) when they stop in the floodplains than geese returning from wintering grounds located in W Europe (~0.40 mg kg^{-1} ww or 2.00 mg kg^{-1} dw). Their western European feeding grounds are fields and permanent grasslands, which are fed with mineral fertilizers containing Mn. This element penetrates from their food to different parts of the body of the geese, including the brain. Thus, in the cases of the great tit, greenfinch and geese, their brains proved to be good bioindicator of the Mn environmental burden (Kalisinska 2000; Deng et al. 2007).

Compared to Mn levels in the avian brain, the concentrations of this metal in the bones of wild birds vary considerably (from ~1 to >20 mg kg^{-1} dw). The highest Mn concentrations in the bones are characteristic of herbivorous geese and swans, as well as omnivorous mallard, in which it exceeds 13 mg kg^{-1} dw (Honda et al. 1990; Kalisinska et al. 2004; Kim and Oh 2013). In passerines (black bird, great tit and rock bunting *Emberiza cia*) and piscivorous birds (great white egret and great cormorant), the level of the bone Mn ranges from 4.5 to 7.0 mg kg^{-1} dw but

sometimes is much lower (1.15 mg kg^{-1} dw), as in the great cormorant from Serbia (Llacuna et al. 1995; Dauwe et al. 2005; Scoric et al. 2012). It appears that the lowest concentrations of this metal (2–3 mg Mn kg^{-1} dw) occur in nocturnal and diurnal predatory birds such as the common buzzard and barn owl *Tyto alba guttata* (Jager et al. 1996; Esselink et al. 1995). Furthermore, it should be noted that Mn concentrations in different bird bones (e.g. the femur and sternum) from individuals of the same species may differ in values, as was noted by Deng et al. (2007).

6 Conclusions

Manganese content in the diet of wildlife significantly influences its concentration in their tissues. The available data indicate that the highest concentrations of this metal are recorded in herbivorous mammals and birds and the lowest in predatory species of both groups. Manganese reaches the highest concentrations in various parts of the digestive tract (including the intestines), but is most commonly assayed in the liver and kidney. Many authors point out that bone and nervous tissues are good bioindicative material for ecotoxicological studies of Mn. However, in comparative studies, attention should be paid to whether samples come from analogous places, as Mn is not evenly distributed in the brain and bones of skeleton.

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Chapter 8
Molybdenum, Mo

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Abstract Molybdenum in plants, animals, and humans occurs in small quantities; however, being an essential element, the metal is a component of a range of enzymes. In animals and humans, these are xanthine oxidase, aldehyde oxidase, and sulfite oxidase. Goats that had been for many generations fed a semisynthetic, Mo low diet exhibited impaired growth, lower fertility, poor fetal survival, and a higher incidence of miscarriages. The importance of molybdenum consists in its toxicity, which affects primarily ruminants, cattle in particular. Molybdenum penetrates animal bodies through oral intake or inhalation. From the gastrointestinal tract, the element is transported to the kidneys, liver, and bones. In monogastric animals, molybdenum is absorbed through the wall of the stomach. In ruminants, its absorption takes place in the intestinal wall. Molybdenum poisoning is accompanied by a range of symptoms, many of which result from secondary copper deficiency. Typical signs of acute, uncomplicated molybdenosis include impaired bone formation, which may be a result of altered phosphorus metabolism. These changes lead to deformation of bones and joints, spontaneous pathological fractures of long bone metaphyses, and exostosis. A decrease can be observed in the activity of alkaline phosphatase and the content of proteoglycans in articular cartilage. Reproductive disorders affecting individuals of either sex also appear. Renal excretion rate of Mo in laboratory animals is rather quick, taking about 2 weeks. So far no biomagnification and bioaccumulation of molybdenum in animal bodies have been confirmed.

Monogastric animals are less susceptible to Mo toxicity, and the most tolerant to elevated doses seem to be horses. Sheep and cattle, on the other hand, exhibit the lowest level of resistance to Mo toxic effects. Regardless of the species, acute

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molybdenum poisoning leads to growth hindrance, reduced body weight, and increased mortality.

Anthropogenic environmental Mo contamination is related to its mining, production of steels for special purposes, and industrial waste discharge. When it comes to fossil fuels, the element accumulates and builds up in coals. Molybdenum contents in soils vary greatly. The highest amounts of molybdenum are found in soils formed from granite and clays. In plants growing on muschelkalk, keuper, and alluvial soils, on the other hand, Mo content is low.

Data on the way molybdenum affects free-living mammals are scarce. Some well-documented sources point to the "mysterious" moose disease in Sweden, caused by copper deficiency and molybdenosis. The latter disease evokes symptoms resembling copper deficiency.

Research is carried out mainly on domesticated avian species in which toxic molybdenum effects were observed at the dietary concentration of its absorbable forms exceeding 200 mg kg^{-1}. Among undomesticated birds, analyses involved bobwhite quail (*Colinus virginianus*) treated with molybdenum disulfide (insoluble) and a soluble form of sodium molybdate dihydrate. Toxicity and bioavailability of both Mo forms were compared. These results are more realistic in showing the susceptibility and the risk birds are exposed to when it comes to environmental molybdenum. Human impact associated with molybdenum environmental contamination involves mainly combustion of fossil fuels, mining, and metallurgy. Molybdenum does not belong to metals of special significance in terms of environmental toxicology. The metal has not been classified as a major toxic element by the EPA. In Central Europe, plants growing on the soils formed from granite, gneiss, rotliegend, and shale, as well as on muck and peat soils, may represent a health hazard for free-living ruminants.

1 Introduction

As a metal, molybdenum was known in the ancient times (Anke 2004). In the 16-km layer of the Earth's crust, the content of molybdenum is approx. 1.4 mg kg^{-1}, making it the 40th most abundant element in nature (Anke et al. 2000). Molybdenum is an essential element for the life and normal growth of plants, animals, and humans (Anke et al. 2000). The biological role of molybdenum was discovered in 1830 by Boussingault, who demonstrated that clover and pea increase their nitrogen contents using *Acetobacter* sp. bacteria, which have Mo in their enzymes. In 1940, after many years of studies, Bortels proved that molybdenum is essential for higher plants (Anke 2004).

As a heavy metal, molybdenum has drawn attention of animal scientists; in 1938 a group of researchers led by Ferguson found that the element was responsible for teart disease in cattle in Mo-rich areas of England (Anke 1986).

In both animals and humans, molybdenum is recognized as an important constituent of three enzymes: xanthine oxidase, aldehyde oxidase, and sulfite oxidase

(Cohen et al. 1971; Feldman and Weiner 1972; Anke et al. 2000). Although Mo is a component of a range of enzymes, no symptoms of molybdenum primary deficiency have been so far observed in humans and animals (Kośla et al. 1989). Only high doses of Mo-antagonistic elements (tungsten) result in sulfite oxidase activation, which leads to Mo deficiency symptoms (Johnson 1997).

Anke et al. (1978, 1985a, b), who administered a molybdenum-poor (<24 μg kg^{-1} dw of feed) semisynthetic dose to several generations of goats, observed depressed growth, reduced fertilization rates, and low fetal survival. A significant increase in the prevalence of miscarriage was also noted. Those experiments demonstrated the essentiality of Mo for animals, without using antagonistic substances (Kośla et al. 1989).

The importance of molybdenum consists in its toxicity (Anke et al. 2000). In combination with Cu and S, molybdenum causes secondary copper deficiency, which is the case primarily in ruminants (Anke et al. 2000). In this group, molybdenum toxicity (molybdenosis) affects mainly cattle (Anke 2004). In horses, a high, species-specific hepatic content of Mo is significantly higher compared to other domestic and wild animals (Kośla et al. 1989).

2 General Properties

Molybdenum occurs in the Earth's crust at a level of 1–2 ppm, only in the form of compounds with other elements (Sebenik et al. 2002; Anbar 2004; Kabata-Pendias and Mukherjee 2007). Its concentrations are highest in granite rocks and loam sediments ("argillaceous sediments") (Kabata-Pendias and Mukherjee 2007). Molybdenum is the 24th most abundant element in the oceans, with an average of 10 parts per billion (Emsley 2001; Considine 2005). Although the most important source is molybdenite, MoS_2, molybdenum can be found in other minerals, i.e., molybdite, MoO_3; wulfenite, $PbMoO_4$; and powellite, $CaMoO_4$ (Kabata-Pendias and Mukherjee 2007). In 1778 Carl Wilhelm Scheele separated molybdenum from graphite and lead and derived the oxide from molybdenite (Mitchell 2003). Three years later Peter Jacob Hjelm extracted the metal by reducing its oxide using carbon.

Molybdenum is a transient metal located in Group VI of the periodic table. It is a silvery white, literary lead-like metal, and very hard, with a Mohs hardness of 5.5. It occurs in several oxidation states, from -2 to 6, with Mo(6) being the most common species in most natural waters, including seawater, in the form of molybdate ion, MoO_4^{2-} (Reid 2012). The boiling point of molybdenum is 4639 °C; its melting point, 2617 °C, is one among the highest of all the elements (Reid 2012). There are seven stable isotopes of molybdenum, 92, 94, 95, 96, 97, 98, and 100. The most common is ^{98}Mo (24.13%), whereas ^{99}Mo has found its application in the nuclear sector (Anbar 2004). Molybdenum does not visibly react with oxygen or water at room temperature; however, at higher temperatures (600 °C), the metal oxidizes quickly and forms molybdenum(6) oxide, MoO_3. In strongly alkaline water, MoO_3 is transformed into molybdates (MoO_4^{2-}). Molybdenum oxidation states four (e.g.,

MoS_2) and six are the most stable species. The element is prone to bioaccumulation and has accumulated in coals, which—if combusted—release dispersing molybdenum that finally reaches the soil and sediments. Volatile ashes may contain 5–-33 mg kg^{-1} of the element (Pasieczna 2012). Under anoxic conditions, concretions containing up to 2000 mg kg^{-1} of molybdenum can form in marine sediments (Anbar 2004; Arnold et al. 2004).

Molybdenum binds into complexes with many inorganic and organic ligands, thereby playing a significant role in the biochemical process. It is involved in redox reactions and is a constituent of many enzymes, which are essential in aldehyde oxidation (aldehyde oxidase), purine and pyrimidine metabolism (xanthine oxidase), or sulfite detoxification (sulfite oxidase) (Skibniewski et al. 2015). No biomagnification and bioaccumulation of Mo in animals have been observed so far (Ikemoto et al. 2008; Reid 2012).

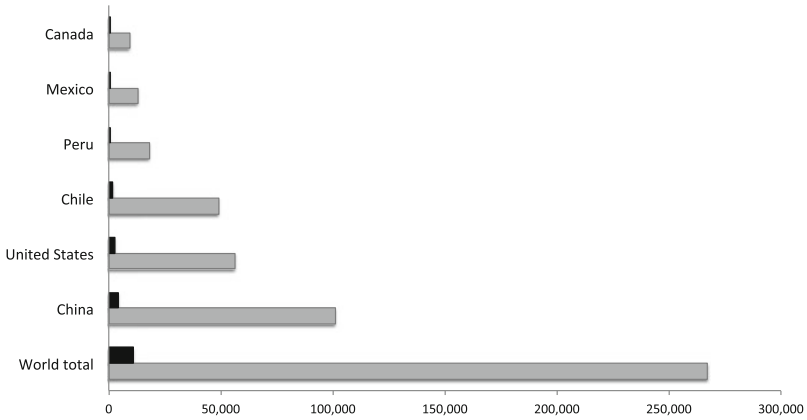
3 Molybdenum Minerals, Production, and Uses

Molybdenum is mostly extracted from its ore, molybdenite, but also produced as a side product in copper smelting (Kabata-Pendias and Mukherjee 2007).

Molybdenum is primarily used as an alloy hardening component, in heat- and wear-resistant steel production (Kabata-Pendias and Mukherjee 2007). Ferromolybdenum and molybdic oxide are the main molybdenum forms used in combination with chromium, manganese, nickel, niobium, tungsten, etc. (Polyak 2016b). It is also used in the aerospace, in arms and electronics industries, in catalyst manufacturing, and in the production of dyes, lubricants, and elements of incandescent lamps; its complexes are also utilized as catalysts in oil-processing industry, especially for sulfur removal from petroleum products (NRC 2004; Kabata-Pendias and Mukherjee 2007). Molybdenum disulfide is an excellent high-temperature-resistant lubricant and is applied in heat-resistant metal coatings. Its role in the so-called green technologies is increasingly more and more important, and it has found applications in the production of biofuels and ethanol, as well as in the manufacturing of solar panels and wind turbines (Polyak 2013). The International Molybdenum Association (IMOA 2014) reports that molybdenum compounds will soon play an important role in the production of stable and environmentally safe dyes.

China, the USA, and Chile are the world's leaders in molybdenum ore mining (Fig. 8.1). Other producing countries (2015 production) include Armenia (7300), Russia (4800), Iran (4000), Mongolia (2000), Turkey (1400), and Uzbekistan (520) (Polyak 2016a).

An upward trend in molybdenum mining is particularly apparent in China, where the production has increased 2.5 times since 2005; this is due to China's galloping economic growth and an improved competitiveness of steel exports (Magyar 2007, 2009; Polyak 2016a). The whole identified Mo resources in the USA reach about 5.4



	World total	China	United States	Chile	Peru	Mexico	Canada
Reserves in thousand tons	11,000	4,300	2,700	1,800	450	130	260
Mine production in tons	267,000	101,000	56,300	49,000	18,100	13,000	9,300

Fig. 8.1 World in total and six of the most important countries in molybdenum mining production (in tons) in 2015 and the estimated reserves (in 1000 tons) (Polyak 2016a)

million tons, which adds to about 14 million tons located in the other parts of the world (Polyak 2016a).

Anthropogenic molybdenum pollution results from its mining processes, production of heat- and corrosion-resistant steel alloys, and industrial wastewater discharge including those from tanneries (Reid 2012).

4 Molybdenum in Nature

Molybdenum is widely distributed in nature. It is found in such minerals as molybdenite (MoS_2—the major ore of molybdenum), wulfenite, ferrimolybdate, jordisite, and powellite (Leichtfried 1990). Environmental release of molybdenum compounds from industrial activities affects the air (stack emissions), water (liquid effluents), or earth in the form of solid wastes (sludge) (Leichtfried 1990).

The content of molybdenum in rocks depends on their type (Table 8.1). Lithosphere molybdenum is mainly associated with acid igneous rocks or argillaceous formations (Kabata-Pendias 2011; Pasieczna 2012). In respect to rock type, caustobioliths and copper and oil shales are the richest rocks in Mo, followed by argillaceous sediments and clays. The lowest molybdenum content is found in limestones, sandstones, and graywackes (Thornton 1981; Wedepohl 2004; He et al. 1998, 2005; Kabata-Pendias and Mukherjee 2007). The continental crust contains Mo in the range 1–1.5 mg kg^{-1}, whereas the oceanic basalt crust contains 0.8 mg kg^{-1} (Budaveri 1996; Wedephol 2004).

The content of molybdenum in soils is presented in Table 8.2. The average soil concentration of molybdenum may range between 1.0 and 2.0 mg kg^{-1} (Kubota

Table 8.1 Concentrations of molybdenum in rocks (mg kg^{-1})

Rock	Content	References
Continental crust	1–1.5	Budaveri (1996)
	1.1	Wedepohl (2004)
Oceanic basalt crust	0.8	Wedepohl (2004)
Caustobioliths	>2%	Enzmann (1972) and Pasieczna (2012)
Copper and oil shales	>200	Enzmann (1972) and Pasieczna (2012)
Argillaceous sedimentary rocks	2.5–3.0	Thornton (1981), Reimann et al. (1998), He et al. (1998, 2005), and Pasieczna (2012)
Clays	2–2.5	Kabata-Pendias and Mukherjee (2007)
Granites	1.0–6.0	Thornton (1981), Wedepohl (2004), and He et al. (1998, 2005)
Shales	1.3–2.5	Thornton (1981), Wedepohl (2004), and He et al. (1998, 2005)
Gneisses	1.5	Wedepohl (2004)
Basalts, gabbroic rocks	0.9–7.0	Thornton (1981), Wedepohl (2004), and He et al. (1998, 2005)
Igneous rocks	0.3–2.0	Reimann et al. (1998) and Pasieczna (2012)
Graywackes	0.7	Wedepohl (2004)
Sandstones	0.2–0.8	Kabata-Pendias and Mukherjee (2007)
Limestones	0.2–0.4	Thornton (1981), Wedepohl (2004), Kabata-Pendias and Mukherjee (2007), and He et al. (1998, 2005)

Table 8.2 Concentrations of molybdenum in soils (mg kg^{-1} dry wt)

Soil type	Content	Reference
Soils of the world	0.1–7	Kabata-Pendias and Mukherjee (2007)
On average	1.8	Kabata-Pendias and Mukherjee (2007)
	1.2	Koljonen (1992)
	1.0–2.0	Kubota (1977), Adriano (1986) and USGS (2015)
European topsoil	<0.1–17.2	de Vos and Tarvainen (2006)
Median	0.62	de Vos and Tarvainen (2006)
Soils used for agricultural purposes	0.6–72	Reimann et al. (2003)
Light sandys	0.1–3.7	Kabata-Pendias and Mukherjee (2007)
Medium clays	0.4–6.4	Kabata-Pendias and Mukherjee (2007)
Heavy clays	0.7–7.2	Kabata-Pendias and Mukherjee (2007)
Calcareous soils	0.3–7.4	Kabata-Pendias and Mukherjee (2007)
Organic soils	0.3–3.2	Kabata-Pendias and Mukherjee (2007)
Soils in the USA	0.1–4.0	Friberg et al. (1975) and Chappel et al. (1979)
On average	1.2	Friberg et al. (1975) and Chappel et al. (1979)

1977; Adriano 1986; Koljonen 1992; Kabata-Pendias and Mukherjee 2007; USGS 2015). Soils containing more washable particles also contain more molybdenum. Molybdenum content in the soils of Saxony averages 0.30–6.0 mg kg^{-1} (Barth et al.

1996), 0.2–48.6 mg kg^{-1} in Slovakia (Eurlik and Šefeik 1999), 0.24–3.13 mg kg^{-1} in Lithuania (Kadűnas et al. 1999; Gregorauskiené and Kadűnas 2000), and from <1 to up to 20 mg kg^{-1} in the Kola Peninsula (Reimann et al. 1998).

Soils in arid and semiarid areas, especially ferrasoils, usually contain relatively high amounts of molybdenum. Reclamation of such soils involves reduction of Mo phytoavailability (Kabata-Pendias and Mukherjee 2007). Eisler (1989) states that the levels of Mo are higher in the vicinity of molybdenum mines and combined heat and power plants. The soil may contain up to 35 mg kg^{-1} Mo in the areas around molybdenum processing plants in the USA and up to 38 mg kg^{-1} in Chile (Kabata-Pendias and Mukherjee 2007). Molybdenum is different from most trace metals in a way that its compounds are poorly soluble at a low soil pH (<4.5) and highly soluble in alkaline soils (pH > 6.5), which is reflected in Mo uptake by plants growing on different soil types (Kabata-Pendias 2011).

Molybdenum is likely to form compounds with organic matter and some metals (Kabata-Pendias and Mukherjee 2007). Some soils require supplemental enrichment with Mo. These are soils with low organic matter content, exposed to severe erosion or strongly weathered, low in total molybdenum, as well as sandy and acidic soils (pH < 6.3) (Hornick et al. 1977). In the USA, Mo concentrations in soils increase moving from east to west (Kubota 1977; Adriano 1986).

Water and wind are the main factors of molybdenum spreading across the surface of the Earth (Wedepohl 2004). The median of Mo concentration in the oceanic waters was calculated at the level 10 μg L^{-1} (Reimann and de Caritat 1998; Wedephol 2004; Nozaki 2005). Rainwater Mo content may vary depending on the pollution from 0.01 to 2.6 μg L^{-1}, between 0.04 and 1.3 μg L^{-1} in river water (Gaillardet et al. 2004), or 1 μg L^{-1} according to Wedephol (2004). In the USA, molybdenum concentrations are noted at levels ranging 1.2–4.1 μg L^{-1} in rivers, <1 μg L^{-1} in groundwaters, and 5–57 mg kg^{-1} dw in fluvial deposits (Friberg et al. 1975; Chappell et al. 1979). Surface water concentration of this element ranges from 0.4 μg L^{-1} in unpolluted rivers of North America to 100,000 μg L^{-1} in mining wastewater. In the groundwaters of the USA, Mo concentration is usually lower than 1 μg L^{-1}; however, high levels reaching 50,000 μg L^{-1} were measured near uranium mills in Colorado (Eisler 1989). Natural molybdenum concentrations in surface waters seldom exceed 20 μg L^{-1}; higher levels are probably due to industrial pollution (Eisler 1989).

The average molybdenum content in the atmosphere is below 0.2 ng m^{-3}, ranging from <0.5 ng m^{-3} in the isles of Svalbard and 0.2 ng m^{-3} in Greenland to 1–10 ng m^{-3} in urban areas (Kabata-Pendias and Mukherjee 2007).

If we look at the concentration of Mo in fossil fuels (Table 8.3), it appears that the element accumulates and builds up in coals. If combusted, these fuels release molybdenum, which spreads around and finally gets into soils and sediments. Fly ash contains Mo at a level between 5 and 33 mg kg^{-1} (Bhattacharyya et al. 2009; Pandey et al. 2009; Pasieczna 2012).

Table 8.3 Molybdenum content in fossil energy materials (mg kg^{-1})

Fuel	Content	Reference
Coal	3–6	Kabata-Pendias and Mukherjee (2007)
On average	4	Wedephol (2004)
Lignite	2.8	Wedephol (2004)
Fly ash	5–33	Bhattacharyya et al. (2009), Pandey et al. (2009) and Pasieczna (2012)
On average	14.6	Kabata-Pendias and Mukherjee (2007)
Petroleum	10 mg L^{-1}	Wedephol (2004)
Gasoline	10 mg L^{-1}	Kabata-Pendias and Mukherjee (2007)

5 Biological Status of Molybdenum

In human and animal bodies, molybdenum occurs in low concentrations; still, Mo is an essential element, a component of several enzymes (Stiefel 2002; Williams and da Silva 2002; Kabata-Pendias 2011; Reid 2012), which catalyze redox reactions. In plants, on the other hand, molybdenum causes reduction of molecular nitrogen and nitrates (Sellman 1993; Kim et al. 1993; Burris and Roberts 1993; Reid 2012), which is important in plant growth processes. Despite its key role, Mo is present in plant tissues in very small amounts, 0.5 mg kg^{-1} dry matter on average (Spears 1992; Turnlund et al. 1995). According to Kabata-Pendias (2011), normal concentrations in plants may vary, ranging from 0.1 to 1.5 mg kg^{-1} dw. In areas where intensive industrial activities take place, herbaceous plants contain Mo in amounts of up to 231 mg kg^{-1} dw. Molybdenum is poorly absorbed from acid soils; hence it is recommended to provide the plants with additional amounts of this element through soil liming or by applying Mo supplementation on pastures (Hornick et al. 1977). Its deficiency signs are pale patches on leaves, withering of buds, and impaired leaf development; particularly susceptible are brassicas (Pasieczna 2012).

Molybdenum concentration in the range 0.1–0.5 mg kg^{-1} suffices for the plant metabolism, whereas levels of 10–50 mg kg^{-1} are toxic to most plants. Molybdenum deficiencies are likely in acid soils (pH < 5.5), in those where a low Mo content is coupled with a high level of iron oxide, or in peat soils (Kabata-Pendias and Mukherjee 2007; Kabata-Pendias 2011).

Average Mo content in grain is 0.45 mg kg^{-1} in rye, 0.5 in barley, 0.55 in oats, and 1.0 in wheat (always mg kg^{-1} dw). There is 1.2–1.8 in peas, 0.9–1.6 in beans, 0.1–0.25 in potatoes, and 0.07 in apples on average (always mg kg^{-1}). In grasses growing over Mo-contaminated areas, the concentrations of the metal range from 1.5 mg kg^{-1}, in Great Britain, to 50 mg kg^{-1}, in Russia; in legumes, the levels range from 5.2 mg kg^{-1}, in Canada, to 26.6 mg kg^{-1}, in Poland (Kabata-Pendias and Mukherjee 2007). Excess soil molybdenum supply will increase its content in plants, which may lead to molybdenosis in ruminants (Underwood 1977; Kabata-Pendias and Mukherjee 2007). In soils, molybdenum is likely to form complex anionic

Table 8.4 Effect of soils formed from various soils on relative molybdenum (Mo) content in plants

Geological origin of the soil	Relative Mo content in plants
Granite	100
Clay	88
Phyllite—a fine-grain shale	88
Gneiss—a metamorphic rock	78
Buntsandstein	78
Peat, muck soils	71
Rotliegend	71
Loess	64
Diluvial sands	64
Shale soils (Devonian, Siluran, Culm Supergroup)	51
Alluvial soils	47
Keuper	47
Muschelkalk	38

Anke et al. (2000)

compounds, which are mobile in neutral and alkaline substrates. In acid substrates, on the other hand, Mo binds to a hydroxide of aluminum, iron, or manganese or to organic matter and argillaceous minerals, which limits its phytoavailability (Pasieczna 2012). Legumes require more molybdenum compared to other plants, since symbiotic bacteria of their root nodules use it for binding atmospheric nitrogen (Sequi 1973; Ivanova 1973; Regius and Anke 1989; Schnabel and Bunke 1989; Kabata-Pendias 2011).

Plants sometimes exhibit explicit symptoms of Mo deficiency, such as classic whiptail in cauliflower or yellow patches on citrus plants; however, most often Mo deficiency symptoms are invisible, and nitrogen deficiency symptoms may appear instead (Hornick et al. 1977; Lăcătuşu and Borza 1989).

The highest levels of molybdenum available for plants, despite a low pH, are in soils formed from granite rock (Table 8.4). Also vegetation growing on soils created from clays, phyllite, and gneiss contain much molybdenum. Muschelkalk, keuper, and alluvial soils, on the other hand, are low in terms of molybdenum levels in plants (Anke et al. 2000). Plants growing on these soils are likely to suffer Mo deficiencies (Holzinger et al. 1998).

Although animal molybdenum deficiencies are rare, broiler chickens are susceptible, and slow growth rates and poor plumage quality may be symptoms of such (Kabata-Pendias and Mukherjee 2007). Higher concentrations of molybdenum are said to stimulate growth; hence some groups of animals (chickens, rainbow trout) obtain Mo supplementation to enhance growth (Reid 2012).

Anke et al. (1983, 1985b) measured molybdenum in calves, lambs, and newborn children and found that Mo levels in all studied tissues were significantly lower during the period of maternal milk feeding, as compared with those during further, post-suckling nutrition period. Similar pattern was observed in various ungulate species. Studies on herbivorous mammals in the San Diego Zoo (California, USA)

Table 8.5 The content (mg kg^{-1} dw) of Mo in the liver in different species of wild ruminants

Name of species		Adult	Newborn
Species (n;n)	Latin name	Mean ± SD	Mean ± SD
Sable antelope (4;3)	*Hippotragus niger*	1.51 ± 0.96	0.28 ± 0.14
Gemsbok (15;15)	*Oryx gazella*	1.78 ± 0.37	0.98 ± 0.40
Pampas deer (5;2)	*Ozotoceros bezoarticus*	1.89 ± 0.63	1.29 ± 0.14
Chital or cheetal (8;14)	*Axis axis*	1.95 ± 0.85	1.12 ± 3.39
Gaur or Indian bison (3;5)	*Bos gaurus*	2.09 ± 0.88	1.13 ± 0.27
Hog deer (7;6)	*Axis porcinus*	2.18 ± 0.93	1.23 ± 0.38
Sika deer (8;6)	*Cervus nippon*	2.21 ± 0.98	1.59 ± 0.25
Impala (4;2)	*Aepyceros melampus*	2.29 ± 0.78	0.41 ± 0.02
Markhor (6;4)	*Capra falconeri*	2.37 ± 0.91	1.69 ± 0.35
European bison (4;5)	*Bison bonasus*	2.59 ± 0.85	1.28 ± 0.39
Nilgai (4;5)	*Boselaphus tragocamelus*	2.59 ± 0.24	0.85±0.52
Kudu (4;3)	*Tragelaphus imberbis*	2.66 ± 0.10	1.09 ± 0.19
Barasingha or swamp deer (6;8)	*Rucervus duvaucelii syn. Cervus duvaucelii*	2.83 ± 0.80	0.98 ± 0.12
Blackbuck/Indian antelope (4;17)	*Antilope cervicapra*	3.03 ± 0.47	0.63 ± 0.17
Mufflon or mouflon (12;12)	*Ovis musimon*	3.27 ± 0.39	1.30 ± 0.63
Grant's gazelle (6;3)	*Nanger granti*	3.81 ± 0.89	0.94 ± 0.53
Alpine ibex (12;17)	*Capra ibex*	3.88 ± 0.85	1.86 ± 0.44
Thomson's gazelle (7;3)	*Eudorcas thomsonii*	3.89 ± 1.01	0.70 ± 0.15
Dama gazelle (5;6)	*Nanger dama*	4.31 ± 0.85	0.69 ± 0.34
Gazella subgutturosa (7;8)	*Gazella subgutturosa*	4.64 ± 2.88	1.83 ± 1.21
Mountain gazelle (8;6)	*Gazella gazella*	4.67 ± 2.11	0.84 ± 0.35
Soemmerring's gazelle (5;5)	*Nanger soemmerringii*	5.15 ± 1.07	1.31 ± 0.18

Anke et al. (2000)

revealed that hepatic Mo content in neonates was significantly lower compared to adult animals (Table 8.5); nonsignificant differences were found only in 3 out of 22 species studied. Also, molybdenum hepatic levels in adult animals differ significantly ($p \leq 0.001$) between species; between the liver of Soemmerring's gazelle (*Nanger soemmerringii*) (5.15 mg kg^{-1}), in which Mo content is highest, and the sable antelope (*Hippotragus niger*) (1.5 mg kg^{-1}), with the lowest Mo hepatic content, the difference was 342%. A similar pattern can be seen in their neonates; the difference between extreme species reached 664% (Anke et al. 2000).

Molybdenum is present in all tissues in humans and animals. The lowest level in a human body occurs in blood, 3.4–14.9 ng L^{-1}, and the highest in the kidneys and liver, 0.4 mg kg^{-1} (Li 2000). In animals, molybdenum is involved in oxidation (hydroxylation) of xanthine to uric acid and other purines and aldehydes (Schindelin et al. 1996; Reid 2012). Molybdenum in animals also affects protein synthesis and metabolism of a range of elements, i.e., phosphorus, sulfur, potassium, iron, copper, zinc, and iodine (Reid 2012).

Molybdenum is also an essential element for humans. The molybdenum cofactor is necessary for the functioning of at least three enzymes: (1) sulfite oxidase (catalyzes sulfite-to-sulfate oxidation and is necessary for sulfur amino acid metabolism), which occurs in the liver (Mills and Davis 1987; Anke and Risch 1989; Hille et al. 2011; Kabata-Pendias 2011); (2) xanthine oxidase (catalyzes purine and pyridine hydroxylation, including conversion of hypoxanthine to xanthine and xanthine to uric acid); and (3) aldehyde oxidase (oxidizes purines, pyrimidines, and pteridines and is involved in nicotinic acid metabolism), which are both present in the liver and intestine. Xanthine oxidase has been isolated from cow's milk. Molybdenum in milk occurs mainly as a component of this enzyme (Mills and Davis 1987).

The main sources of Mo in the human diet are vegetables, legumes, and offal (Combs 2005). Excess dietary molybdenum reflects in its elevated levels in serum, urine, or hair (Kabata-Pendias and Mukherjee 2007). Low intake of Mo reduces the concentrations of uric acid in urine and serum and leads to excessive excretion of xanthine. Molybdenum deficiency in humans leads to neurological symptoms and premature death (Spears 1992; Van Gennip et al. 1994; Turnlund et al. 1995).

6 Toxicity of Various Molybdenum Forms in Homeothermic Animals

Symptoms of either acute or chronic molybdenum toxicity depend on its chemical form and the species of the exposed organism. Generally insoluble Mo compounds are characterized by a lower toxicity compared to its soluble forms. These include primarily MoS_2, MoO_2, and the metallic form of the element (Stokinger 1981; EFSA 2006). Those of higher toxicity—apart from such water-soluble compounds as calcium molybdate and molybdenum trioxide—include thiomolybdates and oxythiomolybdates, as well as molybdenum forms present in plants. Their bioavailability for laboratory animals and ruminants ranged between 75 and 97% of ingested quantity (EFSA 2006). If we consider molybdenum toxicity in terms of the species, a regularity is that monogastric animals are less susceptible to its toxic effects, as compared to ruminants (Davis and Mertz 1987; Mills and Davis 1987; Blood and Radostits 1989; Frank et al. 2004a, b; Hall 2012).

Excess molybdenum is a commonplace phenomenon, especially in cattle, affecting the growth and health of the animals. It may lead to osteoporosis and bone deformities, since it interferes with Ca and F metabolism in the bone (Anke and Groppel 1985; Kabata-Pendias and Mukherjee 2007). Copper deficiency caused by Mo elevated levels is often the case in ruminants (Jones 2005). Some pastures may have an extremely high concentration of Mo (as a rule, this is the vegetation associated with alkaline soils), which may result in Mo toxicity in sheep and cattle (Hornick et al. 1977). The recommended molybdenum concentration in soils used

for agricultural purposes has been established at the level 50 mg kg^{-1} dry weight, dw (Hornick et al. 1977).

Most reports on animal Mo research carried out so far concern laboratory mammals and domesticated species; those on free-living animals are sparse. Underwood (1977) claims that animals of different groups vary in relation to dietary molybdenum dose tolerance. This is particularly dependent on copper and inorganic sulfates contents in the diet. In the group of domesticated animals, horses are the most tolerant species to elevated molybdenum intake, followed by pigs, rats, rabbits, and guinea pigs. Cattle and sheep, on the other hand, are definitely the most susceptible species to Mo toxicity (Underwood 1977; Anke and Groppel 1985; Rajagopalan 1988; Tallkvist and Oskarsson 2015). In cattle, a concentration of 20 mg Mo kg^{-1} dw of feed results in severe diarrhea and body weight loss (teart); this level causes no effect in horses and very little in sheep (Underwood 1977).

In pigs, administration of 1 g Mo kg^{-1} dw of feed lasting for several months produced no symptoms of toxic effect. With acute Mo toxicity, all animal species exhibit growth inhibition, body weight loss, and increased mortality (Underwood 1977). Laboratory animals affected by molybdenosis, however, do not suffer diarrhea, which is the case in cattle. A strong protective activity of copper and inorganic sulfates has been found (Underwood 1977). The LD_{50} for rodents in response to oral administration of molybdenum trioxide was 188 mg kg^{-1} body weight, which corresponds to 125 mg Mo kg^{-1} body weight; for ammonium molybdate, on the other hand, the value was 680 mg kg^{-1} body weight, i.e., 370 mg Mo kg^{-1} body weight. The LD_{100} after oral administration of ammonium molybdate to guinea pigs, rabbits, and cats were, respectively, 2200, 1870, and 2400 mg kg^{-1} body weight, which corresponds to 1200, 1020, and 1310 mg Mo kg^{-1} body weight (Venugopal and Luckey 1978). Reproducible lethal dose for mice, guinea pigs, and rabbits ranges between 60 and 330 mg Mo kg^{-1} body weight (Mills and Davis 1987). The NOAEL for rats is 40 mg Mo kg^{-1} body weight per day, whereas for rabbits 23 mg Mo kg^{-1} body weight per day (Bompart et al. 1990; Vyskocil and Viau 1999).

Studies on the effects of molybdenum on ruminants revealed that symptoms of acute molybdenosis in cattle appear at the concentration of 7400 mg kg^{-1} of feed, in the form of sodium molybdate. This dose caused focal necrosis in the kidneys and liver of the animals (Swan et al. 1998). As in the case of acute toxicity, chronic toxicity also depends on the animal species. An oral lethal dose of the chronic exposure in rats, mice, rabbits, and guinea pigs remains in the range from 60 to 333 mg Mo kg^{-1} of body weight per day. Ruminants are much less resistant to molybdenum, as similar outcomes are observed at only 3 mg Mo kg^{-1} body weight per day (Hall 2012).

Molybdenum toxicity symptoms include diarrhea (cattle only), anorexia, achromotrichia, and disturbation of neurological conditions and may lead to premature death (Anke 2004). Contamination with molybdenum caused in cattle severe diarrhea, which occurred during the period of grazing. This was accompanied by secondary copper deficiency (Anke 1986). Sulfur levels also played a role here. With participation of sulfates, inorganic Mo compounds were converted to

thiomolybdates (e.g., MoS^{2-}) by microorganisms in the rumen. Thiomolybdates immediately react with various proteins, thereby forming Cu-binding complexes (Mills et al. 1978; Anke 1986). High concentrations of Mo in the diet of cattle, sheep, horses, rabbits, and rats damage the animal skeleton (Anke and Groppel 1985).

Under natural conditions, toxicity of molybdenum starts immediately after ingestion. Some compounds of the metal may also penetrate the body through inhalation or cause skin irritation. These include molybdenum trioxide. As in the case of the gastrointestinal tract, absorption in the airways also depends on the solubility of the substances. It has been found that soluble species are absorbed in the lungs, whereas insoluble compounds are not (Stokinger 1981; Friberg and Lener 1986). Chan et al. (1998) observed that rats and mice exposed to this compound in an amount of 10–100 mg m^{-3} for 6 h a day over the period of 5 days developed adenomas in their respiratory system, as well as chronic inflammation of the lining of the respiratory system and degeneration of the cartilage structure of the bronchial tree. In rabbits treated intratracheally with molybdenum trioxide in particulate form, in an amount of 70–80 mg kg^{-1} body weight for a period of 9 months, induced pneumoconiosis accompanied by effusion into the lumen of pulmonary alveoli and bronchi (Friberg and Lener 1986). Molybdenum compounds inhaled into the airways also have system-wide effects. Lukashev et al. (1971) observed that rabbits and rats exposed to molybdenum trioxide in particulate form administered in the dose changing from 210 to 10 mg m^{-3} in 25-min intervals, for 4 h per day, over the period of 3.5 months, resulted in renal tubular atrophy. Compounds causing skin irritation include Na_2MoO_4, which induces dermal reaction within 24 h following the contact. The changes disappear within 72 h from the cessation of irritation (EFSA 2006).

Data concerning the effects of molybdenum on free-living mammals are sparse. Good documented sources deal only with a cervid species inhabiting Scandinavia. Particular focus has been on copper and molybdenum contents in the tissues of the moose living in Sweden in connection with the "mysterious" moose disease, which affected the population in this country in the mid-1980s. It was then a disorder of unknown etiology (Frank et al. 2000). The clinical symptoms and organ changes observed postmortem resembled those caused by copper deficiencies and molybdenosis in cattle and sheep (Frank 1998, Frank et al. 2000). Several years of investigations revealed that in the period 1982–1994, copper hepatic levels in unaffected individuals dropped twofold, whereas molybdenum concentrations in the same period and in the same animals increased 20–40% (Frank et al. 1994, 2000; Frank and Galgan 1997; Frank 1998). Based on microbiological and anatomopathological examinations and chemical composition analyses of parenchymal organs in the moose, it was eventually concluded that the most probable cause of the disease is copper deficiency and molybdenosis (Frank 1998; Frank et al. 2000). Frank (2003) also reported another case of molybdenosis in a moose in Sweden, which was caused by imbalance in the proportion between Cu and Mo in the liver, and this affected the metabolism of sulfur.

There is little information on molybdenum toxicity in free-living birds. As compared with mammals, reports on avian species are sparse and deal mainly with domestic birds. Toxic levels of dietary Mo in birds have been found at its absorbable

form concentration of 200 mg kg^{-1}. The most apparent symptom was growth inhibition. Molybdenum applied to turkey chicks at a dose of 300 mg kg^{-1} feed caused a considerable growth inhibition (Underwood 1977). At a Mo level of 500 mg kg^{-1} in feed, reproduction disorders were observed, whereas a feed concentration of 6000 mg kg^{-1} applied over 4 weeks resulted in 33% mortality. An increase of Mo dose to 8000 mg kg^{-1} feed over the same period of time killed 61% of chicks. Those that survived weighed 16% less than the control group birds (Friberg et al. 1975; Eisler 1989).

Stafford et al. (2016) analyzed toxicity of molybdenum disulfide (MoS_2, a dominant form found in molybdenite ore) in relation to bobwhite quail (*Colinus virginianus*). The chemical form and bioavailability of Mo are important in terms of its toxicity. The trial on birds involved a soluble Mo form, sodium molybdate dihydrate (SMD, $Na_2MoO_4 \cdot 2H_2O$), whereas MoS_2 is generally insoluble, poorly available under special environmental conditions. The observations included survival and health status (body weight and feed intake) of 9-day-old bobwhite quails exposed to soluble Mo (SMD) and Mo ore (MoS_2) in the diet for 30 days. The two forms of Mo were compared in terms of toxicity and bioavailability (also tissue penetration). Histopathological examinations and analyses of the serum, kidneys, liver, and bone were carried out. Copper, linked with Mo in terms of toxicity, was also determined in the diet and the tissues. There were no deaths or changes in groups of any form of Mo.

Analyses of tissues revealed increased levels of Mo in the serum, kidneys, liver, and bone during the experiment with SMD. After the period of exposure, a reduction in Mo was observed in these tissues. For the soluble form, the no-observed-adverse-effect concentration (NOAEC) was 1200 mg Mo as SMD/kg feed (134 mg SMD/kg body weight per day). There was no adverse exposure effect of MoS_2 at the maximum dose 5000 mg MoS_2 kg^{-1} feed (545 mg MoS_2 kg^{-1} body weight per day). This reveals that the effect of MoS_2, a more common and less bioavailable form of Mo, is similar to that of SMD. The NOAEC of MoS_2 is 5000 mg (545 mg MoS_2 kg^{-1} body weight per day). These results are more realistic in showing the susceptibility and the risk birds are exposed to when it comes to environmental molybdenum (Stafford et al. 2016).

7 Toxicokinetics and Effects of Molybdenum in Wildlife

There are two main routes by which the animal body may be exposed to molybdenum, namely, a dietary and a respiratory pathway. The latter has been relatively poorly described and reports refer mostly to laboratory animals (Tallkvist and Oskarsson 2015). Aerial exposure of guinea pigs to 285 mg Mo m^{-3} in the form of molybdenum disulfide powder did not result in elevated absorption of the metal via airways (Fairhall et al. 1945). The ingested dose of molybdenum is predominantly responsible for its uptake. Animal studies show that a single dose of hexavalent molybdenum compounds will be efficiently absorbed in the

gastrointestinal tract. Experimental data reveal that from 40% to 90% of ingested metal is absorbed in the gut (Friberg and Lener 1986; Turnlund et al. 1995; Anke 2004). The metal is next transported to the kidneys, liver, and bone; this applies to both short- and long-term exposure. It should be stressed, however, that molybdenum absorption levels differ greatly between monogastric organisms and ruminants (Miller et al. 1972; Nielsen 1996; Frank et al. 2000; Hall 2012). In the former group of animals, molybdenum is absorbed through the walls of the stomach, but also in the other parts of the gastrointestinal tract. In ruminants, on the other hand, absorption takes place via the intestinal walls, whereas the walls of the multi-chambered ruminant stomach create a barrier preventing molybdenum penetration. Molybdenum is absorbed by active transport, which is also used for sulfate intestinal absorption; hence, sulfates present in the lumen of the gastrointestinal tract can significantly reduce the absorption of molybdenum (Mason and Cardin 1977). Sulfates or sulfites present in ruminal digesta lead to formation of di-, tri-, and tetramolybdates, which are strong copper-binding ligands. These capture copper by forming insoluble Cu-thiomolybdate complexes (Price et al. 1987; Gooneratne et al. 1989; Smith and White 1997; Gu et al. 2015; Skibniewski et al. 2016). This type of binding is much stronger than that with metallothionein, which is the main copper-binding tissue protein (Allen and Gawthorne 1987; Frank et al. 2000). The complexes are inhibitory in relation to the activity of copper enzymes resulting from their strong affinity to copper ions (Humphries et al. 1983). Price et al. (1987) observed that about 30% of ruminal fluid molybdenum occurred in the form of di-, tri-, and tetrathiomolybdates combined with the solid phase—thus being undetected in the liquid phase. Tetrathiomolybdates are thought to be bound to the solid phase of the digesta and, in consequence, cannot be absorbed through the walls of the rumen. Probably, large quantities of molybdenum, reaching toxicity levels, may limit the ability of SO_4-reducing ruminal bacteria to live in an environment with high sulfur content, which in consequence leads to an increased production of H_2S (Kessler et al. 2012). The main function of molybdenum is to take part in redox reactions in cells, since the element may assume a valency of +4, +5, or +6 in the catalytic reactions of the enzymes it is bound to. Molybdenum-containing enzymes have been identified in all living organisms. In mammals, they are involved in the metabolism of purines, pyrimidines, pteridines, and aldehydes, as well as in the oxidation of sulfites. Most prominent molybdenum enzymes include aldehyde oxidase, sulfite oxidase, and nitrate reductase (Hille et al. 2011). Generally, reactions catalyzed by Mo enzymes consist in oxygen atom transfer from water to or from the substrate as a result of a redox reaction, in which molybdenum changes its valency from IV to VI (Mason 1986; Kisker et al. 1997; Hille 2002; Mendel and Bittner 2006).

Molybdenum toxicity is linked with a wide spectrum of symptoms, of which many arise from molybdenum-caused secondary copper deficiency. Typical symptoms of acute uncomplicated molybdenosis include impaired bone formation, which may be a result of impaired phosphorus metabolism. This leads to bone and joint deformities and spontaneous pathological metaphyseal fractures of the long bones and may cause exostosis. Molybdenosis leads to a decrease in alkaline phosphatase activity and a lower content of proteoglycans in the articular cartilage. Reproductive

disorders affecting both sexes may also be the case. Females suffer inhibition of the estrous cycles, while interstitial testicular degeneration may afflict males, probably by affecting sex hormone receptors. Laboratory animals exhibit growth inhibition as well as morphological and functional changes in the liver, kidney, and spleen. Long-term exposure also results in anemia and diarrhea (Tallkvist and Oskarsson 2015).

Molybdenum causes disorders of the copper metabolic functions. This is due to the fact that the elements are antagonistic to each other, which is due to the electron configuration of the atoms in their ionic forms. The effect of copper deficiency caused by excess molybdenum is apparent mainly in ruminants; however, some studies suggest that excessive levels of molybdenum disrupt copper metabolism also in monogastric animals (Halverson et al. 1960; Mills and Davis 1987). In ruminants, the nutritional requirement of the ruminal microbiota is an extremely important issue. The microbial demand for copper, which is lower than that of the tissues of the host organism, is 1.57 μmol kg^{-1} dw of feed. As far as molybdenum is concerned, this value is much higher, from 104.2 to 2.85 mmol kg^{-1} dw of feed (Dziekan et al. 2007). The copper-molybdenum antagonism is based primarily on molybdenum reactions with sulfides formed through bacterial reduction of sulfates in the lumen of the gastrointestinal tract. Another mechanism of copper content reduction involves copper reactions with thiomolybdates. In monogastric animals and in humans, considerable amounts of sulfates may form in the colon. As a consequence, active sulfur compounds are inhibited. Molybdenum is removed from the body with urine and, to a lesser extent, with bile (Vyskocil and Viau 1999; NRC 2006). Molybdenum urinary excretion in laboratory animals is relatively quick, as its total removal in guinea pigs, rats, goats, and pigs takes about 2 weeks. In goats, small amounts of molybdenum, 2% and 0.2% of molybdenum uptake, respectively, have also been observed to be removed with milk and lost hair (Anke et al. 1983).

There is little information on molybdenum toxicity in free-living birds, and the research carried out so far has been focusing on domesticated avian species. In the latter group of birds, molybdenum hepatic concentrations, ranging from 22 to 36 mg kg^{-1} dw, positively correlated with the toxicity symptoms (Puls 1988). Experiments revealed that the level of the element in the avian liver depended not only on molybdenum content in the diet but also on the dietary concentrations of sulfates and copper. The problem of the interaction between these elements in terms of their absorption, excretion, and kinetics belongs to the most important issues of veterinary toxicology, and to date the complex nature of these processes has not been fully explained. The toxicity threshold for avian embryos is 23–33 mg Mo kg^{-1} of egg. Accordingly, in natural conditions molybdenum toxicity to avian embryos is thought to be extremely rare (Eisler 1989).

As is the case of birds, data on molybdenum toxicity in relation to undomesticated mammals have been reported sparsely. The only species well described in terms of this issue is the moose (*Alces alces*). In the mid-1980s, moose population inhabiting the southwestern part of Sweden started showing symptoms of a previously unknown disease. The number of dead or culled animals reached about 150 individuals a year, which represented about 3% of the total regional population (Frank

1998). Investigations revealed that the most possible cause of the "mysterious" moose disease was copper deficiency and molybdenosis (Frank 1998; Frank et al. 2000, 2004a). The molybdenosis hypothesis of the moose illness was later supported by unexpected manifestation of type 2 diabetes mellitus in those of the afflicted animals in which protein glycation occurred due to prolonged hyperglycemia (Frank et al. 2002). The clinical signs of the disease, as well as anatomopathological changes, were similar to those of copper deficiency and molybdenosis in cattle and sheep (Gooneratne et al. 1998; Frank 1998; Frank et al. 2000). The symptoms included diarrhea, anorexia, emaciation, achromotrichia, alopecia, apathy, abnormal behavior, and motor dysfunction. The anatomopathological changes included mucosal edema, hyperemia, and petechiae of the mucosa in the gastrointestinal tract, spleen and liver hemosiderosis, dilation of the heart, lung alveolar emphysema, neuropathies, as well as uni- or bilateral corneal opacity (Frank et al. 2000, 2004a, b; Frank 1998). Reports on molybdenum-exposed mule deer reveal that the species has a similar tolerance to molybdenum as pigs and horses. Animals fed a dose of 2500 mg Mo kg^{-1} body weight for 25 days exhibited only reduced feed intake and moderate diarrhea. At a dose of 5000–7000 mg Mo kg^{-1} body weight administered for 3–15 days, the symptoms aggravated; however, relief of symptoms was observed nearly immediately on the restoration of the normal diet (Chappell et al. 1979; Eisler 1989).

8 Bioaccumulation of Molybdenum

Molybdenum is a constituent of numerous enzymes found in all living organisms. This gets into the body as a molybdate anion; however, its biochemical marker has not been identified yet. In order to attain biological activity, molybdenum must be complexed by a pterin compound, this way forming molybdenum cofactor (Mendel and Bittner 2006). Its structure is unique and probably results from the necessity to control and sustain the oxidation-reduction properties of molybdenum. The role of this cofactor consists in maintaining the catalyst, i.e., molybdenum, in the active center, which in consequence enables electron exchange between the pterin ring and molybdenum atom (Kisker et al. 1997).

In both humans and animals, the tissue content of molybdenum and the processes of its removal mostly depend on the dose ingested orally; however, this level does not fully reflect molybdenum status in the body due to numerous interactions with other metals and substances present in the tissue (Kisker et al. 1997; Mendel and Bittner 2006).

Molybdenum is distributed to all the tissues of the living system, although its highest concentrations occur in the liver, kidney, and bone. In the light of its role and importance for metabolic processes, it must be noted that the quantities of this essential element present in the system are relatively low. After absorption, molybdenum is transported with erythrocytes and in the form of molybdate ions (Allway et al. 1968; Versieck et al. 1981). In the red blood cells, molybdenum binds to their

membrane proteins, particularly with spectrin, whereas Mo present in the plasma binds with α_2-macroglobulin (Bibr et al. 1983). Either taken in or produced on an ongoing basis, thiomolybdates may bind copper, forming copper-thiomolybdate complexes which—remaining in the bloodstream—cannot be used by the cells of the living system (Hall 2012). It has been generally accepted that molybdenum is accumulated in parenchymal organs, primarily in the kidney and liver (Rousseaux et al. 2002).

Studies on molybdenum distribution in the tissues of laboratory animals show that—within 1–24 h following a single intravenous injection of Mo-99 isotope—the highest levels occurred in the kidney, liver, and pancreas. With a lapse of time, molybdenum concentrations decreased in the kidneys and pancreas, whereas the hepatic level of the element did not change significantly over the entire period of the experiment (Rosoff and Spencer 1973). A similar pattern of molybdenum tissue distribution was found in cattle and goats subjected to long-term exposure, with the highest values observed in the kidneys (Anke et al. 2007; Tallkvist and Oskarsson 2015). An experiment on rats that were orally or subcutaneously administered a dose of 25–40 micrograms molybdenum per kilogram of body weight revealed that within 14 days Mo concentration reached a high level in the kidneys, liver, and skin. The levels in these tissues of the rats depended on the dose (Rosoff and Spencer 1973). Pott et al. (1999) report that two compartments may be present in the liver, of which one is responsible for free molybdenum circulation, whereas the other is characteristic for its rapid distribution. Molybdenum also binds to dermal collagen. It is also accumulated in the bone tissue and hyaline cartilage; hence it may be found in the cancellous bone of epiphyses and the epiphyseal plates. The metal may also penetrate dentition, the highest concentrations being found in the dentin and much lower in the enamels (Lener 1978). Pott et al. (1999) claim that plasma, muscle, and kidney levels are the best measure of molybdenum bioavailability.

9 Ecological Effects of Molybdenum

Molybdenum is a relatively rare element, finding its application mostly in smelting steel used in many industries and medicine. Anthropogenic activities causing molybdenum contamination of the environment involve mainly fossil fuel combustion, mining, and metallurgical industry. In a general outline, molybdenum chemistry is complex and not fully understood (Eisler 1989). The metal was discovered about 200 years ago and found a wide application in metallurgy, superseding the traditionally used toxic metals, such as hexavalent chromium (Heijerick et al. 2012b; Shields 2013; Wang et al. 2016). In nature, molybdenum does not occur in its pure form, but in compounds with sulfur, oxygen, tungsten, lead, uranium, iron, magnesium, cobalt, vanadium, bismuth, or calcium (Eisler 1989).

If molybdenum concentration in fodder plants exceeds 5 or 10 mg kg^{-1} dw, it may cause molybdenosis in ruminants. This may be the case in plants growing on undrained soils rich in organic components (He et al. 2005). In terms of

environmental toxicology, the most important molybdenum form is molybdate anion, MoO_4^{2-}, which is of particular significance to animals inhabiting aquatic ecosystems, including freshwater systems. It was found to form under similar environmental conditions from various molybdenum-containing substances (De Schamphelaere et al. 2010; Heijerick et al. 2012a, b). Currently, the most common molybdenum-containing chemicals include ammonium molybdate, potassium molybdate, sodium molybdate, molybdenum disulfide, molybdic acid, and molybdenum trioxide, the latter being produced on the largest scale (Wang et al. 2016). Although environmental levels of molybdenum are relatively low, human impact may lead to a considerable increase, which in aquatic ecosystems may reach toxic concentrations. According to Shan et al. (2012), Mo concentrations in industrial wastes range from 4 to 145 mg L^{-1}. It must be stressed, however, that various forms of molybdenum have a different toxicity. In rainbow trout, the median lethal concentration (LC_{50}) for sodium molybdate was found to be 800 mg L^{-1}, whereas for ammonium molybdate 420 mg L^{-1} (Sigma-Aldrich 2015a, b, c). Similar results were reported by Wang et al. (2016), who found that acute toxicity of various molybdenum compounds against *Daphnia magna* after 48-h exposure increased in the following order: sodium molybdate, molybdenum trioxide, and ammonium molybdate. Bioconcentration of molybdenum on each level of the trophic chain, however, was found to be low. In aquatic organisms living in uncontaminated waters, average molybdenum concentration remains at a level below 1 mg kg^{-1} dw, whereas in strongly polluted areas, it does not exceed 10 mg kg^{-1} dw (Ikemoto et al. 2008; Regoli et al. 2012). Considering fish inhabiting polluted waters, the highest levels of molybdenum are measured in the liver, gills, and kidney. Contrary to these organs, Mo levels in the muscle tissue are much lower (Regoli et al. 2012). Given the research on various species inhabiting terrestrial ecosystems, molybdenum is not a metal of significant importance for environmental toxicology; hence, no legal regulations have been established so far on molybdenum dietary exposure for fish and terrestrial wild animals. Molybdenum has not been classified as an element of major toxicity by the EPA (US EPA 1992; US Department of Interior 1998).

10 Bioindicators and Biomarkers of Molybdenum in Ecotoxicological Studies

Environmental molybdenum contamination may be an outcome of using fertilizers containing this element but also results from mining and metallurgical industry emissions (Buekers et al. 2010). It may accumulate in animal tissues and is removed primarily with feces and urine. Herbivorous animals, both small (like the muskrat) and big (e.g., the moose), are more susceptible to increased Mo levels in the tissues than carnivorous and omnivorous animals, since the element accumulates in aquatic and terrestrial plants, reaching concentrations exceeding 1000 mg kg^{-1} dw (Fitzgerald et al. 2007). Mochizuki et al. (2002) report that—depending on the way ducks

feed (Table 8.6)—their molybdenum hepatic levels increase in the following order: carnivorous > omnivorous > herbivorous ones. Also, the authors point out that molybdenum hepatic and renal levels are higher in dabbling ducks (including spot-billed duck (*Anas poecilorhyncha*), pintail (*A. acuta*), wigeon (*A. penelope*)) compared to diving duck species such as scaup (*Aythya marila*) and tufted duck (*A. fuligula*) (Table 8.6).

Both in birds and mammals, molybdenum is mainly taken in with food and water, absorbed in the gastrointestinal tract. The highest Mo contents are usually found in the liver, kidney, and spleen (Table 8.6). Such all species of ducks, as well as muskrat and moose, may accurately reflect their natural habitat status in terms of the levels of molybdenum, which accumulates in plants, is present in the water column, and occurs in the benthic deposits, where these animals forage for food (Mochizuki et al. 2002; Frank 1998; Custer et al. 2004). Diet difference and its influence on Mo bioaccumulation in small terrestrial animals were also observed. Anke et al. (2007) investigated carcasses of two groups of micromammals (rodents and shrews) from habitats on Triassic (Muschelkalk) soils in Germany. In seven species rodent group (mainly herbivorous), Mo concentrations in their carcasses were similar and mean values ranged from 0.35 to 0.65 mg kg^{-1} dw. However, insectivorous common shrew (*Sorex araneus*) and pigmy shrew (*Sorex minutus*) accumulate significantly more Mo in their body (2.40 and 1.40 mg kg^{-1} dw, respectively) than rodents.

Elevated levels of Mo in ecosystems may result from the presence of large industrial objects or intensive agricultural production in the area but may also be a consequence of natural changes, as is the case of copper deficiency in the soils of northern Saskatchewan and Manitoba and parts of Alaska (North America). Frank (1998) demonstrated that in the livers of moose living in the region affected by acid rains (southwest Sweden), the content of molybdenum increased by 40% (Table 8.6).

Analyses presented by Anke et al. (2000) reveal that molybdenum contents in the liver and kidneys of red deer differ significantly ($p \leq 0.001$; Table 8.6) depending on the region (East Germany—Erzgebirge, Germany). Wild animals are susceptible to molybdenum tissue accumulations due to high concentrations of molybdate, copper deficiencies, and excess dietary sulfur, which is crucial in the case of ruminants. Mule deer and Alaskan moose tolerate high doses of molybdenum, compared with cattle. Mouflons (*Ovis musimon*) respond with immediate diarrhea if a Mo level in alfalfa reaches 300 mg kg^{-1} dw (Anke 1986).

In Central Europe, plants growing on soils formed from granite, rotliegend, or shale, as well as on peat and muck soils, may cause Mo contamination in free-living ruminants (Anke et al. 2000).

Table 8.6 Molybdenum in soft tissues of birds and mammals in mg kg^{-1}

Species	Place and years	*n* dw or ww	Liver	Kidney	Muscle	Brain	Lung	References
Birds								
Ducks								
Spot-billed duck *Anas poecilorhyncha*	Japan, 1993–1995	19 dw	9.27 ± 3.59 0.02–53.84	5.76 ± 1.78 0.02–32.34				Mochizuki et al. (2002)
Pintail *Anas acuta*		11 dw	3.30 ± 0.56 0.04–6.97	9.17 ± 3.21 0.06–33.03				Mochizuki et al. (2002)
Wigeon *Anas penelope*		15 dw	13.04 ± 5.80 0.08–91.78	8.58 ± 2.46 0.07–35.47				Mochizuki et al. (2002)
Scaup *Aythya marila*		6 dw	3.35 ± 1.52 0.66–10.75	3.11 ± 1.61 0.70–10.81				Mochizuki et al. (2002)
Tufted duck *Aythya fuligula*		6 dw	1.76 ± 0.98 0.02–6.32	2.63 ± 0.65 1.00–5.67				Mochizuki et al. (2002)
Other aquatic birds								
Grey heron *Aldea cinerea*	Japan, Kanto, 2001–2002	31 dw	3.18 ± 0.72 2.04–5.15	2.64 ± 0.58 1.82–4.69	0.06 ± 0.03 0.02–0.16	$n = 10$ 0.11 ± 0.13 0.03–0.47	0.19 ± 0.13 0.07–0.80	Horai et al. (2007)
Great white egret *Egretta alba*		22 dw	1.55 ± 0.27 1.03–2.09	2.17 ± 0.389 1.28–2.84	0.05 ± 0.02 0.02–0.09	$n = 18$ 0.15 ± 0.27 0.024–1.20	0.20 ± 0.16 0.07–0.76	Horai et al. (2007)
Intermediate egret *Egretta intermedia*		17 dw	1.69 ± 0.20 1.35–2.10	2.63 ± 0.436 1.94–3.52	0.08 ± 0.02 0.04–0.13	0.16 ± 0.19 0.05–0.69	0.31 ± 0.35 0.08–1.57	Horai et al. (2007)

(continued)

Table 8.6 (continued)

Species	Place and years	*n* dw or ww	Liver	Kidney	Muscle	Brain	Lung	References
Great cormorant *Phalacrocorax carbo*		4 dw	1.69 ± 0.38 1.27–2.17	1.57 ± 0.207 1.37–1.86	0.05 ± 0.02 0.03–0.07	$n = 1$ 0.18	0.10 ± 0.04 0.06–0.16	Horai et al. (2007)
Moorhen *Gallinula chloropus*		3 dw	5.87 ± 6.09 1.79–12.9	1.80 ± 0.154 1.64–1.94	0.11 ± 0.04 0.08–0.16	0.11 ± 0.01 0.10–0.13	0.30 ± 0.01 0.29–0.31	Horai et al. (2007)
Predatory birds								
Northern goshawk *Accipiter gentiles*		12 dw	2.13 ± 0.64 1.01–3.53	2.95 ± 1.03 1.75–5.10	0.09 ± 0.04 0.04–0.21		0.12 ± 0.07 0.06–0.30	Horai et al. (2007)
Japanese sparrowhawk *Accipiter gularis*		5 dw	1.64 ± 0.46 1.18–2.22	1.88 ± 0.41 1.47–2.47	0.08 ± 0.03 0.049–0.12		0.12 ± 0.05 0.07–0.20	Horai et al. (2007)
Black kite *Milvus migrans*		14 dw	1.61 ± 0.48 0.85–2.53	1.83 ± 0.689 0.570–2.83	0.07 ± 0.02 0.04–0.11	$n = 8$ 0.10 ± 0.04 0.06–0.19	0.18 ± 0.14 0.01–0.45	Horai et al. (2007)
Brown hawk-owl *Ninox scutulata*		7 dw	1.19 ± 0.31 0.76–1.66	1.61 ± 0.40 1.12–2.23	0.09 ± 0.04 0.05–0.19		0.13 ± 0.03 0.08–0.17	Horai et al. (2007)
Ural owl *Strix uralensis*		12 dw	1.20 ± 0.42 0.38–1.84	1.41 ± 0.985 0.190–3.10	0.07 ± 0.02 0.04–0.12		0.21 ± 0.11 0.07–0.39	Horai et al. (2007)
Others								
Feral pigeon *Columba livia*		11 dw	6.30 ± 1.98 3.41–8.94	8.54 ± 1.92 4.5–11.1	0.12 ± 0.06 0.07–0.26	$n = 10$ 0.48 ± 0.23 0.26–0.98	0.33 ± 0.27 0.12–1.00	Horai et al. (2007)

Jungle crow *Corvus macrorhynchos*		14 dw	2.17 ± 0.52 1.43–3.03	1.33 ± 0.27 0.93–1.98	$n = 12$ 0.13 ± 0.04 0.08–0.21	$n = 8$ 0.64 ± 0.25 0.425–1.20	0.39 ± 0.32 0.14–1.39	Horai et al. (2007)
Carrion crow *Corvus corone*		5 dw	2.32 ± 0.53 1.52–2.95	1.52 ± 0.54 0.986–2.21	$n = 4$ 0.03 ± 0.03 <DL-0.08	$n = 4$ 0.13 ± 0.08 0.07–0.25	0.27 ± 0.14 0.15–0.51	Horai et al. (2007)
Mammals								
Ungulates								
Red deer *Cervus elaphus*	Poland, 2008–2009	27 ww			0.05 median 0.04–0.07			Skibniewski et al. (2015)
Red deer *Cervus elaphus*	Germany, E part	35 22 dw	1.2 ± 0.62 2.1 ± 0.80	0.85 ± 0.46 1.7 ± 0.76				Anke et al. (2000)
Elk *Alces alces*	Poland, NE part, 2010	35 ww	0.92 ± 0.46	0.42 ± 0.62	0.05 ± 0.03			Skibniewski et al. (2016)
Moose *Alces alces*	Sweden, SW part, 1982 reference area	ww						Frank (1998)
		124	0.80–0.90 0.24–0.27					
	1988	26	1.20–1.30 0.36–0.39					
	1992	84	1.0–1.1 0.30–0.33					
	1996	67	1.10–1.20 0.33–0.36					

(continued)

Table 8.6 (continued)

Species	Place and years	*n* dw or ww	Liver	Kidney	Muscle	Brain	Lung	References
Wild boar *Sus scrofa*	Germany	dw	$n = 95$ 3.38 ± 1.40	$n = 10$ 2.08 ± 1.10				Anke et al. (2007)
Fallow deer *Dama dama*	Germany	dw	$n = 99$ 1.95 ± 1.17	$n = 100$ 1.62 ± 0.92				Anke et al. (2007)
Red deer *Cervus elaphus*	Germany	dw	$n = 35$ 1.19 ± 0.62	$n = 25$ 0.85 ± 0.46				Anke et al. (2007)
Roe deer *Capreolus capreolus*	Germany	dw	$n = 16$ 0.62 ± 0.37	$n = 3$ 0.21 ± 0.14				Anke et al. (2007)
Horse *Equus ferus caballus*	Germany	dw	$n = 152$ 6.30 ± 5.80	$n = 133$ 1.44 ± 0.71				Anke et al. (2007)
Porcupine caribou *Rangifer tarandus granti*	Canada, Yukon, 1996	25 dw		2.07 ± 0.53				Gamberg (1997)
Moose *Alces alces*	Canada, Yukon, 1996	63 dw		1.39 ± 0.62				Gamberg (1997)
Moose *Alces alces*	USA, Minnesota, 1998–1999, bog and forest agricultural areas	dw						Custer et al. (2004)
		32	2.3					
		47	3.4					
White-tailed deer *Odocoileus virginianus*	USA, Texas, 2005	20 dw	20% of samples <2		50% of samples <2			Bruckwicki et al. (2006)

Carnivores								
Lutra lutra Eurasian otter	England and Wales, 2007–2008	dw						Walker et al. (2010)
		48	1.24					
			1.04–1.43					
		57	1.2					
			0.95–1.33					
American mink *Neovison vison*	Poland, W part, 2009–2011	dw 30	1.16 ± 1.01	0.87 ± 1.461				Brzezinski et al. (2014)

dw dry weight or *ww* wet weight, *DL* detection limit

11 Conclusion

No symptoms of primary molybdenum deficiency have ever been observed in humans or animals. The importance of molybdenum consists in its toxicity. Molybdenosis, or molybdenum toxicity, primarily affects ruminants, mainly cattle. Monogastric animals are less susceptible to Mo toxic effects. No biomagnification and bioaccumulation of Mo in animals have been confirmed so far. Anthropogenic environmental Mo contamination is linked with Mo ore mining, production of steels for special purposes, and industrial waste discharge. Excess molybdenum, especially in cattle, is a commonplace phenomenon in the world. Data on the effects of molybdenum in free-living mammals are sparse. Well-documented sources deal only with a cervid inhabiting Scandinavia. Moose in Sweden suffer from a disease most probably caused by copper deficiency and molybdenosis. The symptoms include diarrhea, anorexia, emaciation, achromotrichia, alopecia, apathy, as well as behavioral and motor disorders. Necropsy findings included mucosal edema, atrophied lymphoid tissues of the mucous membranes of the alimentary tract, splenic and hepatic hemosiderosis, hypertrophic cardiomyopathy, alveolar emphysema, neuropathy, and uni- or bilateral corneal opacity. Hepatic molybdenum concentrations have reportedly increased by 40% in the moose inhabiting areas affected by acid rain.

There is very little information on molybdenum toxicity in free-living birds. Research was carried out on bobwhite quail (*Colinus virginianus*) treated with molybdenum disulfide (insoluble) and soluble sodium molybdate dihydrate. Toxicity and bioavailability of both forms of Mo were compared. For the soluble form, the NOAEC (no-observed-adverse-effect concentration) was 1200 mg Mo kg^{-1} feed (134 mg kg^{-1} body weight per day). For MoS_2, the NOAEC was found to be 5000 mg (545 mg kg^{-1} body weight per day). These results reflect how avian species are exposed to environmental Mo. Molybdenum does not belong to metals of special significance in relation to environmental toxicology; hence no dietary exposure regulations for fish and free-living terrestrial animals have been established. The metal has not been classified by the EPA as an element of major toxicity. In Central Europe, plants growing on the soils formed from granite, gneiss, rotliegend, and shales, as well as on muck and peat soils, may cause Mo contamination in free-living ruminants.

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Chapter 9
Nickel, Ni

Łukasz J. Binkowski

Abstract Nickel (Ni) is a transition metal whose average concentration in the Earth's crust is not high. Very high concentrations are thought to be found in the Earth's inner core and have been discovered in soils based on serpentine rocks. The most common forms of Ni are oxides, and of the five stable isotopes, ^{58}Ni is the most abundant. The present occurrence of Ni in the environment is mainly connected with industrial use, especially in metallurgy. Because of its density, Ni is considered a heavy metal. It is an essential element for plants and microorganisms, but its physical role in vertebrates is still not fully understood. On the other hand, its toxic, genotoxic, and carcinogenic properties are known. Nickel concentrations considered normal in birds and mammals fall into a range of 0.05–0.5 for kidneys and 0.04–0.3 mg kg^{-1} for liver, but other materials, such as feathers and fur, usually accumulate it in higher amounts. Studies on the evaluation of possible biomarkers of Ni exposure have been carried out mainly on humans, but no clear and measurable relationship has been found so far. Some initial findings linked Ni exposure with a decrease in δ-aminolevulinic acid dehydratase activity, but the most useful methods of its detection continue to be based on the measurement of concentrations in select tissues or materials.

1 Introduction

Nickel (chemical symbol Ni) belongs to the group of transition metals. According to the most common definition of heavy metals (based on density), Ni can be considered one of these elements (Duffus 2002). Its concentration in the Earth's crust is not high, 0.008% (IARC 1990). However, significant Ni content is thought to occur in the Earth's inner core (around 5.5%), where it likely is found as part of the alloy known as FeNi (also called NiFe) (McDonough and Sun 1995).

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The main use of Ni is in industry; thus, the main source of this metal in the environment is metallurgy. Nickel is mainly used in the production of stainless steel and iron magnetic alloys known as alnico (an acronym formed from the symbols for aluminum, nickel, and cobalt).

The essentiality of Ni in plants and microorganisms is generally known. Its role in animals, especially vertebrates, remains incompletely understood. Numerous studies have shown its toxicity, genotoxicity, effect on reproduction, and even carcinogenic properties (Nordberg et al. 2007; Kong et al. 2014; Wang et al. 2016). Additionally, the ecotoxicological status of Ni nanoparticles (whose use has increased significantly) has not been fully elucidated, but their toxicity for animals and whole ecosystems is suspected (Ray et al. 2009; Magaye et al. 2012).

The main organizations that study Ni reserves, as well as market trends for the metal, are the International Nickel Study Group (INSG 2016) and the United States Geological Survey (USGS 2016).

2 General Properties

Nickel (Latin *Niccolum*) lies between cobalt and copper in the tenth group of the periodic table with atomic number 28. Ni's atomic mass and density are 58.7 and 8.90 g cm^{-3}, respectively. This metal, which is silver-white at room temperature, occurs in a solid state; it is hard but malleable; it reaches its melting point at a high temperature of 1455 °C (Hammond 2004). The most common Ni form is the oxide, so the metallic form is rarely observed. Properties of the metallic form are quite similar to those of cobalt (Sienko and Plane 1979). Nickel has 5 naturally occurring stable isotopes (58, 60, 61, 62, and 64) and 19 unstable ones (Hammond 2004). In nature, nickel exists for the most part in the form of isotope ^{58}Ni (68.3%). The element is often encountered in the 0, +1, +3, and +4 oxidation states in compounds, but states −2 and −1 are also known (Earnshaw and Greenwood 1997).

3 Nickel Minerals, Production and Uses

Nickel resembles iron and cobalt in that it occurs in rocks; its largest deposits are found in alkaline (up to 160 mg kg^{-1}) and ultraalkaline (up to 2000 mg kg^{-1}) rocks. Acidic rocks contain substantially lower concentrations (Kabata-Pendias 2011). In rocks, Ni occurs most often in the form of oxides, sulfides, and silicates. Over 100 minerals contain a significant substratum of Ni; the most common of these are garnierite, millerite, nickeline, nickel galena, and pentlandite (Cempel and Nikel 2006; NPI 2015). Nickel is also abundant in iron meteorites in taenite and kamacite alloys (Rasmussen et al. 1988).

Identified land resources that contain at least 1% of Ni are estimated to hold at least 130 million tons of Ni. The largest part (ca. 60%) is bound in laterites, with the rest in sulfide deposits. The world total available Ni reserves is estimated at 80 million metric tons, of which the largest parts lie in Australia (24 million tons), New Calcedonia (12 million tons), and Brazil (8.7 million tons) (USGS 2012a).

The global market demand for steel (38.13 million tons in 2013) (Statista 2015a) entails an increase in global Ni production (Fig. 9.1). Approximately 20 countries mine Ni ore, and around 25 countries smelt it (INSG 2016). In the fourth quarter of the twentieth century, the largest Ni mining operations were located in the USSR and Canada (USGS 1980, 1995). Since then different leaders in production have emerged. In 2013 the leading producers were the Philippines and Indonesia, where annual Ni production was estimated at 440,000 tons. Filipino production almost doubled over 2011 levels. Russian production has remained stable in recent years and has been hovering around 260,000 tons (Statista 2015b).

Because of Ni's high resistance to oxidation and corrosion, it is widely used around the globe in industry (including nickel plating on steel) and daily life (e.g., in coin production). The industry that uses Ni most intensively is metallurgy for the production of stainless steel, estimated at 65% of global use (INSG 2016). A rather recent new use has been observed in the hunting industry. Owing to regulations banning lead shot use in waterfowl hunting, a few so-called nontoxic forms of ammunition have been produced. One is produced from an alloy of iron, tungsten, and nickel (Brewer et al. 2003; Binkowski and Sawicka-Kapusta 2015).

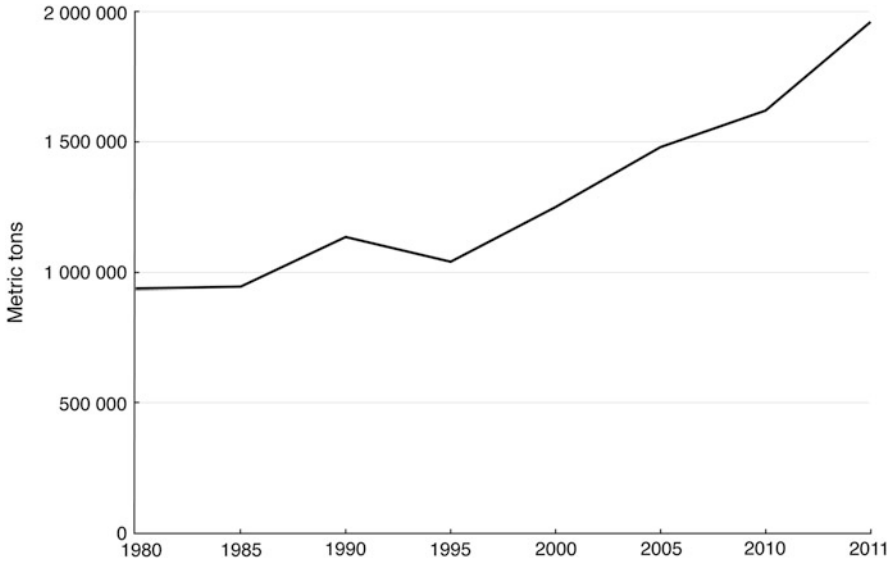

Fig. 9.1 Dynamic of Ni mining production between 1980 and 2011 (USGS 1980, 1985, 1990, 1995, 2000, 2007, 2012b, 2013)

The general Ni usage is divided into two branches. The so-called first use is the use of metal produced indirectly from ores mainly in the production of stainless steel, alloyed steels, high-nickel alloys, castings, and chemicals. The second branch is the use of recycled metal from scrap, which has enjoyed very wide usage (INSG 2016).

4 Nickel in Nature: Geogenic and Anthropogenic Sources

Apart from ores, which consist of minerals rich in oxides, sulfides, and silicates of nickel, the element occurs widely in carbon deposits (around 15 mg kg^{-1}) and in petroleum (the range 20–100 mg $kg^{-1)}$ (Fig. 9.2) (Kabata-Pendias 2011).

Nickel background levels are hard to assess currently since numerous pollutant sources are distributed around the world. The range of normal values in the air over the continents is 0.1–1 ng m^{-3} (Livett 1992; Kabata-Pendias and Pendias 1999). The concentrations observed over Spitsbergen in the 1980s were up to 0.95 ng m^{-3} (Maenhaut et al. 1989). Concentrations in natural waters varied between fresh waters (2–10 μg L^{-1}) and marine waters (0.2–0.7 μg L^{-1}) (Rojas et al. 1999). Nickel concentrations in nonpolluted soils significantly depend on the soil type. Usually the entire range fits between 10 (organic soils) and 34 mg kg^{-1} (rendzinas) (Kabata-Pendias 2011), but soils based on serpentine rocks reach significantly higher concentrations—in some cases even up to 2% of the soil composition (Shallari et al. 1998; Brooks 1999; Marsh and Anderson 2011; Altinozlu et al. 2012).

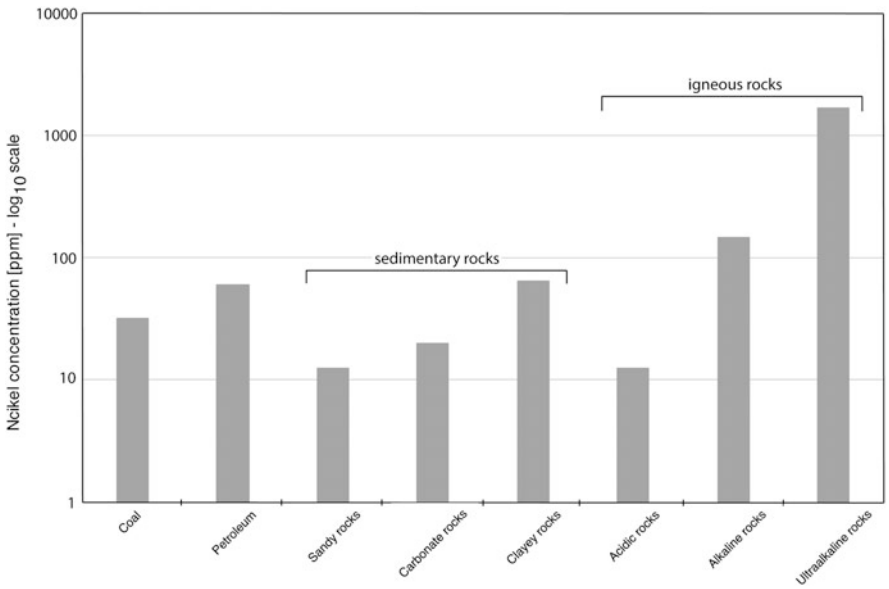

Fig. 9.2 Nickel concentrations in biolites and rocks (Kabata-Pendias and Pendias 1999; Adriano 2001; Chmielnicka 2002; Kabata-Pendias 2011)

In anthropogenically changed environments, concentrations in air usually fit the range 1–150 ng m^{-3} (Kabata-Pendias and Pendias 1999). In European cities, the average values are 9–60 ng m^{-3}, but in strictly industrialized areas, concentrations reach 110–180 ng m^{-3} or more (Bennett 1994; WHO 2000; Cempel and Nikel 2006). Concentrations in potable water are generally low (around 10 μg L^{-1}), but levels in waters of most European rivers reach 75 μg L^{-1} or more (Kabata-Pendias and Pendias 1999; Cempel and Nikel 2006; EEA 2009). Nickel concentrations in soils and deposits from industrial regions significantly depend on the industry type and intensity, for example, in some areas, following the emergence of a particular industry, a 25-fold increase (up to 3073 mg kg^{-1} dw) in Ni concentrations in superficial sediments has been observed (Dauvalter 2003).

5 Biological Status of Nickel

The essentiality of nickel in microorganisms and plants is generally known (Muyssen et al. 2004; Sydor and Zamble 2013). Some studies have pointed out the side effects of low Ni intake in birds and mammals. Nevertheless, the study of physiological role of Ni in animals remains incomplete (Nielsen 1974, 2000). Nickel activates numerous enzymes, regulates hormonal activity, and stabilizes the structure of ribonucleic acid. Some observations have led researchers to conclude that the metal is under homeostatic regulation in mammals but not in birds (Gamberg 1998). Research on Ni deficiency has revealed pigmentation changes, thicker legs, dermatitis, and ultrastructural changes in liver (Sunderman et al. 1972; Nielsen 1974). The physiological influence of Ni in rats and chickens is connected with lipid metabolism in liver and erythrocytes and in serum lipoproteins (Nielsen et al. 1975; Stangl and Kirchgessner 1996, 1997), as well as with Ni flux in everted intestinal sacs (Stangl et al. 1998). Nickel deficiency causes iron deficiency in rats owing to the impairment of iron absorption by the intestines (Kirchgessner and Schnegg 1976). Nickel deficiency may also lower reproductive performance in rats as a result of diminishing sperm movement and quantity (Yokoi et al. 2003). Supplementing pigs with nickel and cobalt can ameliorate vitamin B-12 deficiency and hyperhomocysteinemia (Stangl et al. 2000).

On the basis of various sources of information about Ni essentiality in animals, its recommended daily allowance for animals and humans was estimated at 0.5 mg kg^{-1} body weight (Nordberg et al. 2007). Other sources suggest 25–35 μg day^{-1}. Such amounts should be easily supplied by conventional diets (which usually provide 100–150 μg Ni day^{-1}). Diets rich in chocolate, nuts, grains, peas, and beans may even provide 900 μg day^{-1} (Pennington and Jones 1987; Anke et al. 1993; Nielsen 2000).

5.1 Toxicity of Various Forms of Nickel in Homoeothermic Animals

Most studies on Ni toxicity relate to plants, microorganisms, invertebrates, and fish (Chen et al. 2009; Parsons et al. 2010; Macomber and Hausinger 2011). Research on mammals is scant, and the number of studies on birds is even smaller.

Exposure to Ni varies between animals and humans. In animals, the main route of exposure is the gastrointestinal tract. In contrast, absorption through the skin from various products, such as nickel-plated tools, medical instruments, jewelry, and household consumer products, constitutes the major pathway of human exposure (Basketter et al. 2003). The harmful effects of Ni in organisms depend significantly on the properties of the compound, the time and strength of exposure, and individual variables (Adriano 2001). The most toxic Ni compound for animals is nickel carbonyl, known generally as one of the most toxic inhaled poisons. According to the International Agency for Research on Cancer (IARC), metallic Ni and its alloys are classified as possibly carcinogenic to humans (group 2B) and nickel compounds as carcinogenic to humans (group 1) (IARC 2016). Carcinogenic Ni activity is mostly connected with its inhaled compounds. Such problems are diagnosed in the nose and lungs of workers in nickel-connected industries (Adriano 2001; Denkhaus and Salnikow 2002). Experiments on intratracheal instillation of Ni compound also showed histopathological and bronchoalveolar changes in rat lungs (Bajpai et al. 1999). There have even been occurrences of deaths from adult respiratory distress syndrome following occupational Ni exposure (Sandström et al. 1989; Rendall et al. 1994). In the second example cited, a man spraying Ni did not use protective equipment. After several days of exposure, his urinary Ni concentrations reached 700 μg L^{-1}. The estimation of air concentrations during work was 382.1 mg m^{-3} (with 64.6% of the particles smaller than 1.4 μm) and the total amount of Ni inhaled ca. 1 g (Rendall et al. 1994).

After entering the body, Ni induces synthesis of metalothioneine. Next to genotoxicity, developmental toxicity, hematotoxicity, immunotoxicity, neurotoxicity, hepatoxicity, and reproductive toxicity noted in birds and mammals, Ni induces an oxidative stress and crosses the placental barrier (Hoffman 1979; Domingo 1994; Chen and Lin 1998; Mathur and Shanker 2001; Das et al. 2008; Thomas et al. 2009; Saini et al. 2014; Casalegno et al. 2015). Induction is probably connected with further cancerogenesis, but still the direct correlation is not fully understood (Salnikow et al. 1994; Das et al. 2008). Following oral administration in rodents of higher doses of Ni compounds (chloride or sulfate), deleterious effects on organisms, such as histological lesions, liver and body mass decrease, liver cell apoptosis, necrosis, enzyme-level changes, and others, have been observed (Obone et al. 1999; Pari and Amudha 2011; Gathwan et al. 2012). Administration of Ni in food can also disturb reproduction efficiency through its effects on the level of sex hormones such as testosterone (Pandey and Singh 2001; Mathur et al. 2010; Forgacs et al. 2012). Apart from hormonal changes, Ni's influence on reproduction

has been additionally observed in the histological level of testis structure in rats (Toman et al. 2012). The connection between increased Ni concentrations ($NiCl_2$ per os) and decreased egg production and quality has also been reported in the literature (Arpasova et al. 2007). Moreover, it has also been found that birds exposed to nickel per os revealed lower concentrations of magnesium and triglycerides in blood serum, as well as activity of alanine aminotransferase. Other biochemical parameters did not appear to be disturbed (Capcarova et al. 2008; Kolesarova et al. 2008). The lowest-observed-effect concentration (LOEC) noted by oral administration in chickens and mallards was respectively equal to 300 and 700 mg kg^{-1} in diet (DeForest et al. 2012).

Injections of Ni compounds also revealed deleterious effects. Pancreatic, hepatic, and osteogenic toxicity and tumor formation at injection points have been observed in rats (Novelli et al. 1998).

5.2 Toxicokinetics and Effects of Nickel in Wildlife

Most studies concerned with Ni concentrations in animals also address other metals. Nickel alone and its concentrations in vertebrates are rarely studied, so suspicions regarding Ni toxicity in live wild animals are usually explained as Ni's partial influence together with other metals (e.g., Sánchez-Chardi et al. 2008). Laboratory experiments have revealed that the general scheme of increasing concentrations in mammals exposed to Ni is heart = liver < spleen < lung = brain < testes < kidneys (Obone et al. 1999). In birds, the scheme seems to be different (Table 9.1). The highest concentrations are usually encountered in external matter such as fur or feathers, especially in polluted areas. Among internal tissues, usually bones accumulate the highest concentrations (Outridge and Scheuhammer 1993). Some studies have also revealed high Ni concentrations in bone marrow, even six times higher than in liver (Hassan et al. 2012).

Nickel inhalation is connected with higher bioaccumulation than other routes (Reichrtova et al. 1988). Accumulation from food and water is weak, on the level of 5%. This is supported by studies that revealed significant concentrations in ingesta and low concentrations in internal tissues (Hui et al. 1998; Hui 1998; Kabata-Pendias and Pendias 1999). However, in cases of significant exposure, accumulation is observed in bones and several soft tissues (including heart muscle, lungs, skin, fur, and feathers) (Kabata-Pendias and Pendias 1999; ATSDR 2005; Nordberg et al. 2007). Oral absorption of soluble Ni forms is higher than insoluble ones. Soluble Ni compounds are usually accumulated in liver and kidneys and insoluble forms mainly in lungs and pancreas (Casalegno et al. 2015).

Table 9.1 Nickel concentrations (mg kg^{-1} dry weight; mainly means) in chosen tissues and materials collected from birds in the Northern Hemisphere

Species	Area	Kidneys	Liver	Muscles	References
Birds					
American coot *Fulica americana*	USA, San Francisco Bay area		<0.05–1.61		Hui (1998)
Blue-winged teal *Anas discors*	USA, Southern Texas		0.95		Warren et al. (1990)
Canvasback *Aythya valisineria*	USA, San Francisco Bay area		Up to 3.5		Miles and Ohlendorf (1993)
Eider *Somateria mollissima*	Norway, Taura	2	1	2	Lande (1977)
Gray plover *Pluvialis squatarola*	France, Southwest Atlantic coast	0.8	0.4	0.7	Lucia et al. (2010)
Greylag goose *Anser anser*	France, Southwest Atlantic coast	0.8	0.7	1.8	Lucia et al. (2010)
Mallard *Anas platyrhynchos*	Belarus, Swisloch River (above Minsk)	1.7	1.0	1.3	Kozulin and Pavluschick (1993)
Mallard *Anas platyrhynchos*	Belarus, Swisloch River (below Minsk)	3.7	4.3	1.1	Kozulin and Pavluschick (1993)
Red knot *Calidris canutus*	France, Southwest Atlantic coast	0.3	0.4	0.3	Lucia et al. (2010)
Peregrine falcon *Falco peregrinus*	Poland, northwest	1.15	0.11	0.07	Kalisińska et al. (2008)
White-tailed eagle *Haliaeetus albicilla*	Poland, north and northwest	6.5	13		Falandysz et al. (2000)
Great tit *Parus major*	Belgium, Antwerp	0.024	0.014	0.09	Dauwe et al. (2005)
Great tit *Parus major*	Finland, various regions		0.3		Ingervo et al. (1995)
Blue tit *Parus caerulescens*	Finland, various regions		0.3		Ingervo et al. (1995)

(continued)

Table 9.1 (continued)

Species	Area	Kidneys	Liver	Muscles	References
Mammals					
White-tailed deer *Odocoileus virginianus*	USA, Texas		<0.5–3.0	<0.5–2.1	Bruckwicki (2006)
Wild boar *Sus scrofa*	Poland, central and central-east		0.47		Długaszek and Kopczyński (2011)
American mink *Neovison vison*	Poland, Drawa National Park	0.29	0.27		Brzeziński et al. (2014)
American mink *Neovison vison*	Poland, Narew National Park	1.17	0.16		Brzeziński et al. (2014)
Marten *Martes americana*	Canada, British Columbia	1.20			Harding (2004)
Volwerine *Gulo luscus*	Canada, British Columbia		2.00		Harding (2004)
Eurasian otter *Lutra lutra*	Ireland and Great Britain		0.035–0.54		Mason and Stephenson (2001)
Eurasian otter *Lutra lutra*	England and Wales, various regions		0.10		Walker et al. (2011)
Eurasian otter *Lutra lutra*	France, various regions		1.51		Ruiz-Olmo et al. (2000)
Wild rat *Rattus rattus*	Portugal, Tapada Grande	0.06	0.06		Pereira et al. (2006)
Algerian mouse *Mus spretus*	Portugal, Tapada Grande	0.36	0.19		Pereira et al. (2006)
European hare *Lepus europaeus*	Poland, central and central-east		0.41		Długaszek and Kopczyński (2011)

Concentrations in tissues in mg kg^{-1} dw but where needed recalculated from ww according to Binkowski (2012)

5.3 Bioaccumulation of Nickel

Nickel has not been commonly studied in wild living birds and mammals as cadmium or lead. Comprehensive reviews of Ni concentrations in wildlife have been conducted by Outridge and Scheuhammer (1993) and Eisler (1998), but the presented data mainly focus on birds and mammals of North America. The information gathered concerns mainly liver and kidney concentrations; other biological

samples have been significantly less studied. Most studies were carried out on tissues taken during necropsy.

Some evidence suggested that in the same areas birds accumulate higher Ni concentrations than mammals (Outridge and Scheuhammer 1993). The tissues of wild birds and mammals from pristine environments generally contain up to 5 mg kg^{-1}, whereas in Ni-polluted environments, concentrations reached 10 in mammals and even 80 mg kg^{-1} dw in birds. Concerning liver and kidneys, the higher concentrations occurred in kidneys and generally do not exceed 3 mg kg^{-1} dw (Outridge and Scheuhammer 1993). This statement can be supported by several other studies, but average values in kidneys of birds and mammals were established in the range 0.06–0.12 and 0.05–0.5 mg kg^{-1}, respectively (Table 9.1). The average values noted for liver are 0.04–0.1 mg kg^{-1} in birds and 0.1–0.3 mg kg^{-1} in mammals (WVDL 2015).

In vivo studies of birds are scarce, but mostly such projects reveal the current state of exposure. In the Northern Hemisphere, only Ni concentrations in mallard (*Anas platyrhynchos*) blood collected in Poland are known, where small but significant variation between concentrations in birds from industrialized and country areas was observed. There, the maximum value was 3.71 and the minimum was $<$0.04 mg kg^{-1} ww (Binkowski and Meissner 2013). A comparison can be done only with the results of studies from southern Africa where concentrations found in the blood of red knobbed coot (*Fulica cristata*), sacred ibis (*Threskiornis aethiopicus*), and reed cormorant (*Microcarbo africanus*) were significantly higher (van Eeden and Schoonbee 1996). Thus, the means were 4.76, 3.65, and 5.12 mg kg^{-1} ww. The likely reason for such differences is the quality of food and the environment because in birds exposed to higher Ni concentrations, the Ni showed up in, among other places, blood accumulation (Eastin and O'Shea 1981).

Apart from internal bird tissues, Ni is also found in eggs. Some studies revealed increased concentrations in egg yolk and egg white, and some has been found in eggshells of birds inhabiting polluted areas (Darolova et al. 1989; Orłowski et al. 2014). Values noted in eggshells of rook (*Corvus frugilegus*) in Poland fell within the range 1.15–4.07 mg kg^{-1} dw. Seabirds occupy a different position in the trophic net. Nickel studies of this group remain very scarce, but the available data suggest that Ni levels in seabirds are not high (Barbieri et al. 2010; Jerez et al. 2013).

Comprehensive data on Ni concentrations in human tissues (mainly blood) can be found in the literature (Tomei et al. 2004; Stridsklev et al. 2004; Nordberg et al. 2007; Ikeda et al. 2011; Silva et al. 2013; Caciari et al. 2013; Khlifi et al. 2013). Among other mammals, rodents have been widely studied. This group represents popular and efficient Ni bioaccumulators, very tolerant to its deleterious effects and easily adaptive to long-term exposure (Marques et al. 2007). Research on bank voles (*Myodes glareolus*) in Slovakia revealed that Ni in bones reaches rather low concentrations (up to 9.52 mg kg^{-1} dw). Concentrations in soft tissues are low, often below the detection limit of the methods used (Cloutier et al. 1986). An increase in Ni concentrations in soft tissues may be observed in connection with in the aspect of environmental pollution, but generally, even statistically increased values are low (Marques et al. 2007; Sánchez-Chardi et al. 2007). Research studies from Spain

showed that concentrations in the liver and kidneys of the shrew (*Crocidura russula*) in a reference pristine area were 0.67 mg kg^{-1} dw and 5.40 mg kg^{-1}, which were ca. three times lower than at a mining site—respectively 1.48 and 15.28 mg kg^{-1} dw (Sánchez-Chardi et al. 2007). Studies on roe deer (*Capreolus capreolus*) antlers in Poland revealed that exposure over the course of 40 years in the middle of the twentieth century did not increase, and no relationship between concentrations in samples and environmental pollution was noted (Sawicka-Kapusta 1979). Renal Ni concentrations in wild Yukon moose (*Alces alces*) and caribou (*Rangifer tarandus*) revealed concentrations comparable to those in domestic cattle, with a maximum mean up to 0.78 mg kg^{-1} dw (Gamberg 1998).

Nickel concentrations may be correlated with chromium in liver, as well as in hair (Pereira et al. 2006). The explanation of this observation is not clear, but it may be due to a mutual source of the metals in the environment. Concentrations in soft tissues of mammals can show a significant negative correlation with age (Smith and Rongstad 1982; Sánchez-Chardi et al. 2007). Also, in some studies, a sex dependency of Ni concentrations was observed. Furthermore, observations were inconsistent with the generally suspected mechanism of the reduction in concentrations in females during reproduction (Sánchez-Chardi et al. 2007). Seasonal fluctuation in general is not observed (Cloutier et al. 1986).

5.4 Ecological Effects of Nickel

Apart from indirect contact with environmental pollution, some herbivorous birds and mammals can be potentially exposed through the trophic net. Generally, most plants are sensitive to higher Ni levels in soil, which results in a distribution of plants of optimum concentration areas. In such places concentrations in plants are low, so exposure of herbivores is also low. However, in places of significantly elevated concentrations in soil (lying on ultramafic bedrock) some plant species (ca. 400 species of various families around the world) evolved mechanisms to tolerate and safely accumulate Ni (van der Ent et al. 2015). In such plants, accumulation can reach on average 1000 mg kg^{-1} in the foliage (particular specimens can even accumulate 20,000 mg kg^{-1} ww) (Reeves et al. 1996; Robinson et al. 1997; Li et al. 2003; Altinozlu et al. 2012; van der Ent et al. 2013). In such cases the exposure of animals can be extremely high.

Debate about metal biomagnification has been ongoing for dozens of years. Many authors have questioned its occurrence in terrestrial environments, but generally it is believed that it can occur only in specific food chains (Laskowski 1991; van Straalen and Ernst 1991). Few research studies on Ni biomagnification have been carried out. However, data available for aquatic and terrestrial ecosystems do not confirm the process in birds and mammals (Gamberg 1998; Phipps et al. 2002; EPA 2011; Iamiceli et al. 2015). The groups that might be exposed the most through the trophic net are those that forage on aquatic animals, fish, and invertebrates, but only in

specific aquatic environments, and bivalves, gastropods, and barnacles may show signs of Ni biomagnification (Gamberg 1998; Cardwell et al. 2013).

5.5 *Bioindicators and Biomarkers of Nickel in Ecotoxicological Studies*

The most advanced works on the potential biomarkers of Ni exposure have been carried out among people, especially industrial workers (Nordberg et al. 2007). No clearly measurable relationships with physiological parameters and enzyme activities have been identified. There were some suspicions that connection between the exposure and genotoxic effects may be useful, but after the evaluation it seems to be not accurate (Kiilunen et al. 1997; Burgaz et al. 2002). However, recent studies have demonstrated a connection between Ni concentrations in organism and the activity of δ-aminolevulinic acid dehydratase (ALA-d), which is a heme biopathway enzyme. The activity of ALA-d is widely used as a biomarker of lead poisoning that causes a significant drop (even up to 99% in blood) of activity (Binkowski and Sawicka-Kapusta 2015). Animals injected with Ni salts also revealed a similar negative correlation, but the observed decrease in activity was not very significant, up to 38% in liver and 53% in blood (Sulinskiene et al. 2014).

Still the most useful and reliable practice is measuring the concentrations in tissues, especially in liver, kidneys, and bones. In the case of humans, some thresholds in urine or serum have been established (Nordberg et al. 2007). Among animals, no certain values have been given, but some studies have presented common ranges of concentrations (Sect. 5.3).

6 Conclusions

- Nickel is a transition metal that is toxic for birds and mammals at higher concentrations. However, there is also evidence that it is essential in birds and mammals.
- The main source of Ni in the environment is industry (mainly metallurgy), but some areas have naturally very high concentrations in so-called serpentine soils.
- Nickel bioaccumulation in tissues and materials of birds and mammals depends on environmental factors, but in most cases, in pristine areas, values do not exceed 5 mg kg^{-1} dw. In Ni-polluted regions, birds seem to be more efficient accumulators since concentrations in their soft tissue may reach 80 mg kg^{-1}, while in mammals this figure is 10 mg kg^{-1} dw.
- No efficient and reliable biomarkers of Ni exposure have been found, and the best method of evaluating exposure is still to measure Ni concentrations in wildlife and the environment.

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Chapter 10
Selenium, Se

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Abstract Selenium (Se), in small amounts, is necessary for the proper development and health of humans and animals. This element plays a structural and enzymatic role in the organism. Soils in many regions of Europe are Se deficient in comparison to the USA, Canada, and China. Anthropogenic activity contributes to the introduction of selenium into the environment, as well as to mobilization from subsoils from various land exploitation processes. From the beginning of the twenty-first century, China has emitted the most Se into the atmosphere from anthropogenic sources and, significantly, shows dynamic growth in this matter. The measurement of Se levels in animal tissues is the most commonly used biomarker in evaluation of exposure to this element. Wild ruminants from Cervidae like moose, red deer, roe deer, mule deer, white-tailed deer, and elk, as well as some representatives of the Bovidae family (pronghorn and bighorn sheep), are considered as good bioindicators of environmental selenium levels. From the carnivorous animals, common selenium bioindicators are a fox, mink, and raccoon. The content of Se in the organism is usually evaluated in the liver and kidneys.

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1 Introduction

Selenium (Se) was discovered in 1817 by Swedish chemist J. J. Berzelius. For many years it was considered to be a dangerous element to human beings and animals as it had been identified by its toxic features. Only in 1957 did Schwarz and Foltz in their studies on rats demonstrated that Se had prevented necrosis of the liver, which indicated the important biological role of selenium (Brown and Arthur 2001). It was proven then that this element in small concentrations is crucial for the proper development and health of humans and animals.

The Earth's crust is the most significant source of selenium, although the distribution and concentration of this element vary greatly between regions. For this reason some regions of the world are characterized by excessive levels of Se, and some remain Se deficient. The amount of selenium available to humans and animals depends on its content in soils, the chemical forms in which selenium occurs, the pH and redox potential of the soil, as well as the presence of other organic compounds, climatic factors, and the activity of soil microorganisms. Anthropogenic activity contributes to the introduction of Se into the environment, as well as to mobilization from subsoils in various land exploitation processes (Rayman 2000; Fordyce 2013).

Most Se in vertebrate tissues is integrated into selenoproteins, with only a small amount in a free form. Selenium plays a structural and enzymatic role in the organism. The most important selenoproteins include glutathione peroxidase, iodothyronine deiodinase, P and W selenoproteins, as well as thioredoxin reductase (Flohe et al. 2000; Rayman 2000; Gladyshev 2001). Selenium participates in thyroid hormone metabolism as part of the important enzymes engaged in the functions of this organ, including thyroxine 5-deiodinase which catalyzes the deiodination of thyroxine and its conversion into an active form of triiodothyronine. A deficiency of Se in humans and animals causes disturbances in bone mineralization and tooth growth (Moreno-Reyes et al. 2001; Fordyce 2013; Flueck 2015). In humans, dilated cardiomyopathy (Keshan disease) and osteochondropathy (Kashin-Beck disease) are the most well-known examples of Se deficiency (Kim et al. 2001; Zhang et al. 2010).

Selenium assists in the functions of the immune system and stimulates the production of antibodies, where a deficiency may contribute to a suppression of the immune response to bacterial, viral, and fungal infections by inhibiting the synthesis of prostaglandin and immunoglobulin, as well as by decreasing the activity of T lymphocytes, NK cells, and macrophages, which are engaged in the immunological mechanisms of homeothermic vertebrates (Johnson et al. 2000; Rayman 2000; Arthur et al. 2003; Hartikainen 2005).

A surplus of Se in the organism causes some symptoms of intoxication (selenosis endemica). Typical disorders caused by excessive levels of Se include liver damage, depression, emaciation, nervous system dysfunction, tooth gnashing, salivation, hair loss or rough hair coat, improper growth or necrosis of hooves, stiffness and irritation of limbs, dyspnea, hearth muscle atrophy, and anemia. An excessive intake of Se leads to the inhibition of cellular proliferation, DNA replication, and protein

synthesis and supports oxidative stress (Kim and Mahan 2001; Dodig and Cepelak 2004; Tinggi 2005; Zachary and McGavin 2014).

Soils across a large part of Europe are relatively selenium deficient in comparison to the USA, Canada, and China. In recent years, Se content in northern European ungulates has fallen. This deficiency is likely the effect of a decrease of selenium levels in the environment, caused by the introduction of new technologies in agriculture, which adversely influence the assimilation of selenium into plants. The limited transport of Se from soils to plants, and later to animals, manifests through the diminishing content of this element in these organisms (Winkel et al. 2015).

In wild animals, clinical and subclinical cases of Se deficiency remain practically unnoticed. The situation however is different in farm animals, especially in grazing livestock, in which the symptoms of selenium deficiency have been described frequently. In contrast, in free-ranging animals, even in highly Se-deficient areas, by ranging across much larger areas, they can benefit from a more diversified diet. Moreover, they have probably developed more effective mechanisms of Se management (Wichtel 1998; Spears 2011; Flueck et al. 2012). Pathological changes caused by a Se and iodine deficiency have been found in one wild and endangered species of deer in a Se- and iodine-deficient area in Chile (Wichtel 1998; Spears 2011; Flueck 2015).

Due to the important role of Se in vertebrate organisms, as well as the health threats caused by its deficiency or surplus in other regions of the world, ecotoxicological research (including comparative studies) and biomonitoring of this important microelement are indicated, especially in wild-ranging birds and mammals.

2 General Properties

Selenium belongs to the group of trace elements, with the average concentration of Se in the Earth's crust estimated at 0.05 mg kg^{-1} (Taylor and McLennan 1995). The Se concentration in the Earth's crust is ~0.09 mg Se kg^{-1} (NRC 1983). It is located in the group VI of the periodic table. The atomic mass of Se is 78.96 (Table 10.1). Together with sulfur, oxygen, tellurium, and polonium, it builds the oxygen family, known also as chalcogens.

Selenium has been discovered in slime from the production of sulfuric acid from pyrites. This element comprises two amorphous and four crystalline forms. In nature, six stable isotopes of Se are present: ^{80}Se (79.61%), ^{78}Se (23.77%), ^{76}Se (9.37%), ^{82}Se (8.73%), ^{77}Se (7.63%), and ^{74}Se (0.89%) (Taylor and McLennan 1995). Selenium may occur in the following oxidation states: −2 (selenide), 0 (elementary Se), +4 (selenite), and +6 (selenate). It composes selenides with metals, hydrogen selenide H_2Se with hydrogen (selan), and oxides with oxygen (SeO_2 and SeO_3), which are the selenic (IV) and selenic (VI) acid anhydrides H_2SeO_3 and H_2SeO_4, respectively (Broadley et al. 2006; Kabata-Pendias and Szteke 2015).

Table 10.1 Basic physicochemical properties of selenium

Feature	
Atomic number	34
Atomic mass	78.96
Density (g cm^{-3})	4.26–4.79
Melting point (°C)	217
Boiling point (°C)	685.4
Electronegativity	2.55 (Pauling)
Electronegativity (eV)	2.4
Oxidation states	−2, 0, +4, +6
Mass of stable isotopes	74, 76, 77, 78, 80, 82
Electron configuration	$1s^2\ 2s^2\ p^6\ 3s^2\ p^6\ d^{10}\ 4s^2\ p^4$

Newland (1982)

3 Selenium Minerals, Production, and Uses

Many factors influence the presence and circulation of Se in nature. It is not usually distributed evenly—there are some areas abundant in Se (large areas of North and South America, part of China) as well as Se-deficient areas (a large part of Europe, including some regions of Poland, a few Chinese provinces, New Zealand). A significant diversity occurs in China, where the southwestern and northeastern parts are characterized by extremely low Se levels and the central provinces represent the Se-rich soils, with a risk of intoxication in grazing animals (Xu and Jiang 1985; Amouroux et al. 2001; Blazina et al. 2014).

Particularly high contents of Se in the soil are present in Wyoming and North and South Dakota in the USA (Reilly 1996), Enshi County in China, and in parts of Ireland, Colombia, and Venezuela (Combs 2001). As noted by Haug et al. (2007), many European soils show relatively high concentrations of Se from the naturally high deposition of this element from the sea (e.g., Ireland, England, Scotland, and the Netherlands).

Selenium is a natural and widespread component of the Earth's crust, despite its disparate distribution. It is contained in a variety of rocks, minerals, and soils and moreover occurs in volcanic material. Selenium does not appear individually, but 40 minerals are known to be mostly formed with this element and 37 others where Se is a minor component, mainly as sulfides (NRC 1983; Butterman and Brown 2004). The average Se concentration is much higher in sedimentary rocks, especially shales and coal, than in igneous rocks (Krauskopf 1982). Selenium is found in nature in pyrites of copper and iron and sulfide ores of copper, lead, nickel, gold, or silver, at variable levels between 0.1 and 2 mg Se kg^{-1} dry weight dw (ppm). The most important selenium minerals are berzelianite (Cu_2Se), naumannite (Ag_2Se), and chalcomenite ($CuSeO_3{\cdot}2H_2O$). High content of Se is accompanied by deposits of sulfur and sulfides. However, its ratio to sulfur in these deposits is only 1:6000. Minerals particularly rich in selenium are sulfides (up to 120 mg Se kg^{-1} dw) and volcanic soils, where Se content can reach 200 kg^{-1} dw (Smakowski et al. 2011).

Table 10.2 Concentrations of selenium in rocks and other natural sources

Material	Concentration (mg kg^{-1} dw)	Range (mg kg^{-1} dw)	References
Earth's crust		0.05–0.09	Lakin (1972) and Frost and Ingvoldstad (1975)
Igneous rocks			
Ultrabasic (dunit, peridotite, pyroxenite)		0.02–0.05	Kabata-Pendias and Pendias (2000)
Basic (basalt, gabbro)		0.01–0.05	Kabata-Pendias and Pendias (2000)
Intermediate (syenite)		0.02–0.05	Kabata-Pendias and Pendias (2000)
Intermediate to acidic (rhyolite, trachyte, dacite)		0.02–0.05	Kabata-Pendias and Pendias (2000)
Acidic (granite, gneiss)		0.01–0.05	Kabata-Pendias and Pendias (2000)
Basic volcanic rocks	0.155		Koljonen (1973)
Acid volcanic rocks	0.116		Koljonen (1973)
Volcanic tuff (China, South Qinling Mountain)	32		Kunli et al. 2004
Black carbonaceous slate (China, South Qinling Mountain)	22		Kunli et al. (2004)
Sandstones	<0.05	<0.01–0.05	Turekian and Wedepohl (1961) and Ebens and Shacklette (1982)
Carbonates	0.08		Turekian and Wedepohl (1961)
Ocean sediments		0.34–4.8	de Goeij et al. (1974)
Chondrites	8.0		Ebens and Shacklette (1982)
Shales (general)	0.06	0.05–0.06	Green (1959) and Ebens and Shacklette (1982)
Limestones	0.08		Ebens and Shacklette (1982)
Phosphate rocks		1–300	Mayland et al. (1989)

Parent materials with the highest concentration of Se are black shales and phosphate rocks, with about 600 and 1–300 mg Se kg^{-1} dw, respectively (Presser 1994). Black shales of the Selwyn Basin (Yukon) contain a relatively high amount of selenium, up to 1 mg kg^{-1} dw (Gamberg et al. 2005b). Much higher concentrations were found in cretaceous sedimentary rock formations in central Saskatchewan, especially in White-Speckled Shales from the Lower Cretaceous: up to 11.7 mg kg^{-1} dw (Dunn 1990). Magmatic rocks (granites and basalts) do not contain much Se, mostly <0.05 mg kg^{-1} dw. Some sedimentary rocks with the exception of sandstone (0.02–0.05 kg^{-1} dw) contain much higher selenium concentrations (shales 0.6 mg kg^{-1} dw; argillaceous sediments 0.4–0.6 mg kg^{-1} dw, limestones and dolomites 0.03–0.10 mg kg^{-1} dw) (Kabata-Pendias and Pendias 2000) (Table 10.2). Selenium is also present in fossil fuels in concentrations ranging from 0.046 to 10.65 kg^{-1} dw

in coal (3.0 mg kg^{-1} dw average) and from 0.006 to 2.2 mg kg^{-1} in oil (0.6 mg kg^{-1} average) (Marier and Jaworski 1983). Natural background concentrations of Se in air in nonvolcanic areas are within the range 0.01–1.0 ng m^{-3} (Frankenberger and Karlson 1994).

Selenium is obtained almost exclusively as a coproduct of copper processing (anodic slimes produced by copper refining contain roughly 5–25% selenium), as well as furnace dust from copper ironworks. It is estimated that in the known deposits of copper ore, world Se resources amount to about 90,000 tons (NRC 1983; Plant et al. 2003). The authors suggested that the amount of selenium in undeveloped and potential deposits may even be 2.5 times higher.

Although a relatively high concentration of Se is present in coal (1.5 ppm on average, 80–90 times more than in copper ores), the technical potential of it is not being recovered from coal. Small amounts of Se are also present in lead, nickel, platinum, gold, and zinc ores. The Wolverine deposit of zinc–silver (Zn–Ag) ore in Canada is an exception, where the proportion of Se is very high. Wolverine is the richest of Se deposits and has a very high concentration compared to all known deposits. Other similar massive volcanogenic sulfide deposits characterized by high selenium content include those in the Mattagami District, Quebec, and Skellefte District in Sweden (both of which are nearing depletion). The mining and smelting of copper–nickel ores at Sudbury, Ontario, Canada, alone release about 2 tons of Se into the environment daily, representing the greatest single source of Se emitter in the world (NRC 1983; Plant et al. 2003). The production of Se recovered from secondary sources (electrical equipment) in 2000 reached about 20% of total supply; however, in recent years this has almost entirely disappeared (Smakowski et al. 2011). Over the next years, the recovery of selenium from secondary sources may increase due to the recycling of solar batteries (with Cu-In-Ga-Se-CIGS).

Selenium is widely spread in nature, and in most rocks and soils, the content ranges from 0.1 to 2.0 ppm (Fishbein 1983). In soils, the concentration usually does not exceed 2 mg kg^{-1} dw (with the exception of loamy soils: 2.3–4.2 mg kg^{-1} dw). The mean concentration of Se in the soil is usually between 0.1 and 0.7 mg kg^{-1} dw. In clay soils it is usually higher (from 0.8 to 2 mg kg^{-1} dw) and is highest in tropical soils: from 2 to 4.5 mg kg^{-1} dw. Volcanic soils and granite are lacking in Se. These soils are found, for example, in the mountainous countries of Northern Europe, such as Finland, Sweden, and Scotland (Table 10.3; Fig. 10.1). The low content of Se in Scandinavian soils is due to the commingling of postglacial material by water and wind as well as by leeching of maternal rocks in geological processes (Winkel et al. 2015). So-called selenium provinces can be found in the world. The content of Se in such soils may reach 1200 mg kg^{-1} dw in provinces located in Japan, China, Canada, and the USA, among others (Winkel et al. 2015) (Figs. 10.2 and 10.3). Selenium in soils is positively correlated with the amount of atmospheric precipitation and negatively with the distance to the sea as the content of Se in the precipitation decreases (Wang et al. 1994; Blazina et al. 2014).

The presence of Se in natural waters is mostly the result of seleniferous rock erosion (Callahan 1979). The concentration of Se in such waters depends on the geochemical surrounding, the elution from rocks, and possible contamination (Table 10.4). In natural waters, selenium is present in various forms (SeO_3^{2-}, $HSeO_4^-$, $HSeO_3^-$, H_2SeO_3). As reported by Kabatas-Pendias and Pendias (2000), the highest

Table 10.3 Concentrations of selenium in various soils

Material	Concentration (mg kg^{-1} dw)	Range (mg kg^{-1} dw)	References
Worldwide	0.4	0.1–2	Berrow and Ure (1989)
Asia			
China (general)		0.02–3.81	Tan (1989)
India	3.63	0.25–4.55	Dhillon and Dhillon (2003)
Taiwan		0.03–0.65	Wang and Chen (2003)
Japan		0.11–2.72	Kang et al. (1990)
Europe			
Denmark		0.14–0.52	Hamdy and Gissel-Nielsen (1976)
Finland		0.05–1.24	Aro and Alfthang (1998)
Norway		0.043–2.73	Wu and Lag (1988)
France		0.10–0.70	INRA (2008)
Germany	0.123	0.02–0.42	Hartfield and Bahners (1988)
Poland (PL)		0.04–0.64	Piotrowska (1984)
Kujawy and Pomorze, PL	0.138	0.035–0.332	Borowska et al. (2007)
Wielkopolska, PL	0.19	0.00–0.57	Tomza-Marciniak et al. (2010)
Lithuania		0.144–0.228	Antanaitis et al. (2008)
Slovakia		0.2–0.33	Ducsay et al. (2007)
Romania		0.143–0.237	Lăcătuşu et al. (2010)
Serbia		0.12–0.44	Jakovljeviã et al. (1995)
Great Britain		0.1–4	Broadley et al. (2006)
Great Britain	0.5	0.01–4.66	Thornton (1983)
Scotland, Glasgow	1.0	0.1–6.60	Fordyce et al. (2009)
Northern Ireland	0.80	0.1–7.8	GSNI (in preparation)
North America			
Canada		0.41–2.09	Levesque (1977)
USA (general)		0.10–4.30	Jacobs (1989)
USA, New Mexico	0.23	0.039–1.4	Shacklette and Boemgen (1984)

levels of selenium are present in ground and underground water that flushes through formations rich in this element, for example, over pyrite shales, and through landfill areas that contain dusts with a high Se content from coal combustion. It is estimated that only about 15% of selenium occurs in a dissolved form, while large amounts are deposited as suspensions and sediments (Kabata-Pendias and Szteke 2015). The content of Se in rain and snow is usually similar to fresh water and ranged between 0.03 and 0.3 μg L^{-3} (Ĉuvardić 2003) but may change according to the part of the world.

In atmospheric air, the concentration of Se ranges from 0.008 to 5 ng m^{-3} (Wang et al. 1994). The lowest concentration of selenium was noted over the South Pole 0.004 ng m^{-3}, with the highest air concentration over urban and industrial areas (up to tens of ng m^{-3}). Moreover, considerable concentrations of Se (1 ng m^{-3}) have

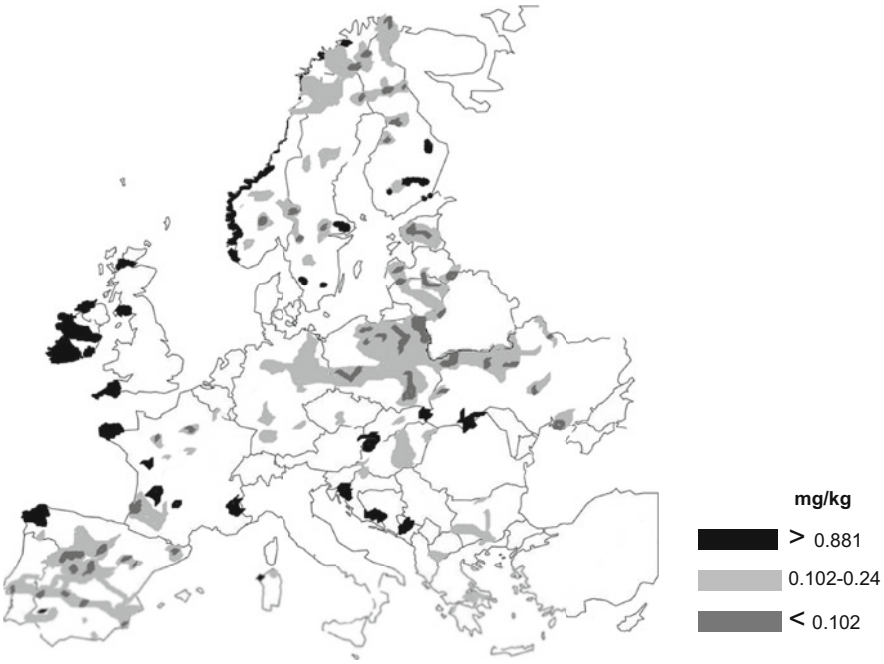

Fig. 10.1 The content of selenium in the soils of Europe (based on the map by Reimann et al. 2013)

been found over dumps and swamps (Beavington et al. 2004; Wen and Carignan 2007).

Selenium is emitted into the atmosphere mostly by the combustion of minerals (including coal and oil processing products) in volatile forms (elementary selenium, selenium dioxide, dimethyl selenide). These compounds may persist in the atmosphere for up to 45 days (Wang et al. 1994; Blazina et al. 2014).

4 Selenium in Nature: Geogenic and Anthropogenic Sources

As an effect of volcanic rock erosion, Se is transferred to the atmosphere and then to oceans, seas, and lakes as well as soils. Selenium is also transferred from the eroding rocks directly to underground and groundwaters, and via the soil-forming processes, also to soils. The process of rock erosion releases to the atmosphere from 100,000 to 200000 tons of this element every year (Andren and Klein 1975). Selenium is assimilated from the soil by plants and through them moves to humans and animals, mostly by ingestion and to a smaller extent by inhalation from the fresh atmospheric air. It returns to soil by the dry and wet deposition from decaying plants and animals as well as from human and animal excrements (Fig. 10.4).

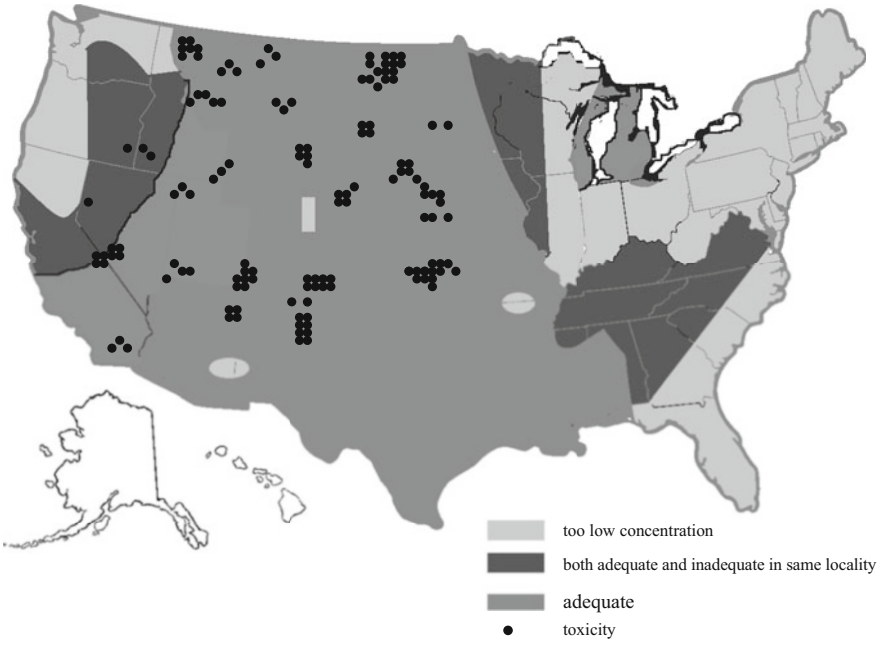

Fig. 10.2 The content of selenium in the soils of USA, based on the map http://www.swampyacresfarm.com/SeleniumSupplements.html

In Europe, a toxic soil selenium level was found in a few places, including Wales and Ireland (Fleming 1962). These seleniferous soils are typically low lying, poorly drained, and of high pH and organic matter status. The soils have been influenced to a large degree by percolating waters from Se-rich rocks where black shales are the predominant facies. Seleniferous soils may contain very much selenium, even up to 200 mg kg^{-1}. Soils that contain more than 5 mg kg^{-1} are considered as toxic (McGrath et al. 2008). Toxic concentrations of Se are found in some parts of China, Hawaii, Mexico, Columbia, and western part of the USA (McNeal and Balistrieri 1989; Blazina et al. 2014). However, to a global scale, the deficiency of selenium is a more severe problem than its abundance.

The atmosphere is an important temporal reservoir of Se in the global store of this element, while the main sources of emission are the oceanic and continental biospheres (Table 10.5). It is estimated that natural and anthropogenic sources emit into the atmosphere 60% and 40%, respectively, and in recent decades, the total annual emission of Se in a global scale was evaluated at 13–19 thousand tons (Mosher and Duce 1987; Wen and Carignan 2007; Winkel et al. 2015).

Selenium evaporates from the surface of the seas and oceans as a dimethyl, which is then incorporated in processes carried out by microbes and higher plants. Selenium is also emitted from volcanoes, such as the European Mt Etna (Mosher and Duce 1987).

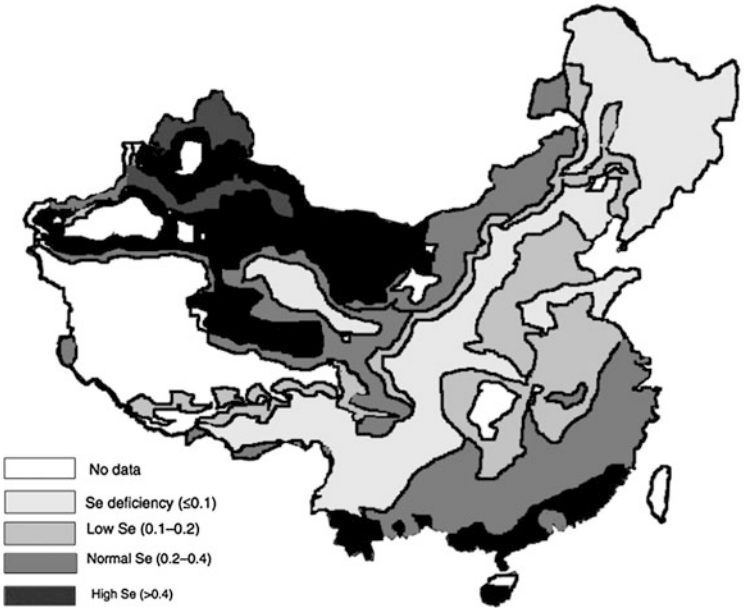

Fig. 10.3 Distribution of total selenium in the soils of China, based on the map by Blazina et al. (2014)

The contamination of the environment by Se is caused by fossil fuels combustion (oil, hard coal) and emissions from industrial plants (Pezzarossa et al. 2007). In the past, Se was used in pesticide production, but due to its stability in soils and subsequent contamination of food crops, its use has been limited (ATSDR 2003). An increased concentration of Se in land plants, lichens, and mosses located at a distance from anthropogenic sources of emission suggests that precipitation is an important vector of contamination (Wen and Carignan 2007).

Selenium is also present in coal as well as in coal dust and ash (Tian et al. 2011). In the industrialized areas, the processes of coal combustion have contributed to a large release of Se into the atmosphere; however, the simultaneous emission of SO_2 caused a decrease in its assimilation. Studies in coal power plants have demonstrated that as a result of coal combustion, 10–60% of the Se associated with coal was released to the atmosphere (Klusek et al. 1983; Conzemius et al. 1984). Modern technologies in coal combustion limit the emission of contaminants such as Se, for example, wet flue gas desulfurization (WFGD) in power plants (Tian et al. 2010). The washing of coal before combustion is an effective way to reduce ash and SO_2 emission. It can reduce sulfur pyrite content by 40%, along with trace elements concentrations (You and Xu 2010). The biggest amount of Se emission from combusted coal is in China, which is connected with the rapid growth of the economy in that country. The use of coal provides more than 75% of the country's total energy sources (You and Xu 2010). From 1980 to 2007, ~145% increase in Se emissions took place in China (Fig. 10.5) (Tian et al. 2010). The World Coal

Table 10.4 The content of selenium in waters

Water type	Content (μg L^{-1})	References
Rain water		
Worldwide	0.03–1.7	Reimann et al. (1998)
	0.04–1.4	Plant et al. (2004)
Polar ice	0.02	Frankenberger and Karlson (1994)
Rivers		
Worldwide	0.07 (0.02–0.5)	Gaillardet et al. (2003)
USA, Gunnison	10	Jacobs (1989)
Germany	0.015	Ebens and Shacklette (1982)
Jordan, River Jordan	0.25	Nishri et al. (1999)
Brazil, Amazon River	0.021	Ebens and Shacklette (1982) and Jacobs (1989)
Japan	0.03–0.09	Nriagu and Wong (1983)
USA	0.14	Robberecht and Grieken (1982)
China	0.04–5	Wang and Gao (2001)
Seas and oceans		
Worldwide	0.2 (0.1–0.35)	Reimann et al. (1998)
Seawater		
Worldwide	0.009–0.045	Ebens and Shacklette (1982)
Dead Sea	0.09–0.45	Whittle et al. (1977)
	0.8	Robberecht and Grieken (1982)
Atlantic Ocean	0.075–0.096	Schutz and Turekian (1965)
Pacific Ocean	0.104	Schutz and Turekian (1965)
Freshwater	0.2 (0.02–10)	Reimann et al. (1998)
Drinking water		
Worldwide	0.12–0.44	Robberecht and Grieken (1982)
Germany	0.02–0.03	Veber et al. (1994)
Slovenia	0.2	Veber et al. (1994)
New Mexico	5	Martin (1975)
USA, New York	0.12–0.44	Cutter (1989)
Belgium	0.13–0.14	Ediger (1975)
Australia	<1	Mesman and Thomas (1975)
Groundwaters		
Argentina	48–67	Robberecht and Grieken (1982)
Australia	0.008–0.33	Robberecht and Grieken (1982)
Israel	0.9–27	Robberecht and Grieken (1982)
Poland	0.25–1.80	Siepak et al. (2003)
Slovakia	0.5–45	Rapant et al. (1996)
Norway	0.01–4.82	Reimann et al. (1998)
Italy	0.002–1.94	Dall'Aglio et al. (1978)
USA	<1–480	Engberg (1973)
Lake waters		
Poland	0.15–0.35	Siepak et al. (2003)
USA, Lake Michigan	0.8–10	Jacobs (1989)

(continued)

Table 10.4 (continued)

Water type	Content (μg L^{-1})	References
Sweden	0.04–0.21	Nriagu and Wong (1983)
Australia, Lake	0.3–5.0	Peters et al. (1999)
Macquarie	<0.5	Maier et al. (1979)
Germany	<0.1	Speyer (1980)
Canada	0.16–0.25	Kucukbay and Demir (2001)
Turkey, Malta Poland	0.12–0.45	Niedzielski (2006)

Institution estimates that global coal production in 2030 will reach 7000 Mt, of which about a half will be made in China (Wen and Carignan 2007). Also, the production of energy in many other countries is based on coal and contributes to a lesser extent to selenium contamination of the atmosphere, relative to the content of selenium in the coal as well as to the appropriate filters in the power plant equipment preventing dust and exhaust gases (Table 10.6). For example, about 50% of electricity is generated from coal combustion in the USA, 70% in India, Australia, Greece, and the Czech Republic, while in Poland and South Africa, it is nearly 95%. The content of Se in coal ranges from 0.13 to 4.30 mg kg^{-1}, and in the ash from 0.5 to 15.5 mg kg^{-1} (Table 10.6; Bielowicz 2013).

As reported by Wen and Carignan (2007), the northern hemisphere is more burdened with anthropogenic activity, so 70–80% of total Se emission is located there. From the beginning of the industrial era, Se emissions from anthropogenic sources have increased. Anthropogenic sources mainly comprise combustion (coal, oil, wood, biomass), nonferrous metal smelting, manufacturing, and utilization of agriculture products (Mosher and Duce 1987). In the USA, more than 90% of Se production comes from the anodic slime release by the electrochemical refining of copper (Nriagu and Pacyna 1988). The emission of Se to the atmosphere in European Union countries (EU) changed to a limited extent, showing a slight decreasing tendency. A comparison of 1990 and 2011 has shown a decrease in annual Se emission from 267 to 234 tons, which is 12% (EEA 2013) (Figs. 10.6 and 10.7). In 2011, the highest percentage shares in industrial selenium emissions were from Spain, Portugal, and the UK. As noted by Dodig and Cepelak (2004), in the USA about 1500 tons of annual emissions of Se come from fuel combustion. The same amount is emitted by municipal landfills and industrial plants.

It seems that since the beginning of the twenty-first century, the highest amount of Se emitted into the atmosphere from anthropogenic sources was by China, which additionally shows a constant and dynamic increase in this matter. Between 2000 and 2012, this emission increased by 44.9%. In 2000 and 2015, the emissions of Se into the environment by the UK were 2113 and 3062 tons per year, respectively, which was at least 10 times higher than the rest of the EU.

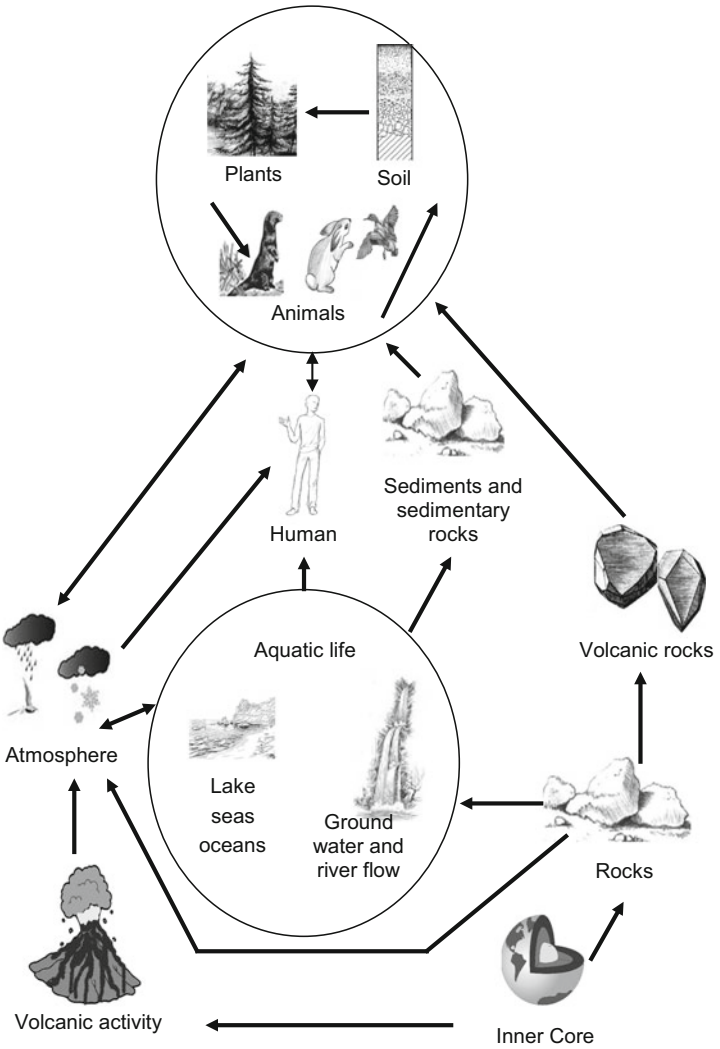

Fig. 10.4 The circulation of selenium in nature (based on the diagram by Diplock 1985)

Table 10.5 The estimated global flux of atmospheric Se from natural sources (10^9 g $year^{-1}$)

Source	Amount
Crustal weathering	0.003–0.035
Sea salt	Up to 1.1
Wild forest fires	Up to 0.52
Marine biosphere	0.4–9
Volcanoes	0.1–1.8
Continent biosphere	0.15–5.25

Sources: Mosher and Duce (1987), Nriagu and Pacyna (1988), Nriagu and Wong (1983)

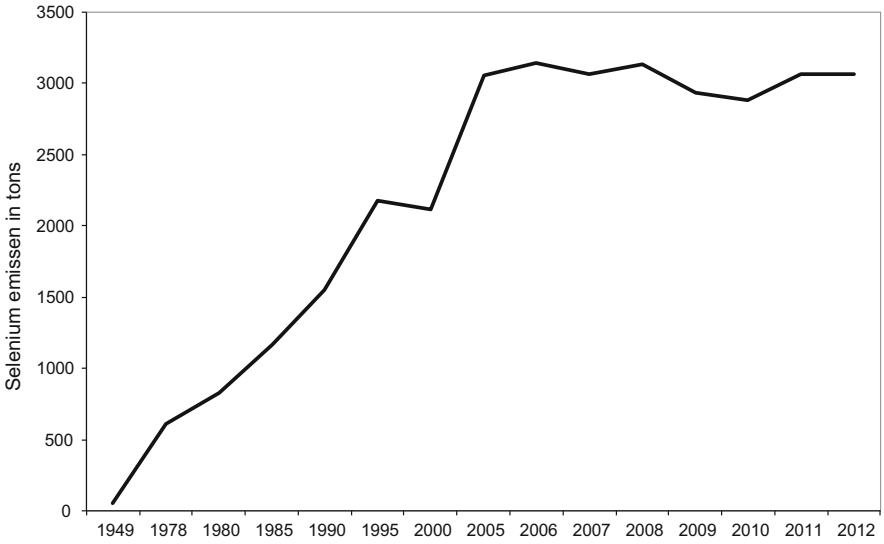

Fig. 10.5 Emission of Se from the main anthropogenic sources in China (Data source: Tian et al. (2015)

Table 10.6 Concentrations of selenium in coals and other natural fuel sources

Country and material	Concentration (mg kg^{-1})	Range (mg kg^{-1})	References
USA, coals	3.36	0.46–10.65	Kuhn et al. (1980)
Hard coal	1.6		Yudovich and Ketris (2006)
Brown coal	1.0		Yudovich and Ketris (2006)
Brown coal	1.0		Ketris and Yudovich (2009)
Kentucky coals	4.3	2.9–5.5	Eble and Hower (1997)
Poland, coals	0.13	0.11–0.49	Symanowicz et al. (2013)
Brown coal	3.08		Goldsztejn (2007)
Brown coal	<3		Bielowicz (2013)
Germany, coals	2.9		Sabbioni et al. (1983)
Indonesia, coals	0.52		ACARP (2006)
China, coals	1.5	0.36–12.10	Tian et al. (2010)
	3.91		Wang et al. (2010)
China, fossil fuels		1–10	Harr (1978)
China, petroleum		500–1650	USPHS (1996)

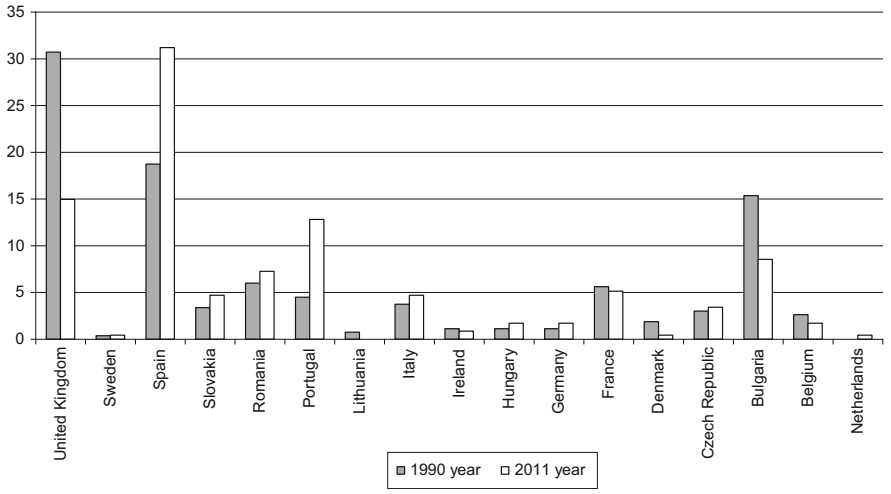

Fig. 10.6 The percentage share of EU countries in the anthropogenic emission of selenium (Data source: EEA 2013)

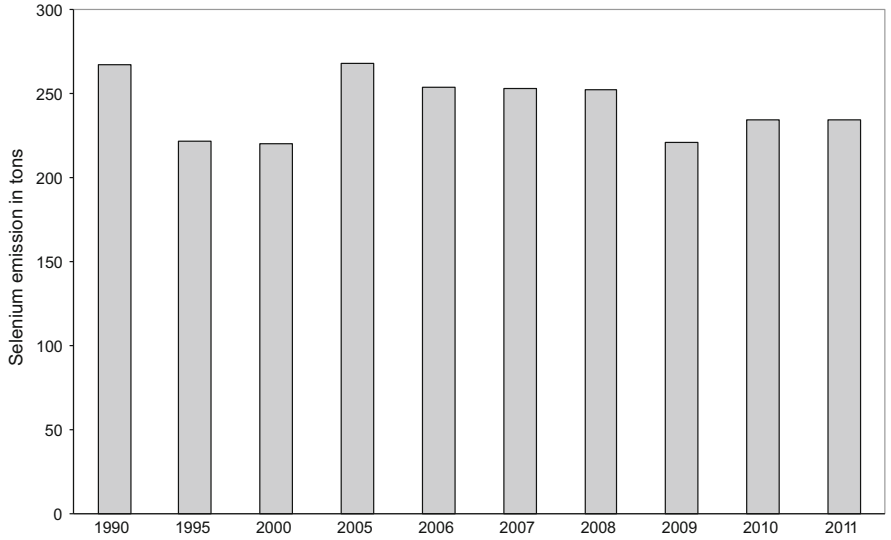

Fig. 10.7 Anthropogenic selenium emissions in the European Union (Data source: EEA 2013)

5 Production and Uses

Four types of Se are offered in the world trade: (1) high-quality Se, purity above 99.99%; (2) pigment selenium, purity above 99.8% Se; (3) standard Se, purity from 99.0 to 99.9% Se; and (4) trade Se, purity above 97.0% Se (George 2004). It is hard

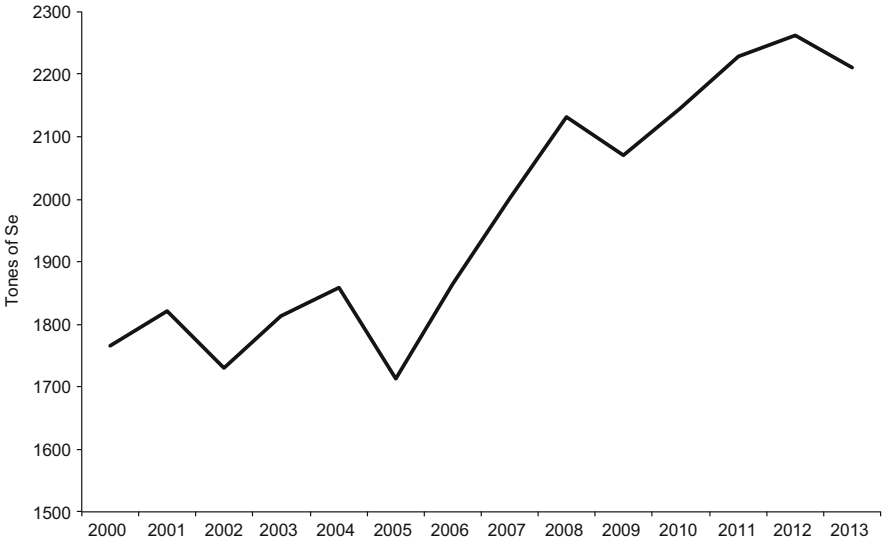

Fig. 10.8 Global production of selenium (data sources: British Geological Survey 2015; World Mineral Production 2009–13)

to say how the demand for Se will look in future years, yet it is expected that demand will increase due to the development of some new technologies (including nanotechnologies). In industry, Se is used as a semiconductor in rectifiers, photocells, and anticorrosive shells (e.g., on steel), as an addition to some copper alloys, and in coloring glass. Red Se at 2–3% will dye glass ruby red (signal glass). According to the ordinance no. 1272/2008 from the European Parliament and EU Council, Se has been classified as Acute Tox 3 (H331, toxic after swallowing; H301, toxic after inhalation), STOT RE 2 (H373, may cause organ damage by prolonged or repeated exposure), Aquatic Acute 1 (H400, very toxic for water organisms), and Aquatic Chronic 1 (H410, very toxic for water organisms, causing prolonged effects). Selenium compounds in pollution are usually selenites (SeO_3^{2-}) and selenates (SeO_4^{2-}), and to a lesser extent its organic forms, as selenomethionine (George 2004; Pilon-Smits and LeDuc 2009). In 1987, the world production of Se was 1400 tones (USPHS 1996). The present production of Se cannot be precisely evaluated as there is no comprehensive data available, but a clear increasing tendency is visible (Fig. 10.8). In 2014 it surely exceeded 2275 tones (U.S. Geological Survey 2015).

In recent years, Japan and Germany have been considered as the largest Se producers (34% and 30% of world production, respectively) (Table 10.7), with the major consumers of selenium in order of importance: Europe, the USA, and Pacific Asia, in particular China. The scale of selenium demand in China correlates with the use of manganese in the steel industry.

Table 10.7 Production of selenium metal (tones)

Country	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Belgium	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200	200
Canada	335	238	175	253	277	107	117	141	191	173	97	35	144	159	154	154
Chile	47	84	–	–	–	–	–	–	–	–	–	–	–	–		
China	65	65	65	65	65	65	65	65	65	65	65	65	65	65	65	65
Finland	37	42	37	52	65	66	70	52	65	59	73	86	93	101	94	93
Germany	100	100	100	100	100	120	120	120	250	230	250	250	250	250	700[a]	700[a]
India	10	10	6	2	–	8	–	–	–	–	–	–	–	–	–	–
Japan	612	735	752	734	599	625	730	806	754	709	804	809	820	739	782	772
Kazakhstan	40	40	40	40	100	60	70	155	130	120	130	130	130	130	130	130
Mexico	–	–	–	–	–	–	–	–	–	–	62	95	95	132	120	107
Peru	21	16	21	24	76	70	75	59	60	61	59	54	42	40	49	50
Philippines	38	43	40	40	48	68	65	65	65	65	65	65	70	70	70	70
Poland	65	65	68	78	83	82	87	85	82	80	79	85	90	80	90	87
Russia	41	48	60	81	85	100	110	110	110	160	170	265	172	155	131	143
Serbia and Montenegro	21	14	17	7	–	–	–	–	–	–	–	–	–	–	16	16
Sweden	104	88	118	107	131	122	135	126	139	129	72	70	70	70	20	20
Uzbekistan	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20
Zambia	10	13	11	10	10	–	–	–	–	–	–	–	–	–	–	–

Sources: British Geological Survey (2015, 2017), World Mineral Production 2009–2013; British Geological Survey (2006), World Mineral Production 2000–2004; British Geological Survey (2010), World Mineral Production 2004–2008

[a]Includes selenium produced from imported material

According to analysts, the greatest respective increases in selenium demand will be connected with the progress in photovoltaic technologies, especially the development of thin-layer solar batteries in the latest Cu-In-Ga-Se (CIGS) technology, as well as in the boom in demand for glass in architecture (Andersson 2005). In many countries, especially in the USA, CIGS and CdTe battery recycling facilities are well developed, from which the demand for selenium and tellurium for thin-layer cells will be partially covered (George 2004).

The structure of selenium use in 2004 was dominated by the glass industry (35%) while in 2009, by metallurgic use (40%), the glass industry dropping to 25% (this decrease is explained by the crisis in that real estate market). The share of other directions of Se use is as follows: agriculture 10%, chemical pharmaceutical and pigment industries 10%, electronics 10%, and others 5%.

Considerable amounts of selenium are used in the glass and ceramic industries for red mosaic dying and in agriculture as an additive for selenium-enriched fertilizers in Se-deficient soils, for instance, in China, New Zealand, and Australia, and as a fodder supplement for farmed animals. Cadmium sulfoselenide until recently was used as a dye to manufacture colored artistic glass and intensive red lamps in traffic lights. In the metallurgy industry, selenium is used as an additive to improving the casting, forming, and machining properties of iron, steel, copper, and lead alloys, of which the last is used in car batteries (George 2004).

In the pharmaceutical industry, selenium is used to produce anti-dandruff shampoos and anti-inflammatory and antifungal drugs for dermatology. The use of selenium in the electronics industry is still high due to the constant demand for devices that use photoelectricity and DC converters (Canadian Council of Ministers of the Environment).

6 Biological Status of Selenium

The concentration of selenium in soils and plants varies depending on the geographic location (including the distance to sea), type of maternal rock, intensity of flushing and washing of rock particles into water reservoirs, climatic conditions (temperature, amount of precipitation), type of soil and its pH and salinity, processes of sorption by iron oxides and loamy minerals in the soil, content of organic matter, level of environmental contamination (presence of antagonistic elements as Pb, Cd), the chemical form of Se, and finally the specific composition of soil microorganisms and plants (Pezzarossa et al. 2007; Kabata-Pendias and Mukherjee 2007; Kabata-Pendias and Szteke 2015; Winkel et al. 2015). In soils rich in iron and organic matter, as well as in salified soils, a higher content of selenium is found, while lower levels pertain to acidic soils. The soils of the central region of North America are formed from cretaceous shales, having favorable pH characteristics that increase Se availability for uptake (Mayland 1994; Kabata-Pendias and Mukherjee 2007).

In selenites, Se may occur as Se (IV) or Se (VI). Selenites (IV) may be absorbed to a higher extent by iron oxides/hydroxides than selenates (VI) (Barrow and Whelan

1989). The intensity of this process decreases with a rise in pH. Iron oxy-hydroxides (hematite, getite) are characterized by a high potential to absorb Se, which causes an inhibition in their transport and retention in soil (Rovira et al. 2008).

In soil, selenium is present in nonvolatile forms, as selenides, seleno-amino acids, and dimethyloselenium—as an ion or as a volatile methylated (DMSe) and dimethylated (DMDSe) form (Cooke and Bruland 1987). Due to the activity of microorganisms, inorganic selenium compounds after methylation change into volatile compounds that may be transferred into the atmosphere from the surface of both water and soil (Zayed et al. 1998; Azaizeh et al. 2003). In anaerobic conditions, microorganisms convert the elementary selenium into hydrogen selenide (Barrow and Whelan 1989). The process of methylation depends on the content and source of carbon, on soil temperature and type, as well as on the redox conditions. Selenium may also be released into the atmosphere by higher-order plants (Laser 2004).

The binding of Se (IV) to solid soil particles occurs by ligand exchange pathway, using the hydroxyl group that is present on the surface of colloid soil particles and hydrated metal oxides. This mechanism is very dependent on the pH. Se (VI) is different, as the connection to other solid components in the soil, water molecules are used between the external layer and the adsorbed ion (Neal 1995).

The content of selenium in plants depends on the abundance of Se in the soil, its chemical form, and the species of plants, which assimilate selenium mostly as selenite Se (IV) and selenate Se (VI), and some species—as selenides. A significant difference in the interaction of selenites (IV) and selenates (VI) has been found which concerns the different mechanism of transport of both chemical selenium forms through cellular membranes. Inorganic Se (VI) ions easily penetrate the root, but are transported by the apoplastic way—without entering the root cells, but rather in the water stream in an unchanged chemically ionic form. In turn, inorganic Se (IV) ions, after penetrating the root, are able to enter the cellular plasmalemma (symplastic transport) and are biotransformed into organic compounds. Selenium is stored by plants as different organic compounds, including amino acids, such as selenomethionine, selenocysteine, Se-methylselenocysteine, selenocystathionine, and selenohomocysteine. Translocation of selenium from the roots to the shoots depends primarily on the chemical form. Selenates (VI) are more easily transported than selenites (IV). This is caused by the quicker transformation of selenites (IV) to forms that are retained in the roots. Therefore the transfer of selenium to the above ground parts of a plant is limited (Terry et al. 2000; Li et al. 2008; Michalska-Kacymirow et al. 2014).

Most crop plants contain less than 25 mg Se kg^{-1} dw, and in only some of them does the concentration exceed 100 mg Se kg^{-1} dw. However, a low content of Se in plants is not always requisite with a low selenium content in the soil, as the concentration of Se in plants depends on many factors: plant species, type of soil and its Se content, climatic and vegetative conditions, fertilizers, chemical form of Se and its bioavailability for plants, pH of the soil, organic matter content, and the presence of competitive anions (Bell et al. 1992; Ellis and Salt 2003; Fig. 10.9).

Due to the varying ability of plants to assimilate and accumulate Se, they can be divided into three groups (Bell et al. 1992; Ellis and Salt 2003): selenophilic plants

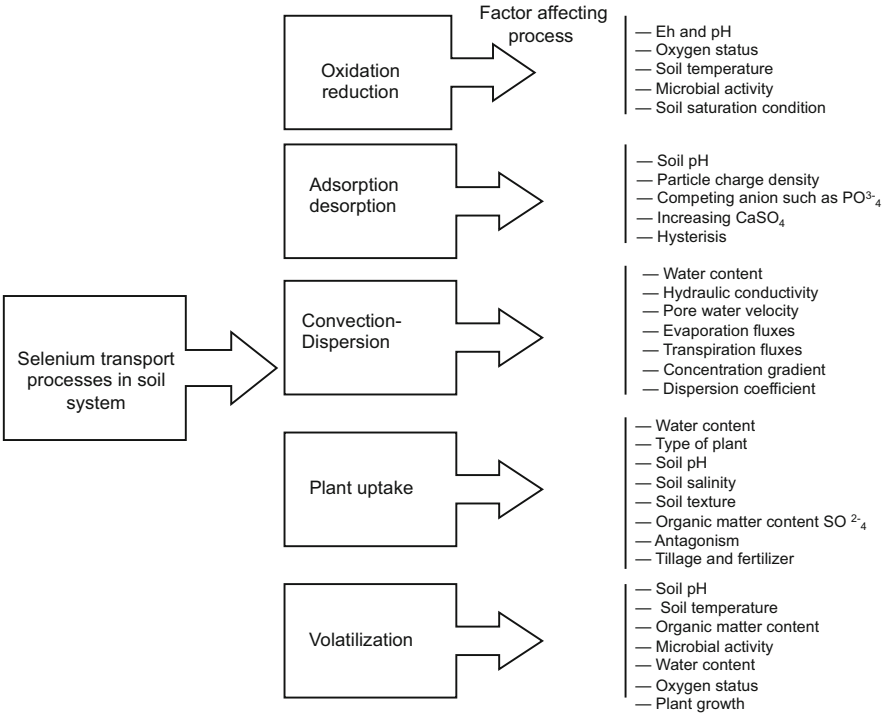

Fig. 10.9 The transport processes and the related factors, based on the diagram by Mirbagheri (2004)

(selenium accumulators), which can store from a thousand to a few thousands mg of Se kg^{-1} dw in their overground parts and are toxic to humans and animals; plants that moderately accumulate selenium (secondary selenium accumulators); and plants that assimilate low amounts of selenium and are characterized by a lower tolerance to this element and do not develop well in selenium-abundant soils.

The concentration of Se in the soil decreases with depth, and in the lowest layers is low, so plants with a deep root system do not have wide access to this element (Hartfiel and Bahners 1987). The location of Se in different parts of a plant depends on the species, development stage, and physiological status. Plants classified as Se accumulators store this element mostly in the leaves in early stages of development and in seeds during the reproductive stage. Then, a decrease of selenium in the leaves is observed. In mature grain plants, the content of Se is at a similar level in the caryopses and roots, with a lesser level in the stalks and leaves (Terry et al. 2000).

The concentration of Se in the animal organism depends on the content of this element in food and on its digestibility. Food is the main route of Se intake for vertebrates and invertebrates. Animals can (depending on the species, the form of selenium and other factors) intake from 44% to 95% of the selenium contained in the food (Opresko 1993). For most of the Se forms (selenite, selenate,

selenomethionine), the level of assimilation is very high (from 80% to over 90%). Selenium can also enter organisms through inhalation, while some Se compounds, such as selenyl chloride, are easily absorbed by the skin. The assimilation of Se is strictly dependent on the chemical form of Se. Vertebrates assimilate Se better in organic forms: selenomethionine (SeMet) and selenocysteine (SeCys). The absorption of organic Se forms is via the active intestinal transport, while the inorganic forms are absorbed by the passive transport (diffusion in the presence of sodium ions) in the small intestine (Fordyce 2013; Sampaio da Silva et al. 2013). Absorbed Se is bound by erythrocytes and blood plasma albumins and globulins and is transported to the tissues. Inorganic Se forms are converted into organic selenocomplexes in the muscles, hemoglobin, and blood plasma. Selenates (VI) in the liver, spleen, blood, and plasma are reduced by enzymes to selenites (IV) or selenium. Selenites (IV) may build complexes with proteins and in this way are more easily bound to glutathione peroxidase than selenates (VI). Selenites (IV) penetrate the blood-placenta barrier and enter the fetus. Selenites (IV) show a higher affinity to tissues than selenates (VI). The excretion of selenium from the organism happens in the urine ($TMeSe^+$), sweat, and as DMeSe with exhaled air. Much lower amounts of this element are excreted with feces (Fishbein 1991; Fordyce 2013). In homeothermic animals, 85%–100% of dietary Se in plants is absorbed, compared to 20%–50% of Se present in meat and fish (Fordyce 2013). The main vector of Se intake in fish is not the water but the food chain (Luoma et al. 1992).

Selenium shows a tendency to bioaccumulate in tissues and causes toxicological effects. Bioaccumulation of Se in lower trophic level invertebrates (zooplankton, clams) is important in evaluating the effect of Se on the higher trophic levels of predators (fish and birds that feed on invertebrates). Absorption of Se dissolved in the water is not as significant as the assimilation from the diet (Luoma et al. 1992; Lemly 1993). Direct uptake of particulate selenium by invertebrates via filter feeding or deposit feeding is the primary route for Se to enter the food chain (Luoma and Presser 2000). Microorganisms connected with the detritus of sediments may be important in the incorporation of Se into the aquatic food chain (Hamilton and Buhl 2003; Sampaio da Silva et al. 2013). It has been shown that differences in the structure of the food chain in lentic and lotic habitats affect the level of Se in the aquatic food chain. Organisms from the higher trophic levels in lentic habitats collect higher concentrations of selenium than organisms in lotic environments (Orr et al. 2006; Sampaio da Silva et al. 2013). The cycle of Se in dentric sediment is where Se is transformed into selenomethionine and is subsequently transferred to superior trophic levels (Sampaio da Silva et al. 2013).

One of the many factors that affects selenium assimilation by animals is their taxonomic affiliation, with the biggest such differences described between single-stomached and ruminant animals (which absorb selenium less effectively). It has been concluded that in monogastric animals, about 80%–90% of Se is absorbed in the digestive tract, while in ruminants it is much less—about 30%–35% (Spears 2003; Lyons et al. 2007; Fordyce 2013). This dependence is caused by the processes of bacterial reduction in the rumen, which leads to a conversion of mineral selenium links into nondigestible forms, the consequence of which is a low biological

availability of the Se. An additional factor that reduces the absorption of Se in ruminants is the low pH in the rumen. Selenium assimilation also depends on the concentration of calcium in particular ingredients of the diet, which also relates to sulfur (Cristaldi et al. 2005; Mynhardt et al. 2006).

6.1 *Toxicity of Various Selenium Forms in Homeothermic Animals*

In the thirteenth century, Marco Polo had already described symptoms typical for selenosis, such as hair loss in horses and humans, salivation, tooth loss, and hoof crumbling, in his China travel diary. Selenite, selenate, and selenomethionine are among the most acutely toxic selenium compounds (Högberg and Alexander 1986). The particular chemical forms of selenium are categorized by toxicity. A lethal dose of Se (IV) for rats is 3.2 mg kg^{-1} body weight (bw), while for dimethyl selenide—1600 mg kg^{-1} b.w. Inorganic selenium compounds such as selenite (IV) and selenate (VI) are the most toxic forms of this element. In nature, selenium most often occurs as selenomethionine and selenocysteine, so in a form connected to amino acids. The least toxic forms of selenium are volatile methyl compounds of Se that are the metabolites of the detoxification process (Orr et al. 2006).

A surplus of Se in food causes symptoms of intoxication in animals (selenosis endemica), while in humans, hair loss, nail cracking, skin changes, and polyneuritis have been observed. The toxic activity of Se in animals may not only occur in places environmentally abundant in this element but also in the areas polluted by metallurgical and mining industry wastes (Wayland and Crosley 2006). Cases of selenosis have been recorded in those regions of the world where the natural Se content in the environment is very high (e.g., some regions of China, northwestern USA). Selenophylic plants (Se accumulators) located in soils abundant in Se are almost always responsible for cases of acute or chronic intoxication with selenium in animals, as the above ground parts of such plants may contain thousands of mg of Se to 1 kg dw converted (Ellis and Salt 2003). Cases of an acute intoxication with selenium have been observed in animals after consuming plants containing 400–800 mg Se kg^{-1} dw, yet as noted by Mayland (1994), a content of Se in fodder above 3 mg kg^{-1} dw may already be toxic for some species of mammals. Raisbeck (2000) claims that a content of Se higher than 0.5 mg kg^{-1} dw in cattle fodder may cause appetite loss, hair loss, inflammation, horn and hoof fragility, hobbling, or even death in these ruminants. The medial lethal doses of Se for adult cattle and for lambs (LD_{50}) are 0.501 and 0.455 mg kg^{-1} bw, respectively (Grace 1994; Tinggi 2005). A toxic concentration of Se in the blood is >2 mg L^{-1} in cattle and >0.6–0.7 mg L^{-1} in sheep (Levander 1986).

The afflictions caused by an excessive supply of Se in animals occur in two clinical forms: chronic (called the alkali disease) and acute (called blind circling). The symptoms of the chronic form include liver damage (metabolic discrepancies

and lack of appetite), depression, emaciation, hair loss, roughness of hair, improper development or necrosis of hooves, limb stiffness, heart atrophy, and anemia (NRC 1980; Clayton and Clayton 1994; Raisbeck 2000; Tinggi 2005). An acute form of intoxication manifests in disturbances in the nervous system, including increased excitability or, conversely, stupor. In some cases, animals blindly push forward, grate their teeth, and salivate. Moreover, sometimes animals suffer colic, diarrhea, and impairment of vision. The final phase includes dyspnea and limb paralysis. Death is caused by respiratory failure (Raisbeck 2000; Kim and Mahan 2001; Dodig and Cepelak 2004).

An excessive concentration of Se in vertebrates causes an increased substitution of sulfur by Se in cysteine, named the "sulfuric amino acid," which is very common in keratin (which composes the hair, feathers, and other horny formations of vertebrates), as well as in other sulfur-containing molecules. Moreover, an excess of Se leads to inhibitions of cellular proliferation, replication of DNA, and protein synthesis while supporting an increase in oxidative stress, intensified lipid peroxidation, and metal complexing, which then accumulate in brain cells (Raisbeck 2000; Kim and Mahan 2001; Dodig and Cepelak 2004; McKittrick et al. 2012; Zachary and McGavin 2014).

Studies performed before 1987 in animals and humans, by the International Agency for Research on Cancer (IARC), have not shown any carcinogenic activity of selenium nor of its compounds, so these substances have been classified within group 3 "Not classifiable as to its carcinogenicity to humans" (IARC 2015). However, since that time it has been shown that selenium sulfide is likely a human carcinogen. Selenium sulfide is the only Se compound that causes tumors in laboratory rats and mice (ADSTR 2003).

It is commonly believed that selenium has a preventive activity against some tumors (of the large intestine, lungs, larynx, prostate gland, stomach, and esophagus) when Se supplementation is used in animals with a deficiency of this element. In the case of animals with a marginal concentration of Se, any additional supplementation with selenium did not cause any benefits and may even cause an opposite effect (Goodman et al. 2001; Duffield-Lillico et al. 2002; Grau et al. 2006; Lippman et al. 2009).

Data concerning the genotoxicity of Se compounds are unambiguous. It has been observed that inorganic Se compounds may act twofold: genotoxically and antigenotoxically. Antigenotoxic effects usually occur in lower levels of exposure than genotoxic activity (ATSDR 2003).

6.2 The Role of Selenium in the Organism

The concentration of Se in an organism is the main factor regulating the activity of glutathione peroxidase and other selenoproteins that participate in metabolic pathways. In the processes of cellular protection against the effects of reactive oxygen forms, a group of five glutathione selenoperoxidases, three thioredoxin reductases,

and a selenoprotein P are engaged (Arthur 2000; Flohe et al. 2000; Gladyshev 2001; Behne and Kyriakopoulos 2001). Selenium, as an antioxidant, limits the harmful effects of the peroxidation of lipids, DNA, and RNA, protecting cells from deformation and genetic damage. Moreover it causes the apoptosis of tumor cells (Griffin 1982; Behne et al. 1996). Epidemiological studies have shown a relationship between a deficiency of selenium and the growth of some types of tumors. Selenium has an inhibiting effect on tumor cell proliferation by enhancing the expression of suppressor gene (p53), as well as on regulating the expression of apoptosis suppressor gene (Bcl-2) (Jackson and Combs 2008; Björkhem-Bergman et al. 2012).

In males, Se accumulates in the testes and is excreted from the organism with semen (Hansen and Deguchi 1996). A deficiency of this element negatively affects the development, motility, and number of sperm cells in an ejaculate, as well as the volume of seminal fluid. A low concentration of Se increases the susceptibility of sperm to free oxygen radicals, which disturb the biochemical processes in the acrosome (Kantola et al. 1988). In males, the large level of Se deposited in the testes is used for the protection of sperm mitochondria from oxidation processes (Roveri et al. 2001). Sperm glutathione peroxidase protects the DNA of the sperm against oxidation damage and participates in the condensation of chromatin (Pfeifer et al. 2001). Some authors also suggest that Se may play a role in the biosynthesis of testosterone (Bedwal et al. 1993).

Selenium is a deactivator of toxic heavy metals (including mercury, cadmium, and lead), as well as organic compounds, which are released in infections, injuries, and stress (Rayman 2000; Kalisińska et al. 2014). In mammalian organisms, selenites of cadmium, mercury, lead, silver, and tallium are easily formed, which enables the removal of these metals from the organism. Selenium is also a factor that decreases the toxicity of methylmercury (Ralston and Raymond 2010). Selenium is also an element that neutralizes the activity of carcinogenic aflatoxins (Navarro-Alarcon et al. 1998; Maehira et al. 2002).

The activity of Se in the cardiovascular system includes protecting LDLs from oxidants, interaction with alpha-tocopherol, and heavy metal detoxication, influencing the metabolism of homocysteine and tissue sensitivity to insulin (Marcus 1993). The protection of LDL cholesterol fractions against oxidative modification is via the antioxidative properties of glutathione peroxidase and other selenoenzymes present in blood plasma, including selenoprotein P (Köhrle et al. 2000).

Administration of Se reduces rheumatic pain and increases mobility in inflamed joint, as well as induces antiviral (e.g., inhibits the progression of HIV virus) and antidepressive activity (Stone et al. 2010). Moreover, it seems that Se is relevant for the proper functioning of the brain, where in the brain tissues of patients diagnosed with Alzheimer's and Parkinson's disease, a lower concentration of selenium was found in comparison to the tissues of healthy people (Atroshi et al. 2007).

6.2.1 Deficiency of Selenium in Animals

Deficiency of selenium in homeothermic vertebrates causes a decrease in the concentration of glutathione, glutathione peroxidase, and the enzymes responsible for thyroid hormone metabolism, including thioredoxin reductase, which causes a decrease in thyroid activity (Arthur et al. 1993; Fischer et al. 2008). A deficiency in selenium can also be seen in oxidative damage to thyroid tissues and in a decreased activity of T3 in the metabolism of an organism (Corvilain et al. 1993). In farm animals, the most well-known disease connected with selenium deficiency is white muscle disease (WMD), which manifests with limb stiffness, mioglobinuria, and difficulties in food uptake and swallowing, which often leads to aspiration pneumonia (McCann and Ames 2011).

6.2.2 High Levels of Selenium in Animals

High concentrations of Se in males lead to a decrease in the number of sperm cells as well as an increase in the number of improperly shaped sperm. Other typical symptoms are changes in sperm motility indicators (progression or forward velocity), testicular hypertrophy, changes in the female reproductive cycle in rats, and changes in the menstrual cycle (anovulation, short luteal and follicular phases) in monkeys (Cukierski et al. 1989). In pregnant women who drank water with a chronically increased dose of Se, a slightly increased number of spontaneous abortions were observed, although recent studies have not proven that a surplus of Se could cause any birth defects in humans or other mammals. In people exposed to Se dust and selenium compounds in workplace air, dizziness, fatigue, and irritation of the mucous membranes, and in extremal cases also accumulation of fluid in lungs (pulmonary edema) and severe bronchitis, were observed (ATSDR 2003).

6.2.3 Toxicokinetics and the Effects of Selenium in Wildlife

According to the amount of consumed Se, clear differences in its distribution are observed. At a Se deficiency, firstly it is incorporated into specific proteins (such as selenoprotein P, 5′-thyronin deiodinase). Next, Se is delivered to non-specific proteins. The brain, endocrine glands, and reproductive organs are the first to accumulate selenium before the liver, heart, and skeletal muscles. For this reason, in a Se deficiency, the discrepancies refer to these tissues and organs first (Behne et al. 1996). The highest amounts of selenium accumulate in the cortical part of the kidneys, pancreas, pituitary, and liver, but a lot of selenium is also transferred to hair, feathers, and horns (Daun and Akesson 2004). The organs in which the highest concentrations of Se are found are the kidneys, as they produce glutathione peroxidase (GSH-Px) for blood plasma (Zachara et al. 2006).

In a proper supply of selenium in an organism, its concentration in the liver and kidneys is higher than in the other organs. It is estimated that in humans, about 30% of the total Se pool is located in the liver, about 15% in the kidneys, 30% in the muscles, and 10% in blood plasma (WHO/FAO 2002). However, in mammals, significant differences in these values are observed (Whanger 1996).

The concentration of selenium in bird tissues depends on age, health, diet, presence of metals, and many other factors. The highest concentrations of Se are observed in the tissues of piscivorous birds and the lowest in herbivorous birds. Middle levels are noted in omnivorous birds (Mora and Anderson 1995). In birds, a deficiency of Se contributes to a decrease in the reproductive potential and immunocompetence, which results in an increased susceptibility to numerous infections. However, too high a concentration of Se is the cause of many illnesses that sometimes lead to death, which also correlates with the size of the population. The most well-known case of wildfowl selenium intoxication happened in Kesterson Reservoir (located on the Kesterson National Wildlife Refuge) in California in the 1980s (Ohlendorf 1989, 2002). Reproductive disorders and high mortality rates of the birds were observed. An excess of Se in the diet of female birds during the period just before egg-laying can result in the transfer of harmful levels of Se to the eggs or other tissues. This incident has shown a close relationship between the transfer of Se from an aquatic habitat rich in this element to the vertebrate organisms that feed in such habitats. In aquatic ecosystems, inorganic Se is rapidly assimilated by primary producers (bacteria, fungi, algae, and plants) and is transformed into organic selenium compounds (Ohlendorf 1989, 2002).

In nature, Se occurs in two different chemical forms that differ in toxicity to birds. The four common oxidation states are selenide (−2), elementary Se (0), selenite (+4), and selenate (+6). Elemental Se is virtually insoluble in water and presents little risk to the birds. Both selenite and selenate are toxic to the birds, but organic selenides pose the greatest hazard. Among the organic selenides, selenomethionine has been shown to be highly toxic to birds and to be the form most likely to harm wild birds, as it results in high bioaccumulation of Se in their eggs (Golubkina and Papazyan 2006; Ohlendorf and Heinz 2011a, b). The negative consequences of an excess of Se in birds have been described by many authors (Heinz 1996; Eisler 2000; Hoffman 2002; Ohlendorf 2003). In Se-rich areas, this element may accumulate in plants and invertebrates, which may then become part of birds' diet and cause intoxication through bioaccumulation.

Literature offers various values as the highest Se level that does not cause any toxic effects in birds (no-observed-adverse-effect level, NOAEL) (Table 10.8). Lam et al. (2005) suppose that an estimated value of NOAEL for medium concentrations of Se in eggs is from 0.9 to 1.45 mg kg^{-1} dw, whereas Latshaw et al. (2004) did not note any effect of 2.05 mg kg^{-1} dose on the development of pheasant embryos. Other authors propose much higher NOAEL values for selenium (Table 10.8). In studies on mallard *Anas platyrhynchos*, an addition of 3.5 mg kg^{-1} of selenium (as seleno-DL-methionine) to fodder did not affect reproductive performance with the lowest Se level that caused a negative effect was 7 mg kg^{-1} (Stanley et al. 1996).

Table 10.8 Values of NOAEL (no-observed-adverse-effect level) and LOAEL (lowest-observed-adverse-effect level) for selenium

Species	Selenium form	Endpoint	NOAEL mg kg day^{-1}	LOAEL mg kg day^{-1}	References
Birds					
Mallard *Anas platyrhynchos*	Sodium selenite	Reproduction	0.5	1.0	Heinz et al. (1987)
	Selenomethionine	Reproduction	0.4	0.8	Heinz et al. (1989)
Screech owl *Otus asio*	Selenomethionine	Reproduction	0.44	1.5	Wiemeyer and Hoffman (1996) and Sample et al. (1996)
Black-crowned night heron *Nycticorax nycticorax*	Selenomethionine	Reproduction	1.8		Smith et al. (1988)
Osprey[a] *Pandion haliaetus*	Selenomethionine	Reproduction	0.44	1.5	Sample et al. (1996)
Great blue heron[a] *Ardea herodias*	Selenomethionine	Reproduction	0.40	0.8	Sample et al. (1996)
Wild turkey[a] *Meleagris gallopavo*	Selenomethionine	Reproduction	0.40	0.8	Sample et al. (1996)
Belted kingfisher[a] *Megaceryle alcyon*	Selenomethionine	Reproduction	1.8		Sample et al. (1996)
Great blue heron	Selenomethionine	Reproduction	1.8		Sample et al. (1996)
Mammals					
Lab mouse *Mus musculus*	Selenate	Reproduction	0.076	0.76	Schroeder and Mitchner (1971)
	Sodium selenite	Reproduction	0.46	4.6	Chernoff and Kavlock (1982)
Lab rat *Rattus norvegicus*	Potassium selenate	Reproduction	0.20	0.33	Rosenfeld and Beath (1954)
Long-tailed macaques *Macaca fascicularis*	L-Selenomethionine	Reproduction	0.025		Tarantal et al. (1991)

[a]Estimated wildlife

Hoffman (2002) in his field studies on two species of wading birds has demonstrated that even a high mean concentration of Se in the water, reaching 190 μg L^{-1}, did not translate into discrepancies in their reproduction. Biochemical indicators in the liver as well as the weight of chick livers did not indicate a toxic activity of selenium, yet the different sensitivity of the examined species to a particular concentration of Se was observed. These studies suggest that the lowest adverse effect level (LOAEL) of selenium, which is already dangerous for health, may vary across the different species of birds. This relationship results from the differences in earlier life history, habitat interactions, and other factors (Table 10.8).

6.3 Bioaccumulation of Selenium in Wildlife

In environmental studies concerning biomonitoring, the measurement of selected elements is mostly performed using internal organs, body fluids, and the hair/feathers of animals typical for the particular habitats (Kalisińska and Salicki 2010; Jarzyńska and Falandysz 2011). The concentrations of Se in animal tissues show a tendency to reflect Se levels in the food consumed from the different habitats, particularly when the diet includes natural ingredients (Heinz et al. 1989; Stowesand et al. 1990). Ecotoxicologists for years have been evaluating and indicating the most useful animal species and types of biological samples which could be used in bioindication of environmental Se levels.

6.3.1 Selenium in the Soft Tissues of Endothermic Vertebrates

Tables 10.9, 10.10, 10.11, and 10.12 show various data concerning the concentrations of Se in biological materials from homeothermic vertebrates related to land ecosystems and inland waters. A proper interpretation of the data requires knowledge of the physiological concentrations of Se in the tissues and organs, values of selenium reflecting the geological background, and the effect of the species specificity. For most of the wild animal species, no data is available in this topic, although it has been developed for some groups of mammals and birds.

In European ruminants, the concentrations of selenium were most often analyzed in roe deer *Capreolus capreolus* and red deer *Cervus elaphus*, while in North America in mule deer *Odocoileus hemionus*, white-tailed deer *O. virginianus*, and elk *Alces alces*. The majority of studies concerned the liver, kidneys, and muscles. European ruminants, in comparison to American, were characterized by much lower concentrations of Se in the examined organs. Studies on Se content in cervids have been performed in Europe, including countries deficient in Se such as Poland and Norway, as well as in North America where the environment contains much higher amounts of this element. The highest level of selenium was found in North American herbivorous white-tailed deers and omnivorous raccoons *Procyon lotor* (Tables 10.9 and 10.10). In Europe the highest content of Se was noted in red deer livers in Poland

Table 10.9 Selenium concentrations in soft tissues and blood of ruminants and other herbivorous mammals

Species	Localization	Concentration	References
Liver (mg kg^{-1} dry wt)			
Red deer *Cervus elaphus*	Norway	0.39[a]	Vikøren et al. (2005)
		0.71[a]	Frøslie et al. (1984)
	Poland	0.34[a]	Pilarczyk et al. (2011c)
		0.23[a]	Jarzyńska and Falandysz (2011)
		0.36	Pilarczyk et al. (2009)
	Croatia	0.86[a]	Lazarus et al. (2008)
	Spain	0.31	Berzas Nevado et al. (2012)
		0.23 (M)	Reglero et al. (2009)
		0.16	Reglero et al. (2009)
Elk (or wapiti) *Cervus canadensis*	USA	0.25[a]	Fielder (1986)
Moose *Alces alces*	Sweden	0.89[a]	Galgan and Frank (1995)
	Norway	1.68[a]	Vikøren et al. (2011)
		1.50[a]	Frøslie et al. (1984)
		0.46–4.28[a]	Ytrehus et al. (1999)
	USA, Minnesota	1.07–2.43[a]	Custer et al. (2004)
	Canada, Yukon	5.71[a]	Gamberg et al. (2005a)
Roe deer *Capreolus capreolus*	Poland	0.18–0.35[a]	Pilarczyk et al. (2011c)
		0.62	Pilarczyk et al. (2009)
		0.57[a]	Pilarczyk et al. (2009)
		0.71	Pilarczyk et al. (2008)
		0.31[a]	Nowakowska et al. (2014)
	Germany	0.96[a]	Humann-Ziehank et al. (2008)
	Norway	0.61[a]	Vikøren et al. (2011)
Reindeer *Rangifer tarandus*	Norway	0.75[a]	Vikøren et al. (2011)
		1.79[a]	Frøslie et al. (1984)
	Greenland	0.90[a]	Aastrup et al. (2000)
Mule deer *Odocoileus hemionus*	USA, Washington	0.43[a]	Fielder (1986)
	USA	2.29[a]	Zimmerman et al. (2008)
White-tailed deer *Odocoileus virginianus*	USA	0.86[a]	Brady et al. (1978)
		0.68[a]	McDowell et al. (1995)
		2.89[a]	Zimmerman et al. (2008)
		0.29[a]	Sleeman et al. (2009, 2010)
Pronghorn *Antilocapra americana*	USA	0.40[a]	Dunbar et al. (1999)
		0.43–0.99[a]	Stoszek et al. (1980)
Mountain goat *Oreamnos americanus*	USA	0.07[a]	Fielder (1986)
Bighorn sheep *Ovis canadensis*	USA	0.57[a]	Cox (2006)
European hare *Lepus europaeus*	Croatia	0.51(P)[a]	Linšak et al. (2014)
		1.10[a]	Linšak et al. (2014)
	Poland	0.27[a]	Drozd et al. (2015)
		0.84[a]	Dębski et al. (2005)

(continued)

Table 10.9 (continued)

Species	Localization	Concentration	References
Kidneys (mg kg^{-1} dry wt)			
European hare	Croatia	2.71 (P)[a]	Linšak et al. (2014)
		2.80[a]	Linšak et al. (2014)
Red deer	Spain	2.60	Berzas Nevado et al. (2012)
Roe deer	Poland	2.18[a]	Nowakowska et al. (2014)
		3.09	Pilarczyk et al. (2008)
		2.99	Pilarczyk et al. (2009)
		2.72	Pilarczyk et al. (2009)
Skeletal muscle (mg kg^{-1} dry wt)			
Red deer	Poland	0.15[a]	Jarzyńska and Falandysz (2011)
	Croatia	0.19[a]	Lazarus et al. (2008)
	Spain	0.12	Berzas Nevado et al. (2012)
	Czech Republic	0.058[a]	Kursa et al. (2010)
		0.13[a]	Kursa et al. (2010)
White-tailed deer	USA	0.14[a]	Ullrey et al. (1981)
		0.25[a]	Brady et al. (1978)
Reindeer	Greenland	0.37[a]	Aastrup et al. (2000)
European hare	Croatia	0.43 (P)[a]	Linšak et al. (2014)
		0.40[a]	Linšak et al. (2014)

P polluted area, *M* mine
[a]Values were converted from wet weight into dry weight

(Pilarczyk et al. 2009) but slightly less than in the studies by Vikøren et al. (2005) in west Norway (Table 10.9).

Bioaccumulation of trace elements depends on many factors such as sex, age, and trophic level in a food chain. The results of studies on the dependency between selenium level and sex of the animals were ambiguous in the analyzed species. In an examination of roe deer livers from Poland, no significant differences were found between males and females in Se concentration (Pilarczyk et al. 2011a). This lack of differences between the sexes was also observed in other species, including ungulates (wild boar *Sus scrofa*) and carnivores, for example, in the domestic dog *Canis lupus f. domestica* and polar bear *Ursus maritimus* (Nicpoń et al. 2005; Rush et al. 2008; Pilarczyk et al. 2010b). In contrast to those works, Millán et al. (2008) showed significant differences in the concentrations of Se in the liver between males and females in the red fox *Vulpes vulpes* and Egyptian mongoose *Herpestes ichneumon* from Spain, as well as Vikøren et al. (2005), who analyzed hepatic concentrations of Se in mature Norwegian red deer.

In the case of free-living birds, not many such studies on this topic have been performed. Pilarczyk et al. (2012) in their analysis of marine ducks (velvet scoter *Melanitta fusca*, common scoter *M. nigara*, and long-tailed duck *Clangula hyemalis*), wintering in the south coast of the Baltic Sea, did not find any significant differences between selenium concentrations in the liver, kidneys, lungs, or heart

Table 10.10 The content of selenium in selected tissues of omnivores

Species	Localization	Concentration	References
Liver (mg kg^{-1} dry wt)			
Wild boar *Sus scrofa*	Spain	0.84	Berzas Nevado et al. (2012)
		0.45 (M)	Reglero et al. (2009)
		0.59	Reglero et al. (2009)
	Poland	0.68[a]	Pilarczyk et al. (2010b)
		0.86[a]	Jankowiak et al. (2015)
Raccoon *Procyon lotor*	USA, Illinois	7.06[a]	Levengood and Hubert (2001)
	Canada	9.24[a]	Wren (1984)
	USA, East, Central Michigan	7.56[a]	Herbert and Peterle (1990)
	USA, New York	3.17[a]	Valentine et al. (1988)
	USA, California (Kesterson)	14.52–34.65[a]	Clark et al. (1989)
	USA, Volta	1.69	Clark et al. (1989)
Kidneys (mg kg^{-1} dry wt)			
Raccoon	USA, Illinois	7.28[a]	Levengood and Hubert (2001)
	Canada	7.60[a]	Wren (1984)
	USA, New York	12.32[a]	Valentine et al. (1988)
Wild boar	Poland	5.45[a]	Pilarczyk et al. (2010b)

P polluted area, *M* mine
[a]Values were converted from wet weight into dry weight

between males and females of the mentioned species. An analogous conclusion was made by Conover and Vest (2009) in comparison studies on the livers of males and females of the black-necked grebe *Podiceps nigricollis* from Great Salt Lake (Utah, USA).

Recent studies on the relationships between the age of wild mammals and Se concentrations in their organs were also ambiguous. For example, McDowell et al. (1995) stated that age made a significant difference in the content of selenium in the kidneys of white-tailed red deer, with the animals younger than 12 months characterized by the lowest concentrations of selenium. Also Vikøren et al. (2005) found the lowest hepatic Se concentrations in the youngest group of Norwegian red deer. A similar tendency was observed by Pilarczyk et al. (2010b) in studies on Polish wild boar—the individuals under 1 year old were characterized by higher concentrations of selenium than the older animals. The lower concentration of selenium in the livers of the youngest ungulates was most probably caused by their faster metabolism, which contributed to the formation of larger amounts of free radicals and neutralized by Se released by the liver. In a representative of predators (Eurasian otter, *Lutra lutra*), a significant difference in Se concentration was found between young and adult individuals in the kidneys—higher values were typical for adults, yet hepatic concentrations of this element were similar (Kang et al. 2015). In contrast to the above, Pilarczyk et al. (2011a) and Jankowiak et al. (2015), in studies on ungulates (roe deer and wild boar) from Poland, where a deficiency of selenium in the environment is noted, did not find any dependence between the age of the animals

Table 10.11 The concentration of selenium in selected tissues of carnivores

Species	Localization	Concentration	References
Liver (mg kg^{-1} dry wt)			
Red fox *Vulpes vulpes*	Poland	0.88	Pilarczyk et al. (2011)
	USA, Central New York	1.90	Valentine et al. (1988)
Eurasian otters *Lutra lutra*	South Korea	1.90	Kang et al. (2015)
	England and Wales	6.15	Walker et al. (2010)
	England and Wales	6.92	Walker et al. (2011)
American mink *Neovison vison*	Canada, Yukon	4.62[a]	Gamberg et al. (2005a)
	Canada, British Columbia	2.24	Harding et al. (1998)
	Norway	1.50	Norheim et al. (1984)
	Poland	2.40	Brzezinski et al. (2014)
River otter *Lontra canadensis*	Canada, British Columbia	6.13	Harding et al. (1998)
Wolverine *Gulo luscus*	Canada, British Columbia	6.28	Harding (2004)
Kidneys (mg kg^{-1} dry wt)			
Red fox	Poland	2.36	Pilarczyk et al. (2011b)
	USA, Central New York	5.50	Valentine et al. (1988)
Eurasian otter	South Korea	3.40	Kang et al. (2015)
American mink	Canada, Yukon	8.28[a]	Gamberg et al. (2005a)
	Canada, British Columbia	4.00	Harding et al. (1998)
	Poland	4.92	Brzezinski et al. (2014)
American marten *Martes americana*	Canada, British Columbia	<4.00	Harding (2004)

[a]Values were converted from wet weight into dry weight

and the concentration of selenium in their organs. Between the predators, a connection between Se in the liver and age was analyzed in the Canadian American mink *Neovison vison*, and no significant relationship was found (Gamberg et al. 2005a).

Stussy et al. (2000), basing on the results of studies on female elk aged from 1 to 23 years, denied the usefulness of hepatic Se measurements as a good indicator of this element's status in the organism. The authors did not note any relationship between liver Se concentration and the age of the animals, as well as no dependence between Se content and the condition and progression of pregnancy or lactation. The authors claim that the total pool of selenium in the liver did not fully reflect the level of the bioactive forms of this element available for the biosynthesis of glutathione peroxidase and other selenium-dependent enzymes. Moreover they indicated that a low concentration of Se in the blood may occur with either a low or high content of selenium in the liver.

Some studies have indicated that one of the relevant factors determining the concentration of Se in wild ungulates may be the season. Such studies were performed in Poland in roe deer and red deer showing selenium deficiencies during winter and spring in all of the sampled deer (Pilarczyk et al. 2008, 2009). An optimal concentration of hepatic Se was found only during autumn and in about 30% of the

Table 10.12 The concentration of selenium in selected soft tissues of birds

Species	Localization	Concentration	References
Liver (mg kg^{-1} dry wt)			
Common merganser *Mergus merganser*	Poland	3.08	Kalisińska et al. (2014b)
	Canada, Ontario	9.7	Scheuhammer et al. (1998)
Bald eagle *Haliaeetus leucocephalus*	USA, Alaska islands	10.2	Stout and Trust (2002)
Black-tailed godwit *Limosa limosa*	France	16	Lucia et al. (2012)
Great cormorant *Phalacrocorax carbo*	Japan	7.3	Nam et al. (2005)
Mallard *Anas platyrhynchos*	Japan	3.4	Nam et al. (2005)
Spot-billed duck *Anas poecilorhyncha*	Japan	2.3	Nam et al. (2005)
Pintail *Anas acuta*	Japan	23	Nam et al. (2005)
Common teal *Anas crecca*	Japan	2.3	Nam et al. (2005)
Common loon *Gavia immer*	Canada, Ontario	15	Scheuhammer et al. (1998)
Eurasian coot *Fulica atra*	Spain	1.19 (P)[a]	Taggart et al. (2006)
Mallard	Spain	1.32 (P)[a]	Taggart et al. (2006)
Gadwall *Anas strepera*	Spain	1.25 (P)[a]	Taggart et al. (2006)
Common pochard *Aythya ferina*	Spain	1.25 (P)[a]	Taggart et al. (2006)
Red-crested pochard *Netta rufina*	Spain	1.12 (P)[a]	Taggart et al. (2006)
Western swamphen *Porphyrio porphyrio*	Spain	0.59 (P)[a]	Taggart et al. (2006)
Bufflehead *Bucephala albeola*	Canada	10.35	Braune and Malone (2006)
	USA	5.30	Michot et al. (1998)
	USA	32.1	Custer and Custer (2000)
Common goldeneye *Bucephala clangula*	Canada	7.3–13	Braune and Malone (2006)
	USA	16.0–36.2	Custer and Custer (2000)
Canvasback *Aythya valisineria*	USA	20	Custer and Custer (2000)
Lesser scaup *Aythya affinis*	USA	21.7	Custer and Custer (2000)
Black-capped chickadee *Poecile atricapillus*	USA, Alaska	4.2	Handel and Hemert (2015)
Great tit *Parus major*	China, Beijing	4.17	Deng et al. (2007)

(continued)

Table 10.12 (continued)

Species	Localization	Concentration	References
Greenfinch *Chloris chloris*	China, Beijing	3.46	Deng et al. (2007)
Cliff swallow *Hirundo pyrrhonota*	USA, Arizona	3.86	Estrada and Maughan (2000)
Red-winged blackbird *Agelaius phoeniceus*	USA, Arizona	12.30	Estrada and Maughan (2000)
Western kingbird *Tyrannus verticalis*	USA, Arizona	6.86	Estrada and Maughan (2000)
Kidney (mg kg^{-1} dry wt)			
Common merganser	Poland	2.32	Kalisińska et al. (2014)
	Canada, Ontario	8.50	Scheuhammer et al. (1998)
Black-tailed godwit	France	11.0	Lucia et al. (2012)
Bald eagle	USA, Alaska islands	13.1	Stout and Trust (2002)
Great cormorant	Japan, Izumi	9.5	Nam et al. (2005)
Mallard	Japan, Izumi	4.9	Nam et al. (2005)
Spot-billed duck	Japan, Izumi	4.3	Nam et al. (2005)
Pintail	Japan, Izumi	16.0	Nam et al. (2005)
Common teal	Japan, Izumi	4.1	Nam et al. (2005)
Common loon	Canada, Ontario	15.0	Scheuhammer et al. (1998)
Great tit	China, Beijing	5.47	Deng et al. (2007)
Greenfinch	China, Beijing	5.5	Deng et al. (2007)
Muscle (mg kg^{-1} dry wt)			
Common merganser	Poland	0.54	Kalisińska et al. (2014)
	Canada, Ontario	1.80	Scheuhammer et al. (1998)
Black-tailed godwit	France	3.20	Lucia et al. (2012)
Bald eagle	Aleutian Islands, Alaska	12.87[a]	Burger et al. (2012)
Great cormorant	Japan, Izumi	1.80	Nam et al. (2005)
Mallard	Japan, Izumi	1.10	Nam et al. (2005)
Spot-billed duck	Japan, Izumi	2.30	Nam et al. (2005)
Pintail	Japan, Izumi	3.00	Nam et al. (2005)
Common teal	Japan, Izumi	1.10	Nam et al. (2005)
Common loon	Canada, Ontario	2.80	Scheuhammer et al. (1998)
Great tit	China, Beijing	1.47	Deng et al. (2007)
Greenfinch	China, Beijing	2.91	Deng et al. (2007)

P polluted area, *M* mine
[a]Values were converted from wet weight into dry weight

examined red deers (Pilarczyk et al. 2011a). The lower level of selenium in animals that manifested strongly in particular seasons is probably the effect of the limited period of availability of selenium-rich foods such as mushrooms. In roe deer, in each of the analyzed organs (liver, kidneys, lungs, heart), the highest concentrations of selenium were noted in spring and the lowest in autumn and winter (Pilarczyk et al.

2011a). This seems to have a biological explanation. The autumn period is a time of increased food intake and intensive metabolic changes related to the energetic reserve storage in adipocytes for winter.

According to Pollock (2005), the biochemical criteria used to diagnose the presence of a selenium deficiency based on hepatic selenium levels in game animals are as follows: below mg kg^{-1} dw, deficiency; 0.6–0.88 mg kg^{-1} dw, marginal level; and above 0.88 mg kg^{-1} dw, optimal level. In studies by McDowell et al. (1995) in white-tailed deer in South Florida (USA), a low concentration of selenium was found in 13% of liver samples (<0.25 mg kg^{-1} dw) and in 36% of kidney samples (<3.0 mg kg^{-1} dw). This situation was caused by a limited availability of Se-rich food at that time. The situation is different for the hare. Drozd et al. (2015) found a higher Se level in hare livers in winter, during which a diversified diet seems to be quite unavailable.

In wild boar, Pilarczyk et al. (2010b) noted the highest hepatic concentration of Se in spring and the lowest in autumn. The differences were statistically significant. In the kidneys, the highest concentration was noted in summer and was significantly higher in comparison to the spring and autumn periods. This situation shows that wild boar consumes, apart from forest and meadow plants, also field crops (corn, potatoes, cereals) as well as animal feed. For this reason, wild boar feed is more diversified during the whole year than in roe and red deers (Pilarczyk et al. 2010b).

One of the most interesting research problems is the analysis of relationships between Se concentrations in the different tissues and organs. In wild land mammals and birds, the most commonly examined organs are the liver and kidneys and less frequently the muscles, lungs, heart, and gonads. The presence of a correlation between selenium content in the particular organs and tissues of free-ranging animals has not been unambiguous and not always statistically confirmed. For example, a positive correlation between Se levels in the liver and kidneys has been found in ungulates (wild boar and roe deer) from Poland (Pilarczyk et al. 2010b; Nowakowska et al. 2014), yet no such correlation was found in foxes from the same country (Pilarczyk et al. 2011a). Moreover, in the roe deer and fox, a positive and statistically significant relationship between selenium levels in two other pairs of organs, liver-lungs and liver-heart, has been found (Pilarczyk et al. 2011a; Nowakowska et al. 2014).

In juvenile ducks from the Kesterson Reservoir in California, a relationship between Se content in the muscles and the liver was observed ($r = 0.67$) (Ohlendorf et al. 1990).

McDowell et al. (1995) suppose that concentrations of selenium in the kidneys of red deer lower than 3.0 mg kg^{-1} dw indicate a deficiency. Using the criteria for roe deer from Poland, Pilarczyk et al. (2009) also showed a deficiency of this element in the kidneys, mostly during the summer period (87.5%) and less in autumn (40.9%).

In the herbivorous European hare, *Lepus europaeus* in Croatia and Poland, a deficiency of this element was shown in the both countries, with the mean concentration between 0.08 and 0.33 mg kg^{-1} ww and the lowest concentration in the individuals from Poland (Dębski et al. 2005; Drozd et al. 2015; Linšak et al. 2014) (Table 10.9).

In predator mammals, depending upon the species, diet, and place of origin, differences in hepatic Se levels are also present (Table 10.11).

According to Puls (1994), in canids when the Se concentration in the liver does not exceed 0.3 mg kg^{-1} ww, a deficiency of this element can be declared, while optimal values are placed between 0.50 and 1.50 mg kg^{-1} ww. In the Arctic fox *Vulpes lagopus* from the Canadian Arctic and Svalbard (Norwegian archipelago in the Arctic Ocean), about 0.8 and 2.7 mg Se kg^{-1} ww, respectively, was observed in the livers, which is classified as an optimal value for the first population and visibly raised for the second (Prestrud et al. 1994; Hoekstra et al. 2003). In comparison to the Arctic fox, in red foxes from central and southern Europe, the hepatic Se concentrations turned out to be lower. In individuals from Poland, where there is a deficiency in environmental selenium supply, the concentration was extremely low (<0.3 mg kg^{-1} ww), and in the red fox from Spain, it was optimal, reaching slightly more than 0.50 mg kg^{-1} ww (1.72 mg kg^{-1} dw) (Millán et al. 2008; Pilarczyk et al. 2011a).

In ecotoxicological studies on Se, birds play a significant role, including the species connected with freshwater habitats (Ohlendorf et al. 1988; Albers et al. 1996; Wu 2004; Paveglio and Kilbridge 2007). The natural level of selenium in the liver of birds ranges from 4 to 10 mg kg^{-1} dw (Ohlendorf 1989). Aquatic birds with a mixed diet (plants, insects, small crustaceans, and fish), such as the black-headed gull (*Chroicocephalus ridibundus*), consume more Se in an organic form (selenomethionines) and smaller amounts of Se as selenocysteines (Spallholz and Hoffman 2002).

The liver reacts quickly to Se intoxication in food (Heinz et al. 1990). Such a situation occurred in adult birds (coots, stilts, and ducks) from Kesterson Reservoir. Ohlendorf et al. (1990) demonstrated the difference in Se content according to the place and time of exposure. In the livers of water birds classified as selenium intoxicated, hunted directly in Kesterson Reservoir or in its neighborhood, but without any symptoms of intoxication, the content of this element was several times higher than normal ranging between 26 to 86 and 38 to 85 mg kg^{-1} dw (Ohlendorf et al. 1988; Wu 2004). This may be evidence of the adaptation of birds to high levels of this element in the environment and in the diet. Experimental studies on mallard *Anas platyrhynchos* indicated that with Se concentrations higher than 10 mg kg^{-1} dw, disturbances in the reproductive process may be expected, and above 33 mg kg^{-1} dw can adversely affect health and survival (Heinz et al. 1989; Heinz 1996). A comparative analysis of selenium concentrations in water bird livers from California (USA), in three species of ducks, mallard, northern shoveler *Anas clypeata*, and northern pintail *A. acuta,* has shown that hepatic Se background levels, respectively, reached 4.1, 8.1, and 5.5 mg kg^{-1} dw. All these species of ducks collect mixed food with different proportions of invertebrates and plants (both land and aquatic), while in another species from that area—American coot *Fulica americana*—which feeds mostly on algae, the background level turned out to be the lowest at 3.2 mg kg^{-1} dw (Paveglio and Kilbridge 2007). Mentioned authors suppose that values of hepatic Se background level may be diverse due to the diet.

For some time, interest in heavy metal and Se contamination in urban and suburban environments increased, requiring an appropriate selection of species to study with regard to their food preferences. In China (Western Mountains of Beijing), a study was performed on two settled passerine species (insectivorous great tit *Parus major*), seed- and fruit-eating greenfinch *Chloris chloris*, in which 11 elements including Se were measured in 10 different parts of the body (Table 10.12). In both species the highest (and similar) concentrations of Se were found in the kidneys and liver (about 5.5 and 4 mg kg^{-1} dw, respectively), with statistically significant differences in levels found only in the muscles and feathers. Clearly more selenium in the muscles and feathers was observed in the greenfinch in comparison to the insectivorous great tit (Deng et al. 2007). Because the concentration of Se in the pectoral muscle of the greenfinch exceeded 3 mg kg^{-1} dw (reflecting the background level), we may conclude that in Beijing and the surroundings of the Chinese capital city, an elevated level of selenium in the environment exists.

Ohlendorf and Heinz (2011a, b) have proposed the thresholds for bird tissues. For the liver and muscles of freshwater species, <10 and 1–3 mg Se kg^{-1} dw were established as concentrations that reflect the background level. Kalisińska et al. (2014) found neither hepatic nor muscle concentrations of Se exceeded background levels in common merganser *Mergus merganser* form Poland. Puls (1994) reported that an adequate level of Se in the muscle of poultry is 0.49–4.9 mg kg^{-1} dw. Between Polish common mergansers examined by Kalisińska et al. (2014), muscle values $\leq$0.5 mg kg^{-1} dw were noted in 37% of the analyzed birds, and the mean concentration (0.54 mg kg^{-1} dw) was close to the lower value of the adequate range. A background Se level in the avian kidney has not been clearly defined, but an adequate value for poultry ranges from 2.2 to 5.2 mg kg^{-1} dw (Puls 1994; Ohlendorf and Heinz 2011a, b). Kalisińska et al. (2014) found the Se concentration in the kidneys $\leq$2.2 mg kg^{-1} dw in 42% of the studied birds. Mean concentrations of hepatic and nephric Se in the piscivorous ducks were 3.1 and 2.3 mg kg^{-1} dw, respectively, and were 70–130% and 60–180% lower than analogous values for the nearby sea ducks (*Melanitta fusca, M. nigra*, and *Clangula hyemalis*) feeding on zoobenthos and wintering in the Pomeranian Bay (Pilarczyk et al. 2012). These birds nest in areas considered as selenium deficient (Scandinavia). In studies from other European countries (Leonzio et al. 1986; Lucia et al. 2012) not classified as Se deficient, mean concentrations of Se were several times higher than in the study by Kalisińska et al. (2014). In the liver, kidney, and muscles, the selenium levels were between the following respective ranges: 10–16, 7–18, and 3.2–6.7 mg kg^{-1} dw. In comparison to two piscivorous avian species from North America (Scheuhammer et al. 1998), the Polish common mergansers were characterized by much lower Se levels in all three types of tissues. In Canadian common merganser and common loon (*Gavia immer*), Se concentrations in the liver were 9.7 and 15 mg kg^{-1} d.w, in the kidneys 8.5 and 15 mg kg^{-1} d.w, and in the muscles 1.8 and 2.8 mg kg^{-1} dw, respectively. These values are higher than those found in Polish common merganser by 3–6 times, depending on the tissue and compared species.

In contrast to the liver, background Se levels in bird kidneys have not been clearly set, similarly to the proportion between the concentration of selenium in the liver and kidneys expressed as the liver/kidney ratio, although usually a significant correlation between Se levels in these organs is indicated. In birds from areas with an optimal Se content, nephric Se concentrations are usually slightly higher, similar to found in contaminated areas (Ohlendorf et al. 1988, 1990; Agusa et al. 2005; Deng et al. 2007). However in the piscivorous common merganser from eastern Canada, Scheuhammer et al. (1998) found higher concentrations of Se in the liver than in the kidneys, at 9.7 and 8.5 mg kg^{-1} dw, respectively (the L/K factor value: 1.14). In the same species located in European selenium-deficient areas, the content of this element in the liver and kidneys was three times lower than in those from Canada, and also the hepatic concentration was higher than the nephric: 3.08 and 2.32 mg kg^{-1} dw, respectively (Kalisińska et al. 2014). Apart from the liver and kidneys, Se is also measured in avian muscle. Background Se concentrations in birds muscles usually range from 1 to 3 mg kg^{-1} dw. It was found that there is a clear relationship between the concentration of Se in feed and its content in muscles.

Because changes in Se content in bird muscles progress slowly, they are not considered a good indicator of Se levels, either in the organism or in the environment (Ohlendorf and Heinz 2011b).

In contrast to water birds, in land birds from the passeriformes group, Se is much less frequently measured, but there are some reports on this topic from the USA and China (Estrada and Maughan 2000; Deng et al. 2007), for example, related to the red-winged blackbird *Agelaius phoeniceus* and western kingbird *Tyrannus verticalis* (mostly insectivorous species).

Although the concentration of Se in the avian liver depends on the amount contained in food, this organ is still not treated as a good estimator of the pathological condition of a bird (Hoffman et al. 1991). When birds consume Se-rich food, the level of this element quickly passes to the eggs, liver, and blood and slowly to the muscles. A similar situation occurs when birds change from a Se-rich diet to a diet with lower selenium content or when they migrate from a high-Se area to a Se-normal area (Ohlendorf et al. 2008). The study by Albers et al. (1996) has also shown that the concentration of selenium in the liver is 2–3 times higher than in the food, while in the kidneys, it is about 1.8 times higher.

In the study by Santolo et al. (1999), selenium bioconcentration factors for diet-blood and diet-eggs in the American kestrel *Falco sparverius* are 1.0 and 2.2, respectively.

Between many tissues, blood is in a small extent used in studies of Se content in birds because collection in free-ranging animals is quite complicated, while in ecotoxicological studies in this matter, a more important role is played by eggs.

6.3.1.1 Selenium in Avian Eggs

Because eggs, as one of bird's stages of life, are particularly sensitive to selenium, they are often used in biomonitoring studies mostly concerning water habitats and

wetlands (Ohlendorf et al. 2008). Selenium levels of 3 mg kg^{-1} dw in the bird egg are considered to be the threshold for concern for teratogenesis (Lemly 1993). Mean background concentrations of Se in eggs in freshwater and terrestrial birds have been established at <3 mg kg^{-1} dw (usually from 1.5 to 2.5 mg kg^{-1}). Generally in various species, Se concentrations in avian eggs range from roughly equivalent to about three or four times the concentrations in the diet of the female during the laying period (Ohlendorf 2003). It has to be underlined that in different species of birds, the concentrations of Se in eggs that would affect a decrease in the reproductive parameters of birds may strongly differ, as some species are able to regulate the amount of selenium transferred to the eggs or they are characterized by an increased tolerance to this element during embryonic development (Harding 2008; Ohlendorf et al. 2008). It seems that the species that show a high level of tolerance to Se in eggs include red-winged blackbirds from North America, with a threshold for reduced egg hatchability estimated at 22 mg kg^{-1} dw, while in other bird species, it ranges from 5 to 16 mg kg^{-1} dw (Harding 2008; Ohlendorf et al. 2008).

Like the concentration of Se in different internal tissues of the birds, a significant impact on the amount of Se in the eggs is exerted by the diet of females. Moreover, it has been recently shown that the concentration of this element in eggs correlates with Se concentrations in the mother's liver (Ackerman et al. 2016). In passerine birds in the USA (from the border of Arizona and California, where the habitat is rich in Se), quite high concentrations of Se were found in the eggs of five bird species, with higher levels found in the insectivorous species in comparison to the grain eaters (Estrada and Maughan 2000; Table 10.13). In comparison to the number of reports concerning the presence of Se in the eggs of birds that live in Se-rich and selenium-excessive habitats, not many analogous studies in medium and poor level habitats are available, which impedes making proper comparisons of the results obtained in this research field (Guitart et al. 2003; Ohlendorf and Heinz 2011a, b).

6.3.1.2 Selenium in Hair and Feathers

The content of selenium in animal hair may be successfully used to diagnose both a deficiency and a surplus of this element in the organism. The concentration of Se in human hair turned out to be proportional to the concentration of this element in the blood (Yang et al. 1989). Selenium in the hair or feathers is incorporated instead of sulfur into sulfuric amino acids (Wichert et al. 2002). Animal hair is a valuable research material due to its stable level of selenium (Dunnet and Lees 2003), the simple and noninvasive collection (no stress caused by blood sampling), and ease in storage (Wichert et al. 2002). In the case of free-ranging animals, hair for selenium measurements is used occasionally due to problems with obtaining material intravitally.

Background concentrations of Se in feathers range from 1 to 4 mg kg^{-1} dw but are usually <2 mg kg^{-1} dw (Ohlendorf and Heinz 2011b). Chemical analysis of feathers may deliver useful information about the exposure to pollutants consumed with food. However it has to be mentioned that different types of feathers from one

Table 10.13 Concentration of selenium in avian eggs

Species	Localization	Concentration (mg kg^{-1} dry wt)	References
Yellow-breasted chat *Icteria virens*	USA, Arizona	3.1	Mora (2003)
Yellow warbler *Setophaga petechia*	USA, Arizona	2.8	Mora (2003)
Bell's vireo *Vireo bellii*	USA, Arizona	1.93	Mora (2003)
Willow flycatcher *Empidonax traillii*	USA, Arizona	3.43	Mora (2003)
Common yellowthroat *Geothlypis trichas*	USA, Arizona	4.95	Mora (2003)
Black-throated gray warbler *Setophaga nigrescens*	USA, Arizona	3.8	Mora (2003)
Summer tanager *Piranga rubra*	USA, Arizona	2.4	Mora (2003)
Vermilion flycatcher *Pyrocephalus obscurus*	USA, Arizona	3.2	Mora (2003)
Song sparrow *Melospiza melodia*	USA, Arizona	2.77	Mora (2003)
Brown-headed cowbird *Molothrus ater*	USA, Arizona	2.3	Mora (2003)
Lesser goldfinch *Spinus psaltria*	USA, Arizona	2.1	Mora (2003)
Red-winged blackbirds *Agelaius phoeniceus*	British Columbia	0.89–9.9	Harding (2008)
	USA, Arizona	4.54	Estrada and Maughan (2000)
Cliff swallow *Hirundo pyrrhonota*	USA, Arizona	2.56	Estrada and Maughan (2000)
Verdin *Auriparus flaviceps*	USA, Arizona	2.9	Estrada and Maughan (2000)
Western kingbird *Tyrannus verticalis*	USA, Arizona	5.99	Estrada and Maughan (2000)

bird may be characterized by different selenium concentrations. Also in a feather itself, differences in levels of Se are possible: the highest concentration is usually found at the tip and the lowest at the base. For this reason feathers for analysis should be chosen very precisely. It is considered that feathers are not a good indicator of the current exposure of birds to Se, as the accumulation of this element takes place during the feather growth period, and not constantly (Burger 1993; Eisler 2000). The content of Se in feathers depends on the species and origin of birds (Table 10.14).

Table 10.14 Concentration of selenium in bird feathers

Species	Location	Concentration (mg kg^{-1} dry wt)	References
Golden eagle *Aquila chrysaetos*	USA	0.89	Harmata and Restani (2013)
Black-tailed godwit *Limosa limosa*	France	1.90	Lucia et al. (2012)
Black skimmer *Rynchops niger*	USA	1.22	Burger and Hochfeld (1992)
Song sparrow *Melospiza melodia*	USA, Arizona	1.20	Lester and Riper (2014)
Great tit *Parus major*	China, Beijing	2.17	Deng et al. (2007)
	Portugal	0.93	Costa et al. (2013)
Greenfinch *Chloris chloris*	China, Beijing	1.24	Deng et al. (2007)

6.4 Ecological Effects of Selenium

Selenium belongs to the group of trace elements, which are crucial for the proper functioning of terrestrial vertebrate organisms. In nature and biotas, Se may be present in inorganic and organic forms with diverse bioavailability. Vertebrates are characterized by different demands for this microelement in global areas of low, proper, and excessive amounts of selenium. A review study concerning the "soil to small mammal" selenium bioconcentration factor derived final mean and median factors of 0.35 and 0.16, respectively (Sample et al. 1998). In global ecotoxicological literature, many reports concern the effects of too high selenium levels in aquatic and soil habitats, as well as the interactions with organisms from different trophic levels.

The Se concentration in water, at which toxicity is observed, ranges widely and varies between organisms like algae, invertebrates, and vertebrates: 0.01–80, 0.07–200, and 0.09–82 mg Se L^{-1}, respectively (Maier et al. 1987). Environmental intoxication also concerns organisms that live on land. Relevant studies have indicated that Se mobilization is caused by earthworks from changing land use (Ohlendorf et al. 1988; Albers et al. 1996). In California National Park, 20% of water bird offspring developed abnormalities along with increased chick morbidity due to the flow of excessively polluted water from a nearby reservoir (Lenz and Piet 2009). Coal and crude oil combustion are a considerable source of Se contamination, as well as copper and lead ore smelting, and some specific branches of industry (fat processing, pharmacy, dyes etc.)

Clinical symptoms of Se deficiency in free-ranging animals are noted occasionally; however, it is suspected that some subclinical symptoms may be noted by woodsmen, veterinary doctors, and hunters. In European wild ungulates, including roe deer, red deer, elk (*Alces alces* in Eurasia), and fallow deer *Dama dama*, WDM may occur to a level, which impairs the ability to escape quickly from predators. This

disease occurs mostly between the 3rd and 6th weeks of life, where in such young individuals damage to the heart muscle may also be caused by the deficiency (Flueck et al. 2012).

In females with a deficiency in Se, milk production may decrease which in turn results in early weaning of offspring and added risk from predators. A deficiency of selenium may also manifest as a decrease in female fertility and a higher number of weak offspring. In males, it may reduce reproductive potential, which would result in discrepancies in the gender and age structure of the population (Flueck and Smith-Flueck 2008; Flueck et al. 2012). Moreover in males, due to a deficiency in this microelement, diarrhea, weight loss, weak growth, and antler deformations may take place. It was also shown that a deficiency of Se in free-ranging animals causes disturbances in bone mineralization and osteoblast activity, decrease of bone density, arthritis, improper teeth formation, premature tooth loss, as well as periodontal diseases. These various consequences of a selenium deficiency may together contribute to a decrease in the wild ruminant population size in a selected area (Hnilicka et al. 2004; Flueck and Smith-Flueck 2008; Flueck et al. 2012).

In other groups of free-ranging mammals (e.g., in representatives of omnivores, wild boar; carnivores, raccoon dog *Nyctereutes procyonoides*, red fox, American mink), a prolonged deficiency of Se influences the condition of the animals, litter size, embryo and fetal morbidity, placenta retention, decreased fetal growth rate, and delay in puberty onset (Flueck and Smith-Flueck 2008; Flueck et al. 2012). One of the reasons of a reduced population in some free-ranging animals may also be a decrease in their immunity caused by a lack of Se (Flueck et al. 2012). In wild boar, as in pigs, a deficiency of this element may be a cause of MHD (mulberry heart disease), as well as hepatosis diaetetica, while in sows it may cause premature fetal death due to impaired development, postparturitional placenta retention, and genital tract inflammations (Radostits et al. 2000). In Canidae (wolf, dog, foxes), a deficiency in selenium may be (as in dogs) a reason behind liver alimentary myopathy, muscle degeneration, tumors, subcutaneous endemas, shortness of breath, myocardial necrosis and kidney failure (Kuchan and Milner 1991; Green et al. 2001; Evans et al. 2004; Pilarczyk et al. 2010a, 2013).

In wild fowl, as in domestic fowl, a deficiency of Se may cause exudative diathesis and skeletal, stomachic and cardiac muscle degeneration (necrotic centers), increased morbidity, decreased fertility, weak feathering fibrosis and atrophy of the pancreas, as well as decreased digestive enzyme synthesis (Paton et al. 2002; Pappas et al. 2005).

Al-Dissi et al. (2011) in red deer, at liver Se concentrations reaching 2.7–8.97 mg kg^{-1} ww, found symptoms of intoxication characterized by myocardial necrosis, muscle mineralization, and heart fibroplasia, with impaired hoof development and necrosis. The skin over the antler pedicles had areas of erosion and ulceration extending to the bony cranium. Within the meninges and Virchow Robin's spaces, an inflammatory infiltrate composed of neutrophils, lymphocytes, plasma cells, and macrophages was present. The pyloric area of the abomasum had isolated areas of erosion and ulceration.

6.5 *Bioindicators and Biomarkers of Selenium in Ecotoxicological Studies*

Selenium is present in every tissue of mammals and accumulates mostly in the liver, kidneys, hair, and nails. About 30% of the total Se pool is located in the liver, 15% in the kidneys, 30% in muscles, and 10% in blood plasma (Navarro-Alarcón and López-Martínez 2000). The content of selenium in body fluids is usually low. Erythrocytes contain more Se than whole blood in total, wherein the content of Se in serum and blood plasma is the same. The ratio of Se in red cells to its content in blood plasma is 3:1 (Sager 1993).

In the evaluation of Se status, it is important to obtain data about the geochemical background and anthropological sources of Se located within the examined areas, and to develop so-called typical (physiological) values for the most important organs and tissues in ecotoxicological studies, in order to interpret the obtained results in the proper way. The present knowledge database in this area is lacking (Table 10.15). The difference between a necessary (physiological) and toxic dose of selenium is very little. Many authors claim that the content of selenium in blood plasma or in full blood does not reflect the real level of this element in the organism (Burk and Hill 1994; Breedlove et al. 2006). It is said that an interrupted conversion of thyroxine to triiodothyronine, glutathione peroxidase activity, and the ratio between liver and kidney Se content in homeothermic mammals are good markers of Se levels (Oh et al. 1976).

Some Se-biomarkers, such as the selenoproteins and particularly GPX3 and SEPP1, provide information about the functioning of the organism directly and are

Table 10.15 Levels of Se in animal organisms (mg kg^{-1} ww), according to Puls (1994)

Tissue	Animal group	Deficient	Marginal	Normal	High	Toxic
Kidney	Avian	0.1–0.4	0.4–0.5	0.5–1.2	1.5–5.2	–
	Bovine	0.18–0.4	0.4–1	1–1.5	2–2.5	2.5–8
	Canine	–	–	1–1.5	–	–
	Lapine	< 0.4	0.6–0.8	1–2	–	12
	Ovine	0.05–0.6	0.7–1.1	0.9–3	4–6	6–15
	Porcine	0.4–0.77	0.7–1.1	1.5–2.9	3–18	3.8–90
Liver	Avian	0.05–0.25	0.25–0.35	0.35–1	2–6	4–23
	Bovine	0.02–0.17	0.12–0.25	0.25–0.5	0.75–1.25	1.25–47
	Canine	0.1–0.3	0.3–0.5	0.5–1.5	–	–
	Caprine	0.01–0.1	0.1–0.2	0.25–1.2	–	–
	Cervid	–	–	0.25–1.4	–	–
	Lapine	<0.4	0.6–1	1–2	–	7
	Ovine	0.01–0.1	0.15–0.25	0.25–1.5	2–10	15–30
	Porcine	0.03–0.1	0.12–0.25	0.4–1.2	1.5–12	3–120
Muscle	Bovine	0.01–0.05	0.05–0.07	0.07–0.15	0.25–0.5	0.08–1.5
	Cervid	0.05–0.26	–	0.25–0.49	–	–
	Ovine	–	0.9–1.2	1–1.3	1.1–1.6	–

of value in identifying a nutritional Se deficiency and in tracking the responses to Se-treatment in deficient individuals (Combs 2015).

Pollock (2005) stated that the concentration of selenium in liver is a better indicator of its status in the organism in comparison to the kidneys, as liver is the main organ responsible for selenium homeostasis in an organism. Selenium is stored in hepatocytes where the synthesis and distribution of not only Se-GSH-Px and other enzymatic selenoproteins take place. In a selenium deficiency, the organism is emptied of Se reserves, and the reserves located in the liver are mobilized first (Georgieva 2005). However Hoffman et al. (1991) indicated that liver does not reflect the selenium level in an organism in a precise way due to the fact that the concentration of Se in the liver depends on the absorbed dose of selenium, the relatively quick process of Se concentration balancing in the liver (7–8 days), as well as short half-life period of Se in this organ (18.7 days). For these reasons, the liver should be treated as a medium-term indicator of Se levels in an organism. Oh et al. (1976) claim that the relative proportions between Se content in the kidneys and liver are very important. In the case of Se-poor fodder, a higher concentration of this element is found in the kidneys than in the liver. Inversely, in selenium-rich fodder, the hepatic Se concentration is higher than the kidneys.

For toxic Se levels in a selected area, some authors consider bird eggs (as well as fish muscle) as good indicators. Selenium concentration in the eggs reflects the unfavorable changes in the environment to a higher extent, as selenium is very easily transferred to eggs (Focardi et al. 1988), which makes them good indicators of this element (Ohlendorf et al. 2011) as selenomethionine readily accumulates in the protein of egg albumen. Reproductive impairment is considered to be the most sensitive indicator of selenium toxicity in birds (Ohlendorf 2003; Seiler et al. 2003). As reported by Ohlendorf et al. (2011) eggs are treated as good Se indicators, while the feathers are considered weak indicators (Ohlendorf and Heinz 2011a, b). Bird embryos are very sensitive to the toxic effects of Se, including the teratogenic activity on embryonic development, which in turn translates into a decreased number of chicks hatching (Janz et al. 2010).

Information about the environmental Se status may be obtained through studying samples of inanimate (soil, water, air) and active (tissues, body fluids) parts of the habitat. The most used biomarkers of selenium exposure in animal organisms are tissue samples. Wild-ranging animals, due to a full integrity with the environment, are a very good indicator of Se levels in ecosystems (Pilarczyk et al. 2010b).

For some time, interest in heavy metal and Se contamination in urban and suburban environments has been increasing, entailing a proper selection of species regarding their nutritional preferences. In homeothermic vertebrates (farm animals), selenium status is usually based on analyses of fresh blood samples. Unfortunately in free-ranging animals, there is almost no possibility to obtain fresh blood, so the level of Se is usually measured in the liver and kidneys and less often in the muscles, blood, brain, feathers (hair), eggs, and bones of hunted or dead animals (Tables 10.9, 10.10, 10.11, 10.12, 10.13, and 10.14).

Despite the good documentation on the usefulness of ducks for Se biomonitoring in aquatic habitats, not many reports concerning the concentration of Se in their

organisms are available outside of North America. Because of the wide spread of the species included into this group of birds (for instance, species belonging to *Anas*, *Aythya*, and *Mergus* genera) and usually the large number of individuals, it is possible to perform studies of a general biological and ecotoxicological character to a much higher extent and to do different comparisons of results between birds from areas rich and poor in selenium. In comparison to water birds, not many studies on samples obtained from typically land birds, for example, Passeriformes, are available, even though they are considered as potentially good indicators of selenium levels in the environment (Den et al. 2007; Costa et al. 2013).

In China (in the Western Mountains of Beijing), a study was conducted on two settled passerine species (the insectivorous great tit *Parus major* and the herbivorous greenfinch *Chloris chloris*), in which concentrations of 11 elements (including Se) were measured in 10 of their body parts (Table 10.12). In both species the highest and similar concentrations of selenium were found in the kidneys and liver (about 5.5 and 4 mg kg^{-1} dw, respectively), and significant differences in Se level were noted only in the muscles and feathers. Clearly more Se was present in the muscles and less in the feathers of the greenfinch (Tables 10.12 and 10.14) than the insectivorous great tit (Deng et al. 2007). As the concentration of Se in the pectoral muscle of the greenfinch exceeded 3 mg kg^{-1} dw (reflecting the background level), we may conclude that in Beijing and its surroundings, the level of Se in the environment is elevated (Table 10.12). To ease identification and systematic classification, the longevity (to evaluate the effects of the environment over time) and mobility (to monitor the level of pollution over a wider area) of birds are great advantages as bioindicators. If a species lives in a tight association with a specific area, it can reflect the pollution in that environment more specifically (air, food, water) (Ohlendorf and Heinz 2011a, b).

Typical land birds, such as tiny Passeriformes, can successfully be used to monitor the environment. They are considered good biomonitors of Se content as they occur commonly, are ubiquitous and abundant, and are eager to live in birdhouses, making it relatively easy to obtain study material from living individuals (blood, feathers, feces, and eggs). Moreover, the size of the population may be easily monitored (Costa et al. 2013).

As reported by Hobson et al. (2000), the use of free-ranging bird chicks in biomonitoring has two main advantages. Firstly, it avoids the consequences of bioaccumulation related to aging, as the exposure time is short and similar in all individuals from the same nest or colony. Secondly, all the chicks are fed by the parents with food collected from the surroundings and rich in local nutrients and contaminants. According to Ohlendorf and Heine (2011a, b), feathers are not a good indicator of selenium content.

In many works on selenium status in organisms of homeothermic mammals, studies mostly focused on evaluating the level of Se in the liver and kidneys, as well as often defining the mutual relationships in the obtained results (Pilarczyk et al. 2010a, b, 2011a; Flueck et al. 2012). However, as it has been shown, a proper evaluation of Se status should be based on the analysis of Se content in several different tissues, like the liver and kidneys as well as the muscles and/or lungs.

Moreover in such an evaluation, age, sex, and season should be taken into consideration (Garcia et al. 2000). Unfortunately such a multifaceted analysis is very rarely possible to conduct in free-ranging animals, as it is very difficult to obtain enough research material from the same year and the same area (region) to perform a reliable statistical interpretation of the results, representing different age and sex groups and in a particular season.

Wild ruminants from cervid group like the moose/elk, red deer, roe deer, mule deer, white-tailed deer, as well those of the Bovidae family, such as pronghorn and bighorn sheep, are considered good bioindicators of selenium levels in the environment. From the carnivores such as a role may be played by the fox, mink, and raccoon.

The concentration of Se in males and females living in the same area may differ. No unambiguous results of studies are available that would describe the dependence between sex and the content of selenium in the body. For this reason future experiments should regard both males and females settling in the same area (Nicpoń et al. 2005; Pilarczyk et al. 2010a; Rush et al. 2008; Pilarczyk et al. 2012). Also, data on the dependence of age and Se content are not yet clear enough. (Pilarczyk et al. 2010b, 2011a; Jankowiak et al. 2015; Vikøren et al. 2005; McDowell et al. 1995). Therefore in environmental studies, we should choose animals with regard to the particular age groups. In most of the present publications about selenium levels in animal organs, no such data is provided. With a low number of examined individuals, the results may be distorted due to any large interindividual variability. The evaluation of environmental levels of Se, as well as its status in homeothermic animals, should be performed on the basis of a population.

7 Conclusions

Wild ruminants belonging to the *Cervidae* family, like the moose, red deer, roe deer, mule deer, white-tailed deer, and elk, as well those in the *Bovidae* family, like pronghorn and bighorn sheep, are considered to be good bioindicators of selenium levels in the environment. From the carnivores, such a role may be played by the fox, mink, and raccoon.

In birds, many species of ducks (e.g., *Anas*, *Aythya*, and *Mergus* genera) and Passeriformes (e.g., greenfinch, great tit, song sparrow) may be used as selenium biomonitors. Typical land birds, such as tiny passerines, may successfully be used to monitor the environment.

From the European ruminants, the concentration of selenium has most often been analyzed in roe deer and red deer, while in North America in mule deer, white-tailed deer, and elk, using mostly samples from the liver, kidneys, and muscles. European ruminants, in comparison to North American, are characterized by much lower concentrations of selenium in analyzed organs.

The status of selenium in free-ranging homeothermic organisms should be evaluated mostly in the liver and kidneys. In ecotoxicological studies on Se, the

liver and kidneys should primarily be used and to a lesser extent the muscles, eggs and feathers. It is necessary to assess the mutual relationships between these concentrations. Also age, sex and season should be taken into account. In an evaluation of selenium status, it is particularly important to obtain data about the geochemical background and anthropogenic sources of selenium located in the examined area, to ensure a proper interpretation of the results.

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Chapter 11
Zinc, Zn

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Abstract Zinc (Zn) is an essential trace element having a wide range of biological roles. The presented data concern Zn concentrations in various organs of terrestrial mammals and birds. In studies on terrestrial mammals, a measurable response to Zn pollution is exhibited by canids common in natural and seminatural habitats, including the red fox, raccoon, American mink, otters, and ungulates, such as the white-tailed deer, reindeer, red deer, and wild boar. Birds are used as bioindicators because they are abundant and widely distributed, have long lifespans, and feed at different trophic levels and are often the top consumers. At the same time, they are more sensitive to Zn contamination than other vertebrates and therefore seem to be better bioindicators. Nestling passerines are potential good biomonitors for Zn pollution because Zn is ingested in a clearly defined time period and originates from a limited parental foraging area. Zinc concentrations in the tissues of mammals and birds depend both on biological factors (e.g., age, physiological condition, animal species, sex, and age) and environmental factors (e.g., supply of Zn in the diet). Long-term bioindication research conducted on the organs and tissues of mammals and birds, as well as noninvasive sampling of eggs and feathers, indicates the usefulness of this type of material for evaluating the state of the environment.

1 Introduction

Zinc (Zn) is one of the most common elements in the Earth's crust. It is found in the air, soil, and water and is present in all foods. This essential trace element plays catalytic, structural, and regulatory roles in more than 300 Zn-metalloenzymes identified in biological systems. It plays an important role in the polymeric organization of macromolecules like DNA and RNA, protein synthesis, cell division, and

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stability of biological membranes through protection against oxidative injury. Physiologically, Zn is vital for growth and development, sexual maturation and reproduction, dark vision adaptation, olfactory and gustatory activity, insulin storage and release, and for a variety of host immune defenses. Improvement in sperm production and fertility has been achieved following the supplementary feeding of Zn. Crop residues, which form the bulk of rations in India, are deficient in Zn, and deficiency may lead to male reproductive failure in domestic livestock.

For years, ecotoxicologists have tried to assess and identify the most useful animal species and types of biological samples that could be used in the bioindication of environmental levels of Zn. The herbivorous species, which often forage across very large territories, are not suitable for determining the specific source of a toxic hazard. It seems that species such as the red fox, which adapts to different environmental conditions and ranges within small territories of 0.5 km^2 and less, would be more suitable for biomonitoring research. Another species that seems appropriate in this regard is the American mink, a predatory mammal in which Zn concentrations in the kidney, liver, and bone are similar to those in other mammalian species.

2 General Properties of Zinc

Zinc is an essential trace element appearing in Group II-B of the periodic table, with atomic number 30, atomic weight 65.38, melting point 419.5 °C, and boiling point 908 °C and is a relatively soft metal with a density of 7.13 g cm^{-3} (Adriano 2001). As a fairly active element, Zn dissolves in both acids and alkalis. It has two common oxidation states, Zn (0) and Zn (+2). Zinc forms a variety of compounds such as zinc chloride, zinc oxide, and zinc sulfate (ATSDR 2005). This element has five stable isotopes: ^{64}Zn, ^{66}Zn, ^{67}Zn, ^{68}Zn, and ^{70}Zn, with average natural abundances at 48.89, 27.81, 4.11, 18.56, and 0.62% of the total volume, respectively. There are also six radioactive zinc isotopes: ^{62}Zn, ^{63}Zn, ^{65}Zn, ^{69}Zn, ^{72}Zn, and ^{73}Zn, with ^{65}Zn ($t_{1/2} = 245$ days) and ^{69}Zn ($t_{1/2} = 55$ min) being the most commonly used (Adriano 2001). Zinc has high lability (Stone and Marsalek 1999). In weathering processes, all Zn compounds are readily soluble, especially in acid (Kabata-Pendias and Pendias 1992). According to Goldschmidt's classification, Zn belongs to the chalcophile elements with an affinity to sulfur higher than that of iron, and correspondingly lower relative to oxygen (it mainly creates sulfides) (Goldschmidt 1954). According to the classification by Vernadsky (1945), Zn belongs to cyclical elements.

3 Zinc Production and Uses

Global production of Zn in 2014 was 813.372 million metric tonnes (MT), according to the International Lead and Zinc Study Group. The major world producers include Canada, the former Soviet Union, and Japan, which collectively account for about half the production (Elinder 1986). Zinc is used in many industries, including the production of noncorrosive alloys and brass and in galvanizing steel and iron products. This element undergoes oxidation on the surface, thereby protecting the underlying metal from degradation. Galvanized products are widely used in construction materials, automobile parts, and household appliances (Elinder 1986). Zinc oxide (ZnO) is used in the manufacture of paints, white pigments in rubber processing, the coating of photocopy paper, and in cosmetics, pharmaceuticals, floor covering, plastics, printing inks, soap, textiles, and electrical equipment (EPA 1987; PHS 1989). Zinc sulfate ($ZnSO_4$) is used in making luminous dials, X-ray films, TV screens, paints and fluorescent lights, as a cooperative agent in fungicides, and as a protective agent against Zn deficiency in soils (Maita et al. 1981). Zinc chloride ($ZnCl_2$) is used in vulcanization, refining of oils, and dyes and disinfectants. In 2001 more than 9 million MT of Zn were produced for galvanizing (47%), brass and bronze production (19%), Zn-based alloys (14%), chemicals (9%), and other uses (11%) (NRC 2005).

Zinc has been identified in at least 985 of the 1662 hazardous waste sites proposed for inclusion in the EPA National Priorities List (NPL) (HazDat 2005). This element is released into the environment in the form of particulates from Zn smelters, around which soil Zn concentrations range from 10 to 80 mg kg^{-1}. Another source of this element in the soil are certain plant protection chemicals and phosphate fertilizers. Zinc contained in industrial and mining waste often reaches groundwater. An important source of environmental pollution by Zn is the combustion of coal and petroleum and their products. Incineration of solid municipal waste may be responsible for about 75% of airborne Zn in urban areas; waste waters also generally contain significant amounts of zinc (Senczuk 2006).

4 Zinc in Nature

Zinc is ubiquitous in the environment and is the 24th most abundant element, with an average concentration of 70 mg kg^{-1} in the Earth's crust (Mason and Moore 1982) and in the silicate crust, core, and mantle of the Earth at 55, 0, and 40 mg g^{-1}, respectively (McDonough and Sun 1995). This element is present in nature primarily as zinc sulfide (ZnS) and zinc carbonate ($ZnCO_3$) and it is found in the air, soil, and water and is present in all foods (Kabata-Pendias and Pendias 1992). Most rocks of the Earth's crust contain Zn in various concentrations depending on the type of rock (Aubert and Pinta 1977). Zinc is a chalcophile metallic element, easily combining with carbonates and organic compounds. There are approximately 55 mineralized

Table 11.1 Zinc (Zn) in certain minerals

Minerals	Zinc percentages
Sphalerite (ZnS)	67.0
Hemimorphite ($Zn_4Si_2O_7(OH)_2H_2O$	54.2
Smithsonite ($ZnCO_3$)	52.0
Hydrozincite ($Zn_5(OH)_6(CO3)_2$)	56.0
Zincite (ZnO)	80.3
Willemite (Zn_2SiO_4)	58.5
Franklinite ((Zn, Fe, Mn)(Fe, $Mn)_2O_4$)	15–20

Goodwin (1998)

forms of Zn, with the most significant being sphalerite, smithsonite, and hemimorphite (Table 11.1). Zinc is also widely dispersed as a trace element in pyroxene, amphibole, mica, garnet, and magnetite. Significant deposits of Zn ore can be found in China, the USA, Canada, Australia, Kazakhstan, Peru, and Mexico. World reserves of Zn are estimated at about 180 million MT of pure metal (US Geological Survey 2010).

Although Zn occurs naturally in soils, these levels have risen unnaturally due to anthropogenic additions. Mean Zn concentrations in soils were estimated at about 50 mg kg^{-1}, ranging between 10 and 300 mg kg^{-1} (Malle 1992). It was later found that in noncontaminated soil environments, the average Zn concentration was 63 mg kg^{-1}, while in light sandy, medium loam, heavy loam, calcareous, and organic soils, levels fell in ranges of 31–61, 47–61, 35–75, 50–100, and 57–100 mg kg^{-1}, respectively (Kabata-Pendias and Mukherjee 2007; Kabata-Pendias and Szteke 2012). Zinc concentration is highest in lithosols (95 mg kg^{-1}) and lowest in oxisols (34 mg kg^{-1}). Zinc levels in soils have been found to be very heterogeneous in many parts of the world, especially in areas affected by glacial and periglacial processes, with a wide range of soils developed on drift deposits (Alloway 2008). The element's deficiency in soils and plants is a widespread micronutrient deficiency problem in many countries (Alloway 2008). This problem concerns arid and semiarid regions due to low organic matter and soil moisture, as well as high pH and levels of calcium carbonate ($CaCO_2$) (Cakmak 2008), typically in sampling in Iraq (57% of samples), Turkey (35%), and Pakistan (20%) (Sillanpaa 1982). Zinc is low in the Southeast USA and moderately higher in California, the Southwest, Colorado, and in the Lower Mississippi Valley.

Zinc is present in water in the form of hydrated cations and soluble salts, mainly carbonates and sulfates, as well as compounds with organic colloids (Kabata-Pendias and Szteke 2012). Despite its high mobility, Zn reaches groundwater in relatively low quantities. It has been established that an acceptable Zn level in groundwater is 50 μg L^{-1}; at 200 μg L^{-1} it requires control, while at 800 μg L^{-1} water needs to be treated (VROM 2012). In natural surface waters, Zn concentration is usually below 10 μg L^{-1} and in groundwater 10–40 μg L^{-1} (Elinder 1986). The mean Zn concentrations in ambient water and drinking water range from 0.02 to 0.05 mg L^{-1} and from 0.01 to 0.1 mg L^{-1}, respectively (ATSDR 2005). The average Zn concentrations measured in rainwater, rivers, and seawater were 1.2–6.6, 1.5–3.3,

Table 11.2 Global emissions of Zn into the atmosphere: natural and anthropogenic sources

Sources	Emissions ($\times 10^6$ kg year^{-1})	References
Natural		
Windborne soil particles	19	Nriagu (1989)
Sea salt spray	0.44	
Volcanoes	9.6	
Wild forest fires	7.5	
Biogenic		
Continental particulates	2.6	
Continental volatiles	2.5	
Marine	3.0	
Total in 1983	45	
Total in 2000	301	Rauch and Pacyna (2009)
Anthropogenic		
Stationary fossil fuel combustion	9.42	Pacyna and Pacyna (2001)
Nonferrous metal production	40.87	
Iron and steel production	2.12	
Cement production	2.67	
Waste disposal	1.93	
Total in 1983	131.88	Nriagu (1989)
Total in 2000	99.80	Rauch and Pacyna (2009)

and 0.04–5.0 mg L^{-1}, respectively (Reimann and de Caritat 1998; Kabata-Pendias and Mukherjee 2007)

Zinc may enter waters from a variety of sources, including mine drainage, industrial and municipal wastes, urban runoff, and soil erosion particles containing Zn (US EPA 1980). This element in water is easily bioaccumulated in phyto- and zooplankton and accumulates in bottom sediments. The background levels in river sediments are 110 mg kg^{-1} in the Vistula River and 115 mg kg^{-1} in the Rhein River, while in polluted parts of these rivers Zn concentrations may exceed 2000 and 14,000 mg kg^{-1}, respectively (Kabata-Pendias and Mukherjee 2007).

Mean Zn concentrations in the air at remote and polluted sites are estimated to be 7 and 900 ng m^{-3}, respectively. Such Zn occurs in different forms, for example, as free cations and suspended particulate matter (Reimann and de Caritat 1998). Zinc levels in rural air are between 10 and 200 ng m^{-3}, while in urban air Zn can reach 16,000 ng m^{-3} (Eriksson et al. 2001). The element is released into the environment from both natural and anthropogenic sources; however, anthropogenic emissions are greater than those from natural sources (Table 11.2).

Zinc is an essential trace element (micronutrient) required by plants in small but critical amounts. It is necessary for growth and plays an important role in several plant metabolic processes. It is a functional, structural, or regulatory cofactor of enzymes, participating in protein synthesis, in carbohydrate, nucleic acid, and lipid metabolism, in the regulation of auxin synthesis, and in pollen formation (Pahlsson 1989). When accumulated at excess levels in plant tissues, Zn causes alterations in

vital growth processes and membrane integrity (Doncheva et al. 2001). Zinc is taken up by plants as cations (Zn^{+2}, $ZnOH^{+}$), organic chelates, and insoluble Zn compounds (Kabata-Pendias and Szteke 2012). In general, this element from anthropogenic sources is more accessible for plants. Because of the high solubility of its compounds, the bioavailability of Zn for plants is high, which results in a high risk of Zn being introduced into the food chain (Broadley et al. 2007). Mean Zn levels in the aerial part of plants in noncontaminated areas range from 10 to 70 mg kg^{-1} dry weight (dw) (Kucharczak and Moryl 2010). Most Zn can be found in the roots, especially in the rhizosphere. Zinc is most often associated with low-molecular-weight proteins or other soluble organic compounds. Relatively high levels of Zn can be found in cereal grains (18–23 mg kg^{-1}), vegetables (23–73 mg kg^{-1}), fruit (1.2–2.8 mg kg^{-1}), grass (25–47 mg kg^{-1}), and clover (24–39 mg kg^{-1}) (Kabata-Pendias and Szteke 2012).

5 Biological Effects, Metabolism, and Toxicity of Zinc in Endothermic Animals

Zinc plays a structurally and functionally significant role in more than 300 metalloenzymes from all six classes of enzymes (McCall et al. 2000). Zinc ions exist primarily as complexes with proteins that participate in all aspects of intermediary metabolism; they are also neurotransmitters, with cells in the salivary glands, prostate, immune system, and intestine using Zn signaling (Tapeiro and Tew 2003; Herschfinkel et al. 2007). Zinc serves as a cofactor in RNA polymerase and reverse transcriptase and in zinc-finger proteins that are adducts to DNA (Oberleas and Harland 2008). It plays a role in the synthesis, storage, and secretion of insulin and is necessary for the proper functioning and development of teeth and the skeletal system (NRC 2005; Chausmer 1998; Smrcka 2005). Zinc is a component of thymulin, a thymus hormone necessary for the maturation and differentiation of T cells (Dardenne et al. 1982). This element is also a major regulator of lymphocyte apoptosis in vitro and in vivo (Dardenne 2002). Zinc is involved in the control of oxidative stress and could contribute to membrane stabilization, acting at the cytoskeletal level (Dardenne et al. 1982). It is required for normal testicular development (Merck 1986). In birds, Zn is necessary for the growth and development of the skeleton, the formation and maintenance of epithelial tissues, and for egg production (Gordon 1977). In swine, Zn prevents thickening or hyperkeratinization of the epithelial cells of the skin and esophagus (parakeratosis), while in chicks it prevents a similar disease (Soetan et al. 2010).

Zinc homeostasis is primarily maintained via the gastrointestinal system, especially the small intestine, liver, and pancreas, by a process of absorption of exogenous zinc and gastrointestinal secretion and excretion of endogenous Zn (Krebs 2000). In humans and nonruminant animals, the highest absorption rate for Zn was observed in the jejunum, and in ruminants also in the rumen (Georgieskii et al. 1982;

Krebs 2000). Zinc absorption from the gut is dependent on the level in the diet, and generally ranges from 15% to 60% (McDowell 2003). Many dietary factors influence Zn absorption. Protein in the meal, amino acids, and other low-molecular-weight ions are known to have a positive effect on Zn absorption, while phytate forms, iron (Fe), calcium (Ca), and cadmium (Cd), have a negative effect on Zn absorption (Lonnerdal 2000). A decrease in Zn absorption is associated with age, but zinc excretion also decreases with age, and Zn homeostasis is not downregulated with age (Semrad 1999). The element is transported to the liver via portal circulation and then to other tissues, mainly in a complex with albumin (McMahon and Cousins 1998). In blood, 60% of Zn is bound to albumin, 30% to α2-macroglobulin, and 10% to transferrin (Scott and Bradwell 1983). Other plasma proteins that bind to zinc are transferrin, histamine-rich glycoprotein, and metallothionein (NRC 2005). Zinc physiological concentrations in mammalian serum range from 0.8 to 0.9 μg mL^{-1}, whereas in organs and tissues it has been found at 10–200 mg kg^{-1} wet weight (ww) (Goyer et al. 1995; Kabata-Pendias and Pendias 1999).

Zinc is excreted mainly in the feces and urine (McDowell 2003). Increased Zn excretion in the urine can be caused by trauma, muscle catabolism, and administration of chelating agents (Hambridge et al. 1986). Additional zinc is lost daily in seminal emissions, menstrual losses, and hair and nail growth.

Zinc is not mutagenic and does not represent a carcinogenic risk to humans (Leonard et al. 1986), and it is relatively nontoxic to birds and animals. Rats, pigs, poultry, sheep, cattle, and humans exhibit a tolerance to high intake of Zn. In contrast, a zinc deficiency in animals causes numerous pathological changes, including skin parakeratosis, growth retardation, gastrointestinal malfunction, testicular and lymphoid tissue atrophy, poor wound healing, general debility, lethargy, poor appetite, and increased susceptibility to infection (Prasad et al. 1979; Dardenne 2002). In addition, long-term Zn deficiency increases the susceptibility to damage induced by oxidative stress; a low Zn level increases the level of lipid peroxidation in mitochondrial membranes. A dietary Zn deficiency significantly reduces red blood cell carbonic anhydrase activity, which may impair respiratory functions (Lukaski 2005). Zinc deficiency makes bones thin and fragile with excessive bone resorption and in male rats caused a delay in the growth and development of testes and prohibited spermatogenesis, while in mice it decreased natural killer cell activity and responses to cutaneous sensitization (Charles et al. 2001; Fernandes et al. 1979; Gilabert et al. 1996). Studies in rats, mice, pigs, and sheep showed that a Zn deficiency increased fetal death due to spontaneous abortions or multiple congenital anomalies (King 2000). Zinc deficiency occurs in cattle and calves and is characterized by reduced growth and feed intake, loss of hair and skin lesions that are most severe on the legs, neck, and head and around the nostrils, with excessive salivation, swollen feet with open, scaly lesions, and impaired reproduction (Spears 1994; Radostits et al. 2007). In pigs, Zn deficiency causes a marked depression of appetite, growth rate, and parakeratosis, while in young birds it results in poor growth, severe dermatitis, especially of the feet, poor feathering, abnormal respiration, and skeletal abnormalities causing leg weakness and ataxia (Soetan et al. 2010). Long bones are shortened and thickened and are sometimes crooked, and the joints are enlarged and

rigid (Gordon 1977). The element's deficiency in mothers can cause an increased incidence of congenital malformations in infants (Elinder 1986). Gestational Zn deficiency in mice produced short- and long-term deleterious effects and showed a depressed immune function on offspring. Offspring from marginally Zn-deficient mice reduced lymphoid organ size and immunoglobulin concentrations (Beach et al. 1982).

Zinc toxicity depends on the Zn concentration and duration of exposure, age, sex, species, nutritional status, and composition of the diet. Young animals may be more vulnerable than older animals because they tend to have a higher efficiency of Zn absorption (NRC 2005). The effects of this element's toxicity depend on its chemical forms and presence or absence of other cations in the diet (Abdel-Mageed and Oehme 1990). Perhaps one of the major causes of Zn toxicity is its effect on the metabolism of essential metals. It has been found that the excessive consumption of Zn interferes with the absorption of Cu, probably via the induction of metallothionein, which has a greater affinity to copper (Cu) than to Zn. After binding to metallothionein, Cu is excreted from the body.

High doses of Zn interfere with metabolic processes and accumulate in the kidneys, liver, and gonads. Too high doses of Zn contribute to a gradual reduction in bone mass and calcium ion concentration in bones and blood serum (Charles et al. 2001). The half-life of Zn elimination is 162–500 days, and the content in the body decreases with age. Levengood et al. (1999) found clinical signs of Zn poisoning in mallards, with liver concentrations of 473–1990 mg kg^{-1} dw; similarly, Sileo et al. (2003) diagnosed Zn poisoning in wild waterfowl, with liver concentrations of 280–2900 mg kg^{-1} dw, while Doneley (1992) observed moderate to severe nephrosis in caged and aviary birds with hepatic Zn levels of 320 and 534 mg kg^{-1} dw, respectively. Eisler (1993) concluded that Zn levels in the tissues of birds and mammals are typically <210 mg kg^{-1} dw, and that Zn poisoning usually occurs in birds at liver or kidney concentrations >2100 mg kg^{-1} dw and in mammals when kidney, liver, or pancreas levels exceed 274, 465, or 752 mg kg^{-1} dw. In cattle, adequate Zn levels are 25–100 mg kg^{-1} ww (or 83.33–333.33 mg kg^{-1} dw) in the liver and 18–20 mg kg^{-1} ww (or 72–80 mg kg^{-1} dw) in the kidney, with Zn levels not considered "elevated" (not necessarily toxic) until 300–500 mg kg^{-1} ww (or 1000–1666.66 mg kg^{-1} dw) in the liver and 50–140 mg kg^{-1} ww (or 200–560 mg kg^{-1} dw) in the kidney (Puls 1994).

Zinc poisoning has been described in dogs, cats, ferrets, birds, cattle, sheep, and horses, usually as a result of ingesting galvanized metal objects, certain paints and fertilizers, zinc-containing coins, and skin and sunblock preparations containing zinc oxide (Wentink et al. 1985; Ogden et al. 1988; Lu and Combs 1988; Binnerts 1989; Robinette 1990). In several different species high doses, from 2 to 8 mg kg^{-1}, of orally ingested Zn generally resulted in gastrointestinal distress with nausea, vomiting, abdominal cramps, and diarrhea (ATSDR 2005). Acute Zn toxicosis has been described in dogs that had ingested large numbers of pennies, metal nuts from dog kennels, and other metal objects (Hornfeldt and Koepke 1984; Caldwell 1994; Mikszewski et al. 2003). Signs of zinc toxicosis in dogs include anorexia, vomiting,

depression, fever (39.9 °C), intravascular hemolysis, pigmenturia, acute pancreatitis, hepatomegaly, and renal disease (Mikszewski et al. 2003; Hammond et al. 2004; Gurnee and Drobatz 2007). In chickens, high dietary Zn halted egg production and lowered body weight (McCormick and Cunningham 1984) and at 500 mg kg^{-1} in the diet caused dysfunctions of pancreatic acinar cells and exocrine pancreatic insufficiency (Lu et al. 1990). In mice, the reported LCT_{50} (product of lethal concentration and time to kill 50% of animals) of zinc chloride was 11,800 mg min^{-1} m^{-3} (Schenker et al. 1981). The LD_{50} for several zinc compounds (ranging from 186 to 623 mg kg^{-1} day^{-1}) has been determined for rats and mice (Domingo et al. 1988). In general, mice appear to be more sensitive to the lethal effects of Zn than rats.

Zinc status may be reflected by biochemical markers, i.e., biomarkers that are related to the structural, regulatory, and catalytic roles of Zn (van Riet et al. 2015). Although plasma Zn level is the most used biomarker for Zn status, other markers, such as albumin, metallothionein, and alkaline phosphatase, also play a role in Zn metabolism and homeostasis. Zinc is bound to albumin after absorption, metallothionein is involved in regulating the quantity of absorbed Zn, and alkaline phosphatase is a Zn-dependent enzyme in which Zn ions are present in active center (McDowell 2003; Coleman 1992).

6 Animals in Biomonitoring Studies

6.1 Bioaccumulation of Zinc in Wildlife

Environmental studies, including those concerned with biomonitoring, often use wild animal species as bioindicators due to the processes of bioaccumulation and biomagnification, which are especially pronounced in those species. Wild animals are also suitable bioindicators due to their large geographical distribution, limited feeding range, feeding habits, relatively long life span (sometimes 20–30 years), and easy sampling via regular hunting activities (Duffy et al. 2001). Measurements of trace element concentrations, including Zn, are performed in various organs and tissues, body fluids, hair, or feathers of animals associated with certain habitats (Kalisinska and Salicki 2010; Jarzynska and Falandysz 2011). In wild land mammals and birds, these are most often the liver and kidney and, less frequently, muscle, lung, heart, bone, and intestine.

Tables 11.4, 11.5, 11.6, and 11.7 show summarized data on Zn concentrations in various biological materials from endothermic vertebrates associated with land ecosystems and inland waterways. A correct interpretation of these results requires knowledge of the physiological Zn concentrations in the tissues and organs, Zn levels reflecting the geochemical background, and the specificity of species. For most species of wild animals there are no relevant data in this field, with the exception of domesticated animals. Table 11.3 shows deficient, marginal, optimal, high, and toxic Zn concentrations in the liver and kidney in cattle, dogs, horses,

Table 11.3 Deficient, marginal, optimal, and high Zn levels (mg kg^{-1}) in liver, kidney, and muscle of domestic and wild animals

Animals	Deficient	Marginal	Adequate	High	Toxic
			Liver		
Cervid[a]			30–110		
Cattle[b]	<20–40 <67–133[d]	25–40 83–133[d]	25–100 167–333[d]	300–500 1000–1667[d]	120–500 400–1667[d]
Sheep[b]	20–30 67–100[d]		30–75 100–250[d]	100–400 333–1333[d]	>400 >1333[d]
Canine or dog[a,b]	<15 <50[d]		30–70 100–233[d]		370 1233[d]
Musteline or mink[a,b]			25–100 83–333[d]	200 667[d]	
Mink[c]			27.4 91[d]		
Pig[b]	9.6–25 32–83[d]	25–35 83–117[d]	40–90 133–300[d]	>200 >667[d]	500–3100 1667–10333[d]
Birds/poultry[a,b]	18–40 60–133[d]	20–40 67–133[d]	25–40 117–133[d]	90–300 300–1000[d]	200–700 667–2333[d]
			Kidney		
Cervid[a]			19–33		
Cattle[b]	16–20 80–100[d]		18–25 90–125[d]	50–140 250–700[d]	130–480 650–2400[d]
Sheep[b]	15–30 75–150[d]		20–40 100–200[d]	50–1000 250–5000[d]	240–1600 1200–8000[d]
Canine[a]	<8 <40[d]		16–30 80–150[d]		300 1500[d]
Dog[b]					
Mustaline or mink[a,b]			18–20 90–100[d]		>100? >500?[d]
Mink[c]			19.9 99.5[d]		
Pig[b]	9.6–25 48–125[d]	25–35 125–175[d]	40–90 200–450[d]	>200 >1000[d]	500–3100 2500–15500[d]
Birds/poultry[a,b]	17–22 85–110[d]		22–32 110–160[d]	120 600[d]	300–800 1500–4000[d]
			Muscle		
Sheep[b]			75–130 (dw)		80–130 (dw)
Pig[b]			21–24 105–120[d]		

We assume that the kidneys consist of 80% water and the liver and muscle 70%
dw dry weight, *ww* wet weight
[a]WVDL (2015), [b]Puls (1994), [c]Stejskal et al. (1989)
[d]Values converted from wet weight to dry weight

mink, pigs, and poultry (Puls 1994; WVDL 2015). Importantly, in the liver in waterfowl on the basis of field and laboratory studies, it was found that the background Zn concentration, sublethal effects, and mortality in adults amounted to

Table 11.4 Zinc concentrations in liver, kidney, and muscle of ruminants and other herbivorous mammals

Species	Location	Zn concentration	References
Liver (mg kg^{-1} dw)			
Red deer *Cervus elaphus*	Northwest Poland	100	Jarzynska and Falandysz (2011)
	West–central Poland	126.67[a]	Michalska and Zmudzki (1992)
	Netherlands, Veluwe	108–124 (age: <0.6 and 1.5–5 years)	Wolkers et al. (1994)
	Eastern Croatia	100.00[a]	Lazarus et al. (2008)
	Western Slovakia	87.45[a]	Gasparik et al. (2003)
Roe deer *Capreolus capreolus*	Central Poland	116.67[a]	Dlugaszek and Kopczynski (2011)
	Southern Poland	93.33[a]	Lech and Gubala (1996)
	Northern Slovenia	108.67[a]	Pokorny and Ribaric-Lasnik (2000)
White-tailed deer *Odocoileus virginianus*	Nova Scotia, Canada	99.7	Pollock (2005)
	Illinois, USA,	70	Woolf et al. (1982)
	Georgia, USA	80[a]	Lewis et al. (2001)
Mule deer *Odocoileus hemionus*	California, USA	39	Roug et al. (2015)
Elk *Cervus elaphus*	Ontario, Canada	73.62	Parker and Hamr (2001)
Moose *Alces alces*	Northwest Russia	135.53[a]	Medvedev (1999)
	Nova Scotia, Canada	75	Pollock (2005)
Caribou *Rangifer tarandus*	Northwest Russia	123.33[a]	Bernhoft et al. (2002)
	Norway	103	Vikoren et al. (2011)
	Northern Alaska, USA	153[a]	O'Hara et al. (2003)
	Northwest Canada	276.33[a]	MacDonald et al. (2002)
Kidney (mg kg^{-1} dw)			
Red deer *Cervus elaphus*	Northeast Poland	130	Jarzynska and Falandysz (2011)
	Northern Poland	196[a]	Falandysz (1994)
	Netherlands, Veluwe	144–165 (age: <0.6 and 1.5–5 years)	Wolkers et al. (1994)
	Southern Spain	97.6	Reglero et al. (2008)
	Slovenia	114.4–188.4[a]	Pokorny (2000)
	Eastern Croatia	196.8–202.8[a]	Lazarus et al. (2008)
	Western Slovakia	124.47[a]	Gasparik et al. (2003)
Roe deer *Capreolus capreolus*	Northern Poland	196[a]	Falandysz (1994)
	Southern Poland	140[a]	Lech and Gubala (1996)
	Norway	125	Vikoren et al. (2011)
	Northern Slovenia	188.4[a]	Pokorny and Ribaric-Lasnik (2000)

(continued)

Table 11.4 (continued)

Species	Location	Zn concentration	References
White-tailed deer *Odocoileus virginianus*	Nova Scotia, Canada	79.7	Pollock (2005)
	Virginia, USA	119.33[a]	Sleeman et al. (2010)
	Georgia, USA	116.4[a]	Lewis et al. (2001)
Elk *Cervus elaphus*	Ontario, Canada	164.47	Parker and Hamr (2001)
Moose *Alces alces*	Northwest Russia	114.92[a]	Medvedev (1999)
	Nova Scotia, Canada	99.7	Pollock (2005)
	Yukon, Canada	117.56[a]	Gamberg et al. (2005)
Caribou *Rangifer tarandus*	Svalbard, Norway	146.67[a]	Borch-Iohnsen et al. (1996)
	Northern Alaska, USA	127.6[a]	O'Hara et al. (2003)
	Northwest Canada	464[a]	MacDonald et al. (2002)
Muscle (mg kg^{-1} dw)			
Red deer *Cervus elaphus*	Southwest and North-east Poland	93.32–103.12[a]	Skibniewski et al. (2015)
	Central–Eastern Poland	288[a]	Karpinski (1999)
	Eastern Croatia	144.67[a]	Lazarus et al. (2008)
	Western Slovakia	219.04[a]	Gasparik et al. (2003)
Roe deer *Capreolus capreolus*	Central Poland	124[a]	Dlugaszek and Kopczynski (2013)
	Northern Poland	144[a]	Falandysz (1994)
	Northern Slovenia	206.4[a]	Pokorny and Ribaric–Lasnik (2000)
Elk *Cervus elaphus*	Ontario, Canada	48.19	Parker and Hamr (2001)
Moose *Alces alces*	Northwest Russia	147.36[a]	Medvedev (1999)
Caribou *Rangifer tarandus*	Northern Alaska, USA	134.8[a]	O'Hara et al. (2003)

[a]Values converted from wet weight to dry weight

28.2–54.5 mg kg^{-1} ww (or 94–82 mg kg^{-1} dw), ≥84.8 mg kg^{-1} ww (or ≥283 mg kg^{-1} dw), and >333 mg kg^{-1} ww (or >1111 mg kg^{-1} dw), respectively (Pillatzki et al. 2011).

Table 11.5 Zinc concentrations in selected tissues of omnivorous mammals

Species	Localization	Zn concentration	References
Liver (mg kg^{-1} dw)			
Wild boar *Sus scrofa*	Western Poland	157.27–171.3[a]	Kucharczak et al. (2003)
	Slovakia	94[a]	Gasparik et al. (2012)
	Central Italy	165.87[a]	Amici et al. (2012)
	Southern Spain	113	Reglero et al. (2009)
Raccoon *Procyon lotor*	Illinois, USA	150–186.67[a]	Levengood et al. (2002)
	Michigan, USA	148[a]	Herbert and Peterle (1990)
	Georgia, USA	100.33[a]	Lewis et al. (2001)
	Tennessee, USA, PA	132.83[a]	Souza et al. (2013)
	Tennessee, USA, UA	136.33	
	South Carolina, USA, PA	112.98	Hernandez et al. (2017)
	South Carolina, USA, UA	106.02	
	Ontario, Canada	34.4	Wren (1984)
Kidney (mg kg^{-1} dw)			
Wild boar *Sus scrofa*	Southern Poland	82	Swiergosz et al. (1993)
	Western Poland	111.56–122.12[a]	Kucharczak et al. (2003)
	Slovakia	83.92[a]	Gasparik et al. (2012)
	Central Italy	129.84[a]	Amici et al. (2012)
Rraccoon *Procyon lotor*	Illinois, USA	92–108[a]	Levengood et al. (2002)
	Michigan, USA	74.4[a]	Herbert and Peterle (1990)
	Georgia, USA	65.6[a]	Lewis et al. (2001)
	Tennessee, USA, PA	79[a]	Souza et al. (2013)
	Tennessee, USA, UA	79.4[a]	
	Ontario, Canada	29.5	Wren (1984)
Muscle (mg kg^{-1} dw)			
Wild boar *Sus scrofa*	Central Poland	126[a]	Długaszek and Kopczyński (2011)
	Western Poland	42.68–249.16[a]	Kucharczak et al. (2003)
	Hungary	151.48–204.68[a]	Skobrak et al. (2011)
	Slovakia	53.92[a]	Gasparik et al. (2012)
	Central Italy	212.84[a]	Amici et al. (2012)
Raccoon *Procyon lotor*	Tennessee, USA, PA	221.6[a]	Souza et al. (2013)
	Tennessee, USA, UA	254[a]	

PA polluted area, *UA* unpolluted area
[a]Values converted from wet weight to dry weight

Table 11.6 Zinc concentrations in selected tissues in carnivorous mammals

Species	Localization	Zn concentration	References
Liver (mg kg^{-1} dw)			
Red fox *Vulpes vulpes*	Southwest Poland	128.26	Binkowski et al. (2016)
	Northern Czech Republic	96.17	Jankovska et al. (2010)
	Central Hungary	156.93	Heltai and Markov (2012)
	North-central Switzerland	149.67[a]	Dip et al. (2001)
	Northwest Spain	77	Perez-Lopez et al. (2016)
	Southern Spain	118.7	Millan et al. (2008)
Polar fox *Alopex lagopus*	Svalbard, Norway	106.67[a]	Prestrud et al. (1994)
	Nunavut, Canada	29	Hoekstra et al. (2003)
California gray fox *Urocyon cinereoargenteus californicus*	California, USA, ZOO	109	Arnhold et al. (2002)
Arctic wolf *Canis lupus*	Keewatin, Canada	67.0	Lamothe (1991)
Eurasian otter *Lutra lutra*	Hungary	99.75	Lanszki et al. (2009)
European otter *Lutra lutra*	Central and Eastern Finland	133.6[a]	Skaren (1992)
		120[a]	Lodenius et al. (2014)
	England and Wales	102	Walker et al. (2011)
	Great Britain	111.67	Mason and Stephenson (2001)
	Ireland	83.80	
	Denmark	92.13	
	Netherlands	131	Broekhuizen (1987)
	Austria	92.6	Gutleb et al. (1998)
	Hungary	96.2	
	Czech	60.7	
River otter *Lontra canadensis*	Illinois, USA	80.33[a]	Halbrook et al. (1996)
	Virginia, USA	62.63	Anderson-Bledsoe and Scanlon (1983)
	Ontario, Canada	26.5	Wren (1984)
	British Columbia, Canada	86	Harding et al. (1998)
American mink *Neovision vision*	Poland	67.22–135.38	Brzezinski et al. (2014)
	British Columbia, Canada	95	Harding et al. (1998)
	Virginia, USA	123.24	Ogle et al. (1985)

(continued)

Table 11.6 (continued)

Species	Localization	Zn concentration	References
Kidney (mg kg^{-1} dw)			
Red fox *Vulpes vulpes*	Poland, SW part	58.58	Binkowski et al. (2016)
	Northern Czech Republic	79.29	Jankovska et al. (2010)
	Central Hungary	87.16	Heltai and Markov 2012
	North-central Switzerland	84.8[a]	Dip et al. (2001)
	Northwestern Spain	17	Perez-Lopez et al. (2016)
California gray fox *Urocyon cinereoargenteus californicus*	San Diego, CA, USA, ZOO	74	Arnhold et al. (2002)
Grey wolf *Canis lupus*	USA	28.7–39.1	Hoffmann et al. (2010)
	Northwest Territories, Canada	28.0	
Arctic wolf *Canis lupus*	Keewatin, Canada	85.0	Lamothe (1991)
Eurasian otter *Lutra lutra*	England and Wales	93.5–106.5	Walker et al. (2011)
	Netherlands	95	Broekhuizen (1987)
	Austria	138.2	Gutleb et al. (1998)
	Hungary	55.6	
	Czech	107.2	
River otter *Lontra canadensis*	Illinois, USA	82[a]	Halbrook et al. (1996)
	Virginia, USA	78.91	Anderson-Bledsoe and Scanlon (1983)
	Ontario, Canada	19.6	Wren (1984)
American mink *Neovision vision*	Poland	76.22–115.40	Brzeziński et al. (2014)
	British Columbia, Canada	65	Harding et al. (1998)
	Virginia, USA	93.42	Ogle et al. (1985)
Muscle (mg kg^{-1} dw)			
Red fox *Vulpes vulpes*	Southwest Poland	87.31	Binkowski et al. (2016)
	Northwest Spain	77	Perez-Lopez et al. (2016)
	Southern Spain	118.7	Millan et al. (2008)
River otter *Lutra canadensis*	Illinois, USA	149.2[a]	Halbrook et al. (1996)
	Ontario, Canada	50.5	Wren (1984)

[a]Values converted from wet weight to dry weight

Table 11.7 Zinc concentrations in different organs of birds

Species	Localization	Zn concentration	References
Liver (mg kg^{-1} dw)			
White-tailed eagle *Haliaeetus albicilla*	Poland, NW and E parts	88.67[a]	Kalisinska et al. (2006)
		170	Falandysz et al. (2000)
	Southwest Poland, Baltic Sea coast	62	Falandysz et al. (1988)
Bald eagle *Haliaeetus leucocephalus*	Alaska, USA	127	Stout and Trust (2002)
	Michigan and Minnesota, USA	237	Nam et al. (2012)
Eurasian eagle owls *Bubo bubo*	South Korea	212	Kim and Oh (2016)
Osprey *Pandion haliaetus*	Eastern USA	171.3[a]	Wiemeyer et al. (1987)
Black kite *Milvus migrans*	Central India	84.33[a]	Gupta and Kanaujia (2014)
Eurasian buzzard *Buteo buteo*	Northwest Poland, and Eastern Czech Republic	126.2	Kalisinska et al. (2009)
	Eastern Poland	121.51	Komosa et al. (2012)
	Sicily, Italy	137.5	Naccari et al. (2009)
	Southern Italy	158.33	Zaccaroni et al. (2011)
	Northwestern Spain	297.4	Perez-Lopez et al. (2008)
	South Korea	144	Kim and Oh (2016)
Peregrine falcon *Falco peregrinus*	Sweden	72	Ek et al. (2004)
Common kestrel *Falco tinnunculus*	South Korea	132	Kim and Oh (2016)
Mallard *Anas platyrhynchos*	Southeast Poland	144.67[a]	Bojar and Bojar (2009)
	Northeast and Southern Poland	80.97–87.03[a]	Szymczyk and Zalewski (2003)
	Spain, DNP, 1998	221.33	Taggart et al. (2006)
	Spain, DNP, 1998 and 2000	136.0	Gomez et al. (2004)
	South Korea	103.00	Kim and Oh (2012)
	Southeastern Iran	62.4[a]	Sinka-Karimi et al. (2015)
	Virginia, USA	161	DiGulio and Scanlon (1984)
Greylag goose *Anser anser*	France	355.8	Lucia et al. (2010)
	Southwestern Spain	102–196	Mateo et al. (2006)
Eurasian teal *Anas crecca*	Spain, DNP	83.91	Hernandez et al. (1999)

(continued)

Table 11.7 (continued)

Species	Localization	Zn concentration	References
Spot-billed ducks *Anas poecilorhyncha*	South Korea	131.0	Kim and Oh (2012)
Eurasian wigeons *Anas penelope*	South Korea	88.4	Kim and Oh (2012)
Greater scaup *Aythya marila*	Alaska, USA	139	Badzinski et al. (2009)
	Virginia, USA	117	Di Giulio and Scanlon (1984)
Pochard *Aythya ferina*	Spain, DNP, 1998	345.67	Taggart et al. (2006)
	Spain, DNP, 1998 and 2000	283	Gomez et al. (2004)
	Southeastern Iran	93.4[a]	Sinka-Karimi et al. (2015)
Redhead duck *Aythya americana*	Louisiana, USA	122	Michot and Chadwick (1994)
Great tit *Parus major*	Northeastern and Southern Poland	163	Sawicka-Kapusta et al. (1986)
	Northern Belgium	36.0	Dauwe et al. (2005)
	Central Norway	69.60–72.32	Hogstad (1996)
	Northern China	117.15	Deng et al. (2007)
	Northeastern Spain, UA	112.80	Llacuna et al. (1995)
	Northeastern Spain, PA	98.78	
Rock bunting *Emberiza cia*	Northeastern Spain, UA	71.50	Llacuna et al. (1995)
	Northeastern Spain, PA	91.40	
Blackbird *Turdus merula*	Northeastern Spain, UA	51.00	Llacuna et al. (1995)
	Northeastern Spain, PA	43.00	
house sparrow *Passer domesticus*	Southern Finland, RUA	18.35	Kekkonen et al. (2012)
	Southern Finland, URA	21.08	
	Albania, PA	68.25–94.47	Millaku et al. (2015)
	Albania, UA	61.48	
	Turkey, UA	43.18	Albayrak and Mor (2011)
	Turkey, PA	101.76	
	West Bank, Palestine	131.4	Swaileh and Sansur (2006)
	Northern Pakistan	26.16[a]	Mustafa et al. (2015)
Italian sparrow *Passer domesticus italiae*	Southern Italy, RUA	154	Gragnaniello et al. (2001)
	Southern Italy, URA	204	
Tree sparrow *Passer montanus*	Northern China	104–137	Chao et al. (2003)
	China	65.03–82.90	Gong et al. (2012)
Savannah sparrow *Passerculus sandwichensis*	Northwest Alaska, USA	82.3	Brumbaugh et al. (2010)

(continued)

Table 11.7 (continued)

Species	Localization	Zn concentration	References
Kidney (mg kg^{-1} dw)			
White-tailed eagle *Haliaeetus albicilla*	Northwestern Poland	80.16[a]	Kalisinska et al. (2006)
	Western Poland	140	Falandysz et al. (2000)
Bald eagle *Haliaeetus leucocephalus*	Alaska, USA	96.4	Stout and Trust (2002)
Osprey *Pandion haliaetus*	Eastern USA	171.3[a]	Wiemeyer et al. (1987)
Black kite *Milvus migrans*	Central India	82[a]	Gupta and Kanaujia (2014)
Eurasian buzzard *Buteo buteo*	Northwestern Poland and Eastern Czech Republic	75.0	Kalisinska et al. (2009)
	Sicily, Italy	62.25	Licata et al. (2010)
	Southern Italy	367.6[a]	Zaccaroni et al. (2011)
Peregrine falcon *Falco peregrinus*	Sweden	70	Ek et al. (2004)
Mallard *Anas platyrhynchos*	Southeastern Poland	88.8[a]	Bojar and Bojar (2009)
	Spain, DNP, 1998 and 2000	70.4	Gomez et al. (2004)
	Southeastern Iran	44.88[a]	Sinka-Karimi et al. (2015)
	Virginia, USA	86	DiGulio and Scanlon (1984)
Pochard *Aythya ferina*	Southeastern Iran	54.44[a]	Sinka-Karimi et al. (2015)
Gadwall *Anas strepera*	Spain, DNP	138.9	Taggart et al. (2006)
	Spain, DNP	296.2	Hernandez et al. (1999)
Greylag goose *Anser anser*	France	189.2	Lucia et al. (2010)
Great tit *Parus major*	Northern Belgium	53.4	Dauwe et al. (2005)
	Northern China	85.50	Deng et al. (2007)
	Northeastern Spain, UA	96.43	Llacuna et al. (1995)
	Northeastern Spain, PA	85.89	
Rock bunting *Emberiza cia*	Northeastern Spain, UA	93.80	Llacuna et al. (1995)
	Northeastern Spain, PA	100.22	
Blackbird *Turdus merula*	Northeastern Spain, UA	113.49	Llacuna et al. (1995)
	Northeastern Spain, PA	106.31	

(continued)

Table 11.7 (continued)

Species	Localization	Zn concentration	References
House sparrow *Passer domesticus*	Albania, PA	61.63–77.76	Millaku et al. (2015)
	Albania, UA	47.22	
	Turkey, UA	19.72	Albayrak and Mor (2011)
	Turkey, PA	31.51	
	Northern Pakistan	25.28[a]	Mustafa et al. (2015)
Italian sparrow *Passer domesticus italiae*	Southern Italy, RUA	133	Gragnaniello et al. (2001)
	Southern Italy, URA	162	
Muscle (mg kg^{-1} dw)			
White-tailed eagle *Haliaeetus albicilla*	Northwestern Poland	86.17[a]	Kalisinska et al. (2006)
	Western Poland	12.00	Falandysz et al. (2000)
Eurasian buzzard *Buteo buteo*	Sicily, Italy	52.76	Naccari et al. (2009)
	Sicily, Italy	52.01	Licata et al. (2010)
Mallard *Anas platyrhynchos*	Southeastern Poland	74.33[a]	Bojar and Bojar (2009)
	Northeastern and Southern Poland	34.77–66[a]	Szymczyk and Zalewski (2003)
	Spain, DNP, 1998 and 2000	32.3	Gomez et al. (2004)
	Southeastern Iran	31.53[a]	Sinka-Karimi et al. (2015)
Pochard *Aythya ferina*	Spain, DNP, 1998 and 2000	80.6	Gomez et al. (2004)
	Southeastern Iran	33.07[a]	Sinka-Karimi et al. (2015)
Greylag gees *Anser anser*	France	93.8	Lucia et al. (2010)
	Southwestern Spain	52–111	Mateo et al. (2006)
Great tit *Parus major*	Northern Belgium	11.9	Dauwe et al. (2005)
	Northern China	32.15–92.09	Deng et al. (2007)
	Northeastern Spain, UA	31.57	Llacuna et al. (1995)
	Northeastern Spain, PA	31.14	
Rock bunting *Emberiza cia*	Northeastern Spain, UA	29.18	Llacuna et al. (1995)
	Northeastern Spain, PA	28.24	
Blackbird *Turdus merula*	Northeastern Spain, UA	26.82	Llacuna et al. (1995)
	Northeastern Spain, PA	29.95	
House sparrow *Passer domesticus*	Northern Pakistan	27.5[a]	Mustafa et al. (2015)
	Turkey, UA	19.90	Albayrak and Mor (2011)
	Turkey, PA	34.03	
	West Bank, Palestine	61.9	Swaileh and Sansur (2006)
	India, URA	43.78	Sundaramahalingam et al. (2016)
	India, RUA	32.4	

(continued)

Table 11.7 (continued)

Species	Localization	Zn concentration	References
Tree sparrow *Passer montanus*	Northern China	48.6–75.5	Chao et al. (2003)
	China	22.50–32.03	Gong et al. (2012)
Bone (mg kg^{-1} dw)			
Mallard *Anas platyrhynchos*	Northwestern Poland	97.89 (ad), 111.39 (imm)	Kalisinska et al. (2004)
	Western Poland	87.73 (ad), 111.77 (imm)	
Pochard *Aythya ferina*	Spain, DNP, 1998	154.9	Taggart et al. (2006)
Great tit *Parus major*	Northeastern and Southern Poland	183–284	Sawicka-Kapusta et al. (1986)
	Northeastern Spain, UA	248.5	Llacuna et al. (1995)
	Northeastern Spain, PA	255.9	
Rock bunting *Emberiza cia*	Northeastern Spain, UA	166.2	Llacuna et al. (1995)
	Northeastern Spain, PA	209.8	
Blackbird *Turdus merula*	Northeastern Spain, UA	152.6	Llacuna et al. (1995)
	Northeastern Spain, PA	149.9	
House sparrow *Passer domesticus*	Albania, PA	342.8 and 291.5	Millaku et al. (2015)
	Albania, UA	235.1	
	West Bank, Palestine	150.4	Swaileh and Sansur (2006)
	India, URA	25	Sundaramahalingam et al. (2016)
	India, RUA	27.2	
Tree sparrow *Passer montanus*	Northern China	207–255	Chao et al. (2003)

DNP Donana National Park, *PA* polluted area, *UA* unpolluted area, *RUA* rural area, *URA* urban area, *ad* adultus, *imm* immaturus
[a]Values converted from wet weight to dry weight

6.2 Mammals

6.2.1 Zinc Concentration in Mammalian Tissues

Zinc concentration in mammals can be analyzed on the basis of data on selected animals from different trophic groups. Among European ruminants, Zn levels are most often analyzed in livers, kidneys, and muscles of red deer (*Cervus elaphus*) and roe deer (*Capreolus capreolus*) and in North America in the white-tailed deer (*Odocoileus virgianus*), mule deer (*Odocoileus hemionus*), and caribou (*Rangifer tarandus*). Caribou and reindeer are the same species and occur in the Arctic and

subarctic regions of North America and Eurasia. Some studies have also examined Zn concentrations in moose (North America) and elk (Eurasia) (*Alces alces*), the largest extant species in the deer family. Those data indicate that the mean Zn concentration in ruminant livers is in a range of 70–170 mg kg^{-1} dw (Table 11.4). Zinc levels in the liver below 40 mg kg^{-1} dw were found in mule deer from California, USA (Roug et al. 2015), while levels exceeding 270 mg kg^{-1} dw were found in caribou from the Northwest Territories and Nunavut, Canada (MacDonald et al. 2002). In ruminant kidneys, mean Zn concentrations were 80–200 mg kg^{-1} dw (Table 11.4), while in caribou from the Northwest Territories and Nunavut, Zn levels in the kidney were higher, 77–159 mg kg^{-1} ww or 306–636 mg kg^{-1} dw (MacDonald et al. 2002). In ruminant muscle, mean Zn levels were 93–156 mg kg^{-1} dw (Table 11.4). Lower muscle Zn levels were found in elk in the region of Ontario Sudbury ore smelters, Canada (48.19 mg kg^{-1} dw) (Parker and Hamr 2001).

Higher muscle Zn levels were found in European red deer from central-eastern Poland (72.53 mg kg^{-1} ww or 288 mg kg^{-1} dw) and Western Slovakia (54.76 mg kg^{-1} ww or 219.04 mg kg^{-1} dw) and in roe deer from an industrial area, the Koroska Region, with a centuries-old tradition of mining and manufacturing of lead and zinc (51.6 mg kg^{-1} ww or 206.4 mg kg^{-1} dw) (Gasparik et al. 2003; Karpinski 1999; Parker and Hamr 2001; Pokorny and Ribaric-Lasnik 2000).

In the case of omnivorous animals in Europe, Zn concentrations are most frequently analyzed in wild boar (*Sus scrofa*) and in North America in the raccoon (*Procyon lotor*). Average Zn concentrations in these animals can be arranged in the following descending order: muscle > liver > kidney (Table 11.5). Mean hepatic Zn levels usually ranged from 90 to 190 mg kg^{-1} dw, and in the kidney Zn levels were 70–130 mg kg^{-1} dw (Table 11.5). The one significant exception was in raccoon from Ontario, Canada, in which Zn concentrations in the liver and kidney were 34.4 and 29.5 mg kg^{-1} dw, respectively (Wren 1984). In the muscles of omnivorous animals, mean Zn levels were usually in the range 110–250 mg kg^{-1} dw (Table 11.5), while in some wild boar populations from Poland and Slovakia they were much lower, 10.67 mg kg^{-1} ww (or 42.68 mg kg^{-1} dw) and 13.48 mg kg^{-1} ww (or 53.92 mg kg^{-1} dw) (Kucharczak et al. 2003; Gasparik et al. 2012).

Zinc levels in European carnivores have most frequently been analyzed in the red fox (*Vulpes vulpes*) and Eurasian otter (*Lutra lutra*). In North America such research has been mainly carried out on the Arctic wolf (*Canis lupus*) and river otter (*Lontra canadensis*). Research on American mink (*Neovison vison*) has been conducted on both continents. In carnivores, Zn concentrations have usually been studied in connection with the liver, kidney, and muscle, less often bone, hair, and other tissues. Liver Zn levels usually ranged from 70 to 150 mg kg^{-1} dw (Table 11.6). Much lower hepatic Zn levels were found in river otter from Ontario, Canada, and in the polar fox (*Alopex lagopus*) from the Canadian Arctic, at 26.5 and 29 mg kg^{-1} dw, respectively (Hoekstra et al. 2003; Wren 1984). Higher liver Zn levels were found in the Arctic wolf (*Canis lupus*) from Yukon, Canada (122–130 mg kg^{-1} ww or 406.67–433.33 mg kg^{-1} dw) (Gamberg and Braune 1999) and Eurasian otter from Styria, Austria (556.7 mg kg^{-1} dw) (Gutleb 1992). In the kidney, mean Zn levels were 60–120 mg kg^{-1} dw (Table 11.6). Lower Zn concentrations were found

in the red fox from Galicia, Spain (17 mg kg^{-1} dw) (Perez-Lopez et al. 2016), gray wolf (*Canis lupus*) from different regions in Canada and the USA (25.8–39.1 mg kg^{-1} dw) (Hoffmann et al. 2010), and river otter from Ontario (19.6 mg kg^{-1} dw) (Wren 1984), and higher Zn concentrations were found in the Eurasian otter from some parts of Austria (327 mg kg^{-1} dw) (Gutleb 1992). In muscles in carnivores, mean Zn concentrations were 50–150 mg kg^{-1} dw (Table 11.6).

6.2.2 Factors Affecting Zinc Concentrations in Mammal Tissues

6.2.2.1 Sex of Mammals and Zinc Concentrations

The results of studies on the relationship between Zn concentrations and the sex of wild mammals are not clear. In moose (*Alces alces*) and roe deer from Norway, Vikoren et al. (2011) found significant sex-related differences in Zn concentrations in the liver, with females having lower Zn concentrations than males. Hyvarinen et al. (2003) found that in Eurasian otters from Finland, Zn concentrations in the kidney were higher in males (135.9 mg kg^{-1} ww or 453 mg kg^{-1} dw) than in females (101 mg kg^{-1} ww or 336.6 mg kg^{-1} dw). Similarly, in raccoon dogs from farms in Poland, Hanusova et al. (2007) found significant differences, with kidney Zn concentrations in females higher than in males at 80.05 and 60.14 mg kg^{-1} dw, respectively, and in the liver at 107.04 and 75.83 mg kg^{-1} dw, respectively. Similarly, Suvegova et al. (1993) in silver foxes and Hanusova et al. (2007) in polar foxes from farms found higher Zn concentrations in the livers of females. Hanusova et al. (2007) studied the polar fox (*Alopex lagopus*) and the silver variety of farm fox (*Vulpes vulpes*) from the Research Institute for Animal Production in Nitra, Slovakia, and found that Zn levels in liver and muscle of the polar fox were greater in females (82.27 and 108.27 mg kg^{-1} dw, respectively) than in males (69.5 and 98 mg kg^{-1} dw, respectively). In contrast, Bernhoft et al. (2002) found no difference in hepatic Zn concentrations between male and female reindeer from Rybatsjij Ostrov, northwestern Russia. Similarly, Medvedev (1999) found no sex-related differences in Zn concentrations in various organs of the moose, wild boar, or brown bear (*Ursus arctos*) from Russia. Roslewska et al. (2016) and Dlugaszek and Kopczynski (2013) found no differences in Zn concentrations in the muscles of female and male wild boars from Poland. Similarly, Perez-Lopez et al. (2016) found no sex-related differences in Zn levels in the liver and kidney of red fox from Spain and Ogle et al. (1985) in American mink from the state of Virginia, USA.

6.2.2.2 Age of Mammals and Zinc Concentrations

Existing studies on the relationship between the age of wild mammals and Zn concentrations in their organs do not allow firm conclusions to be drawn. For example, Lazarus et al. (2005, 2008) found a higher Zn level in the kidney of the oldest red deer than in the younger animals. Similarly, Holterman et al. (1984) found that red deer 6–11 years of age had approximately twice as high kidney cortex Zn

levels than younger animals. Lazarus et al. (2005) also found an age-related difference in Zn concentrations in the kidney cortex of red deer. Custer et al. (2004) found that 7-year-old moose had higher Zn concentrations in the liver than 1-year-old moose. Parker and Hamr (2001) found much higher Zn concentrations in the liver and bone of elk fetuses (*Cervus elaphus*) (467 and 227 mg kg^{-1} dw, respectively) than in calves (73.62 and 128.77 mg kg^{-1} dw) and adults (74.77 and 102.02 mg kg^{-1} dw), but the authors found no such regularities in the muscle. It has been found that Zn bioaccumulation usually changes with the age of carnivores, being higher in old individuals (Hyvarinen et al. 2003). Cybulski et al. (2009) found higher Zn concentrations in serum, liver, and kidney in older silver fox in comparison to younger animals. An age-related difference has not been shown in the livers of some ruminants, such as reindeer (Bernhoft et al. 2002). Medvedev (1999) found no age-related Zn concentration differences in various organs of the moose (*Alces alces*). This relationship is also not found in different organs of various carnivore species, including the red fox (Dip et al. 2001), Arctic fox (Prestrud et al. 1994), American mink (Ogle et al. 1985; Stejskal et al. 1989; Brzezinski et al. 2014), Eurasian otter (Hyvarinen et al. 2003; Kang et al. 2015), and raccoon (Herbert and Peterle 1990).

6.2.2.3 Environments and Zinc Concentration

For some time we have seen a growing interest in the heavy metal contamination of polluted and unpolluted environments, which requires a proper selection of species in terms of their dietary preferences. Some researchers believe that small ruminants may be good biomonitors of soil Zn levels. Sileo and Beyer (1985) found that mean hepatic and renal Zn concentrations were significantly higher in white-tailed deer caught near zinc smelters at Palmerton, Pennsylvania, USA, than in deer collected farther away from smelters. In white-tailed deer in the vicinity of zinc smelters (<8 km), Zn levels in the liver and kidney were 310 and 256 mg kg^{-1} dw, respectively, while in animals hunted in areas located >100 km from smelters, the levels were much lower (145 and 132 mg kg^{-1} dw, respectively). Bernhoft et al. (1999) found that reindeer from Rybatsjij Ostrov, Russia, an area with nickel smelters emitting large amounts of trace elements, Zn concentrations in the liver were 1.3–1.8 times higher than was found in reindeer from western Finmark, Norway (Sivertsen et al. 1995; Lovberg and Sivertsen 1997). Also, Lopez-Alonso et al. (2002) found a positive association between Zn concentrations in the soil and levels in the livers of calves. Sileo and Beyer (1985) and Reglero et al. (2008) found no significant differences in Zn level in the liver of red deer living close to lead mines compared to those in control areas in Spain. Dip et al. (2001) found no differences in Zn concentrations in the livers and kidneys of red foxes from urban, suburban, and rural areas.

6.2.2.4 Season and Zinc Concentrations

Some studies have shown that the season can be an important factor determining Zn concentrations in wild ruminants. In some hoofed mammals living in a temperate climate such as roe deer and wild boar, the detected muscle, liver, and kidney Zn levels were greater in autumn than in spring (Michalska and Żmudzki 1992). A likely explanation of this is that in autumn, the animals have already had a few months of eating wholesome food, and at the same time it is also a period increased food intake and intense metabolism related to the storing up of energy reserves for winter. However, the organs of red deer living in the same area exhibited an inverse relationship with Zn levels. Borch-Iohnsen et al. (1996), studying reindeer inhabiting the Norwegian archipelago of Svalbard, found that liver Zn concentrations in summer were 2.5 times higher than in winter, and kidney Zn concentrations in July/August were two times higher than in April. These animals feed mainly on grasses and sedge like horsetail, willowherb, and shoots of deciduous trees (Venalainen 2007). Summer food is high herbaceous plants, while in late summer and early autumn reindeer eat mushrooms, and the winter diet mainly consists of lichen (Elkin and Bethke 1995). Moreover, in coastal reindeer, high hepatic Zn concentrations were found in April, which could be due to the low dietary Fe levels, which would improve Zn bioavailability (Borch-Iohnsen et al. 1996). In addition, in winter, those animals feed on marine algae, which have Zn content higher than normal winter foraging plants. Aastrup et al. (2000) found that Zn concentrations in caribou livers were higher in late winter after a season of feeding on long-lived lichens. It was further found that the Zn concentration increased in plant biomass following burn-off of the meadow (Ohr and Bragg 1985). The regrowing plant formations provided herbivorous mammals with significant amounts of Zn, which resulted in a greater accumulation of this element in the liver and other organs. Zimmerman et al. (2008) showed that in white-tailed deer, hepatic Zn concentration was higher in animals from the southern Black Hills in South Dakota, USA, following burn-off (39.09 mg kg^{-1} ww or 130.3 mg kg^{-1} dw) than in tilled areas (35.69 mg kg^{-1} ww or 118.97 mg kg^{-1} dw). A similar relationship was also found in mule deer, in which liver Zn concentrations were 43.53 mg kg^{-1} ww (or 144.33 mg kg^{-1} dw) in burned-off areas and 40.56 mg kg^{-1} ww (or 135.2 mg kg^{-1} dw) in tilled habitats (Zimmerman et al. 2008). The results of all these studies indicate that research on Zn in wild ruminants should consider seasonal changes in diet.

6.2.3 Correlations in Zinc Concentration in Different Tissues

One of the problems researched in ecotoxicology is the relationship between Zn levels in various tissues and organs. However, the occurrence of such correlations in free-living animals is not always clear and may not always be confirmed statistically. Millan et al. (2008) found correlations between muscle and liver Zn concentrations in a few carnivorous species: red fox, Iberian lynx (*Lynx pardinus*), Egyptian mongoose (*Herpestes ichneumon*), common genet (*Genetta genetta*), and Eurasian

badger (*Meles meles*) ($r = 0.388$, $p = 0.021$). On the other hand, Medvedev (1999) found no relationship between Zn concentrations in the various organs of the moose, wild boar, and brown bear from Russia, similar to Harding et al. (1998), who analyzed the relationship between the concentrations of Zn in the liver, kidney, and spleen of American mink in Canada.

6.2.4 Zinc Versus Other Metals in Mammalian Tissues

Zinc interacts with other trace elements, including Cd and Cu. Cadmium has a slight influence on Zn metabolism, owing to its ability to induce production of metallothionein, as well as a competition with Zn for binding metallothionein (Goyer et al. 1995). It was found that high dietary Cu reduces Zn levels in the liver (Puls 1994). All of these metals and mercury (Hg) have a high affinity to small-molecule proteins from the metallothionein group and may induce their formation and compete for binding sites in those proteins (Henkel and Krebs 2004). Gasparik et al. (2012) found a positive correlation between two metal pairs, Zn–Cu and Zn–Hg, in the muscle of wild boar. In other studies, exposure to Cd led to increased Zn levels in the liver and kidney of rats and cattle (Ashby et al. 1981; Lopez-Alonso et al. 2002). In rats, biliary Zn concentrations greatly increased and Cu decreased following Cd administration (Ashby et al. 1981). In contrast, no correlation between Zn and Cd was found in muscle, liver, or kidney tissues or in cattle in Galicia, Northwest Spain, an area characterized by low environmental concentrations of heavy metals (Lopez-Alonso et al. 2004). Given the aforementioned evidence, it seems that research on Zn concentrations in various organs of mammals should also examine the concentrations of other trace elements, mainly Cd and Cu.

For years, ecotoxicologists have tried to assess and identify the most useful animal species and types of biological samples that could be used in the bioindication of environmental levels of Zn. It seems that data for herbivorous species, which often forage across very large territories, are not suitable for determining the specific source of a toxic hazard. Apparently species such as the red fox, which adapts to different environmental conditions and ranges within small territories of 0.5 km^2 and less, would be more suitable for biomonitoring research. Another species that seems appropriate in this regard is the American mink, a predatory mammal in which Zn concentrations in the kidney, liver, and bone are similar to other mammalian species. Finally, studies of this type must also take into account age, gender, and environmental pollution.

6.3 Birds

6.3.1 Zinc Concentration in Bird Tissues

Various biomonitoring studies on birds have analyzed Zn concentrations in various organs, including the liver, kidney, muscle, and bone. In general, Zn concentrations in birds are highest in the liver, kidney, bone, and feathers and lowest in muscle, blood, feces, and eggs (Eisler 1984; Ek et al. 2004). Birds of prey, piscivores, and insectivores have similar Zn concentration ranges (bone > liver > kidney) (Zaccaroni et al. 2011). Kalisinska et al. (2004) found the highest concentration of Zn in mallards in bone tissues (87.73–111.77 mg kg^{-1} dw) and the liver (34.88–49.78 mg kg^{-1} or 116.27–165.93 mg kg^{-1} dw) and the lowest in the kidney (19.91–24.65 mg kg^{-1} or 79.64–98.6 mg kg^{-1} dw), muscle (11.99–12.96 mg kg^{-1} or 39.97–43.2 mg kg^{-1} dw), and brain (10.63–12.04 mg kg^{-1} or 53.15–60.20 mg kg^{-1} dw).

Zinc concentrations in the liver, kidney, and muscle can be considered indicative of Zn chronic exposure (Naccari et al. 2009). Because the determination of Zn concentrations in internal organs requires that the subject animals be dead, researchers increasingly prefer intravital sampling, for example, blood, excrement, feather, and egg samples (Burger 1993; Dauwe et al. 2000). Birds can excrete Zn through feces or by deposition in the uropygial salt glands (Burger and Gochfeld 1985) and feathers (Burger 1993). Females can also eliminate this metal by deposition in the eggs. Zinc concentrations in feathers may increase with age due to exogenous contamination with atmospheric deposition, so feathers can reflect contamination of the local habitat (Dmowski and Golimowski 1993). This method of research is often used for birds of prey, including the white-tailed eagle (*Haliaeetus albicilla*), bald eagle (*Haliaeetus leucocephalus*), osprey (*Pandion haliaetus*), and Eurasian buzzard (*Buteo buteo*), for water birds, including the mallard (*Anas platyrhynchos*), greylag goose (*Anser anser*), and pochard (*Aythya ferina*), and for passerines such as the great tit (*Parus major*), house sparrow (*Passer domesticus*), and tree sparrow (*Passer montanus*) (Table 11.7).

In Anseriformes, bone Zn levels range from 90 to 120 mg kg^{-1} dw (Table 11.7). However, much higher Zn concentrations in bone have been found in pochard from Donana Natural Park (DNP) (154.9 mg kg^{-1} dw) (Taggart et al. 2006). In passerines, mean bone Zn levels were greater than the average level for Anseriformes at 150–250 mg kg^{-1} dw. Even higher Zn concentrations have been described in the great tit from a polluted zone in Spain (255.90 mg kg^{-1} dw) (Llacuna et al. 1995) and from Niepołomice Forest, Poland (284 mg kg^{-1} dw) (Sawicka-Kapusta et al. 1986) and in a tree sparrow (*Passer montanus*) in Beijing, China (255 mg kg^{-1} dw) (Chao et al. 2003). An even greater Zn concentration has been described in the tibia of house sparrows in two polluted areas in Albania (291.50 and 342.80 mg kg^{-1} dw) (Millaku et al. 2015).

Typical Zn concentrations in avian livers are 25–40 mg kg^{-1} ww (or 83–133 mg kg^{-1} dw) (WVDL 2015). Usually, mean hepatic Zn concentrations in birds of prey

range from 60 to 170 mg kg^{-1} dw (Table 11.7). However, in some species, especially those inhabiting areas with significant environmental pollution with heavy metals, levels can exceed 220 mg kg^{-1} dw. Almost 240 mg Zn kg^{-1} dw was detected in the liver of a bald eagle in the area of the Great Lakes in North America (Nam et al. 2012). An even greater Zn level, nearly 300 mg kg^{-1} dw, was found in a Eurasian sparrowhawk from Galicia, Spain (Perez-Lopez et al. 2008). This could be due to the high Zn concentrations in soils in Galicia, ranging from 25 to 400 mg kg^{-1} dw (Perez-Lopez et al. 2008).

In wild waterfowl, average hepatic Zn levels generally occur over a wider range (80–220 mg kg^{-1} dw) than in birds of prey (Table 11.7). Sometimes the levels are much lower, for example 62.4 mg kg^{-1} dw in mallard from the Gomish International Wetland, Iran (Sinka-Karimi et al. 2015). A few cases of waterfowl research showed very high liver Zn, in excess of 280, and even 2900 mg kg^{-1} dw (Sileo et al. 2003). Experimental studies have shown that in mallards with clinical signs of Zn poisoning, liver Zn was 473–1990 mg kg^{-1} dw (Levengood et al. 1999). Sileo et al. (2003) found Zn poisoning in three Canada geese (*Branta canadensis*) and mallard from the Tri-State Mining District (TSMD), Oklahoma, Kansas, and Missouri, USA, contaminated with Pb, Cd, Zn, and from mining, milling, and smelting. Zinc poisoning was diagnosed based on mild to severe degenerative abnormalities of the exocrine secretions of the pancreas; the liver Zn concentrations in the geese and mallard were 1000–2900 mg kg^{-1} and 280 mg kg^{-1} dw, respectively (Sileo et al. 2003). In addition, Beyer et al. (2005) noted that Zn concentrations in liver in three mallards, also from the TSMD, ranged from 770 to 1100 mg kg^{-1} dw. The mallard with the highest concentration of Zn had caseous typhlitis (inflammation of the caeca). Typhlitis wad has also been observed in mallards experimentally poisoned with Zn shot (Levengood et al. 1999).

The literature also describes Zn poisoning in birds kept in zoos and parks in cages with nets made out of galvanized wire or in birds residing in bodies of water into which people threw coins made of alloys containing Zn. Fragments of such wires and coins are a significant source of poisoning of birds held in captivity. Doneley (1992) observed moderate to severe nephrosis in caged and aviary birds containing hepatic Zn levels of 320 and 534 mg kg^{-1} dw, respectively.

In passerines, mean hepatic Zn levels were lower than the previously mentioned groups of birds, and usually range from 40 to 130 mg kg^{-1} dw (Table 11.7). Lower mean levels were found in house sparrows from Sargodha city and Bhalwal Punjab, Pakistan (7.85 mg kg^{-1} or 26.16 mg kg^{-1} dw) (Mustafa et al. 2015) and from rural and urban areas in Finland (18.35 and 21.08 mg kg^{-1} dw, respectively) (Kekkonen et al. 2012), while higher Zn concentrations in the liver were found in the great tit from Bialowieza and Niepolomice Forests, Poland (163 mg kg^{-1} dw) (Sawicka-Kapusta et al. 1986) and in the Italian sparrow *Passer domesticus Italiae* in rural and urban areas in Italy (154 and 204 mg kg^{-1} dw) (Gragnaniello et al. 2001).

Ecotoxicological reports on Zn concentrations in animals also contain relatively large amounts of data regarding the kidneys. Normal Zn concentrations in avian kidneys are 22–32 mg kg^{-1} ww or 88–128 mg kg^{-1} dw (WVDL 2015). In birds of prey, Anseriformes and passerines, mean nephric Zn is usually from 40 to 190 mg kg^{-1}

dw (Table 11.7). Lower mean nephric Zn levels have been found in house sparrows in reference (village Ciglik, Antalya) and polluted areas (Yatagan Thermal Power Plant in Mugla Province) in Turkey, at about 20 and 30 mg kg^{-1} dw, respectively (Albayrak and Mor 2011). These small nephric Zn concentrations in polluted areas could be due to low levels of Zn in the environment. Demirak and Balci (2005) found that the Zn content in the underground water around the Yatagan Thermal Power Plant in Turkey were lower than those noted in European Economic Community and World Health Organization guidelines. Higher nephric Zn levels have been found in the Eurasian buzzard in Italy, at 91.1 mg kg^{-1} ww or 367.6 mg kg^{-1} dw (Zaccaroni et al. 2011). Also, higher Zn levels were found in the kidney of the gadwall (*Anas strepera*) in DNP, Spain, at 296.2 mg kg^{-1} dw (Hernandez et al. 1999) and in mallard in the TSMD, USA, at 290–620 mg kg^{-1} dw (Beyer et al. 2005). Sileo et al. (2003) found that Zn concentrations in the kidney in three Canada geese and a mallard displaying Zn poisoning from the TSMD were 510–970 and 220 mg kg^{-1} dw, respectively. Experimental studies have shown that in Zn-intoxicated birds, microscopic changes in the kidneys include varying degrees of acute tubular necrosis, occasional secondary renal or visceral gout, and moderate interstitial nephritis in addition to nephrosis (Puschner et al. 1999).

In contrast to the liver and kidney, the average Zn concentration in the muscles of these birds is considerably lower and does not exceed 100 mg kg^{-1} dw. The muscles of birds of prey, waterfowl, and passerines contain an average of 50–90, 30–95, and 10–95 mg Zn kg^{-1} dw, respectively (Table 11.7).

Among the different types of samples taken from birds, ecotoxicologists indicate the significant usefulness of feathers because they can be obtained from living individuals. Some researchers believe that the feathers of nonmigratory bird species are suitable bioindicators of regional contamination (Burger 1993). Metal concentrations in feathers reflect the levels in the blood during the period of growth when the feather is connected with blood vessels and metals are incorporated into the keratin structure (Dauwe et al. 2000). The relative high Zn concentration in feathers is caused by the participation of Zn in the keratinization process (Burger 1993). Because birds can excrete Zn into growing feathers, Zn concentrations in feathers can be higher than in other tissues (Janssens et al. 2002). Metal levels in feathers reflect the levels in food during the period of feather growth, including during the growth of young birds, or during the molting period of fully grown birds (Solonen et al. 1999). In Falconiformes and Strigiformes, mean Zn concentrations in feathers ranged from 30 to 175 mg kg^{-1} dw (Table 11.8). Much higher Zn concentrations in feathers have been found in the barn owl (*Tyto alba*) in contaminated and control sites in Belgium, at about 360 mg kg^{-1} dw (Denneman and Douben 1993).

Zinc concentrations in feathers are higher in nocturnal raptors compared to diurnal raptors and bird eaters (Solonen et al. 1999). This is an essential element, and there seems to be no significant food-chain-related differences in birds of prey. However, Zn levels in feathers in passerines vary greatly, from 50 to 280 mg kg^{-1} dw. Zinc concentrations much higher than this upper limit were found in great tit in the Bialowieza Forest, Poland (~360 mg kg^{-1} dw) (Sawicka-Kapusta et al. 1986)

and blue tit (*Parus caeruleus*) in a reference site in Belgium (~400 mg kg^{-1} dw) (Eens et al. 1999).

Zinc is involved in the formation of certain colored feathers. Pigments such as eumelanin have a great capacity for binding Zn (Niecke et al. 1999). The black-brown pigmentation of feathers often results from the presence of melanin and a high concentration of Fe, Ca, Cu, and Zn (Scanlon et al. 1980; Goede 1985). Darker individuals have higher zinc levels in their feathers compared with paler ones when kept in standardized conditions.

6.3.2 Factors Affecting Zinc Concentrations in Bird Tissues

6.3.2.1 Age of Birds and Zinc Concentrations

The results of research are not unambiguous on the relationship between Zn content and age of birds. Taggart et al. (2006) found a significant difference in bone Zn concentrations between different age groups of birds. Kalisinska et al. (2004) studied two populations of mallards from an area less polluted with heavy metals in the city of Szczecin (including Zn) and a more polluted area of Slonsk (Poland) and found an age-related difference in Zn concentrations between both mallard populations. Zinc concentrations in the kidney of adults in Szczecin (22.87 mg kg^{-1} ww or 91.48 mg kg^{-1} dw) were higher than in juveniles (19.91 mg kg^{-1} ww or 79.64 mg kg^{-1} dw) ($p \leq 0.05$), while immature mallards from Slonsk had higher Zn levels in bone ($p \leq 0.01$) and liver tissues ($p \leq 0.05$) (111.77 mg kg^{-1} ww or 166.82 mg kg^{-1} dw and 49.78 mg kg^{-1} ww or 165.93 mg kg^{-1} dw, respectively) than adults (87.73 mg kg^{-1} ww or 130.94 mg kg^{-1} dw and 43.32 mg kg^{-1} ww or 144.4 mg kg^{-1} dw, respectively). Similarly, in piscivorous osprey from the Eastern USA, Wiemeyer et al. (1980) found higher Zn concentrations in the liver of immature birds (223.33 mg kg^{-1} dw) than in adults (126.67 mg kg^{-1} dw). Their later studies, however, showed that Zn levels in the same osprey were similar in both age groups (Wiemeyer et al. 1987). Swaileh and Sansur (2006) found that Zn concentration in the liver in adult house sparrows were about 1.5 times higher than in 1-month-old juveniles. In contrast, Licata et al. (2010) found no effect of age on Zn concentrations in Eurasian buzzard. Similarly, Hogstad (1996) found no statistically significant differences in Zn concentration in the liver between adults (72.70 mg kg^{-1} dw) and juveniles (67.06 mg kg^{-1} dw) in five passerine species. Changes in Zn concentration can be due to the fact that this metal is involved in many processes occurring in the egg and during feather development (Morera et al. 1997).

6.3.2.2 Sex of Birds and Zinc Concentrations

Gender-related differences in metal concentrations, including Zn, might be expected if males and females eat different food, different sized foods, and different proportions of various types of food (Burger 1995). In addition, some gender-related

Table 11.8 Zinc concentrations in feathers of birds

Species	Localization	Zn (mg kg^{-1} dw)	References
Eurasian buzzard *Buteo buteo*	Sicily, Italy	60.1	Naccari et al. (2009)
	Southern Finland	140	Solonen et al. (1999)
Peregrine falcon *Falco peregrinus*	Sweden	47.0	Ek et al. (2004)
	Alaska	141.9–149.3	Parrish et al. (1983)
Laggar falcon *Falco biarmicus jagger*	Pakistan	110	Movalli (2000)
Eurasian sparrowhawk *Accipiter nisus*	Southern Finland	130	Solonen et al. (1999)
	Belgium	35	Dauwe et al. (2003)
	Sweden	41	Ek et al. (2004)
Northern goshawk *Accipiter gentilis*	Southern Finland	130	Solonen et al. (1999
Barn owl *Tyto alba*	Belgium	62	Dauwe et al. (2003)
	Netherlands, PA	363	Denneman and Douben (1993)
	Netherlands, UA	360	
Little owl *Athene noctua*	Belgium	31	Dauwe et al. (2003)
Tawny owl *Strix aluco*	Southern Finland	120	Solonen et al. (1999)
Laggar falcon *Falco biarmicus jugger*	Pakistan	107.40	Movalli (2000)
Osprey *Pandion haliaetus*	Central California, USA	173	Cahill et al. (1998)
	Southern Finland	110	Solonen et al. (1999)
Mallard *Anas platyrhynchos*	Central California, USA	170	Cahill et al. (1998)
Great tit *Parus major*	Northeastern and Southern Poland	173–357	Sawicka-Kapusta et al. (1986)
	Belgium, PA	172.66	Eens et al. (1999)
	Belgium, UA	178.56	
	Belgium, PA	97.9	Dauwe et al. 2000)
	Belgium, UA	127.2	
	Finland, PA	132.4	Eeva et al. (2009
	Russia, UA	126.5	
	Portugal, PA	111.0	Costa et al. (2013)
	Portugal, UA	112.9	
	Northern China	276.60	Deng et al. (2007)
	Northeastern Spain, UA	185.18	Llacuna et al. (1995)
	Northeastern Spain, PA	166.60	
Blue tit *Parus caeruleus*	Belgium, PA	252.64	Eens et al. (1999)
	Belgium, UA	403.70	
	Belgium, PA	317.4	Dauwe et al. (2005)
	Belgium, UA	311.0	

(continued)

Table 11.8 (continued)

Species	Localization	Zn (mg kg^{-1} dw)	References
Rock bunting *Emberiza cia*	Northeastern Spain, UA	177.60 196.1	Llacuna et al. (1995)
	Northeastern Spain, PA	196.10	
Blackbird *Turdus merula*	Northeastern Spain, UA	131.90	Llacuna et al. (1995)
	Northeastern Spain, PA	155.40	
House sparow *Passer domesticus*	West Bank, Palestine	54.9	Swaileh and Sansur (2006)
	India, URA	48.99	Sundaramahalingam et al. (2016)
	India, RUA	31.5	
Tree sparrow *Passer montanus*	China	83.40–126.97	Gong et al. (2012)
Song sparrow *Melospiza melodia fallax*	Arizona, USA	195.1–206.3	Lester and van Riper (2014)

PA polluted area, *UA* unpolluted area

differences may be associated with differences in the metabolic profiles of metals involved and the activity of sex hormones, the intake or uptake of metals and nutritional requirements, or interactions between elements (Vahter et al. 2007). The sexes may differ in their production of various metalloproteins ,which play fundamental roles in the transport, storage, and excretion of metals (Gochfeld and Burger 1987). Moreover, differences in Zn levels may be due to physiological differences and the ability of female birds to excrete Zn into eggs (Naccari et al. 2009).

Moreover, because some species such as the house sparrow are considered to be sedentary, females are more prone to dispersal from native areas than males, making them less indicative of the area of environmental contamination (Skjelseth et al. 2007). Eeva et al. (2009) suggest that these differences are also due to the higher reproductive effort that makes females more susceptible to the negative health effects of pollution stress. Taggart et al. (2006) found that in female waterfowl, the liver Zn concentration was higher (87.7 mg kg^{-1} dw) than in males (68.8 mg kg^{-1} dw) in DPN, Spain. Danczak et al. (1997), in their research on mallard from the Slonsk Reserve (Poland), showed that the mean Zn concentration in the liver was higher in females (53.9 mg kg^{-1} ww or 179.67 mg kg^{-1} dw) than in males (43.6 mg kg^{-1} ww or 145.33 mg kg^{-1} dw), while both Swaileh and Sansur (2006) and Albayrak and Mor (2011) found no statistical difference in Zn concentrations between the livers of male and female house sparrows.

Despite the ambiguity concerning the relation between Zn content and sex of birds, it seems that this factor should be taken into consideration when analyzing the results of research.

6.3.2.3 Diet of Birds and Zinc Concentrations

Differences in Zn concentration between species and areas of habitation are the result of different diets, feeding strategies, and metabolic rates (Costa et al. 2013), as well as differences in the physiology of bird species (Deng et al. 2007). Animals usually regulate Zn effectively, and consequently hepatic Zn concentrations do not vary in proportion to dietary variability (Sileo et al. 2003). However, homeostatic mechanisms do fail at extremely high concentrations, with significant differences observed between species. In experimental studies on chickens, hepatic Zn levels increased more than 10-fold when the dietary concentration increased to about 2200 mg kg^{-1}, but Zn levels remained constant as the dietary concentration increased from 37 to about 110 mg kg^{-1} ww (Stahl et al. 1989). In domestic mallard liver Zn concentration increased from 54 to 401 mg kg^{-1} ww (or 180 to 336.67 mg kg^{-1} dw) as dietary Zn concentration increased from the control concentration to 3000 mg kg^{-1} (Gasaway and Buss 1972). Mute swans (*Cygnus olor*) fed a contaminated and suboptimal diet accumulated three times higher Zn concentrations in the liver than those fed a commercial waterfowl maintenance diet with the same Zn and other metal levels (Day et al. 2003).

Zinc concentrations in tissues may be related to the amount of plant food in the diet. Parslow (1982) studied the concentration of heavy metals in the liver of 16 different bird species from Ouse Washes, England. They found the highest Zn concentrations in the liver of the Eurasian wigeon (*Anas penelope*) and the lowest concentrations in the shoveler (*Anas clypeata*) and tufted duck (*Aythya fuligula*). They surmised that this could be because wheat (31.2 mg Zn kg^{-1} ww) and barley (31.6 mg Zn kg^{-1} ww) seeds contain more zinc than potatoes (7.7 mg Zn kg^{-1} ww). Similarly, Gochfeld and Burger (1987) observed that birds eating other animals accumulate more metals than birds feeding on vegetation. Zaccaroni et al. (2011) studied Zn levels in groups of species with regard to different feeding habits, with higher Zn concentrations in the liver of piscivorous birds (95.1 mg kg^{-1} ww or 317 mg kg^{-1} dw) than insectivorous birds (82 mg kg^{-1} ww or 274 mg kg^{-1} dw). Bone Zn concentration was higher in birds of prey (217 mg kg^{-1} ww or 324 mg kg^{-1} dw) than in fish-eating birds (194 mg kg^{-1} ww or 290 mg kg^{-1} dw).

Lucia et al. (2008) found that in overfed birds Zn concentrations in the kidney (138.1 mg kg^{-1} dw) were higher than in muscle (73.9 mg kg^{-1} dw) and liver (38.4 mg kg^{-1} dw), and in nonoverfed birds liver Zn levels (271.9 mg kg^{-1} dw) were greater than in kidney (95.5 mg kg^{-1} dw) and muscle (67.4 mg kg^{-1} dw). In feathers of both the nonoverfed and overfed birds Zn concentrations were 102.8 and 164.9 mg kg^{-1} dw, respectively. This suggests that the homogeneity in Zn levels in avian species from different habitats is related to the role of zinc in biological systems. Methallothionein can counteract the effects of exposure to high Zn levels, shifting its metabolism to bone accumulation typical of chronic exposure, which is most evident in piscivorous birds whose Zn levels are low in the kidney (47.5 mg kg^{-1} ww or 190 mg kg^{-1} dw) and much higher in bone (194 mg kg^{-1} ww or 290 mg kg^{-1} dw) (Zaccaroni et al. 2011). Therefore, bioindicative studies should take into account food chain differences between bird species.

6.3.2.4 Habitats and Zinc Concentration

In recent years, many studies have investigated Zn concentrations in the organs of birds from polluted and unpolluted sites. Millaku et al. (2015) found that Zn concentrations were higher in the liver and kidney of the house sparrow from polluted areas (94.47 and 61.63 mg kg^{-1} dw, respectively) in comparison to a reference site (61.48 and 47.22 mg kg^{-1} dw, respectively) in Albania. Beyer et al. (2005) found that Zn poisoning in the TSMD USA, seems to be hazardous primarily to waterfowl. They also found that in waterfowl, including Canada geese, mallard, common pintail (*Anas acuta*), green-winged teal (*A. crecca*), ring-necked duck (*Aythya collaris*), and lesser scaup (*A. affinis*) from the TSMD, Zn levels in the liver and kidney were higher (440 and 210 mg kg^{-1} dw, respectively) than in mallard at a reference site (93 and 80 mg kg^{-1} dw, respectively). In intestinal digesta of the waterfowl from the TSMD, Zn concentration was 1100 mg kg^{-1} dw compared to 130 mg kg^{-1} dw at the reference site. The digesta contained a mixture of plant and invertebrate material with some sediments and soil. Sediments in the TSMD contained an extremely high Zn concentration, for example, in the Spring River, Zn levels in sediments were 22,000–25,000 mg kg^{-1} (Ferrington 1989). Zinc concentrations exceeding 1000 mg kg^{-1} were also found in freshwater vascular plants from several polluted sites (Outridge and Noller 1991). Canada geese and swans may be especially susceptible to metal poisoning because they ingest substantial amounts of sediment when they feed (Beyer et al. 2005). Van der Merwe et al. (2011) studied Canada geese in the TSMD with regard to their mean Zn concentrations in different organs at four mine-waste-contaminated sites and a reference site, where those from the confluence between the Spring River and Short Creek, where mine waste was deposited in the streambed of the Spring River and northwestern Galena, Kansas, mean Zn concentrations in the liver were 83 mg kg^{-1} ww (or 277 mg kg^{-1} dw) and 178 mg kg^{-1} ww (or 595 mg kg^{-1} dw), respectively, and in the kidney 22.8 mg kg^{-1} ww (or 91.3 mg kg^{-1} dw) and 48.7 mg kg^{-1} ww (or 194.6 mg kg^{-1} dw), respectively.

In two birds northwest of Galena, liver Zn levels were above a level indicating Zn poisoning in domestic poultry (>200 mg kg^{-1} ww or >666 mg kg^{-1} dw) (Puls 1994). In April 1998, a holding lagoon containing pyrite-ore-processing waste failed and released acidic metal-rich sludge and water into the Rio Guadiamar flowing through DNP (Galan et al. 2002). Benito et al. (1999) and Hernandez et al. (1999), examining blood, livers, and eggs of birds from the DNP since that accident, found that Zn concentration was elevated in relation to uncontaminated areas. Two years after the spill, Gomez et al. (2004) found increased Zn concentrations in the tissues of waterbirds from DNP, with Zn concentration in the liver 2.92–1084 mg kg^{-1} dw. Taggart et al. (2006) found in waterfowl from the DNP maximum Zn concentration in liver at 220 mg kg^{-1} ww (734 mg kg^{-1} dw). Kozulin and Pavluschick (1993), examining mallards from an unpolluted section of the Svisloch River in Minsk, Belarus, and another section heavily polluted by urban and industrial outflows, found no difference in Zn concentration in the liver (135.1 and 126.1 mg kg^{-1} dw, respectively), kidney (113.4 and 93.6 mg kg^{-1} dw, respectively), and muscle

(50.4 and 41.8 mg kg^{-1} dw, respectively). In contrast, house sparrows studied in Albania had higher Zn levels in the liver and muscle at a polluted site than those from an uncontaminated reference area (Albayrak and Mor 2011).

Kekkonen et al. (2012) found that the livers of house sparrows from an urban area had higher Zn levels than at a rural site. Swaileh and Sansur (2006) found the livers of house sparrows from urban areas (131.4 mg kg^{-1} dw) had significantly higher Zn levels than at a rural site (97 mg kg^{-1} dw). Similarly, Sundaramahalingam et al. (2016) found higher Zn levels in the muscles, bones, and feathers of sparrows from an urban site compared to a rural area. Gragnaniello et al. (2001), studying the liver and kidney of Italian sparrows, found higher Zn concentrations in species collected from an urban area than in those collected from rural localities.

Nestling birds are potential good biomonitors for terrestrial point-source pollution (Burger 1993; Janssens et al. 2002). In areas with significant environmental pollution (especially Cd), Zn deficiency may occur in intensively growing chicks. Zinc concentrations lower than that resulting from adequate nutrition were found in dead nestlings of the rook *Corvus frugilegus* in the liver, kidney, and muscle, with average Zn levels at 3.3, 1.6, and 1.3 mg kg^{-1} dw, respectively (Orlowski et al. 2012).

An excess of Zn in the environment can lead to increased concentrations in the tissues of birds, including adults. Zinc concentrations in various organs or tissues taken from birds from a polluted area were greater than at the reference site in a study by Gomez et al. (2004), who found that, 7 months after a spill accident in DNP, Zn levels in 14 waterbird species were higher than those reported before the spill. In songbirds from a site severely contaminated with Zn from smelting, Zn concentration was only 20% greater than in birds from a reference site, although Zn soil concentration at the contaminated site was >10 times higher than at a reference site (Beyer et al. 1985). Hogstad (1996) found no significant differences in liver Zn concentrations in juveniles of three *Parus* species, the great tit, the marsh tit (*P. palustris*), and the willow tit, and the finches, bullfinch (*Pyrrhula pyrrhula*), and greenfinch (*Carduelis chloris*) from industrial areas (72.50 mg kg^{-1} dw) and forest areas (57.99 mg kg^{-1} dw). This may prove that birds adapt to high levels of this element in the environment and diet.

Interesting results are also provided by the analysis of Zn content in the feathers of birds. Janssens et al. (2001) found that mean Zn concentrations in the tail feathers of great tits near a metallurgical factory were higher than in a reference area (264 vs. 119.5 mg kg^{-1} dw). Similarly, Manjula et al. (2015) found that in the feathers of house sparrows from an urban area, Zn concentrations were higher (98.16 mg kg^{-1} dw) than those from a rural area (75.91 mg kg^{-1} dw) ($p = 0.04$). In contrast, there was no difference between Zn levels in feathers of great tits from polluted and reference sites, but Zn levels in feathers were higher in the blue tit from a reference site than a polluted site (Eens et al. 1999). Based on a field experiment with free-living great tits, Jaspers et al. (2004) stated that Zn concentrations in feathers were probably due to endogenous deposition. Therefore, Zn levels in feathers of adult passerines can be used as monitors of local exposure.

Often studies also used feathers of nestlings, because the metal concentration in such feathers small reflect local pollution levels far better than those from in adults,

because in nestlings, exposure occurs over a defined time period and is limited to the parents' foraging area (Furness 1993). However, it appears that in the case of Zn, rather young birds do not meet the criteria for good material bioindication. Janssens et al. (2002) studied 15-day-old great tit nestlings in Belgium, gathering feathers collected from multiple positions at different degrees from a large nonferrous smelter.

In feathers of nestlings collected at a distance of 400–600 m from the smelter, Zn concentration was significantly lower (16.5 mg kg^{-1} dw) than at locations at distances of 0–350 m (31.3 mg kg^{-1} dw), 2500 m (40.2 mg kg^{-1} dw), and 4000 m (43.35 mg kg^{-1} dw). Furthermore, in other studies, feathers of great tit nestlings from reference and polluted sites showed no significant differences in Zn concentrations (Dauwe et al. 2000; Janssens et al. 2002; Costa et al. 2013). These authors suggested that the feathers of great tit nestlings could not be used as biomonitors for Zn because they may not adequately reflect nestlings' body burden.

Eggs play an important role in ecotoxicological studies. Bird eggs have been used as bioindicators because they come from a specific fragment of the population, namely laying females. They are formed only during a specific period, have a consistent composition, and are easily sampled, and the removal of one egg from a nest has only a minor effect on population parameters (Furness 1993). Trace elements essential to embryonic development including Zn are transferred from the tissues of the females and ultimately reflect the extent of pollution in the females' environment (Nyholm 1998). The mean Zn concentrations are higher in egg content than eggshell because Zn is embedded in the quaternary structure of proteins whose concentrations are higher in eggs than in eggshells. It seems that the Zn supply to eggs, which are the nucleus of the future of the body, is subject to regulation developed during the evolution of the species, because Zn levels in eggs from areas heavily polluted with Zn are similar to those from uncontaminated areas. Dauwe et al. (1999) found no differences between Zn concentrations in eggs and eggshells from great and blue tits in polluted (62 and 69 mg kg^{-1} dw, respectively) and reference sites in Belgium (28 and 19 mg kg^{-1} dw, respectively). Dauwe et al. (1999) found that the eggshell could be used as an indicator for heavy metal pollution, especially at contaminated sites. It has also been found that egg white, ovalbumin, and conalbumin bind Zn (Richards and Steel 1987). Metals excreted in eggs reflect both stored body burdens and food choices of females during egg formation (Ek et al. 2004).

The aforementioned data indicate that Zn pollution is reflected in water and marsh birds (which collect food from the aqueous environment and contaminated sediments) and passerines.

6.3.2.5 Season and Zinc Concentrations

Differences in Zn concentrations in avian organs may also be related to season. Parslow (1982) demonstrated that Zn concentrations in the liver from each of the waterfowl species they studied, including mallard shot in November (119.8 mg kg^{-1}

dw), were lower than in December and January (approximately 166 mg kg^{-1} dw), which could be related to periodic molting and changes in the composition and quality of food. Gomez et al. (2004) found that in 14 waterfowl species from DNP, liver Zn concentrations tended to decrease slightly during summer. Gong et al. (2012) found that Zn concentrations in the pectoral muscle, heart, liver, and primary feathers of tree sparrows from Heilongjiang province, China, were highest in summer. In contrast, Hogstad (1996) found no statistically confirmed differences between hepatic Zn levels in juveniles and adults of three *Parus* species from Central Norway between January–March and October–December. Despite this inconsistency, biomonitoring should take into account the season of the year during which the material was collected and seasonal differences in the composition of the diet.

6.3.3 Zinc Versus Other Metals in Avian Tissues

Zinc is a redox-inactive metal, able to interact with other chemicals and produce altered types of toxicity, accumulation, and metabolism in birds (Koivula and Eeva 2010). In birds, Zn has been found to have antagonistic relations with Pb and Cd (Kaminski 1998). The correlation between Zn and Cd depends on the degree of Cd contamination, the correlation being more significant at a higher Cd burden (Wenzel et al. 1996). Levengood and Skowron (2007) found that Cd was significantly associated with Zn in the livers of sentinel ducks. The relationship between Cd, Zn, and metallothionein in sentinel ducks varied with the location of foraging and diet. Levengood et al. (1999) found that exposure to high Zn concentrations reduced hepatic Zn concentrations and increased renal Cd levels in mallard.

In avian kidneys a positive relationship has been described between Zn and Cd because the increased synthesis of Cd-induced metallothionein at the same time increases the number of binding sites available to Zn (Walsh 1990). Zinc is thought to provide protection against the renal toxicity of Cd (Hutton 1981). It was found that a high concentration of Zn interferes with the absorption of Cd, while a Zn:Cd ratio of about 150:1 probably protects terrestrial food chains from Cd toxicity (Chaney et al. 2001). Kim and Oh (2012) found that in the liver of mallard Zn concentrations were significantly correlated with Pb and Cd. A positive correlation between Zn and Cu has been demonstrated in the avian liver, which is most likely due to the similar metabolism of the metals (Wenzel et al. 1996).

7 Conclusions

In studies on terrestrial mammals, a measurable response to Zn pollution is exhibited by animals that are common in natural and seminatural habitats such as the red fox, raccoon, American mink, otter, and ungulates (including the white-tailed deer, reindeer, red deer, and wild boar). Birds are used as bioindicators because they are abundant and widely distributed, have long lifespans, and feed at different trophic

levels, often being the top consumers. At the same time, they are more sensitive to Zn contamination than other vertebrates and therefore seem to be better bioindicators. Nestling passerines are potential good biomonitors for Zn pollution as Zn is intake in a clearly defined time period and originates from a limited parental foraging area. Zinc concentrations in the tissues of mammals and birds depend both on biological factors (e.g., age, physiological condition, animal species, sex, and age) and environmental factors (such as the supply of zinc in the diet). Long-term bioindication research conducted on the organs and tissues of mammals and birds, as well as noninvasive sampling of eggs and feathers, indicates the usefulness of this type of material for evaluating the state of the environment.

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Chapter 12
Aluminum, Al

Ewa Skibniewska and Michał Skibniewski

Abstract Aluminum is the third most abundant element in nature, after oxygen and silicon. Its content in the Earth's crust has been estimated at a level of 8%. In spite of this, the element has never been engaging in the metabolic processes of the evolving living organisms. Aluminum reaches the body of an animal mostly ingested with food. Crossing the intestinal barrier, the metal gets to the bloodstream and so is transported to various tissues using the iron-transport routes. Of the total aluminum uptake, the majority is deposited in the bone (60%) and lungs (25%), whereas much lower amounts accumulate in the muscles (10%) and the liver (3%). Cerebral accumulation of the total uptake is about 1%. Besides blood, the metal is also found in all the other body fluids of a homeothermic organism, e.g., cerebrospinal fluid, lymph, semen, sweat, or urine. Studies on aluminum toxicity involving various taxonomic groups enable concluding that the mechanisms are similar across the taxa and consist mainly in evoking oxidative stress in cells. At the cellular level, aluminum reacts with cell membranes, cytoskeletal structures, and nucleic acids. In terrestrial vertebrates, aluminum impact results in altered enzymatic activity in the central nervous system and other organs and systems of the body. The metal affects the bone tissue metabolism, impairs the function of the excretory system and liver, and also has a negative effect on erythropoiesis. Human activity observed over the last centuries has led to a rapid growth in the production of aluminum obtained from the natural sources and, as a result, to its inclusion into the trophic chains of various ecosystems. In consequence, since 1970, aluminum has been treated as a xenobiotic accumulating in living organisms, whose bioavailability is continuously increasing.

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1 Introduction

Aluminum (Al), which belongs to the group of light metals, is the most abundant metallic element in the Earth's crust. Naturally found in the soil, rocks, and numerous minerals, Al does not occur in its pure metallic form (de la Fuente et al. 2007; Exley 2009). Since the dawn of history, aluminum-containing minerals have been used in a variety of industries. They were used already in ancient Greece and Rome, mainly in the manufacturing of dyes, in tanning, in water treatment, and as a component of drugs to treat ulcers (Steinegger et al. 1990; Kawahara and Kato-Negishi 2011).

Although the element is ubiquitous in nature, it is considered as a xenobiotic or a foreign substance, which has no role to play in any of biochemical or physiological functions of the organism. As various forms of life were evolving on Earth, many metals were gradually incorporated in the metabolic cycles and became essential nutrients in the biochemical processes running in the cell. Aluminum has remained an element that has no structural or catalytic function in microorganisms, fungi, plants, or animals. Despite this, the metal is biologically reactive and—in excess—is harmful to living organisms (Exley 2003, 2009).

Due to its specific properties, including the electrochemical characteristics, over the last 100 years of industrialization, Al has become an extremely important element and its importance continues to grow. Aluminum has become a ubiquitous component of the human environment, so the times we live now are sometimes referred to as the age of aluminum (Steinegger et al. 1990; Ranau et al. 2001; Exley 2009). In terms of environmental impact, the metal has a major part in the destruction of many ecosystems due to its role in acid rains. Therefore, ecotoxicological studies on the impact of aluminum on aquatic and terrestrial environments have been carried out for decades (Martin 1994). Due to its technological properties, Al is used in many industries. Not only is the metal used in civil engineering, aviation industry, and machine construction, but it is also indispensable in metallurgy and the generally understood chemical industry. Its physical and chemical properties, such as high resistance to moisture, gases, organic solvents, and light, make Al an almost perfect material for containers intended to store various substances. As a result, the metal finds wide application in the manufacturing of packages used in the food processing and cosmetics industry. Its compounds are used as food stabilizers and—as it has been since ancient times—to produce dyes. Moreover, Al compounds are used in medicine to reduce stomach acidity and as antiseptics and astringents (Peterson et al. 1993; Ranau et al. 2001; Codex Alimentarius Commission 2010; Hirata-Koizumi et al. 2011; Sheasby and Pinner 2011). The nanomaterial industry has been developing rapidly over the recent years, and its products find increasingly more applications. Both metallic Al and Al oxide nanoparticles are used in the industry. Therefore, effects of different forms of Al on the environment, including the impact of the nanoparticles, should be investigated (Krewski et al. 2007; Chen et al. 2008).

When it comes to toxic properties, many issues have been described so far in relation to living organisms, especially mammals. One of the most remarkable is Al

ability to penetrate into the structures of the central nervous system (Yokel 2000; Cannon and Greenamyre 2011). Rapid advances are observed in the studies on the Al pro-oxidative function (Exley et al. 1996; Berthon 2002; Exley 2004). Despite intensive research though, there are many unanswered questions as to the effects of aluminum on cellular processes in humans and animals, especially with regard to the central nervous system. Also, there is much to explain and understand in terms of molecular mechanisms of toxicity, especially concerning Al introduced to the environment in the form of nanoparticles (Kearns 2004; Chen et al. 2008; Chaturvedi et al. 2012). A separate but equally important sphere of studies on aluminum is the ecotoxicological research on different groups of organisms, including vertebrates that inhabit inland ecosystems (Rosseland et al. 1990; Barabasz et al. 2002).

2 General Properties of Aluminum

Aluminum (Al, Latin *aluminum*) is a major component of the Earth's crust, as it represents 7.91% of the lithosphere. After oxygen (49.9%) and silicon (26.9%), Al is the third most abundant element in the lithosphere by mass (ATSDR 2008; Kumar and Gill 2009; Stahl et al. 2011). If we consider its oxide, Al is thought to closely follow silicon dioxide, representing 15% of the entire lithosphere mass. Its common occurrence in nature is reflected in the name *sial*, formerly referring to the composition of the outermost layer of the Earth, which consists mainly of silicon and Al. The term *sial* is an acronym that combines the symbols of these elements, Si and Al. Currently the upper layer of the crust is more commonly referred to as the granite layer (Degens 1989; Shenglin et al. 1996). Aluminum occurs mainly in its oxidation state III and, extremely rarely, I or II. In its pure form, it is a silvery-white metal, both malleable and ductile. In contact with the air, the light metal undergoes a slow process of oxidation and passivation, its surface covering with an oxide layer. As a result of its high chemical reactivity, the element does not naturally occur in its metallic form, but in combination with other elements. The minerals include oxides but also silicates, sulfates, and phosphates (ATSDR 2008; Priest 2004; Lide 2005; Kumar and Gill 2009). Aluminum is tasteless and does not corrode. It represents group 13 in the periodic table of elements. Due to its low density, 2.7 g cm^{-3}, aluminum belongs to the group of light metals.

Although being so abundant in the minerals already known since ancient times, aluminum in its metallic form has long remained unknown. The first step to the discovery of metallic aluminum was the work by Johann Heinrich Pott, a German chemist, who extracted aluminum oxide (or alumina, Al_2O_3) in 1746, from naturally occurring alum, a mineral in common use at the time. This discovery caused expectations that alumina could have been an oxide of an unknown metal, which—in a relatively pure state—was eventually extracted by H.C. Ørsted and F. Wöhler in 1825. Some physical and chemical properties of metallic aluminum remained unknown for another 20 years. It was not until 1886 that large-scale

production of metallic aluminum became feasible; at that time, the method was developed allowing extracting aluminum from molten mixture of cryolite and bauxite by electrolysis (Steinegger et al. 1990; Priest 2004; Kawahara and Kato-Negishi 2011). Carl Josef Bayer invented the process of extracting aluminum oxide from bauxite. His method, patented in 1888, has been fundamental to the industrial production of aluminum to this day (Plunkert 2000).

3 Aluminum in Nature: Geogenic Sources of the Metal

If substances that are capable of forming complex compounds are present in the substrate, aluminum may occur in the form of the toxic ion, $Al(H_2O_6)^{3+}$, as a monomeric or polymeric complex with SO_4^{2-} or Cl^-, as well as in the form of other species or complexes with organic ligands. In the natural environment, only a small fraction of aluminum compounds are soluble; therefore it is assumed that the level of its toxic species does not increase significantly as a result of exposure to environmental factors (Klöppel et al. 1997). Although the lithosphere contains enormous amounts of aluminum, its geogenic release is relatively low, especially as compared to quantities released from anthropogenic sources. The geogenic release has been estimated at approx. 26% (Lantzy and MacKenzie 1979; Klee and Graedel 2004; ATSDR 2008; Rauch and Pacyna 2009). Both geogenic and anthropogenic origin aluminum may be found in the geochemical cycle. Natural sources of aluminum include both primary and secondary minerals, as well as colloids, in which previously released aluminum returns to the lithosphere through sedimentation. Its retention is extremely efficient, since as little as estimated 0.001% of released aluminum ions never reach the crust again (Exley 2003). Primary minerals with a high content of aluminum are formed as a result of the weathering of the bedrock, which was formed millions of years ago from solidified magma. Aluminum contents in basalt and granite rocks average 87.6 and 77.0 g kg^{-1}, respectively (Steinegger et al. 1990). Their disintegration underlies the formation of secondary minerals, such as kaolinite, hydroxy aluminosilicates, and aluminum hydroxide (Berg and Banwart 2000).

Aluminum is also mined from other resources, which are thought to be practically inexhaustible, i.e., anorthite (calcium aluminosilicate), alunite (hydrated aluminum potassium sulfate), post-coal wastes, oil shale, sillimanite, and kyanite (disthene). Aluminum compounds appear in the minerals as a result of rock erosion and leaching. Aluminum's most common natural forms are hydroxides, such as bauxites, kaolins, aluminosilicates, and clays. Bauxite is the basic aluminum ore, mostly composed of gibbsite (hydrargillite). Apart from this, boehmite, diaspore, and corundum represent minerals containing aluminum ions (Kabata-Pendias and Mukherjee 2007). Bauxites consist of up to 55% of $Al_2O_3 \cdot H_2O$, and their deposits—although located mainly in the tropical regions—occur in other parts of the world as well. The world's resources of bauxite are estimated between 55 and 75 billion tons. According to the U.S. Geological Survey for 2016, most bauxites

occur in Africa (32%), followed by Oceania (23%), South America and Caribbeans (21%), Asia (18%), and the rest of the world (6%).

Crude oil ash content of aluminum may range widely, from 2000 to 20,000 ppm. The differences result from varied properties of the rock formations found around the oil fields but also may be a result of contamination while drilling, pumping, or preparing oil for transport to refineries.

Aluminum fraction that takes part in the geochemical cycle usually involves monomeric compounds, as polymers are strongly bound to colloids present in the substrate. Released Al may precipitate, forming this way the before-mentioned secondary minerals, of which gibbsite is most common (Steinegger et al. 1990). Cation aluminum species, referred to as mobile Al, are responsible for basic soil properties. Their presence in the soil also increases its sorption capacity (Widłak 2013). Depending on the bedrock and the pH of the soil solution, Al soil concentrations change in a fairly wide range, from 1% to 30%, mostly not exceeding 4% (US EPA 2003; Kabata Pendias and Mukherjee 2007). Solubility of aluminum compounds in the aqueous soil environment is closely related to its pH (Fig. 12.1).

Bedrock weathering processes also release aluminum to aquatic ecosystems, where the element is mostly bound with colloid matrix, representing more than 50% of its content. Soluble fractions in an aqueous medium comprise only 23%, whereas the rest of aluminum remains in its molecular form (Gundersen and Steinnes 2003; Rengel 2004). Particularly important is the mobility of aluminum from water to sediments and back, especially at a changing pH of the environment. Hence, a proper evaluation of a possible threat posed by toxic aluminum species to aquatic

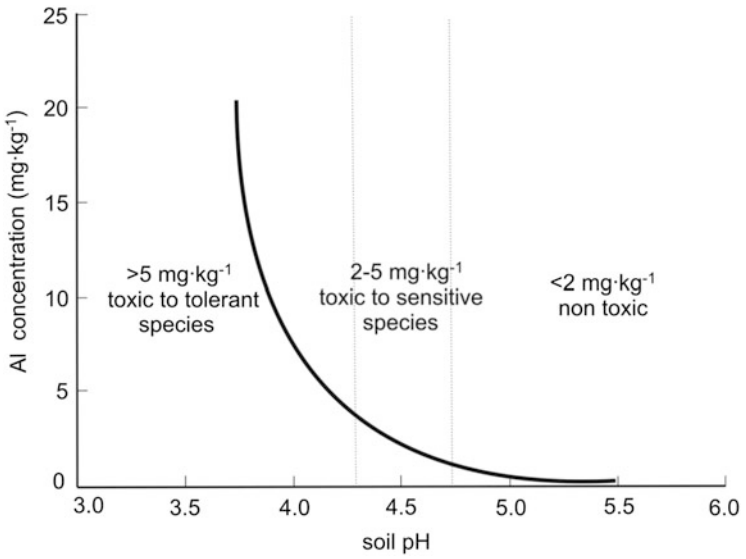

Fig. 12.1 Dependence between soil pH, aluminum concentration, and its toxicity to plants (data source: http://soilquality.org.au/factsheets/soil-acidity-qld)

organisms requires speciation analysis, which should be carried out not only in the water column but also in the sediments. Gardner and Comber (2003) established a threshold value, pH 6.8, at which the concentration of reactive aluminum is lowest. Below this value, $Al(OH)^{2+}$ and Al^{3+} species are dominant; above this pH, the fraction of $Al(OH)^{4-}$ increases. At pH 8 or higher, nearly 100% of dissolved aluminum is represented by the $Al(OH)^{4-}$ ion.

In the surface waters of North America, levels of aluminum range from 0.012 to 2.25 mg L^{-1} (Jones and Bennett 1986). Miller et al. (1984) report that there is much more aluminum in surface waters compared to groundwaters. It was evidenced by their results that detectable quantities of aluminum were observed only in 9% of groundwaters, whereas as much as 78% of surface water contained this metal as well. Aluminum concentrations in European flowing waters vary greatly, depending on the geological formation, topography, and climate. The values range from 0.1 to 812 μg L^{-1}, with an average 17.7 μg L^{-1}. The lowest levels of the metal (below 6.5 μg L^{-1}) occur in the north of France and northeastern Germany, as well as along the continent strip stretching from southeastern France to Greece. The highest values, exceeding 339 μg L^{-1}, are found in the waters of Scandinavia (Salminen et al. 2005). Potable water treated with the most commonly used agents, i.e., aluminum chloride or sulfate, contains mostly the monomeric form of aluminum (Schintu et al. 2000). Going through this process, drinking water may acquire considerable amounts of aluminum, reaching 70 μg L^{-1} on average; its bioavailability, however, is relatively low (Yokel and McNamara 2001). Increased aluminum concentrations in surface waters, resulting from its acidification and exceeding the threshold of toxicity, negatively affect fish and other aquatic organisms (Roux et al. 1996; Bi 2001; Herrmann 2001). A similar effect is observable in acidified soils which contain a high level of mobile aluminum fractions. These are toxic to various taxa of soil organisms (Maňkovská and Steinnes 1995; Markich et al. 2002). Apart from the noxious effects of mobile aluminum species present in terrestrial ecosystem components, one may also observe their negative impact on vegetation. This is thought to be the key factor reducing plant production efficiency on acid soils globally (Foy 1988).

Acidification of the environment, as well as the resulting acidic precipitation containing mostly sulfuric acid and nitric acid, plays an important role in aluminum retention changes. Acid rains are a consequence of emission of sulfur dioxide, nitrogen oxides, and ammonia to the atmosphere. These acids decrease the pH and increase aluminum concentration in surface waters (Bi 2001). This leads to poorer biodiversity in aquatic ecosystems and increases soil acidity (Driscoll et al. 2003; Jönsson et al. 2003).

A fraction of aluminum released from the crust enters the atmosphere. Weathering of rocks is the natural process behind the aluminum's presence in the air. As a result of this process, but also due to the industrial activity of man, aluminum-containing dusts, including particulate matter, are released to the atmosphere (Varrica et al. 2000; ATSDR 2008). Aluminum is the most important metallic component of particulate matter in the environment, where it occurs in the relatively stable form of Al_2O_3 ultrafine particle (Reff et al. 2009).

4 Aluminum Production and Uses: Anthropogenic Sources of Aluminum

Although Al is present in a number of minerals, of which many have been known since ancient times, its metallic form long remained unknown. The first step in obtaining metallic aluminum was a discovery by the German chemist, Johann Heinrich Pott, who in 1746 derived *alumina* (aluminum oxide, Al_2O_3) from then commonly used alum. Originally, alum (aluminum potassium sulfate dodecahydrate) was widely used as astringent, for treating minor bleedings. The discovery by J.H. Pott raised speculations that the new substance was an oxide of an unknown metal, whose relatively pure form was finally obtained by H.C. Ørsted and F. Wöhler in 1825. Some physical and chemical properties had not been described until 20 years later. It was not until 1886 that large-scale production of metallic aluminum was started, as the method was developed of electrolytic extraction of aluminum from molten mixture of cryolite and bauxite (Steinegger et al. 1990; Priest 2004; Kawahara and Kato-Negishi 2011).

Pure, silvery-white metal is obtained in a combination of chemical and electrolytic processes. Aluminum oxide is the main precursor of the metallic form. More than 95% of aluminum production is obtained from bauxites, following the Bayer process. This technology, developed in 1888 by Carl Josef Bayer, consists in heating bauxite ore to high temperatures at high pressure, in caustic soda, to obtain sodium aluminate solution, separated from insoluble residue (Plunkert 2000). In the next step, sodium aluminate is filtered and crystals of aluminum hydroxide are precipitated. Combined with the Hall-Héroult process, the Bayer process has found its application in industrial-scale aluminum extraction (Grojtheim et al. 1982; Steinegger et al. 1990; Lewis 2001).

Aluminum smelting consumes a considerable amount of energy and is responsible for both vast emission of greenhouse gases and extensive environmental acidification (Sheasby and Pinner 2011; Liu et al. 2013). Besides the previously mentioned Bayer process, which is still the basic technology of aluminum production, there exist a limited number of other technologies using different processes. It should be stressed, however, that irrespective of the smelting technology, bauxites remain the main source of the metal, as 95% of world aluminum production is obtained from this ore. Constituent minerals of bauxites are mostly polymorphic aluminum compounds, referred to as gibbsite [$Al(OH)_3$, containing 65% of Al_2O_3], boehmite [AlO(OH)], and diaspore ($HAlO_2$). Bauxite deposits are easily accessible and contain 30–65% of aluminum oxide (Steinegger et al. 1990; Sheasby and Pinner 2011; Reimann et al. 2014). Efforts are being made to use kaolin and other clays of high aluminum content. Since the early twentieth century, the primary aluminum production has been showing a strong, rising trend. According to some forecasts, it is estimated that the total world production of aluminum will have reached 60 million tons by 2020. It should also be emphasized that the process consumes about 2% of global energy production. Including bauxite ore preprocessing, one kilogram of pure aluminum needs about 23–24 kWh of energy. Aluminum production-related

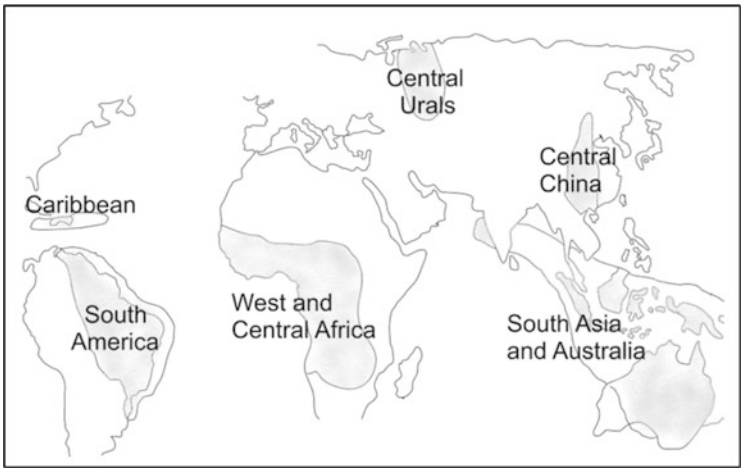

Fig. 12.2 Distribution of major world bauxite reserves. On the base of the data published by U.S. Geological Survey (2016)

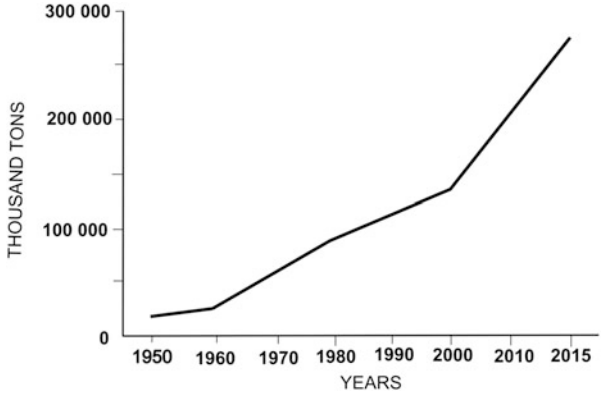

Fig. 12.3 World bauxite mining in the years 1950–2015. On the base of the data published by U.S. Geological Survey (2016)

industries significantly contribute to the global economy and comprise the basis of national economies in more than 30 countries. Globally, 45 million tons of semi-fabricated aluminum products are made annually, including 14 million tons of recycled metal. The sector involved in the production and processing of aluminum is a direct employer for about 1 million people (Das and Yin 2007; Das 2011). Figure 12.2 illustrates the distribution of world bauxite deposits (www.aluminumleader.com).

The global bauxite mine production in 1900 was 88 thousand tons, produced by France, the USA and the UK (Plunkert 2000). In 2015, the production was 3000 times higher, 274 million tons (Fig. 12.3), with the world's total resources of bauxites estimated at 55–75 billion tons (U.S. Geological Survey 2016).

Table 12.1 Top countries in and primary smelter aluminum production

Production	Thousand metric tons
Bauxite mine production in 2015	
Suriname	2200
Kazakhstan	5200
Russia	6600
Jamaica	10,700
Guinea	17,700
India	19,200
Malaysia	21,200
Brazil	35,000
China	60,000
Australia	80,000
World	274,000
Primary aluminum production in 2015	
Iceland	820
Bahrain	960
Norway	1320
USA	1600
Australia	1650
United Arab Emirates	2340
India	2350
Canada	2900
Russia	3500
China	32,000
World	58,300

Data source: U.S. Geological Survey (2016)

In Table 12.1 are presented the countries with the highest mine production of bauxites, exceeding 2 million tons, and with the highest aluminum primary production. Globally, nearly 40% of bauxite in 2015 was produced by four Asian countries (China, Malaysia, India, and Kazakhstan), and the two largest and most populated countries in this group, i.e., China and India, produced nearly 59% of aluminum extracted from bauxites. The global alumina (aluminum oxide) and bauxite production in 2015 increased by 9% and 12%, respectively, as compared to 2014. Particularly dynamic was the increase in China, where nearly 50% of the global aluminum production takes place, i.e., 66 million tons per year. A part of this quantity is obtained from imported ores. In 2015, Australia sold 20 million tons bauxite ore to China. A similar quantity in the same year was exported to China from Malaysia (U.S. Geological Survey 2016).

It is estimated that about 90% of alumina is used in metallic aluminum smelting (www.world-aluminum.org; http://www.alueurope.eu). An important characteristic of aluminum is its resistance to corrosion, as the metal is passivated by a native oxide layer. Aluminum and its alloys are used mainly in transport and civil engineering,

both for support structure construction and in finishing elements (Priest 2004; Menzie et al. 2010).

Natural aluminum minerals, in particular bentonite and zeolite, are used in water purification, sugar refining, and beer production. Large quantities of aluminum hydroxide are used in the production of water treatment agents, refractory products, fuel additives, ceramics, abrasive materials, roofing materials, glass, electrical insulators, catalysts, medications, and cosmetics. Aluminum finds its applications in the chemical industry, mining (production of explosives), and food packaging industry (cans, foil). Aluminum oxides are used as food additives (Priest 2004; Krewski et al. 2007; Kawahara and Kato-Negishi 2011; www.world-aluminum.org; http://www.alueurope.eu).

Since aluminum smelting from bauxite ore is a highly energy-consuming process, it is important to reclaim the metal from waste materials. Recycling aluminum from scrap saves 95% of the energy that would otherwise be consumed to smelt this metal from its virgin source. Typical recycled aluminum materials include machining scrap, used beverage cans (UBC), foils, industrial scrap, shaves, and old metal. Aluminum recycling reduces air pollution by 95% and water pollution by 97%, as compared with its virgin source production. Aluminum scrap represents a significant resource of the metal and is used to manufacture a standard value product in the form of clean aluminum or its alloys. Moreover, recycling may be a highly profitable business, as the total production costs of secondary aluminum are 60% lower compared to aluminum production from bauxite ore (Fundacja RECAL—www.recal.pl. 12 June 2008).

Over the past few decades, we have been witnessing a significant increase in the demand for aluminum, which is applied in numerous conventional sectors of economy. Moreover, with new emerging technologies, the ways the metal and its compounds are used are changing rapidly (Menzie et al. 2010; Nappi 2013; Chaturvedi et al. 2012). The properties of nano- and micron-sized aluminum particles, as well as aluminum oxide nanoparticles, have drawn much attention lately, particularly in terms of their application as a catalyst (Kearns 2004). They are used as fuel additives or in ready-made mixtures of fuel and aluminum-based oxidants. They find application as combustion catalysts in propellants and pyrotechnic chemicals. In the thermite reaction, alumina rapidly reduces metal oxides, which is accompanied by one of the highest industrially attainable temperatures, about 3000 °C—or even 3800 °C, if temperature-boosting materials are added. Also, an intensive emission of light is released. Nanoscale aluminum particles have also found application as high-speed fuel combustion agents in jet engines (Piercey and Klapötke 2010; Gan and Qiao 2011; Sahu et al. 2014; Venkatesan 2015). Trimethylaluminum (TMA) is added to aircraft fuel. During a flight of a jet-propulsion aircraft, TMA is degraded to carbon dioxide, carbon monoxide, and aluminum oxide. The latter occurs in the form of nanoparticles, which remain suspended in the atmosphere for up to 18 months, to finally fall with precipitation and reach both aquatic and terrestrial ecosystems.

A separate and very poorly understood issue is the problem of how aluminum nanoparticles behave in the biotic and abiotic environments. It is presumed that they

might be toxic to plants and other organisms (Chen et al. 2008; Li et al. 2009; Burklew et al. 2012; Chifiriuc et al. 2016). Bearing in mind a constantly increasing proportion of the air transportation, we may presume that the amount of aluminum oxide particulate dust affecting the natural environment will be increasing too. As it was mentioned earlier, the mining and processing of aluminum have a negative impact on ecosystems in many parts of the world. Not only does the primary aluminum production contribute to the emission of greenhouse gases but also entails the necessity of production wastes disposal. The most common waste is the red mud (or red sludge), a side product in the Bayer process. Estimates range between 70 and 120 million tons of red mud produced per year (Mayes et al. 2011a, b). It is usually composed of oxides and hydroxides of iron (hence its color), aluminum and titanium, contains radionuclides, ^{266}Ra and ^{230}Th, as well as a range of heavy metals, such as As, Cr, Co, Cd, Ni, and V (Mayes et al. 2011a, b; Ruyters et al. 2011; Burke et al. 2013). The strongly alkaline sludge is stored in open holding ponds. On October 4, 2010, a broken dike of a red sludge pond in Hungary caused an ecological disaster, in which approximately 1 million cubic meters of released sludge contaminated an area of about 40 square kilometers (Burke et al. 2013).

5 Biological Status of Aluminum

Although aluminum is a ubiquitous element, there is no evidence of any biological function for the metabolism of human or animal body (Exley 2003, 2009). Its complex electrochemical nature makes aluminum able to migrate from a solid phase to an aqueous phase, which eventually defines the role of the metal in the natural environment (Kabata-Pendias and Mukherjee 2007). The element penetrates into any form of life on Earth and, in consequence, passes from one level of the trophic chain to another. This effect results from the fact that the biosphere is formed of overlapping biotic cycles of microorganisms, plants, invertebrates, and vertebrates, with aluminum possibly penetrating each of them (Watanabe and Osaki 2002; Exley 2003).

Human activity over the last centuries has led to a rapid growth in the production of aluminum derived from its virgin sources, which results in an extra amount of the metal available for the trophic chains of various ecosystems. As a consequence, since 1970, aluminum has been regarded as a harmful element, accumulating in the tissues of living forms, constantly increasing in bioavailability (Gromysz-Kałkowska and Szubartowska 1999; Anke et al. 2001; Berthon 2002; Olariu et al. 2004; Kucharczak et al. 2005; Druga et al. 2005; Trif et al. 2005).

Microbial interactions with aluminum present an interesting issue. Illmer et al. (1995) found that the level of aluminum is the main limiting factor for the biomass of soil microorganisms. Studies on how aluminum affects microorganisms, however, show significant limitations, since it is hard to sort out the effects of the culture medium pH from those possibly resulting from the level of aluminum. This is a direct consequence of the fact that the availability of aluminum in the medium

depends on its pH but also significantly affects its acidity (Illmer and Mutschlechner 2004). To date, little attention has been paid to the effects of aluminum on microbial cells, as can be compared with the research effort spent on plants and animals. The complex chemistry of aluminum, which is capable of polymerization and may form complexes with phosphates and medium-acidifying organic acids, often makes result interpretation complicated (Garcidueñas-Piña and Cervantes 1996). Guida et al. (1991), who studied aluminum toxicity in *Escherichia coli*, observed that growth inhibition of bacterial colonies was markedly dependent on pH. Aluminum concentrations below 100 μmol, or even 50 μmol, were found to have an inhibitive effect toward *Bradyrhizobium* spp. (Wood et al. 1988; Vargas and Graham 1988). Appanna et al. (1994) report that *Pseudomonas fluorescens* is tolerant to 50 mmol of aluminum if it occurs in the medium as aluminum citrate complex. The citrate residue, which is the only carbon donor in this aluminum complex, is utilized by the bacteria (Appanna and St. Pierre 1994). Plant nodulation is a process linked with the presence of aluminum in the soil. Johnson and Wood (1990) found in *Rhizobium* cells that aluminum binds to bacterial DNA, which disrupts its synthesis in susceptible strains and has no effect for the strains characterized by a high tolerance to aluminum. Richardson et al. (1988) observed that even a small amount of aluminum such as 7.5 μmol may restrain the expression of genes responsible for the processes of nodulation. Data reported by Brady et al. (1993) demonstrate that aluminum substrate concentrations below 5 μmol may inhibit soybean nodulation. Husaini and Rai (1992) demonstrated that aluminum is toxic to *Cyanobacterium*, and the toxicity increases with acidity of the medium, within pH decreasing from 7.5 to 4.5. The authors claim that with decreasing pH values, aluminum present in the medium affects the ATP level. The studies revealed that aluminum inhibits ATP synthesis at a high pH, whereas in an acidic medium, the metal binds to ATP making it biologically unavailable.

Aluminum belongs to metals that are important to plant growth. Its concentrations in plants depend on the species, variety, and developmental status. Some plants are more resistant to aluminum and tend to accumulate large amounts of the metal. Generally, plants growing on acidic soils contain large quantities of mobile, available fractions of aluminum (Domingos et al. 2003; Rengel 2004). The sensitivity to aluminum has been found to be regulated genetically. The tolerance level varies not only between species but also between varieties of the same plant. For instance, some cultivars of barley (*Hordeum* sp.) were demonstrated to have a varying susceptibility to soil aluminum (Steinegger et al. 1990). Plants tolerating high concentrations of aluminum in the soil may belong to one of two groups: one group is represented by species that do not accumulate the element, and the other comprises those being capable of storing considerable quantities of aluminum in their tissues. It has been found that the aluminum level in the leaves of plants belonging to the latter group may reach up to 37 g kg^{-1} dry weight (dw), which corresponds to the content of potassium and nitrogen, the essential nutrients needed for a normal growth and development of the plant (Masunaga et al. 1998). The median value of aluminum content in Chinese tea shrubs (*Camellia sinensis*) is 2969 mg kg^{-1} dw (Houba and Uittienbogaard 1994). Equally high aluminum

Table 12.2 Mean aluminum contents in selected plants in mg kg^{-1} dry weight

Species	Al
Wheat (*Triticum*)	31
Barley (*Hordeum*)	38
Oat (*Avena*)	47
Onion (*Allium cepa*)	63
Potatoes–tubers (*Solanum tuberosum*)	76
Mushrooms (*Fungi*)	25–130
Grass (*Poaceae*)	7–3410

Kabata-Pendias and Mukherjee (2007)

concentrations have been measured in grasses and legumes, in which these may exceed 3000 mg kg^{-1} dw (Kabata-Pendias and Mukherjee 2007) (Table 12.2).

Aluminum toxic effects involve disrupted intake and transport of nutrients, lower biomass growth, as well as changes in the genotype of the plant. First symptoms of aluminum toxicity include inhibited root growth (Zhang et al. 1998; Zhang and Rengel 1999; Matsumoto 2000; Ahn et al. 2001; Barcelo and Poschenrieder 2002; Ma et al. 2002; Yamamoto et al. 2003). This response results mainly from disrupted metabolism in the growth zone of the root. The disorder may be a consequence of oxidative stress, disrupted calcium homeostasis, inhibition of ATPase activity, and changes in the cytoskeleton. Excess aluminum in plant cells damages polysaccharide-degrading enzymes, slows down the process of cellular respiration, and hampers the transport and absorption of water and macronutrients, including phosphorus, calcium, and magnesium (Ahn et al. 2002, 2004; Schwarzerova et al. 2002; Ma et al. 2003; Rengel and Zhang 2003; Rengel 2004).

Aluminum-caused oxidative stress is manifested in lipid peroxidation in cell membranes (Yamamoto et al. 2003). It also affects calmodulin, a modulator protein in eukaryotic cells, and changes the structure of chromatin in plant cells (Haug and Shi 1991). Plants have a specific protection system against the adverse effects of xenobiotics, which includes vacuoles, relatively large organelles that are able to accumulate aluminum ions and, in consequence, reduce their impact on the cell metabolism (Rengel 1997, 2004). Pathological changes in plants caused by aluminum are not limited to roots. They are also evident in the leaves; however, accurate diagnosis is difficult as the symptoms mimic calcium and phosphorus deficiency (Steinegger et al. 1990). Compared to animal studies, the research on aluminum uptake by plant cells requires a different approach, as the wall present in plant cells may bind large quantities of various forms of the metal (Haug and Shi 1991; Rengel 2004). Aluminum is thought to penetrate into the cells though endocytosis. Aluminum-dependent reactions with the components of intracellular signaling pathways affect the metabolism of plant cells (Haug and Shi 1991).

Freshwater invertebrates, which are food organisms for many species, play an important role in mediating aluminum to the bodies of terrestrial organisms. Results of analyses indicate that aquatic invertebrates may contain considerable amounts of aluminum, which is mostly deposited in the outer layers of their bodies and does not penetrate into the deeper structures and organs (Krantzberg 1989). The

bioconcentration factor (BCF) for aluminum in the commonly found cladoceran, *Daphnia magna*, ranges from 10,000 to 0, with the value decreasing with an increase in water acidity (Havas 1985; Frick and Hermann 1990). A similar relationship was also found in freshwater crayfish, *Trichoptera* caddisflies, *Unionidae* mussels, and *Chironomidae* flies (Malley et al. 1988; Otto and Svensson 1983; Servos et al. 1985; Young and Harvey 1991). Toxic aluminum afflicts the gills of freshwater bivalves and crayfish, as the metal stimulates excessive production of mucus, which prevents an efficient gaseous exchange and disrupts the osmotic regulation (Exley et al. 1996; Woodburn et al. 2011). Crayfish inhabiting the bodies of water with low aluminum concentrations do not accumulate the metal in their internal organs, and only a small fraction of the aluminum uptake reaches the hepatopancreas (Alexopoulos et al. 2003). Crayfish caught in strongly aluminum-contaminated waters, or those kept in crayfish farms and fed freshwater snails obtained from polluted waters, may accumulate considerable amounts of aluminum in the hepatopancreas, which proves that the metal gets to their bodies by ingestion (Walton et al. 2010).

Aluminum bioconcentration factor in fishes ranges between 400 and 1365 (Roy 1999). As in the case of the gill-breathing invertebrates, the gills are a particularly affected organ in bony fishes too. Aluminum accumulates both on the surface and within the inner parts of the organ (Spry and Weiner 1991). Its presence in the gills leads to acute respiratory disorders, which, in consequence, kill the fish. Aluminum binds with piscine gills in a complex process, comprising three individual mechanisms. One consists in attracting water-dissolved positively charged aluminum species onto the gill parts that have a negative potential. The other mechanism involves polymerization and precipitation of aluminum within the gill due to a higher pH of the gill tissue in relation to the water. Finally, aluminum binds of the mucus covering the gills (Wilkinson and Campbell 1993; Playle and Wood 1989; Teien et al. 2006).

Excess aluminum in the food may pose a threat to the health of both humans and animals. The metal penetrates into the body of a homeothermic vertebrate in three ways: by ingestion, by respiration, and transdermally—ingestion being the most important route. The fraction of aluminum intestinally absorbed from food and water is relatively low. Animal studies show that intestinal uptake of aluminum averages around 1%; however, a strong interspecific variability has been observed, with the absorbed fractions ranging from 0.06% to 27% (Berthon 1996, 2002). It is generally accepted that aluminum ions are not absorbed spontaneously from the digesta, since they are unable to cross the lipoprotein membrane of the duodenum epithelial cells. Only a small fraction of ingested aluminum is absorbed as organic ligand complexes, which naturally occur in the food (Schuping 1996; Ranau et al. 2001).

The levels of aluminum or its various compounds in the air, water, and foodstuffs are regulated by law. The levels are set on the basis of the research carried out by Golub and German (2001), who studied nervous system developmental effects of dietary aluminum lactate ingestion in mice. The substance was administered to test animals as from the first day of gestation until birth, as well as in lactation, i.e., until 35 days of the postnatal life. The NOAEL (no-observable-adverse-effect level) was

established at 26 mg aluminum per kg of body weight per day, whereas the LOAEL (lowest-observable-adverse-effect level) at 130 mg per kg of body weight per day. The estimates were used to set the MRL (minimal risk level) for humans, which is 1 mg Al per kg body weight for both intermediate- and chronic-duration daily oral exposure (ATSDR 2008). According to the WHO (2004) recommendations, potable water aluminum level should not exceed 0.1 mg L^{-1}, for large water treatment plants, or 0.2 mg L^{-1}, for small facilities. The publication by EPA (2006) does not include information on an RfD (reference dose) of aluminum; however, an RfD has been set for aluminum phosphate, a substance commonly used as insecticide, rodenticide, and fumigant. The reference dose of this substance is 4×10^{-4} mg kg^{-1} per day. The NOAEL of aluminum phosphate is 0.043 mg kg^{-1} body weight per day (IRIS 2008).

According to the EFSA (2008, 2012), the ADI (acceptable daily intake) of aluminum is 0.14 mg kg^{-1}, whereas the TWI (tolerable weekly intake) is 1 mg kg^{-1} of body weight. According to the SCAN (2003), an average concentration of aluminum in pasture soils is below 100 mg kg^{-1} dw. Under adverse environmental conditions, which to a large extent include soil acidification, aluminum concentrations may reach as much as 1000 mg kg^{-1} dw. Animals grazing on such pastures may take up aluminum, which under these conditions represents 1.5% dry weight of the forage. Although there are no compelling evidence that aluminum is essential for the proper metabolism in homeothermic animals, it has been suggested that, in certain concentration ranges, its presence in the tissues may be needed. Hence, Anke et al. (2005), basing on their own research, recommend a level of aluminum intake for animals below 10 mg kg^{-1} dry weight of the feed. In addition, the authors suggest that the possible aluminum requirements of animals are satisfied from its natural presence in feed and water.

The available literature sources lack data on the maximum tolerated levels (MTLs) of aluminum in free-living homeothermic animals inhabiting terrestrial ecosystems. Based on research data, the MTL for rodents was set to 200 mg kg^{-1} dry weight. For farm animals, such as poultry, cattle, sheep, pigs, and horses, the level is five times higher. It should be noted that there is no experimental data for horses and pigs; instead, estimates have been made by interspecific extrapolation (NRC 2005).

5.1 Toxicity of Various Forms of Aluminum in Homeothermic Animals

As long as the life has been evolving on Earth, aluminum was never incorporated into the metabolic processes of the living organisms (Exley 2003, 2009). According to the National Research Council (NRC 2005), aluminum belongs to elements that are not essential in terms of body homeostasis, as no evidence has ever been found that it should be needed for growth, reproduction, or survival of animals. This is

probably due to two basic reasons, i.e., low aluminum bioavailability and its adverse chemical properties in terms of biochemistry (Berthon 2002; Anke et al. 2009). At this point, aluminum is thought to have no biological function (Kawahara et al. 2007; Verstraeten et al. 2008). As a xenobiotic, the element is generally considered toxic; however, its effects on living organisms should be analyzed in the evolutionary context (Nicolini et al. 1991; Berthon 1996).

Although aluminum has been classified as a nonessential element by the NRC (2005), many reports suggest that its deficiency symptoms may be induced under controlled laboratory conditions. Chickens fed a synthetic, low aluminum diet showed reduced weight gains, whereas goats exhibited a higher rate of miscarriages, slower growth, weakness and motor impairment of the pelvic limbs, as well as a shorter lifespan (Nielsen 1996; Anke et al. 2005). The literature, however, is predominated by reports on harmful effects of aluminum in relation to living organisms. Research on aluminum toxicity, which has been carried out over recent years on animals representing various taxonomic groups, reveals that aluminum has similar activity mechanisms in all organisms. These predominantly involve oxidation stress leading to cellular death (Strong et al. 1996; Yokel 2000; Crisponi et al. 2012). The interest in aluminum as a toxic metal affecting various organs and systems in the human body increased when dialysis in patients suffering from renal failure became widespread. In such patients, long-term treatment results in accumulation of aluminum in the structures of the central nervous system, which cause neurodegenerative diseases, as well as bone metabolism disturbances leading to osteomalacia. A high concentration of aluminum salts, used in dialysis fluids as phosphate-binding agent, is considered as the main cause of these disorders (Ward et al. 2001; Exley and House 2011; Crisponi et al. 2012).

The gastrointestinal tract is most important route of aluminum reaching the bodies of homeothermic vertebrates, although a negligible amount of this element contained in the intestinal digesta penetrates into the bloodstream. This extremely low level of absorption (usually $<1\%$) results from the fact that the gastrointestinal tract is an effective barrier protecting the body against aluminum penetration (Yokel and McNamara 2001; Yokel 2004; Kośla et al. 2006; EFSA 2010). Absorption of aluminum compounds heavily depends on their water solubility and their concentration in the liquid of the lumen of the intestine (Crisponi et al. 2012). Highly soluble compounds are absorbed more efficiently compared to poorly soluble substances (Berthon 2002). Highly water-soluble aluminum chloride and aluminum nitrate were found more toxic than much less soluble aluminum sulfate, which have been confirmed experimentally on rats (Steinegger et al. 1990). The solubility of aluminum compounds is determined by the content of Al^{3+} ions in the intestinal lumen, whose fate depends on the pH and the presence of neutralizing anions, which are thought to facilitate the penetration of the metal through the intestinal barrier (Berthon 2002). At a pH ≤ 5.0, aluminum in biological fluids exists mostly as a hexahydrate $[Al(H_2O)_6]^{3+}$. As the pH of the medium increases, other ion forms appear, such as $[Al(OH)]^{2+}$ or $[Al(OH)_2]^{+}$, as well as chemically inert aluminum hydroxide, $Al(OH)_3$. The latter species appear at the neutral pH and—at a further pH increase—form a soluble ionic species $[Al(OH)_4]^{-}$ (Crisponi et al. 2012). The

presence of highly soluble fractions of aluminum ions their transport with the fluids in the paracellular space of enterocytes. Absorption is also possible via routes used for essential nutrients, which may be substituted by or absorbed along with aluminum ions (Berthon 2002). Aluminum adverse effects can be seen in the gastrointestinal tract, where phosphate binding takes place and where, at high doses, aluminum may cause hypophosphatemia. This leads to bone tissue metabolic disorders. Rats fed a diet containing aluminum at a dose of 6–10 mg kg^{-1} body weight (BW) for 4 weeks exhibited growth impairment and rickets. Some experiments on effects of aluminum on the bone tissue involved intraperitoneal injections of aluminum preparations; this allowed bypassing the alimentary tract, where the binding of phosphates takes place, preventing their absorption. After 63 days of the experiment, in which the animals were administered 38–109 mg aluminum per 1 kg BW, its content in the bone reached a level of 163 mg kg^{-1}, which also caused osteomalacia (Steinegger et al. 1990). Bone metabolic disorders caused by aluminum occur at extremely high concentrations, which as a rule do not happen in nature. The problem of a possible linkage between aluminum and osteomalacia was first addressed in 1978 (Ward et al. 1978). It was noticed that excessive aluminum supply in dialysis patients leads to qualitative and quantitative changes in the bone tissue resulting in the weakening of the structure and spontaneous fractures. Aluminum is capable of being transferred to the structures responsible for the bone mineralization, in which it acts as inhibitor of the process. Osteoblasts, responsible for bone formation, have transferrin receptors on their surface, which are sites of transferrin-bound aluminum uptake. Aluminum acts as an antiproliferative agent, and osteoblast activity inhibition results in abnormal mechanical properties of the bone and, consequently, in fractures (Van Landeghem et al. 1998; Kasai et al. 1991; Crisponi et al. 2012). Apart from this, aluminum is an inhibitor of bone tissue metabolic processes through acting on parathyroid glands, as aluminum and transferrin complexes bind also to the cells of the glands. Therefore, the presence of aluminum in the parathyroid glands results in hypoparathyroidism (Smans et al. 2000).

Despite the negligible fraction of aluminum absorbed from the gastrointestinal tract, the element is definitely negative in relation to both bone and nervous tissues. As far as nervous tissue is concerned, aluminum toxicity is thought to result primarily from the oxidation stress affecting cells of the central nervous system (CNS). It is also stressed that any quantity of bioavailable aluminum that reaches CNS inflicts a neurotoxic damage and results in neurochemical response disturbances with the symptoms depending on the degree of the damage to particular structures. Numerous experiments on animal models have proven the toxic effects of excessive $Al^{3+}_{(aq)}$ concentrations against the encephalic tissue, which mainly results from aluminum inhibitory activity in relation to many enzymes (Zaida et al. 2007; Exley and House 2011). Sharma et al. (2013) demonstrate that long-term exposure to aluminum results in oxidative damages as a consequence of increased levels of reactive oxygen species (ROS) in cells, oxidation of mitochondrial DNA, and reduced activity, allosterically inhibited by ATP citrate synthase. This reaction chain leads to reduced expression of the mitochondrial genes, which in consequence impairs the functioning of neurons, as the nervous tissue is particularly sensitive to

mitochondrial dysfunction (Fiskum 2000). Moreover, aluminum in CNS cells reduced the expression of COX-1, a marker protein of mitochondrial biogenesis. The protein is a component of the electron transport chain encoded for in the mitochondrial genome. Its reduced expression is inevitably linked with a drop in the activity of other enzymes involved in electron transport and leads to disturbances in the functioning of the cellular energy centers (Sharma et al. 2013). In addition, the presence of aluminum ions inhibits the activity of cytochrome oxidase, the final component in the mitochondrial electron transport chain. This leads to a cascade of biochemical reactions involving oxygen utilization disturbances, which result in ATP depletion and increased calcium concentration outside the cell; in consequence, the cell dies (Crisponi et al. 2012). Besides biochemical disturbances, aluminum induces morphology changes in the CNS (Strong et al. 1996). These involve formation of protein aggregates called neurofibrillary tangles, first described by Alzheimer in 1907, as well as amyloids—also referred to as senile plaques. Aluminum plays a role in the deposition of the insoluble proteins, i.e., amyloid beta and hyperphosphorylated tau protein, which form these neurofibrillary tangles (Paik et al. 1997; Uversky et al. 2001; Rengel 2004; Exley 2012). Besides the studies on $Al^{3+}_{(aq)}$ ions, also those on aluminum oxide nanoparticles reveal their potential negative impact on the mammalian brain (Chen et al. 2008; Li et al. 2009).

Aluminum-caused changes in the enzymatic activity do not pertain only to the nervous system but also affect other organs and systems of the body. The metal may interfere with the process of erythropoiesis through an impact on heme biosynthesis. This interference is manifested with changes in the activity of enzymes involved in the formation of heme (including delta-aminolevulinic acid) and reduced activity of uroporphyrinogen decarboxylase and ferrochelatase. High aluminum doses reduce the lifespan of red blood cells and cause a decrease in the activity of ATPase and such enzymes as hexokinase, alkaline phosphatase, choline acetyltransferase, and ferroxidase (Barabasz et al. 2002). At the cellular level, aluminum reacts with cell membranes, cytoskeletal elements, and the genetic material. Experiments have revealed that the metal interacts with both DNA and RNA. Its presence in the nuclei and a well-documented adverse effect on gene expression are facts that confirm interactions between aluminum and the nucleic acids (Exley 2012). Moreover, aluminum may be nephrotoxic; its increased concentration in the kidney will result in changes in the renal function, including impaired renal removal of the metal from the body. Increased aluminum concentrations in the kidney reduce the viability of its cells, destroy the cell membrane integrity, and damage intercellular junctions (Meshitsuka and Inoue 1998; Shirley et al. 2004). These processes do not severely disrupt the renal function in general; they modify, however, the regulatory processes in the cells, which affect the transport of certain substances and their metabolism. Aluminum in renal tubular cells induces oxidation stress, as well as disorders in p-aminohippuric acid transport and phosphorus absorption, which leads to changes in the body water management and problems with sodium retention. In such cases, female sex hormones act protectively in relation to the kidney, whereas male sex hormones contribute to its gradual damage. Aluminum may also have adverse effects on the liver, to which it is transported from the site of absorption via the

portal circulation. Accumulation of aluminum in the liver induces oxidative stress accompanied by an increase in the content of thiobarbituric acid reactive substances (TBARS) and a corresponding reduction in the antioxidant defense, which involves reduced glutathione (GSH) and antioxidant enzymes, such as catalase (CAT) and glutathione peroxidase (GSH-Px). Outcomes of these reactions include abnormal secretion of bile (de Carmen-Contini et al. 2011).

In vitro tests revealed that aluminum compounds, as well as aluminum oxide nanoparticles, are both mutagenic and genotoxic. Most short-term mutagenicity test have shown their negative effects (Krewski et al. 2007; Sjörgen et al. 2007; ATSDR 2008; Hashimoto et al. 2016). A test on human peripheral blood lymphocytes apparently showed formation of micronuclei and chromosomal aberrations caused by aluminum ions (ATSDR 2008). It should be stressed, however, that these responses were observed at relatively high aluminum concentrations, which can be attained in laboratory conditions only (Krewski et al. 2007; Sjögren et al. 2007; ATSDR 2008; EFSA 2010). Interference with CNS cellular function results in changes in the activity of neurotransmitters. Experiments on laboratory rats demonstrate that an elevated aluminum concentration may cause a pronounced cholinergic deficit. In vitro studies have shown that aluminum has a biphasic effect on acetylcholinesterase activity, a marker of cholinergic activity (Kumar 1998).

Research has shown that aluminum, as a strong pro-oxidant, is involved in the processes of carcinogenesis (Exley et al. 2007; Skibniewska 2010). It has been demonstrated that breast tumors accumulate aluminum ions, and this applies to both humans and animals (Majewska et al. 1997; Skibniewska 2010). Most probably, this is related with biochemical properties of a given cancer tissue, which are characterized by overexpression of osteopontin, which forms complexes with aluminum ions; these act in two ways: on estrogen receptors and through binding with DNA in the cells of the mammary gland, which results in genomic instability (Banasik et al. 2013; Pereira et al. 2013; Darbre et al. 2011, 2013). Aluminum salts act as a catalyst of Fenton's reaction, which produces free radicals damaging cellular structures. Female patients suffering from breast cancer exhibited a significant accumulation of certain products of oxidation in the microenvironment of the altered breast tissue, corresponding to the elevated levels of aluminum (Mannello et al. 2009, 2010). Besides its effect on the genome, aluminum has the ability to bind to estrogen receptors; hence it is referred to as metalloestrogen. The signs of its activity include an impact on estrogen-dependent gene expression in response to the activity of these hormones (Darbre et al. 2011, 2013). Moreover, aluminum interacts with other elements. With cations such as Mg^{2+} and Ca^{2+}, aluminum competes for coordination sites in enzymes, signaling molecules, receptors, transport proteins, membrane channels, nucleic acids, and other ligands (Exley and House 2011). Ward et al. (2001) demonstrate that an increase in tissue aluminum concentrations has a dramatic consequence for iron homeostasis, as it leads to its increase being proportional to the aluminum load of the tissues. Their results suggest that both ions may get into cells via similar transport pathways. Aluminum compounds, which interfere with zinc, copper, calcium, and chromium, change their bioavailability (Priest 2004).

The cellular mechanisms discussed above induce various clinical symptoms as a consequence of aluminum excessive content in the tissues and organs of homeothermic organisms. As is the case in mammals, aluminum is not an essential nutrient for birds either. In avian species, aluminum-caused disorders result from its impact on calcium and phosphorus metabolism (Llacuna et al. 1995). Aluminum binds to phosphorus present in the intestine, which creates insoluble complexes, and, in consequence, reduces the bioavailability of this important nutrient element (Sparling and Lowe 1996). Toxicity symptoms in birds are mainly associated with phosphorus deficiency, which leads to impaired growth, loss of appetite, lower laying rates, loss of plumage, and rickets. The morbidity symptoms are most apparent if the diet is low in phosphorus and if the level of aluminum exceeds dietary phosphorus by 50%. If the diet is enriched with phosphorus, the symptoms of noxious aluminum excess retreat (Scheuhammer 1991a, b). In addition, excess aluminum interferes with the formation of the calcareous layer of eggshells and causes bleeding in the uterine part of the oviduct (Nyholm 1981). Birds are generally vulnerable to aluminum poisoning due to its presence in the diet. As in mammals, low intestinal absorption of aluminum and its effective fecal excretion are the metal's toxicity limiting factors. Therefore, even waterbirds are to a lesser degree exposed to the toxic effects of aluminum as compared to fish, amphibians, or aquatic invertebrates. Bones, particularly in young birds, and female reproductive organs are most vulnerable to aluminum toxic activity. The metal also penetrates into the avian brain, kidneys, liver, and integumentary appendages (Sparling and Lowe 1996). Bortolotti and Barlow (1988) found that aluminum content in the feathers of birds of prey is positively correlated with its concentration in the diet.

5.2 Toxicokinetics and Effects of Aluminum in Wildlife

Aluminum is present in all the body fluids, including blood, cerebrospinal fluid, lymph, semen, and urine (Exley 2008; Exley and Mold 2015). The metal penetrates to the body mostly ingested with food. Its concentrations in the diet may vary greatly, with an average of 0.2 g kg^{-1} dry weight (dw). Some plants, mainly those growing on acidic soils, are able to accumulate large amounts of aluminum, with tissue concentrations exceeding 1 g kg^{-1} (Steinegger et al. 1990). The levels of aluminum in the diet of homeothermic vertebrates may range from 0.73 to 3656.7 mg kg^{-1} (Sample et al. 1996).

Aluminum represents a particular case, as its bioavailability from the gastrointestinal tract is relatively low in endothermic organisms. On absorption, the metal is rapidly distributed to all tissues and then effectively removed by the excretory system; hence its concentration measured in biological samples does not in many cases reflect the load of the body with the bioavailable forms of the metal (Berthon 1996, 2002). An excellent example that illustrates this effect is the experiment by Jouhanneau et al. (1997), who used ^{26}Al isotope on rats. The isotope was detected in the bone within an hour from its oral administration and remained there for another

30 days. Contrary to the bone tissue, which is characterized by a relatively slow rate of ion exchange, the content of aluminum in parenchymal organs at retained homeostasis is more labile.

Absorption of aluminum from the gastrointestinal tract in homeothermic vertebrates strongly depends on the solubility of its particular forms (Harris 1996; Crisponi et al. 2012). Soluble aluminum compounds are absorbed much more efficiently than its insoluble substances (Berthon 1996, 2002). The routes that aluminum gets into the internal environment of the body lead mainly across the intercellular spaces, as well as through the inner space of the cell. Comparing to the former route, transcellular transport is slightly less important, due to the fact that aluminum ions may be accumulated inside cells, which represents a barrier preventing its further uptake (Exley and Mold 2015). The form of aluminum that penetrates into the body determines both the way of its transport with the bloodstream and the site of its deposition (Exley et al. 2007). Although aluminum is absorbed mainly within the intercellular spaces and transcellularly, there are also three other ways aluminum can break through biological barriers. These include active transport, membrane channel system, and endocytosis. Exley and Mold (2015) suggest that there are five main aluminum forms that are capable of getting to various parts of the body via these routes of transport. The most important here is free trivalent cation [$Al^{3+}_{(aq)}$], which is capable of crossing biological barriers being transported through the cell membranes and across intercellular spaces. Significant also are aluminum complexes, such as low molecular weight inert soluble complexes, LMW-$Al^{0}_{(aq)}$; high molecular weight inert soluble complexes, HMW-$Al^{0}_{(aq)}$; low molecular weight soluble non-inert complexes, LMW-$Al(L)^{x+/-}_{n(aq)}$; as well as nano- and microparticles, $Al(L)_{n(s)}$. After breaking through the intestinal barrier, aluminum reaches the bloodstream. In animals, its serum concentration was found to have increased immediately after administration (Lote et al. 1995; Glynn et al. 1999a, b, 2001; Swegert et al. 1999; Vanholder et al. 2002). It has been thought until recently that transferrin was the main protein transporting aluminum in the bloodstream, whereas albumins and ferritin seemed to be of little importance for the process (Harris 1996; Ward et al. 2001; Rengel 2004; Krewski et al. 2007; Sjörgen et al. 2007). Aluminum binds to iron-binding sites in the transferrin molecule; however, it does not substitute iron under normal physiological conditions. This is due to the fact that aluminum-transferrin bond strength is much, approximately 100 times, weaker than that of iron. Under normal physiological conditions, about 70% of serum transferrin is not bound with iron and remains "free" for aluminum, which is transported this way (Crisponi et al. 2012). It is accepted now that transferrin is not the only aluminum transporting protein, since the transferrin-$Al^{3+}_{(aq)}$ ion binding/dissociation kinetics do not explain its high rate of urinary excretion through the renal glomeruli. A key feature of transferrin is its high molecular weight, which prevents its glomerular filtration and, in consequence, prevents iron loss. Glomerular filtration barrier threshold in a healthy kidney ranges from 18 to 58 kDa, whereas the molecular weight of the transferrin-aluminum complex is considerably higher (Exley et al. 2007). About 10% of all plasma aluminum is bound to low molecular weight ligands, which include citrates, phosphates, and citrate-phosphate complexes.

Citrates are serum second to transferrin aluminum-binding ligands. They have been estimated to bind 7–8% of serum aluminum (Crisponi et al. 2012).

Exley and Mold (2015) presume that rapid urinary aluminum excretion is a result of its paracellular transport through the glomerular endothelium in the form of inert, low molecular weight complexes [LMW-$Al^0_{(aq)}$]. This effect has not been fully explained though and requires further research to describe both the specific transport mechanisms and the species of aluminum involved in the process.

Relevant literature lacks well-documented sources dealing with the presence of aluminum in the tissues and organs of wild animals. Most reports are on humans and laboratory animals; fewer deal with livestock animals, including ruminants. Authors, however, claim that there are analogies in the aluminum effects on the cellular metabolism that are common to all living organisms. Estimates are that an average daily aluminum intake by an adult human in the USA ranges from 8 to 9 mg in males and is about 7 mg in females. In Italy and the UK, a daily intake of this metal has been estimated at a level of, respectively, from 2.5 to 2.3–6.3 and 3.4 mg (Gramiccioni et al. 1996; Ysart et al. 2000). According to data published by the WHO (1996), an adult human ingests on average 5 mg aluminum with food and water per day, of which as little as 0.1% remains in the body, which is less than 10 μg. The rest is removed from the system (Priest et al. 1998). Acids present in the food enhance the solubility of the compounds of aluminum, which assumes its ionic form Al^{3+}; this species is characterized by a higher bioavailability in the initial part of the gastrointestinal tract, due to its easier transport through the epithelium. This is due to aluminum capability of inert complex formation (Desroches et al. 2000; Dayde et al. 2003). The acidic gastric environment plays the key role by modifying the amount of soluble aluminum species passing to the small intestine, where the absorption takes place (Powell et al. 1999). The alkaline environment of the intestine should prevent the absorption of aluminum; however, acids contained in the diet, such as glutamic, maleic, or tartaric acid, may serve as organic ligands to increase aluminum uptake. For this reason such ligands should be avoided if any aluminum salts are used for therapeutic purposes (Venturini and Berthon 2001). Studies carried out on laboratory rats revealed that absorption of aluminum from drinking water depended not only on the concentration of aluminum in the water but even more on the capability of binding aluminum by the components present in the stomach (Glynn et al. 2001). This information implies that aluminum bioavailability should not be determined based on its concentration in the food and water before ingestion due to ample changes that may occur in the digestive system. Tests using ^{26}Al isotope revealed that as little as 0.06–0.10% of ingested aluminum is absorbed (Moore et al. 2000). Experiments allowed determination that 90–95% of aluminum in the gut is found in its solid phase formed by insoluble and precipitating fractions of the digesta and endogenous material (sloughed epithelial cells of the intestine, bacteria colonizing the digestive tract and mucus). Eventually, most of soluble aluminum forms in the small intestine are bound in the mucus, which occurs in two different fractions. The outer layer is insoluble, adhering to the mucosal surface and forming a kind of “carpet” that lines the surface of the villi, while another layer consists of partially degraded mucus found in the lumen. Aluminum ions were

detected in both fractions, however much more gathered in the insoluble, outer layer. It is responsible also for binding other metals, with particular affinity to trivalent ions, such as Fe^{3+}. It is suggested that intestinal mucus is the main factor limiting aluminum uptake. The relatively low fraction of aluminum passing to the bloodstream—in relation to its high concentration in the mucus lining the intestinal mucosa—may explain this effect (Powell et al. 1999; Berthon 2002). Moreover, some ligands, such as diet citrates, may compete for aluminum with the intestinal mucus. It was found that its absorbability may substantially increase due to the ease with which the resulting complex penetrates the intestinal barrier to reach the systemic circulation and, in consequence, other tissues and organs of the body (Williams 1996; Whitehead et al. 1997; Powell et al. 1999). Experiments show that the presence of such ligands results in doubled retention of aluminum in the liver and brain (Jouhanenau et al. 1997). In both humans and animals, aluminum citrate complex occurs in significant quantities in the blood plasma of healthy individuals and is the main compound which binds aluminum in the cerebrospinal fluid in dialysis patients with acute aluminum toxicosis. It represents also one of the main aluminum forms that penetrate cell membranes of the neurons (Polak et al. 2001; Yokel et al. 2002). It is believed that aluminum citrate may be nontoxic in human and animals cells, but it rather serves as a substance transporting the ions of the metal into the cells, where they interfere with metabolic pathways (Zatta and Zambenedetti 1996; Levesque et al. 2000; Zatta et al. 2002). There are also other ligands, such as polyphenols, phosphates, and silicates, which form insoluble aluminum complexes in the intestinal lumen, thus limiting the uptake of the metal (Powell et al. 1993; Powell and Thomson 1993; Berthon 1996, 2002).

In mammals, the highest concentrations of aluminum uptake are deposited in the nervous tissue (Al-Ganzoury and El-Shaer 2008; Anke et al. 2009), liver, kidneys, and bone (Tang et al. 1999; Al-Ganzoury and El-Shaer 2008; Anke et al. 2009; Teixeira et al. 2013).

Kidneys are most important for the process of aluminum removal from the body (Sutherland and Greger 1998; Berthon 2002). In the cells of the proximal renal tubules, aluminum is absorbed by lysosomes and precipitates in the form of insoluble aluminum phosphate, which is then transferred into the tubular lumen and removed with the urine (Steinegger et al. 1990). Experiments carried out on rodents with the use of ^{26}Al isotope revealed that 45–75% of intravenously administered aluminum is removed from the body within 24 h (Crisponi et al. 2012). It has been confirmed that the body of a healthy human in normal conditions is capable of removing nearly the entire dose of absorbed aluminum via the excretory system. Under heavy aluminum load, its renal excretion rate may be insufficient, and the tissue accumulation may induce cell metabolic disorders (Berthon 2002; Ezomo et al. 2009). Even in physiological conditions, some fraction of aluminum that has not been removed from the bloodstream through the kidneys will be accumulated in the tissues. For this reason, the plasma aluminum level only reflects the current situation and cannot be treated as an indicator of long-term exposure (Boyce et al. 1987). Comparing to other polyvalent ions, aluminum forms relatively weak bonds

with serum components, which facilitates its transport and tissue deposition (Priest 2004).

Aluminum accumulates in the CNS, bone, liver, kidneys, integumentary appendages, and heart (Lote et al. 1995; Glynn et al. 1999b, 2001; Swegert et al. 1999; Vanholder et al. 2002). Molecular mechanisms inducing aluminum uptake in particular tissues differ significantly depending on their type (Crisponi et al. 2012). Therefore, it is not equally distributed to different tissues of the body. In humans, if alimentary exposure is the case, the highest fraction of total aluminum uptake is deposited in the bone (60%) and lungs (25%), and much lower percentage in the muscle (10%) and the liver (3%). The brain accounts for approx. 1% of this (Krewski et al. 2007). Probably the observed pattern of aluminum distribution among the organs may be associated with differences in transferrin receptor density (ATSDR 2008).

The presence of aluminum in the bone is of particular importance, since the tissue represents a specific reservoir which retains the metal for a long period of time. This is due to a long exchange cycle of bone structural components, which in mature individuals is about 3% per year, in the cortical bone, and 20%, in the cancellous bone. The biological half-life of bone-absorbed aluminum is estimated to last several decades (Priest 1990). Aluminum accumulation in the bone interferes its metabolism, which results in osteomalacia. Although molecular mechanisms responsible for aluminum deposition in the bone tissue have not been fully explained, the process is thought to depend on three basic effects. First, aluminum binds on the surface of the bone in exchange of calcium. Ions bound this way belong to the most mobile fraction, which is subject to reversed exchange by binding to complexes in the body fluids located near the bone surface and, next, with plasma transferrin. Another mechanism of binding aluminum to the bone consists in precipitation of aluminum together with calcium in the formation sites of bone mineral, where hydroxyapatite crystals are synthesized. This leads to deposition of aluminum relatively strongly bound with the bone tissue. The third way of aluminum deposition in the bone structures is in the form of ions bound to organic complexes. These ways of aluminum binding to bone tissue result in its presence in all the bone structures, mostly in the surface layers (Priest 2004).

Elevated levels of aluminum in the kidneys are mainly associated with disorders of their excretory function. Impaired renal function leads to deposition of aluminum, which in excess is toxic (Sanches-Iglesias et al. 2007). The renal medulla has a particularly strong capability of accumulating aluminum (Cacini and Yokel 1988).

Although a relatively low fraction of aluminum uptake finally reaches the nervous tissue, it induces a range of negative changes in the CNS, which leads to pathological conditions. Previous studies on the concentration of aluminum in the CNS did not bring much success in terms of clear indication of its toxicity threshold concentration in animals. In humans, the average aluminum cerebral concentration can be found in the range from 0.10 to 4.5 mg kg^{-1} dw, with an apparent age-related increasing trend (Roider and Drasch 1999). Increased cerebral levels of aluminum are linked with such conditions as Alzheimer's disease (11.5 mg g^{-1} dw), dialysis encephalopathy

syndrome (14.1 mg g^{-1} dw), and a variety of other aluminum-dependent encephalopathies (up to 47.4 mg g^{-1} dw) (Exley and House 2011).

Experiments on rats reveal that gray matter concentrations of aluminum are higher (up to 40 mg kg^{-1} dw) compared to those in the white matter (Roider and Drasch 1999; Exley and House 2011). This is probably due to the fact that the metal accumulates mainly in the somata of the neurons, particularly in the nuclei (Galassi et al. 1995; Reusche et al. 2001; Solomon et al. 2001; Shirabe et al. 2002; Exley and House 2011).

5.3 *Bioaccumulation of Aluminum in Mammalian and Avian Species*

Determination of aluminum concentrations in biological samples is prone to uncertainty, since its low uptake from the gastrointestinal tract on the one hand and efficient removal with urine on the other result in the fact that aluminum tissue concentrations are generally low. Additional bias may result from possible contamination of the sample, as various forms of aluminum are ubiquitous in the environment (Cannata-Andia and Diaz-Lopez 1990; Hewitt et al. 1990; Steinegger et al. 1990).

The specificity of aluminum biokinetics is that after entering the systemic circulation, the metal is quickly distributed among all organs and tissues (Exley 2008; Exley and Mold 2015). Bearing this in mind, it is important to decide which tissue reflects the true aluminum load of the body. Diagnostic tests on humans and domestic animals, including laboratory animals, most often involve sampling whole venous blood or serum. However, results of numerous analyses imply that this is not a proper material for aluminum measurement in mammalian bodies, due to the dynamics of its binding and removal. Although data on the aluminum tissue concentration in free-living wild animals are difficult to interpret, we may, to some extent, use for this purpose the results of experiments on laboratory animals or results of medical tests on humans. In the majority of patients suffering from dialysis encephalopathy syndrome, blood serum aluminum levels increase significantly in relation to healthy subjects, reaching values higher than 200 μg L^{-1}. There are reports, however, that these are much lower in patients with aluminum toxicosis and do not exceed 100 μg L^{-1}. It was found that measuring blood serum aluminum in 2- or 3-month intervals may obscure the outcomes of its excessive exposure resulting in its accumulation in body tissues (Cannata-Andia and Diaz-Lopez 1990). Data reported by various authors on blood serum aluminum in people not exposed to its elevated levels in the environment are usually similar and range within 5–7 μg L^{-1} (Mussi et al. 1984; Schaller and Valentin 1984). As compared with human serum aluminum levels, those measured in the serum of cattle managed in Poland on organic and conventional farms are considerably higher, 277 and 1567 μg L^{-1},

respectively (Tomza-Marciniak et al. 2011). In the wild Iberian ibex (*Capra pyrenaica*), whole blood aluminum concentrations ranged between 310 and 390 μg L^{-1} and were similar to bovine plasma levels in the cattle from organic farms but much higher than in human plasma (Ráez-Bravo et al. 2016). This information suggests that herbivorous animals ingest much more aluminum with the fodder than do humans who consume diversified diets.

Ecotoxicological studies on wildlife and domesticated ruminants (Table 12.3) usually involve aluminum determination in the parenchymal organs, such as the liver, kidney, skeletal muscles, and bones, and to a lesser extent in integumentary appendages, such as hair and feathers. Aluminum concentrations in the liver and kidneys were generally found not to reflect elevated environmental levels to which healthy individuals are exposed, though their renal function status plays a significant role in this effect (Scheuhammer 1987; Lucia et al. 2010). Most data on tissue content of aluminum has been collected for ruminants; in the bovine liver, the normal concentration range and the threshold aluminum toxicity values have been established. The normal and toxic values of hepatic aluminum concentrations were estimated at <1–5 and 6.3–11 mg kg^{-1} dw, respectively (WVDL 2015). Hepatic aluminum concentrations in various ruminants may range widely, from 0.83 to 104.3 mg kg^{-1} dw, and exceeds 14 mg kg^{-1} dw in most of farm animals (Al-Ganzoury and El-Shaer 2008; Anke et al. 2009; Gamberg et al. 2016). Typical aluminum levels from 1.53 to 3.6 mg kg^{-1} dw were observed in wild cervids in the USA and Poland (Zimmerman et al. 2008; Długaszek and Kopczyński 2011). Hepatic aluminum levels in wild boars, measured by Kucharczak and Moryl (2012), ranged between 3.37 and 10.67 mg kg^{-1} dw.

Aluminum levels in the bone tissue of ruminants range between 0.36 and 73 mg kg^{-1} dw (Tang et al. 1999; Anke et al. 2009), though much higher values are found in the nervous system, from 48 to 301 mg kg^{-1} dw (Al-Ganzoury and El-Shaer 2008). Anke et al. (2009) report a reversed pattern in the same tissues in lagomorphs; there was 56 ± 20 mg kg^{-1} dw in the nervous tissue and 86 ± 30 mg kg^{-1} dw in the bone of the European hare. A high content of aluminum, at a level of 87 mg kg^{-1} dw, has also been found in the bone of the domestic cat, *Felis catus* (Anke et al. 2001, 2009).

In birds, aluminum significantly affects the quality of the eggshell; hence its analysis is often used for environmental evaluation of exposure to various forms of the metal (Drent and Woldendorp 1989; Oelke 1989; Eeva and Lehikoinen 1995; Miljeteig et al. 2012). The highest aluminum levels in free-living birds were measured in their feathers, where it may vary in a wide range, from 2.25 to 328 mg kg^{-1} dw (Lucia et al. 2010). High concentrations, at a level of 74.49 mg kg^{-1} dw, were also found in avian bone tissue (Llacuna et al. 1995).

Anke et al. (2001, 2009) also found high aluminum concentrations in chickens (*Gallus gallus domesticus*), namely, 50.0 and 69.0 mg kg^{-1} dw, in the nervous and bone tissues, respectively. In terms of analysis of tissue aluminum content, especially in highly mineralized biological materials, a comparative analysis of its concentration in relation to age and sex seems reasonable. Research studies carried out so far have been inconclusive. Some reports suggest that aluminum accumulation in animal

Table 12.3 Aluminum concentrations in wild and domestic ruminants

Species	Country	Liver	Kidney	Muscle	Brain	Bone	References
Cattle *Bos taurus taurus*		Normal value: <1–5 ww or <3.3–16.7 dw					WVDL (2015)
		Toxic value: 6.3–11 ww or 21–36.7 dw					
Cattle	USA					0.66 dw	Tang et al. (1999)
Cattle	Germany	32 dw	32 dw	20 dw	48 dw	68 dw	Anke et al. (2009)
Cattle	Sweden	0.068 ± 0.047 ww	0.063 ± 0.029 ww	0.05 ± 0.006 ww			Jorhem et al. (1989)
		(0.226 ± 0.16 dw)	(0.25 ± 0.12 dw)	(0.2 ± 0.024 dw)			
Cattle	Brazil	70.2 dw	9.63 dw	9.69 dw		4.57 dw	Teixeira et al. (2013)
Cattle	Egypt	14.4 ww	10.5 ww	8.4 ww	33.1 ww		Al-Ganzoury and El-Shaer (2008)
		(48 dw)	(42 dw)	(33.6 dw)	(165.5 dw)		
Buffalo *Bison bison*	Egypt	15.6 ww	11.0 ww	5.7 ww	31.0 ww		Al-Ganzoury and El-Shaer (2008)
		(52 dw)	(44dw)	(22.8 dw)	(155 dw)		
Sheep *Ovis aries*	Germany	37 dw	43 dw		61 dw	59 dw	Anke et al. (2009)
Sheep	Egypt	25.7 ww	20.6 ww	5.9 ww	50.6 ww		Al-Ganzoury and El-Shaer (2008)
		(85.7 dw)	(82.4 dw)	(23.6 dw)	(253 dw)		
Goat *Capra aegagrus hircus*	Egypt	26.3 ww	19.5 ww	7.9 ww	53.0 ww		Al-Ganzoury and El-Shaer (2008)
		(87.7 dw)	(78 dw)	(31.6 dw)	(265 dw)		
Goat	USA					0.36 dw	Tang et al. (1999)
Camel *Camelus* sp.	Egypt	31.3 ww	21.2 ww	8.1 ww	60.2 ww		Al-Ganzoury and El-Shaer (2008)
		(104.3 dw)	(84.8 dw)	(32.4 dw)	(301 dw)		
Fallow deer *Dama dama*	Germany	30 dw	34 dw		56 dw	73 dw	Anke et al. (2009)

(continued)

Table 12.3 (continued)

Species	Country	Liver	Kidney	Muscle	Brain	Bone	References
Roe deer *Capreolus capreolus*	Poland	1.08 ww					Długaszek and Kopczyński 2011
		(3.6 dw)					
Roe deer	Poland			0. 58 ww			Długaszek and Kopczyński (2013)
				(2.32 dw)			
Roe deer	Poland	Herd 1: 0.41 ww (1.37 dw)	Herd 1: 0.96 ww (3.84 dw)	Herd 1: 1.67 ww (6.68 dw)			Kucharczak et al. (2005)
		Herd 2: 1.21 ww (4.27 dw)	Herd 2: 1.92 ww (7.68 dw)	Herd 2: 7.63 ww (30.52 dw)			
Roe deer	Poland	0.59 ± 0.32 ww	0.77 ± 0.12 ww				Kucharczak and Moryl (2012)
		(1.97 ± 1.07 dw)	(3.08 dw)				
Roe deer	Slovakia	0.74 ww	0.65 ww	1.29 ww			Bíres et al. (1992)
		(2.47 dw)	(dw)	(5.16 dw)			
Red deer *Cervus elaphus*	Slovakia	1.18 ww	0.82 ww	0.92 ww			Bíres et al. 1992
		(3.93 dw)	(dw)	(3.68 dw)			
White-tailed deer *Odocoileus virginianus*	USA, Texas	<2 dw		4.1 dw			Bruckwicki et al. (2006)
White-tailed deer	USA, South Dakota	0.46 ww					Zimmerman et al. (2008)
		(1.53 dw)					
Mule deer *Odocoileus hemionus*	USA, South Dakota	1.41 ww					Zimmerman et al. (2008)
		(4.7 dw)					
Caribou *Rangifer tarandus*	Greenland	Herd 1: 2.2 dw	Herd 1: 5.34 dw	Herd 1: 0.79 dw			Gamberg et al. (2016)
		Herd 2: 0.83 dw	Herd 2: 0.87 dw	Herd 2: 0.20 dw			

mg kg^{-1} dry weight, dw; wet weight, ww, was converted to dry weight using the following % moistures: kidney 75%, liver 70%, muscle 75%, brain 80%

tissues increases with age (Yokel and Golub 1997), but others reveal no effect of sex or age on the concentration of aluminum in the bodies of homeothermic vertebrates (Lucia et al. 2010).

5.4 *Ecological Effects of Aluminum*

In the natural environment, aluminum occurs mainly as a component of aluminosilicate minerals, and only its minor amounts are present in a soluble form, which are bioavailable for living organisms (May and Nordstrom 1991). These soluble compounds rapidly increase in quantity along with environment acidity, which is a result of unbalanced nitrogen, sulfur, and carbon cycles (Bolan and Hedley 2003; Tang and Rengel 2003). Apart from these factors, environmental acidification is caused by massive uptake of cations, in relation to anions, and the widespread presence of amides- and ammonia-containing fertilizers (Mahler et al. 1985). Over the last decades, acidic precipitations have been the most serious problem, significantly changing aluminum ions mobility in various environments and, in consequence, changing its bioavailability (Graveland 1990; Ormerod and Wade 1990; Alewell 2003). The phenomenon was first described in the nineteenth century, and the expression "acid rain" was first used in 1852 (Graveland 1990). Intensive research on its effect on aluminum mobility in the ecosystems started in the 1950s, with a majority of reports focusing on aquatic organisms. In subsequent years, more attention was also paid to avian species, which—in response to increasing acidity of the environment—were more exposed to toxic metals, experienced negative changes in food availability and quality, and had to face radical changes in their habitat (Peakall 2000). Aluminum has a significant effect on aquatic organisms, not only under environmental acidification. Freshwater bivalves exhibit severe filtration abnormalities in response to both short-term (1 h) and long-term (15 days) exposure to aluminum at a neutral pH (Kadar et al. 2002). The metal was also found to accumulate in freshwater snails, including the great pond snail, *Lymnaea stagnalis*, at pH 7, which led to sublethal changes in their behavior (Truscott et al. 1995; Elangovan et al. 2000). In this species, aluminum induced changes in the electrical activity of nerve cells, which suggests that the metal interferes with the ion channel electrophysiology in cell membranes (Csoti et al. 2001). This information contradicted the previous opinion that the metal is relatively poorly available in aquatic environments with a pH 6–8, due to its insolubility (Driscoll and Schecher 1989). Acidification of surface waters increases bioavailability of aluminum, but also of other toxic metals, including cadmium. This leads to a simultaneous drop in calcium bioavailability, which hits populations of aquatic invertebrates—food organisms of numerous vertebrate species (Peakall 2000). Markich et al. (2002) found that aluminum becomes toxic to benthic invertebrates at concentrations of its inorganic forms between 0.1 and 0.3 mg L^{-1}. A high level of soluble, toxic aluminum forms observed in surface waters may also be related to the activity of water treatment plants, which use aluminum-containing chemicals as coagulants

(Steinegger et al. 1990). An elevated concentration of aluminum is toxic to fish, whose increased mortality in consequence reduces populations of piscivorous birds (Ormerod and Wade 1990). The gills in fish were found to be most susceptible to aluminum toxic exposure, which causes ion exchange problems in this piscine organ. Aluminum also causes increased secretion of mucus, which hinders gas exchange and causes gill hyperplasia (Dietrich and Schlatter 1989). Reductions in fish populations, which results from water acidification and acidity-related increased aluminum uptake, affect the composition of vertebrates living around the body of water. Although occupying land habitats, these animals rely on the aquatic ecosystems. The group of homeothermic vertebrates includes numerous avian species, such as sandpipers (*Scolopacidae*), dippers (*Cinclidae*), tyrant flycatchers (*Tyrannidae*), wood-warblers (*Parulidae*), and wagtails (*Motacillidae*). In some circumstances, we can observe a growth in a population of insectivorous birds that do not need to compete for food with insect-eating fish (Ormerod and Wade 1990). In conclusion, increased bioavailability of aluminum presumably negatively affects the birds of the terrestrial ecosystems. Graveland et al. (1994), who studied birds living on strongly acidified soils, observed frequent abnormalities in the shell quality of their eggs. The shells were darker, more porous and thinner, which had a consequence in poorer reproduction.

Adverse changes resulting from ecosystem acidification also affect semiaquatic mammals, which nearly entirely feed on aquatic organisms. In Europe, the Eurasian otter (*Lutra lutra*) and water shrew (*Neomys fodiens*) are examples of such mammals. The impact of toxic aluminum forms killing fish and aquatic invertebrates may lead to food shortages affecting these species (Ormerod and Wade 1990). In terms of other terrestrial species, toxicity of aluminum is thought to be relatively low, as compared to other metals and to animals inhabiting aquatic ecosystems (Ormerod and Wade 1990; Steinegger et al. 1990; Roseland et al. 1990). However, a comparative study on two ruminant species revealed that an acidified habitat contributes to elevated levels of tissue aluminum, which can be observed in individuals of the same species living in a non-acidified area, as shown in Table 12.3 (Anke et al. 2009).

Pursuing pro-environmental policies has fortunately reduced the problem of acid rains in Europe and the USA; however, an increase in the pH of stream waters in many recovering areas is not as quick as expected (Menz and Seip 2004; Lajtha and Jones 2013). Contrary to Europe and North America, environmental acidification is increasing in many parts of Asia, especially in China and Russia, due to the intensive development of industries relying on coal-based energy sources and due to inefficient removal of sulfur and nitrogen oxides from combustion exhaust gases (Lu et al. 2010; Bhargava and Bhargava 2013). These oxides (key factors of acid rains) may move over long distances with masses of air, even between continents. Therefore, on a global scale, environmental acidification will long remain a serious ecological problem, which increases the bioavailability of aluminum and other toxic metals, harmful for both humans and ecosystems (Rosseland et al. 1990; Sparling and Lowe 1996; Bhargava and Bhargava 2013). Moreover, the twenty-first century seems to bring another aluminum-related issue in the form of nanoparticles; their impact on living organisms and whole ecosystems is largely a mystery (Burklew et al. 2012; Zhang et al. 2015; Chifiriuc et al. 2016) (Table 12.4).

Table 12.4 Influence of acid rain on aluminum concentrations in tissues of free-living and domestic ruminants in Germany

Tissue	Acidic rain		Statistical significance of difference
	With	Without	
Wild deer: fallow deer (*Dama dama*) and roe deer (*Capreolus capreolus*)			
Bone (rib)	79 ± 20	73 ± 34	NS
Brain	68 ± 16	56 ± 20	NS
Kidney	50 ± 12	34 ± 20	$p < 0.01$
Liver	49 ± 7.1	30 ± 18	$p < 0.01$
Cattle (*Bos taurus taurus*)			
Bone (rib)	73 ± 22	68 ± 15	NS
Brain	69 ± 15	48 ± 20	$p < 0.05$
Kidney	39 ± 24	32 ± 13	NS
Liver	44 ± 16	32 ± 13	$p < 0.05$

mg kg^{-1} dry weight; AM ± SD, arithmetic mean ± standard deviation
NS nonsignificant
Data source: Anke et al. (2009)

5.5 *Bioindicators and Biomarkers for Aluminum in Ecotoxicological Studies*

Selecting terrestrial homeothermic vertebrate species that could be of use as aluminum ecosystem contamination bioindicators is not an easy task. This is partly due to scarce literature sources dealing with aluminum in the wildlife but also due to a small number of organisms in which the level of the element has been established. This is largely associated with a low intestinal uptake of aluminum and its consequent low toxicity to animals but also with a highly varied impact of particular aluminum forms on the metabolic processes in mammals and birds. Aluminum concentrations have been analyzed in various species of these two vertebrate groups; however, ecotoxicologists present different opinions as to whether the animals are of value in terms of environmental biomonitoring of terrestrial ecosystems.

Studies carried out so far indicate that birds may be good bioindicators of aluminum in land ecosystems. Namely, birds—as compared to mammals—are much more intensively exposed to toxic effects of the metal, which they consume with food in much higher amounts. Up till now, mainly herbivorous mammals have been designated as biomonitors of the presence of elevated levels of bioavailable aluminum in terrestrial ecosystems. The most common species include cervids, widely distributed in Eurasia and North America, such as roe deer, fallow deer, white-tailed deer, or mule deer.

Other free-living mammals (Table 12.5), such as fallow deer, reindeer, wild boar, or hare, can also serve as biomonitors (Wren 1986; Bíres et al. 1992; Godal et al. 1995; Kålås et al. 1995; Kucharczak et al. 2005; Kośla et al. 2006; Anke et al. 2001, 2009; Długaszek and Kopczyński 2014). Within small mammals, grey red-backed vole and common shrew are used as bioindicators of aluminum environmental

Table 12.5 Aluminum concentrations in mammalian tissues

Species	Localization	Mean	Liver	Kidney	Muscle	Hair	References
Domestic mouse *Mus musculus f. dom.*	Poland Control group in lab study	AM ± SD	0.07 ± 0.02 ww (0.23 ± 0.07dw)	0.18 ± 0.09 ww (0.72 ± 0.36 dw)			Długaszek and Kopczyński (2000)
Grey-sided vole *Clethrionomys rufocanus*	Norway Svanvik	Med	ad 1.19 dw				Kålås et al. (1995)
Mountain hare *Lepus timidus*	Norway Jarfjord	Med	juv 1.15 dw ad 4.37dw	juv 0.76 dw ad 1.55 dw			Kålås et al. (1995)
Mountain hare	Reference area	Med	juv 2.35 dw ad 4.45 dw	juv 1.39 dw ad 1.27 dw			Kålås et al. (1995)
Snowshoe hare *Lepus americanus*	Northwest, Canada	AM ± SE		1.80 ± 0.28 dw			Poole et al. (1998)
European hare *Lepus europaeus*	Germany	AM ± SD	16 ± 30 dw	33 ± 13 dw	16 ± 6 dw	35 ± 10 dw	Anke et al. (2009)
European hare	Poland, Wroclaw	AM ± SD	1.58 ± 0.62 ww (5.27 ± 2.07 dw)	0.71 ± 0.21w (2.84 ± 0.84 dw)			Kucharczak and Moryl (2012)
European hare	Poland	Med	1.10 ww (3.67 dw)				Długaszek and Kopczyński (2011)
European hare	Poland	Med			1.26 ww (7.04 dw)		Długaszek and Kopczyński (2013)
European hare	Poland	Med				0.34 dw	Długaszek and Kopczyński (2014)

Wild boar *Sus scrofa*	Poland Wroclaw Piaseczno	AM ± SD	3.20 ± 2.40 ww	3.10 ± 1.28 ww	2.18 ± 0.84 ww	350.0 ± 66.5 dw	Kucharczak et al. (2005)
			(10.67 ± 8 dw)	(12.4 ± 5.12 dw)	(8.72 ± 3.36 dw)		
			1.01 ± 0.27 ww	1.44 ± 0.72 ww	2.74 ± 1.36 ww	201.1 ± 29.7 dw	
			(3.37 ± 0.9 dw)	(5.76 ± 2.88 dw)	(10.96 ± 5.44 dw)		
Wild boar	Poland Bogatynia	AM ± SD	0.83 ± 0.22 ww	1.19 ± 0.63 ww			Kucharczak and Moryl (2012)
			(2.77 ± 0.73 dw)	(4.76 ± 2.52 dw)			
Wild boar	Poland	Med	1.02 ww				Długaszek and Kopczyński (2011)
			(3.4 dw)				
Wild boar	Poland	Med			0.54 ww		Długaszek and Kopczyński (2013)
					(2.16 dw)		
Wild boar	Poland	Med				1.53 dw	Długaszek and Kopczyński (2014)
Pig *Sus scrofa f. dom.*	Sweden	AM ± SD	0.028 ± 0.011 ww	0.024 ± 0.014 ww	0.032 ± 0.011 ww		Jorhem et al. (1989)
			(0.09 ± 0.04 dw)	(0.10 ± 0.06 dw)	(0.12 ± 0.04 dw)		
Pig	Germany	AM ± SD	18.0 ± 10 dw	42.0 ± 24dw	12.0 ± 47 dw	39.0 ± 25 dw	Anke et al. (2001, 2009)
Mink *Mustela vision*	USA, Illinois	AM	4.52 ww	6.51 ww	7.85 ww		Halbrook et al. (1996)
			(15.07 dw)	(26.04 dw)	(31.4 dw)		
American mink *Neovison vison*	Northwest, Canada	AM ± SE		8.41 ± 0.75 dw			Poole et al. (1995)
American mink	Northwest, Canada	AM ± SE		5.63 ± 0.76 dw			Poole et al. (1998)
Northern red-backed voles *Myodes rutilus*	Northwest, Canada	AM ± SE	25.35 ± 3.55 dw				Poole et al. (1998)
River otter *Lontra canadensis*	USA, Illinois	AM ± SD			2.46 ± 1.02 ww		Halbrook et al. (1996)
					(9.84 ± 4.08 dw)		

(continued)

Table 12.5 (continued)

Species	Localization	Mean	Liver	Kidney	Muscle	Hair	References
River otter *Lontra canadensis*	Canada, British Columbia Upper Fraser River	AM ± SE	3.33 ± 0.99 dw				Harding et al. (1998)
Wild mink *Mustela vison*	Canada, British Columbia	AM ± SE					Harding et al. (1998)
	Upper Fraser River		3.50 ± 0.47 dw				
	Lower Fraser River		3.63 ± 0.91 dw	7.18 ± 1.75 dw			
Marten *Martes americana*	Canada, British Columbia	AM ± SD		11.3 ± 5.5 dw			Harding (2004)
Marten	Northwest, Canada	AM ± SE		3.51 ± 0.47 dw			Poole et al. (1995)
Wolverine *Gulo luscus*	Canada, British Columbia	AM ± SD	11.0 ± 11dw				Harding (2004)
Dog, Yorkshire terriers *Canis lupus dom.*	Poland	AM ± SD				93.8 ± 72.81 dw	Kośla and Skibniewska (2010)
Cat *Felis catus*	Poland	AM ± SD				Free living 38.0 ± 32 dw	Kośla et al. (2004)
						Homebred 20.8 ± 20.5 dw	
Cat	Germany	AM ± SD	21.0 ± 16 dw	24.0 ± 16 dw		44.0 ± 22 dw	Anke et al. (2001, 2009)

mg kg^{-1} dw, dry weight; ww, wet weight
AM arithmetic mean, *SE* standard error, *SD* standard deviation, *Med* median, *ad* adult, *juv* juvenile

exposure (Kålås et al. 1995). Avian species (Table 12.6) used as environmental aluminum bioindicators include greylag goose, wood grouse, red knot, grey plover, great tit, yellowhammer, rock bunting, or common blackbird (Kålås et al. 1995; Llacuna et al. 1995; Lucia et al. 2010).

The small amount of data on the concentrations of Al in the wildlife collected so far, as well as the progressive environmental changes, imply that this list remains open and will be gradually updated with new species, perhaps more suitable for this type of biomonitoring.

Parenchymal organs, bones, and skin appendages represent the main biomarkers of bioavailable aluminum forms in the bodies of homeothermic vertebrates (Anke et al. 2001, 2009; Kucharczak et al. 2005). The important point is the degree in which they reflect the short- or long-term exposure. Blood, plasma, or urine of wild animals are rarely used for analysis, primarily because the sampling process is usually cumbersome and, also, because the fluids reflect the short-term exposure only (Kowalczyk et al. 2004; Exley 2013).

Studies on birds confirm that bone is the most susceptible tissue in terms of aluminum accumulation, particularly in young individuals and breeding females. Further tissues mentioned are the brain, liver, and kidney (Sparling and Lowe 1996). Numerous studies suggest that arguably the most appropriate biomarkers of long-term aluminum exposure in birds and mammals are keratin appendages of the integumentary system, mainly hair and feathers. The process of their formation consists in transformation of living epithelial cells into dead, cornified, and stable structures showing no metabolic activity; thus the metal ions remain "trapped" within for a long period of time and the lack of metabolic activity prevents their removal (Tomlinson et al. 2004). The metal contamination contained in the feathers or hair may be of either endo- or exogenous origin. Many metals accumulate in the structures during food and water ingestion, though only during their growth; after the completion of growth, various exogenous contaminants from the air, water, or soil accumulate on the surface of feathers and hair. These are usually removed before analysis. Studies on mammals have usually focused on coat samples (Table 12.7), which proved to be a good marker of the effects of long-term exposure to some essential or toxic metals (Anke and Risch 1979; Yokel 1982; Kośla et al. 2004, 2006; Kośla and Skibniewska 2010; Skibniewska et al. 2011).

Birds' feathers have similar properties. Concentrations of endogenous aluminum in feathers vary greatly, ranging from a few to several hundred mg kg^{-1} dw (Bortolotti and Barlow 1988; Lewis and Furness 1991; Monteiro 1996; Bond and Lavers 2011; Lodenius and Solonen 2013; Borghesi et al. 2016). Moreover, in contrast to blood plasma—where metal concentrations change rapidly in response to changes in the physiological status of the body—keratin structures respond to such changes much slower (allowing analysis within at least several weeks before sampling); hence they seem to be a good biomarker of long-term exposure (Kośla et al. 2011; Stachurska et al. 2011).

Table 12.6 Aluminum concentrations

Species	Localization	Mean	Liver	Kidney	Muscle	Feathers	References
Western capercaillie *Tetrao urogallus*	Norway Pasvik	Med	juv 1.13 dw	juv 3.10 dw			Kålås et al. (1995)
			ad 0.20 dw	ad 0.86 dw			
Willow ptarmigan *Lagopus lagopus*	Norway Jarfjord Pasvik Reference area	Med	ad 0.82 dw	ad 1.86 dw			Kålås et al. (1995)
			ad 0.38 dw	ad 0.93 dw			
			ad 0.20 dw	ad 0.73 dw			
Greylag goose *Anser anser*	France	AM ± SE	11.8 ± 12.7 dw	6.1 ± 3.0 dw	11.6 ± 2.4 dw	226 ± 515 dw	Lucia et al. (2010)
Red knot *Calidris canutus*	France	AM ± SE	3.2 ± 0.2 dw	8.9 ± 6.1 dw	2.5 ± 0.4 dw	107 ± 50.1 dw	Lucia et al. (2010)
Grey plover *Pluvialis squatarola*	France	AM ± SE	4.2 ± 1.9 dw	3.4 ± 1.5 dw	7.7 ± 11.3 dw	2.5 ± 3.8 dw	Lucia et al. (2010)
Great tit *Parus major*	North Spain	AM ± SD	21.95 ± 35.0 dw	8.47 ± 6.9 dw	12.71 ± 8.61 dw	170.16 ± 68.8 dw	Llacuna et al. (1995)
Rock bunting *Emberiza cia*	North Spain	AM ± SD	9.88 ± 8.2 dw	7.88 ± 7.68 dw	9.63 ± 5.15 dw	328.2 ± 236.7 dw	Llacuna et al. (1995)
Blackbird *Turdus merula*	North Spain	AM ± SD	7.71 ± 7.37 dw	1.46 ± 1.05 dw	1.88 ± 2.5 dw	113.3 ± 69.7 dw	Llacuna et al. (1995)
Bald eagle *Haliaeetus leucocephalus*	USA, Maine	AM ± SD	3.98 ± 3.19 dw				Mierzykowski et al. (2011)
Great cormorant *Phalacrocorax carbo*	Serbia	AM ± SD				juv 66.19 ± 79.88 dw	Skoric et al. (2012)
						ad 65.94 ± 31.77 dw	
Hen *Gallus gallus dom.*	Germany	AM ± SD	42.0 ± 22 dw		6.40 ± 25 dw	38.0 ± 14 dw	Anke et al. (2001, 2009)

mg kg^{-1} dw, dry weight; ww, wet weight in avian tissues
AM arithmetic mean, *SE* standard error, *SD* standard deviation, *Med* median, *juv* juvenile, *ad* adult

Table 12.7 Aluminum concentrations in the hair of ruminants

Species	Country	Aluminum (mg kg^{-1} dw)	References
Roe deer *Capreolus capreolus*	Poland	0.6 ± 1.1	Długaszek and Kopczyński (2014)
		26.33 ± 3.3	Kucharczak et al. (2005)
European bison *Bison bonasus*	Poland	59.6 ± 63.9	Kośla et al. (2006)
Cattle *Bos taurus taurus*	Germany	19.0 ± 62	Anke et al. (2001, 2009)

6 Conclusion

- Aluminum is the third most abundant element present in the Earth's crust.
- The most common oxidation state of the element is +3, very rarely +1 or +2.
- Metallic aluminum oxidizes in the air, undergoing the process of passivation.
- In the natural environment, aluminum is found in various forms, depending on pH, Eh potential, and the presence of inorganic and organic ligands.
- Minerals containing aluminum include bauxite, cryolite, kaolinite, corundum, albite, orthoclase, gibbsite, and many others.
- Soil content of aluminum varies considerably and depends on the bedrock and the type of soil.
- Despite its abundance and ubiquity, the element has no significant biological function in either animal or human bodies.
- Aluminum is commonly found in plants with its concentrations depending on soil pH.
- In animals, the element occurs in trace quantities in the bone, lungs, and soft tissues.
- The element gets into the tissues of homeothermic vertebrates mainly through alimentary route, followed by aerogenic intake and, to a lesser extent, transdermal absorption.
- Human body may be exposed to aluminum through dialysis fluids or some medications, such as gastric acid suppressors, analgesics, or anti-inflammatory drugs.
- Aluminum nanoparticles, a common aircraft fuel additive, have recently added to aluminum contamination of both aquatic and terrestrial ecosystems.
- Aluminum toxicity to animals representing various taxonomic groups involves oxidative stress resulting in increased cell lethality.
- In homeothermic vertebrates, the toxic aluminum effects are manifested mainly within the central nervous system and in bone tissue and kidneys.
- Aluminum ore mining and processing within the metallic form production pose a threat to the natural environment.

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Chapter 13
Arsenic, As

Łukasz J. Binkowski

Abstract Arsenic is a semimetal that forms a part of more than 200 minerals. In many places of the world concentrations of arsenic in water are high, which is an issue of high importance in connection with human health. It has three allotrope forms; the gray one is the most common. Among numerous arsenic isotopes only ^{75}As is stable. The element is produced mainly in the form of a trioxide. Arsenic is used in electronic, metallurgy, pesticides, and defoliants. The most common use is in the production of wood preservatives (which, along with fossil fuel combustion, represents the largest anthropogenic arsenic source in the environment). In some parts of the world arsenic compounds are used as a supplement in poultry farming. Recent research also shows its potential use in medicine. Arsenic toxicity depends on its form (organic and inorganic), as well as on its oxidation state, solubility, and species exposed. In the body, the methylation of its inorganic form takes place mainly in the liver. Following exposure to arsenic, it can be found in various tissues, organs and materials, as kidneys, blood, lungs, feathers, hair, and fur, but mainly in the liver. Arsenic bioaccumulation is low, and biomagnification is still questioned in terrestrial ecosystems. Some biomarkers of exposure, apart from concentration measurements (especially in urine, blood, hair, fur, and feathers) may be used. Among internal tissues, the liver is the most commonly studied.

1 Introduction

Arsenic (chemical symbol As) is a metalloid (semimetal), but it is commonly included in the list of "heavy metals" based upon its toxicity (IUPAC 1971; Duffus 2002). As a semimetal it presents some properties of metals and nonmetals. It is a component of numerous minerals and reaches a concentration of 2 mg kg^{-1} in rocks (Mandal and Suzuki 2002). Arsenic's main toxicity combines with its inorganic

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forms occurring in groundwater in many places around the world, including more than 70 countries (Ravenscroft et al. 2009). This is the main reason for the global interest in As occurrence, availability, and exposure.

Arsenic, along with its compounds, has been widely used in industry and agriculture. It has found primary application in wood preservatives, insecticides, and poisons (Rahman et al. 2004). It has been also used in medical treatment, pharmaceuticals, and even in supplementation in animals (Jones 2007). Other applications include alloy production, glass processing, and the production of semiconductors, ammunition, batteries, pigments, paper, and metal adhesives. Elevated As concentrations in organisms cause poisoning and stimulate cancer development (IARC 2012). However, numerous studies also reveal that As deficiency in the diet of birds and mammals causes physiological disorders, especially with respect to methionine metabolism (Uthus 2003).

2 General Properties

Arsenic (Lat. *Arsenicum*) lies between germanium and selenium in the nitrogen group (pnictogen) of the periodic table. Its atomic number is 33 and atomic weight is 74.9 Da (Haynes 2014). Among the three As allotropes, the most stable is the gray form (also called α-crystalline). A yellow cubic form is less stable and after warming reverts to the basic form. The black β form is also stable. The density of the gray form is 5.73 g cm^{-3}, and its melting temperature is 817 °C; sublimation occurs at 616 °C (Norman 1998). Generally, 29 As isotopes have been identified (^{64}As–^{92}As). However, some scientists include an additional four (^{60}As–^{63}As). The only isotope considered stable and naturally occurring is ^{75}As and due to that fact As is often treated a monoisotopic element.

Arsenic occurs in four oxidation states: −3, 0, +3, and +5 (Adriano 2001). In nature, two major groups of As compounds occur, inorganic and organic (Lunde 1977; Andreae 1978). Compounds with the element on +3 (arsenite) and +5 (arsenate) oxidation levels dominate (Andreae 1978; Morita and Edmonds 1992; Rosen 2002). Apart from those, compounds as arsines and methylarsines with As on the −3 level also occur, but they are unstable in the air. Free arsenic As(0) is rarely encountered in nature (Eisler 1988). In terms of As use and application, the most important form is As trioxide (As_2O_3).

3 Arsenic Minerals, Production, and Uses

Arsenic constitutes a part of more than 200 minerals, of which 60% are treated as mainly As ones (Kabata-Pendias 2011). The most common are arsenopyrite (FeAsS), arsenolite (As_4O_6), loellingite ($FeAs_2$), orpiment (As_2S_3), and realgar (AsS). Arsenic also occurs in ores of other metals (such as iron, nickel, cobalt, and

Fig. 13.1 Dynamic of arsenic trioxide (As_2O_3) production between 1950 and 2015 (USGS 1950, 1955, 1960, 1965, 1970, 1975, 1980, 1985, 1990, 1995, 2000, 2006, 2011, 2015)

copper) and reaches high concentrations in sulfide deposits: arsenides (27 minerals), sulfides (13 minerals), and sulfosalts (65 minerals) (Adriano 2001; Hammond 2004).

Arsenic is produced mainly in the form of As_2O_3 (most reports present production data expressed in terms of this compound's values). Main global As production in 2015 was estimated at 36,000 metric tons (Fig. 13.1). For many years, largest quantities of As_2O_3 were produced (expressed in metric tons) in China (25,000), Chile (10,000), Morocco (7500), and Russia (1500) (USGS 2015, 2016). The USA has not produced As since 1985 (USGS 2011). At present, As_2O_3 is produced mainly by volatilization during the mining and production of other elements. Probably only China still mines As ores intentionally (Grund et al. 2005). Metallic As is produced in significantly smaller quantities, but detailed data are not available (USGS 2015). Of the total As imported by the USA, no more than 4% is in metallic form, which is usually produced by the reduction of ores or As_2O_3 with coal monoxide (Mandal and Suzuki 2002; Solo-Gabriele et al. 2003; USGS 2006).

The metallic form is used in electronics and nonferrous alloys. As_2O_3 has been used mainly in agriculture and forestry as an ingredient of pesticides and defoliants. The most common use is in wood preservatives (most often chromated copper arsenate, CCA) (USGS 2006). Since the 1980s among various As pesticides only CCA was still approved for use. This is why, in the 1990s, more than 80% of total As in the USA was used as a wood preservative (Solo-Gabriele et al. 2003). In 2004 the US Environmental Protection Agency (EPA) introduced a ban on CCA use for residences, led to a drastic decrease in CCA consumption (Jones 2007). Arsenic compounds have also been used as feed additives for poultry, which resulted in

increased growth rates, improved feed spent, and better pigmentation. However, because of As's toxicity, As compounds were withdrawn from use in the European Union (EU) in 1998. In the USA they are still in use (Nachman et al. 2005, 2013).

Arsenic is known in history as one of the most commonly used poisons for homicidal and suicidal purposes (Mandal and Suzuki 2002). However, previously, around the world but still in many countries today, As and its compounds were widely used in medicine, especially in treatments of syphilis, various parasitic infections, amoebic dysentery, and trypanosomiasis. In the second half of the twentieth century it was also used in stomatology, where As_2O_3 was applied to devitalize the dental pulp (Aso and Abiko 1978). Now recent research has shown the efficiency of As compounds in the treatment of relapsed or refractory acute promyelocytic leukemia (Shen et al. 1997; Antman 2001; Firkin 2014).

4 Arsenic in Nature: Geogenic and Anthropogenic Sources

Arsenic is the 20th most abundant element in the Earth's crust, with an average concentration of 0.00005% (Mandal and Suzuki 2002). A natural source of As in the environment is volcanic activity (USGS 2011). Its concentrations in rocks vary significantly around the world and in some geographical regions reach high values (Duker et al. 2005). Arsenic's highest concentrations are found in sedimentary rocks, especially clayey ones (Fig. 13.2). In some offshore areas, claystone concentrations run as high as 490 mg kg^{-1}.

In river sediments, As concentrations are even higher—up to 4000 mg kg^{-1} (Mandal and Suzuki 2002). The element occurs in almost all soil types and other environmental matrixes, but its major repositories are aquatic systems (Adriano 2001; Smedley and Kinniburgh 2002; Nordstrom 2002; Kabata-Pendias 2011;

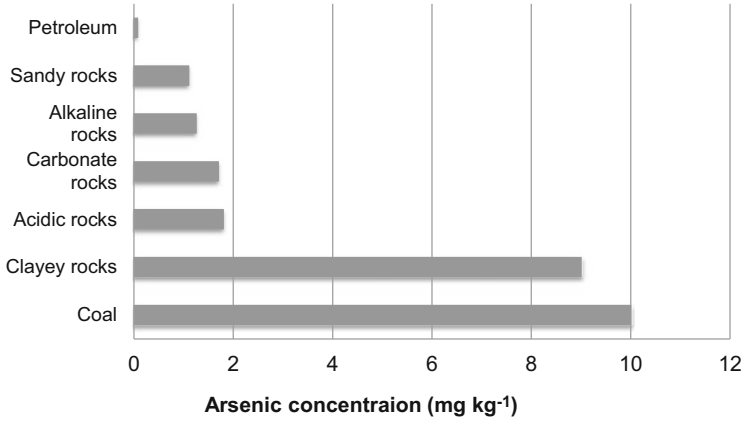

Fig. 13.2 Average arsenic concentrations in fossil fuels and rocks (data from Kabata-Pendias and Pendias 1999)

Magellan et al. 2014). Arsenic occurrence in soils is strictly connected with the initial material from which soils were formed, and As's form depends on many factors, including oxidation, pH, and microbial activity (Xu et al. 1991). Background As levels in various soils usually do not exceed 10 mg kg^{-1} (Kabata-Pendias 2011). However, owing to the common use of pesticides and other As products, concentrations found in agricultural soils are much higher, even up to 2500 mg kg^{-1} in Japan, the UK, and the USA (Adriano 2001; Kabata-Pendias 2011).

Arsenic is released from soils and rocks into the atmosphere by high-temperature processes and erosion. Later these forms are dispersed with the air on land and in water. However, the most dangerous geogenic exposure to inorganic As (the most toxic form) of humans and animals is through drinking groundwater in a number of places around the world, such as Mexico, the USA, Argentina, Chile, Bangladesh, India, and China (Welch et al. 2000; WHO 2010). The biggest problem is in the Bengal Basin (in Bangladesh and partially in India), where almost 60 million people drink water that contains elevated As levels. One million people have already developed strong symptoms of arsenicosis (Henke 2009).

Among fossil fuels, coal has relatively high As concentrations, within a range of 5–15 mg kg^{-1}. Petroleum's concentrations are lower, 0.005–0.14 ppm, with an average value of 0.07 ppm (Fig. 13.2). Concentrations usually found in gasoline fall within a range of 0.02–2 ppm (Kabata-Pendias and Pendias 1999). Fossil fuel combustion and metal smelters are the main anthropogenic As sources next to pesticides and wood-preservative run-off (USGS 2015). In the EU a recent decrease in such activities resulted in a 68% reduction of atmospheric As emissions in the period 1990–2013 (EEA 2016). However, a substantial part of industry still depends on coal combustion, which is linked with As emissions, mainly through particulate matter. Arsenic is observed mainly in the air in the form of arsenites and arsenates. The exceptions are areas where pesticides based on other As forms are sprayed (Davidson et al. 1985). The lowest air As concentration was observed over the South Pole (0.007 ng m^{-3}) and Spitsbergen (0.01–1.5 ng m^{-3}) (Kabata-Pendias and Pendias 1999). Arsenic concentrations in certain American cities average 2 ng m^{-3} (Chen and Lippmann 2009). Average concentrations in remote areas in the USA were estimated to fall within a range of 1–3 ng m^{-3}, in urban areas 20–100 ng m^{-3}, and in industrial areas 70–770 ng m^{-3} (ATSDR 2007a; Geiger and Cooper 2010). Arsenic concentrations in Europe are generally low, and the EU As target value in ambient air was established at a level of 6 ng m^{-3} (EU 2005, 2008; Strincone et al. 2013; Guerreiro et al. 2014).

Arsenic compounds are used as feed additives in animal farming, so the possibility of its deposition in manure arises. Simulations show that using manure to enrich agriculture soils in nutrients may lead to pollution of groundwater and the creation of another pathway of exposure, but environmental studies have not confirmed this problem (Nachman et al. 2005; Jones 2007).

5 Biological Status of Arsenic

Resistance to and metabolism of As is generally known in bacteria that exert an influence on the global As geocycle (Mukhopadhyay et al. 2002; Stolz et al. 2006). Even As's physiological role is suspected in some types of microbial photosynthesis in biofilms, but it has not been fully proven (Kulp et al. 2008; Schoepp-Cothenet et al. 2009). Arsenic is known as a nonessential and toxic element for plants, but some specimens evolved to metabolize it efficiently (Finnegan and Chen 2012). The main mechanism of its detoxification is the reduction process of arsenate into arsenite, controlled by the arsenate reductase enzyme (Chao et al. 2014). Some fern species are even As hyperaccumulators, but still the reaction of most plants to As compounds makes it possible to use them as ingredients in herbicides and defoliants (NAS 1977; Zhao et al. 2009).

Arsenic essentiality in insects is not known either, and the use of herbicides has demonstrated the sensitivity of insects and other invertebrates to this element (Eisler 1988). The sensitivity of different species may vary significantly, and some of them may play an important role in the retention and cycle of As (Riedel et al. 1989; Schaller et al. 2010).

In birds and mammals, the problem of As essentiality is still disputed. Some observations suggest that inorganic As may be an essential nutrient for goats, chicks, minipigs, and rats (EPA 1998; Adriano 2001). The positive influence of As on animal growth has been long observed and resulted in the use of its compounds in animal breeding as food additives. Studies on birds revealed increased body weight and immune organs of chickens after As supplementation (Ai-zhi and Zhen-yong 2007). However, the main mechanism remained unknown for a long time (Anke 1986). Probably the increased growth of animals bred with the aforementioned feed additives is connected with intestinal health. Organoarsenic additives (the most common being Roxarsone) are very toxic to parasites and significantly decrease their number, which results in a better general condition of animals (Lasky et al. 2004; Jones 2007; FDA 2011). Bearing this in mind, such an influence cannot be treated as a positive function in physiology, but rather as a drug treatment.

5.1 Toxicity of Various Arsenic Forms in Homeothermic Animals

Toxic As's effect is undisputed and significantly depends on its form. Arsenic compounds that are still used in medicine showed adverse effects on the body, including lethal cardiac dysfunctions (Ohnishi et al. 2000; Lin et al. 2005). In spite of the fact that various forms stimulate different levels of toxicity, signs of poisoning are similar (Woolson 1975; NRCC 1978). Generally for all organisms, inorganic As forms are more toxic than organic ones (Tamaki and Frankenberger Jr 1992). However, some observations dispute this statement. The positive relationship

between the toxicity of As compounds and solubility in water has been noted (Eisler 1988). The solution showed a toxicity that was as much as ten times higher than that of the undissolved form (Schwartze 1922; Harrisson et al. 1958). Two oxidation states of arsenic are usually discussed in connection with effects on animals: As(III) and As(V). As(III) forms strong bonds with the thiolates of cysteine residues and are regarded as more toxic than As(V)—by as much as 60 times (Rosen 2002; Ventura-Lima et al. 2011). The level of As toxicity also depends on other factors, for example, the species. Comparison of the resistance to As influence between rats and humans revealed that humans are more sensitive than rats (NAS 1977).

The species affects not only the toxicity but also accumulation and distribution of As in the body (Ducoff et al. 1948). The oral LD_{50} of As_2O_3 is on the level of 31.5 mg kg^{-1} in mouse and 14.6 mg kg^{-1} in rat. The LD_{50} of As given intraperitoneally is 46.2 mg for mouse and 13.4 for rat. Adequate values of oral intoxication were consecutively 145 mg kg^{-1} and 763 mg kg^{-1}, respectively (TOXNET 2015). The acute minimum As lethal dose in humans fell in the 70–200 mg range, or 1 mg kg^{-1} per day (Dart 2004).

In addition to toxicity through ingestion, inhalation of As compounds is also harmful. Lethal cases, diarrhea, respiratory distress, and decreased body weight have been observed in rodents exposed to As pesticide fumes (Stevens et al. 1979). The penetration of organic As in fetuses is negligible, but inorganic As compounds may cross the placental barrier and even cause death of newborns (Lugo et al. 1969).

Medical studies that reveal positive As impacts in leukemia treatment point out also observations regarding the further development of thyroid cancer in patients, probably because of As's carcinogenicity (Firkin 2014). Co-occurrence of lung cancer among people chronically exposed to airborne As compounds has also been observed (Nordberg et al. 2007). The carcinogenic properties of inorganic forms have been confirmed, but the main mechanism is not fully understood (Sakurai 2003). Arsenic and inorganic As compounds have been classified in human carcinogen group 1 based on consistent evidence of associations mainly with lung, skin, and bladder cancers. Arsenobetaine and other organic As compounds have not been classified as carcinogens (IARC 2012). The interactions between As and other elements, such as zinc, selenium, and antimony, are suspected in the etiology of carcinogenicity (Gebel 2000).

Most of the organisms already studied show evolved mechanisms of defense against As toxicity (Rosen 2002; Cullen 2014). Arsenic methylation, which leads to the transfer of inorganic forms into less toxic methylarsenic(V) [MMA(V)], was long treated as a very efficient detoxification process. However, further research showed that methylation may lead to the production of other organic compounds such as methylarsenic(III) (Cullen 2014) (Fig. 13.3). Some methylated organic compounds [such as monomethylarsonate MMA(III)] are more toxic to plants and animals (including humans) than inorganic forms and certain organic forms containing As (V) like dimethyloarsenic [DMA(V)] (Meharg and Hartley-Whitaker 2002; Rahman et al. 2012). Research carried out on human liver cells revealed that the toxicity of various As forms can be presented in the order: MMA(III) > arsenite > arsenate > MMA(V) = DMA(V) (Petrick et al. 2000). MMA and DMA may negatively influence enzymes that work in the energetic cycles in cells. Inorganic As interacts

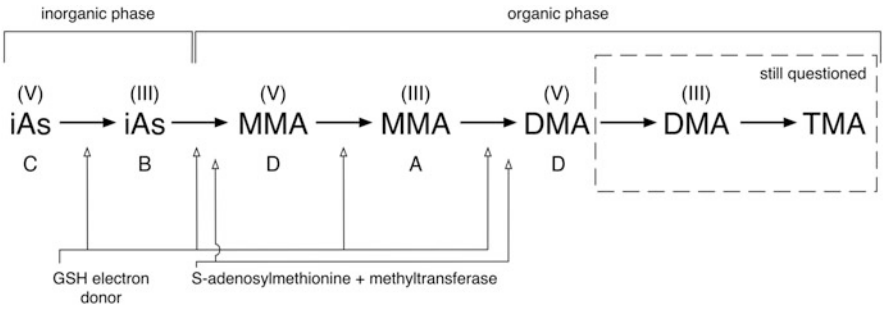

Fig. 13.3 Methylation of arsenic in liver. Letters (A–D) indicate increasing toxicity of compounds. Roman numbers indicate level of oxidation. *iAs*, inorganic arsenic; *MMA*, monomethylarsenic; *DMA*, dimethyloarsenic; *TMA*, trimethyloarsenic (original scheme)

with sulfhydryl groups; the toxicity of MMA is mainly associated with the thiol groups reaction, and the toxicity of DMA with decreasing oxidative phosphorylation (Khan et al. 2014). Some evidence also suggest that MMA(v) is a carcinogen in rodents. There are also suspicions that in humans, DMA may be methylated further into arsenobetaine, which is characterized by a low toxicity for animals (Kaise et al. 1985; Newcombe et al. 2010).

5.2 *Toxicokinetics and Effects of Arsenic in Wildlife*

Both main types of inorganic As—arsenite and arsenate—are well absorbed by ingestion and inhalation. Significantly lower absorption occurs through the skin (ATSDR 2007b). Experiments with As_2O_3 in rats showed elevated As concentration in kidneys, liver, lungs, skin, spleen, and blood 24 h following administration. A similar dynamic was observed in humans (Graeme and Pollack 1998). Arsenic accumulates in blood cells, so concentrations in blood and spleen 2 months after subcutaneous implantation remained high. Interestingly, accumulation was not observed in hair and brain (Vallee et al. 1960; Aso and Abiko 1978), but studies on patients during leukemia treatment revealed elevated concentrations in hair, nails, and urine following intravenous infusion of As drugs (Shen et al. 1997).

In higher animals and humans, following various administrations (including oral, fume, and injection exposure), arsenates are partially reduced to arsenites (Vahter and Marafante 1983; Buchet et al. 1998; ATSDR 2007a). This occurs because of the activity of glutathione, which is an electron donor for the reduction (Styblo et al. 2000). Following parental administration of As_2O_3 to rabbits, As(III) was the major form of the element detected in blood, lungs, and liver (Vahter and Marafante 1983; Lin et al. 2005). However, the main organ containing As following exposure is the liver (Vahidnia et al. 2007b). Inorganic forms of the element in humans are methylated into MMA and DMA, and partially further to trimethylarsenic (TMA) compounds in liver (Yamauchi and Yamamura 1985; Styblo et al. 2000). The process

takes several steps, mainly in the liver, but other organs also showed methylation activity (Fig. 13.3) (Khan et al. 2014). Methylation is catalyzed by methyltransferase, which uses *S*-adenosylmethionine as the methyl group donor (Zakharyan et al. 1995). First, inorganic As(III) is converted into MMA(V). Then MMA(V) is reduced to MMA(III), which is further methylated into DMA(V). Next methylation step (into TMA) is also proceeded by the reduction into DMA(III) (Styblo et al. 2000; Cullen 2014). However, TMA metabolism is still disputed (Kaise et al. 1985; Newcombe et al. 2010) (Fig. 13.3).

The speed of methylation varies among species and is higher, for example, in mice than in rabbits. The excretion of organic forms is faster than that of inorganic forms (Vahter and Marafante 1983). Following absorption, more than 90% of inorganic As is cleared from the blood in 2–4 h and as much as 70% of the intake is excreted in 48 h (Jones 2007).

Arsenic significantly affects the central and peripheral nervous systems. Its effects had already been observed in chronic and acute exposure, but the main mechanisms remain unclear. There are some observations that, not inorganic forms, but organic forms of As are responsible for the impact of the element on nerve cells (Vahidnia et al. 2007a). The time after exposure in single-dose studies varied between 10 days and 3 weeks, but the initial effects may be observed even after a couple of hours (Winship 1984; Vahidnia et al. 2007b). The most characteristic clinical signs of As-induced neuropathy are numbness, paresthesias, and pain (especially in feet soles). They are connected with axonal degeneration and disorganization of the cytoskeletal framework (Vahidnia et al. 2007b).

Studies strictly examining the toxicokinetics and effects of As in birds mainly concern farm species that may be intentionally exposed via feedstuff and unintentionally in some cases through drinking water (Khan et al. 2014). Wild living birds are rarely studied in this respect. Generally, there are numerous observations of lower appetite, weight loss, deterioration of blood parameters, depression, ataxia, dullness, and other neurological disorders among poultry exposed through drinking water or food (Halder et al. 2007; Islam et al. 2009; Sharaf et al. 2013; Khan et al. 2014). Weight loss and even death were observed in mallard (*Anas platyrhynchos*) ducklings (Hoffman et al. 1992). The negative influence of As on the heart (ecchymotic hemorrhages), liver (congestion and hemorrhages), spleen (regression and hemorrhages), kidneys (swelling), and intestinal mucosa (congestion) were already observed in broiler chicks after administration of sodium arsenite (Kalavathi et al. 2011). Studies on bird histopathology showed atrophy of bursa of Fabricius stimulated by a mixture of chemicals including As (also cadmium, lead, benzene, and trichloroethylene), as well as liver lesions (Hoffman et al. 1992; Vodela et al. 1997). Separate analysis of sodium arsenite revealed the substantial negative impact on among others cardiac muscle (disruption of bundles), kidneys (infiltration of mononuclear cells), and spleen (depletion of lymphocytes). The toxic effects of As in these chicks were partially counteracted by supplementation with ascorbic acid and vitamin E (Kalavathi et al. 2011). Increased concentrations of plasma calcium and decreases in plasma glutathione activity are also linked with exposure to As in birds. All toxic effects are more common in birds with limited access to food (Hoffman et al. 1992).

5.3 *Bioaccumulation of Arsenic*

There is a discrepancy in the scientific literature regarding the occurrence and efficiency of As bioaccumulation. Human studies suggest that the element does not bioaccumulate on a large scale, even over time (Jones 2007). Similar observations were made among aquatic organisms, in which the bioconcentration factor (except for algae) is relatively low (Eisler 1988). However, phytoplankton that bioaccumulate As compounds are a major food source for animals of higher levels, so they might be exposed to the element. For this reason, some species of fish are being used in biomonitoring of arsenicals (Rahman et al. 2012).

In terrestrial trophic chains, the situation is different. Generally, inorganic As forms dominate in soil. Soil microbiota may change them into organic ones, methylate and demethylate them, and carry out these processes in opposite ways (Turpeinen et al. 1999). They may get into plants or invertebrates, exposing the animals at higher levels of the trophic pyramid, including birds and mammals, that metabolize the compounds into organic species (Tamaki and Frankenberger Jr 1992; Vahter 2000; Meharg and Hartley-Whitaker 2002).

Despite the fact that As is a known xenobiotic and carcinogen, few studies have been conducted on its concentration and influence in birds. This knowledge gap is especially significant in passerines among which around 75% of studies were conducted only on the great tit (*Parus major*) and pied flycatcher (*Ficedula hypoleuca*). The most often internal tissues have been studied (32.5%), followed by feces (27.5%) and blood (15%) (Sánchez-Virosta et al. 2015). The values considered normal were estimated on levels (mg kg^{-1} dw) 0.01–0.25 for liver and 0.01–0.2 for kidneys (WVDL 2015). Concentrations in internal tissues exceeding 10 mg kg^{-1} wet weight (ww) (~41.6 mg kg^{-1} dry weight, dw, recalculated according to Binkowski 2012) are treated as symptoms of As poisoning (Goede 1985). Such high concentrations are not very common, and in most cases accumulation does not exceed background levels—for liver on average 1.5 mg kg^{-1} dw at pristine sites and 5.8 mg kg^{-1} dw at polluted sites (Berglund et al. 2012; Sánchez-Virosta et al. 2015). However, particular specimens may reach significantly higher concentrations, as high as around 13 mg kg^{-1} dw (pied flycatcher) (Berglund et al. 2012). It is worth mentioning that such high concentrations are harmful to animals since significantly lower concentrations were the cause of disturbances in their biochemistry and growth (Sánchez-Virosta et al. 2015). Among other bird groups, studies on dunlins (*Calidris alpina*) across Europe (including the Netherlands, Norway, and Sweden) revealed that in many cases concentrations were lower than the detection limit. The highest mean concentration was noted for juvenile dunlin and reached 6.2 mg kg^{-1} dw, but the mean value for all studied specimens was lower than 3 mg kg^{-1} dw. Additionally, birds from pristine areas (Scandinavia vs. Western Europe) accumulated significantly lower amounts of the element (Goede et al. 1989). Arsenic concentrations found in the liver of dabbling ducks are similar. A study carried out on common species, including the mallard, blue-winged teal (*Anas discors*), and shoveler (*Anas clypeata*), revealed a mean value of 4.76 mg kg^{-1} dw

(Pereda-Solis et al. 2012). Higher As concentrations were suspected among birds exposed to spent lead shot that contained detectable As levels (Hall and Fisher 1985). Studies verifying this hypothesis in nature did not show high As concentrations in lead-poisoned birds. However, the conclusions are not very obvious because a strong correlation was observed between lead and arsenic in exposed birds (Mateo et al. 2003), so this issue requires further investigation.

Concentrations in feathers are generally lower than in internal organs, and they are used in in vivo biomonitoring. Molting stage and age of the feather are very important here (Burger 1993). The interesting question is whether the contamination of feathers comes mainly from internal distribution or external deposition. A strong argument for the second route is the correlation of As concentrations in preen glands and in feathers (Goede and De Bruin 1984; Goede 1985; Goede et al. 1989). Concentrations of As in feathers of various species of Anseriformes are similar, but a slightly higher one was noted locally for diving duck (pochard *Aythya ferina*), where the mean reached 0.50 μg g^{-1} dw (Karimi et al. 2016). These observations rank Anseriformes in the middle of the common range of species from different trophic levels (e.g., raven, condor, and red knot), whose mean was 0.96 μg g^{-1} dw (Burger 1993). Karimi et al. (2016) also noted an interesting positive but weak correlation between lead and arsenic concentrations in primary feathers of Anseriformes. A similar but stronger relationship was observed in great tit feathers (Janssens et al. 2001). Some studies have also been conducted on As concentrations in bones of birds. The reason for this is that arsenate is structurally very similar to phosphate, which builds bones, so the possibility of phosphate substitution by arsenate may occur (Adriano 2001; WHO 2001; Mateo et al. 2003).

Arsenic is not as widely studied an element in mammals as, for example, lead or cadmium, but because of the potential harm to residential wildlife, studies are being carried out (Saunders et al. 2011). However, among such studies, laboratory acute toxicity issues dominate, and As chronic toxicity studies among wild living animals remain scarce (Drouhot et al. 2014). Normal values, for example in deer, do not exceed 0.5 mg kg^{-1} dw in liver and kidneys. Normal concentrations in other mammals are even lower (WVDL 2015). An interesting procedure for monitoring As levels in shrews was developed by Moriarty et al. (2012). It entails using for analysis the entire torso of an individual. This study revealed that shrews are efficient at processing and excreting As. Animals from heavily contaminated areas may accumulate as much as twice the As body burden as animals from uncontaminated sites. However, not only environmental contamination but also other factors, such as habitat, diet preferences, and animal mobility, play a significant role in exposure and accumulation. Arsenic concentrations in the stomach contents of various small rodent species observed in southern France fell within a very wide range, from below the detection limit to 1669 mg kg^{-1} dw (but in most cases the upper limit did not exceed 50 mg kg^{-1} dw). These values did not correspond clearly to concentrations in soil from different emission zones, and animals from cleaner zones sometimes had higher concentrations in their stomach content. Internal concentrations (mg kg^{-1} dw) fell within a range of 0.05–90.4 for liver, 0.24–50.9 for kidneys, and 0.31–37.7 for lungs (Drouhot et al. 2014). Studies on As accumulation in small

mammals led to varying conclusions (Erry et al. 2000). Some revealed that in polluted areas As is accumulated by animals, some revealed no accumulation, and others only in some organs (Sharma and Shupe 1977; Smith and Rongstad 1982; Ismail and Roberts 1992; Peles and Barrett 1997). Studies on large animals, like cattle, showed that particular tissues, such as blood, kidneys, liver, and muscles, accumulate As at statistically different rates of efficiency. What is more, these animals accumulate As only in areas of higher soil concentrations. Maximum values (mg kg^{-1} dw) may reach 122.6 in liver, 135.6 in kidneys, and 8.55 in muscles [values recalculated from ww according to Binkowski (2012)] (López Alonso et al. 2002).

5.4 *Ecological Effects of Arsenic*

The main processes under dispute in terms of the ecological aspects of a given element or compound are bioaccumulation and biomagnification. They are usually separately evaluated for aquatic and terrestrial environments, but generally they are more efficient in aquatic ones. In aquatic environments (both marine and freshwater), inorganic As species dominate, but they are methylated into organic species by aquatic organisms. Because bioaccumulation of total As in fish reaches as high as 22.1, the exposure of predators through fish is likely (Kar et al. 2011). These may include aquatic birds and mammals. In some areas, to limit exposure, As bioremediation with algae is proposed (Magellan et al. 2014).

In the case of terrestrial ecosystems, As bioaccumulation may be observed, as mentioned earlier (Sect. 5.3). However, studies on mammals also reveal that the bioaccumulation factor is lower than 1 (0.69), which means that As bioaccumulation does not occur in these animals (Erry et al. 2000). In both types of environment, a further step in bioaccumulation—As biomagnification—has been widely questioned (Woolson 1975; NRCC 1978; Eisler 1988; Jones 2007). However, the lack of biomagnification does not mean that As does not affect the ecosystem as a whole. It does affect the ecosystem in areas of polluted water or massive amounts of poultry feces deposition, where animals are supplemented with As compounds (Eisler 1988).

5.5 *Bioindicators and Biomarkers of Arsenic in Ecotoxicological Studies*

Metabolomic studies on As bioindicators and biomarkers are mainly done on rodents. Only a few studies have been carried out on humans. It is worth emphasizing that As, after cadmium, is the most frequently studied element in these aspects (García-Sevillano et al. 2015). Despite the fact that the main mechanisms of its toxicity remain unclear, its connection with enzymatic inhibition and oxidative stress

is widely observed, which may be employed in biomarker studies. However, there is still a need for As-sensitive and appropriate biomarkers in environmental studies (Marchiset-Ferlay et al. 2012).

It is known that As affects certain enzymes in heme biosynthesis, such as aminolevulinate synthase, porphobilingoen deaminase, and heme oxygenase (Garcia-Vargas and Hernandez-Zavala 1996). The exposure to a mixture of elements (arsenic, cadmium, lead) causes perturbations in lipid and amino acid metabolism in blood serum (Dudka et al. 2014). Additionally, the connection between As exposure and blood porphyrins and their urinary excretion has been observed (Garcia-Vargas and Hernandez-Zavala 1996; Marchiset-Ferlay et al. 2012). All these relationships may be implied to some extent as biomarkers, but their usefulness, especially in animal studies, awaits confirmation. In the range of genotoxicity, DNA damage, chromosomal aberrations, sister chromatic exchange and micronuclei formation are linked with As exposure. Based on these effects, genotoxicity biomarkers may be used (Liou et al. 1999; Chen et al. 2005; Marchiset-Ferlay et al. 2012).

Blood and urine are the most frequently used biomarkers of As exposure. Arsenic is purged from the blood, so the concentration in blood reveals only present and recent exposures (Andrade et al. 2015). A better biomarker is probably concentration in urine, because it reflects chronic exposure. Other very good biomarkers of chronic exposure are hair and nails (thus feathers and claws in animals), but the concentrations here cannot be recalculated as the dose ingested (Marchiset-Ferlay et al. 2012). Arsenic exposure may also be evaluated on the basis of its concentration and distribution in internal tissues. Probably the most commonly studied and useful tissue in this connection is liver tissue.

6 Conclusions

- Arsenic is a semimetal that is toxic for birds and mammals at elevated concentrations. Inorganic forms of arsenic possess carcinogenic properties. Additionally, the occurrence of arsenic in water in many parts of the world is an issue of high importance because of the high incidence of arsenicosis in people. Despite its toxicity, As has been used in medicine and as a supplement for farm poultry in some parts of the world (e.g., USA).
- Arsenic forms a part of more than 200 minerals, and its natural sources are rocks, soils, and volcanic activity. In industry, arsenic is used and produced mainly in the form of trioxide. The most prevalent uses of As are in the production of wood preservatives (such as chromated copper arsenate), pesticides, nonferrous alloys, and electronics.
- Bioaccumulation of As in birds and mammals is not high, and biomagnification is still disputed. Concentrations of up to 0.25 mg kg^{-1} dw in bird liver and kidneys are treated as normal. In mammals such values do not exceed 0.5 mg kg^{-1} dw.
- A potential relationship between exposure to arsenic and enzyme activities has been observed, but the precise biomarker needs to be found. Exposure may be

evaluated on the basis of internal concentrations in hair, fur, nails, claws, urine, and organs, preferably in liver.

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Chapter 14
Cadmium, Cd

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Abstract Cadmium (Cd) is a nonessential and toxic element to animals and plants. In recent years, clear changes in the use of this element have been evident, which has resulted in reduced amounts of Cd being released into the environment. Despite the emissions of Cd gradually decreasing since the 1990s, its presence in different components of the environment is still a severe ecological and health problem. Cadmium, due to its short biological half-life period, acts as a cumulative poison. It shows an explicit tendency to bioaccumulate and even at low levels of exposure can accumulate in animal tissues, reaching values significant as toxic interactions. The highest concentrations of Cd are found in the tissues of free-ranging animals that live in the impact range of Cd emitters. Internal concentrations may even be up to dozens of times higher than in animals from nonpolluted areas. In the tissues of game animals, sometimes levels are found so high that they are rejected for human consumption. Such contamination in the environment causes not only numerous disorders within the organism itself but may also result in changes in the whole ecosystem, especially the negative effects of cadmium in reproductive disorders and increased infant mortality in animals.

1 Introduction

Cadmium (Cd) is a toxic element that occurs naturally in the earth's crust. Its average concentration in the lithosphere ranges between 0.10 and 0.20 mg kg^{-1} (or part per million, ppm). Cadmium is emitted from numerous natural and anthropogenic

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sources into the atmosphere as well as into aquatic and terrestrial ecosystems. It is thought that Cd is emitted mainly by human industrial activities (mining, metal production, fuel combustion, various industrial processes, as well as the use of phosphate fertilizers in agriculture), yet natural emissions may even be 30 times higher than anthropogenic sources (UNEP 2010). Air mass movements play a particular role in the global distribution of Cd. Depending on the atmospheric conditions, dust-suspended Cd may travel up to 1300 km in 3 days, so that even areas located at large distances from the main sources of cadmium emissions are still endangered by its influence. The contamination of soils, water, and air with cadmium is a severe problem as this element does not decompose in the environment and may remain for years, being tied into the net of trophic dependencies. For this reason, as it becomes available to plants, it then follows to animals and humans. Cadmium is toxic to microorganisms, plants, and animals (ATSDR 2012). In birds and mammals, it has been showed that the absorption and accumulation of Cd depend on age and, in a lower level, on gender. Usually old individuals accumulate more Cd in their tissues in comparison to the young, and females accumulate more than males (Scheirs et al. 2006; Mayack 2012). In the body, Cd accumulates mostly in the liver and kidneys, the target organs for the toxic influence of this element. In these organs, Cd induces the synthesis of metallothioneins (MT) that bind Cd ions Cd (II) into CdMT complexes (Klassen et al. 1999). On the basis of the mutual proportions of Cd levels between the kidneys and the liver, we can suppose about the nature of the exposure. A higher concentration of Cd in the liver compared to the kidneys suggests exposure to high doses of Cd, while a higher level in the kidneys indicates chronical exposure to low doses of Cd.

Environmental exposure does not usually cause acute intoxication. Definitely long-term exposure causes intoxication more often. The harmful effects of Cd are more pronounced by disorders in liver and kidney function. Cadmium shows carcinogenic and teratogenic activity and may also induce oxidative stress in cells. This metal has been considered as an endocrine modulator that acts in estrogenic and antiandrogenic ways. By disrupting the hypothalamus-pituitary-gonad axis, Cd affects reproductive potential by interfering with the regulation of the reproductive system. In birds, dietary exposure to Cd resulted in reduced egg production and eggshell thickness. Cd is also a neurotoxin that in wild animals may affect sexual behavior. Moreover, Cd acts negatively on bone metabolism, causing a decrease in bone formation and an increase in bone resorption. Long-term exposure to low environmental levels of Cd results in a decrease in mineral bone density, which is the effect of calcium (Ca) release from bones, as well as disorders in collagen production (ATSDR 2012).

In general, in the tissues of wild animals, different levels of cadmium have been observed. For example, in terrestrial birds, it varies over a wide range in the liver, from undetectable to about 18 mg kg^{-1} dry weight (dw), and in the kidneys from undetectable to almost 60 mg kg^{-1} dw. In the liver and kidneys of terrestrial mammals from different regions of the world, it differs in an even larger scale—from below the limits of detection (<DL) to as high as 75 mg kg^{-1} dw in the liver and from <DL to about 390 mg kg^{-1} dw in the kidneys. Animals from contaminated

regions (both rural and industrial) are characterized by a few to a dozen times higher concentrations of Cd in comparison to uncontaminated reference regions. For this reason, it is believed that wild animals reflect the degree of environmental pollution in which they live. Thus, research on such groups provides useful information on the state of the environment, the scale of exposure, and the possible toxicological threat in a selected area.

2 General Properties

Cadmium (Cd, Latin *cadmium*) is a chemical element in the group of transitional metals placed in the group 12 of the periodic table (IIB). It was discovered in 1817 by German chemist Friedrich Strohmeyer, and the name comes from the word *kadmeia*, the Greek name of the zinc ore calamine in which this element was found. Cadmium is a silver-white metal with a blue gloss belonging to the zinc family. Its molecular weight is 8.642 g cm^{-3}, which classifies it as a heavy metal. It develops a hexagonal structure. Vapor pressures at 400 °C and 500 °C are 0.2 kPa (1.4 mmHg) and 2.1 kPa (16 mmHg), respectively. The melting point of Cd is 321 °C and boiling point is 767 °C. Compounds of cadmium are characterized by their differing solubility in water. Some of them, e.g., cadmium acetate, cadmium chloride, or cadmium sulfate, are well soluble, while cadmium oxide and cadmium sulfide are almost insoluble. In nature, cadmium does not exist in a free form and creates many compounds in which it is always in a 2^+ oxidative state. It has six natural, stable isotopes, including ^{106}Cd, ^{108}Cd, ^{110}Cd, ^{111}Cd, ^{112}Cd, and ^{114}Cd, as well as two radioactive isotopes: ^{113}Cd (double beta decay, half-life period of 7.7×10^{15} years) and ^{116}Cd (two-neutrino double beta decay, half-life period of 3.0×10^{19} years). There are also a few isotopes than do not occur naturally in the environment. The most common natural isotopes of Cd are ^{110}Cd, ^{111}Cd, ^{112}Cd, and ^{114}Cd and constitute 12%, 13%, 24%, and 29% of natural cadmium, respectively (Peterson 2001).

Cadmium is a natural compound of the Earth's crust and is about 0.00005% of its total weight. In general, it is combined with zinc and lead ores. This element is strongly dispersed in the Earth's crust, and its average concentration in the lithosphere ranges between 0.15 and 0.20 mg kg^{-1}. This element is located mostly in alkaline igneous rocks, less frequently in acidic (>0.2 mg kg^{-1}) and sedimentary rocks (>0.3 mg kg^{-1}). Higher concentrations of Cd are observed in phosphate sediments, which may contain even up to 15 mg kg^{-1}. Still, in the phosphorites of oceanic islands, levels of Cd may reach even 100 mg kg^{-1} (Adriano 2001).

3 Cadmium Minerals, Production, and Uses

The geochemical properties of cadmium are similar to zinc (Zn), but it is more mobile and susceptible to bind with sulfur (S). Cadmium rarely builds its own minerals, e.g., greenockite (CdS), cadmoselite (CdSe), and octavite ($CdCO_3$). Usually Cd occurs as an addition to sulfides of zinc, mercury, lead, and copper, most often in sphalerite (ZnS) in which its content may reach 0.1–5% and 0.3% on average. It also composes wurtzite (ZnS) and galena (PbS). Despite the fact that in none of these Cd-containing minerals does this metal occur in a concentration sufficient to extract it as an ore, the main source of Cd is zinc ores (Butterman and Plachy 2002; De Vos et al. 2006). World resources of Cd have been estimated at about 6 million metric tonnes (based on zinc resources), and world reserves of Cd were estimated at 500,000 tonnes (USGS 2014).

Cadmium is mobilized in the processes of aeration and is bound by loam materials, iron hydroxides, and organic matter, which may explain its susceptibility to accumulate in biolites (Kabata-Pendias and Pendias 1999). The typical levels of Cd in selected biolites are shown in Table 14.1. Mostly the content of Cd in hard coal is higher than in brown coal.

Cadmium, like other elements, may come from natural or anthropogenic sources. Parental rock is the most significant natural source, and more specifically the products of its aeration or weathering, for example, by flowing water. The concentration of cadmium in soils is very varied and usually reaches 0.01–2 mg kg^{-1} dw and most often depends on the content of this element in the paternal rock and the granulometric composition of the soil. The highest concentrations of Cd (even up to 11 mg kg^{-1}) are found in soils from very small or small crumb rock, while the lowest are from igneous rock. Soils from metamorphic rock usually contain about 0.1–1 mg kg^{-1} Cd. In general, heavy soils are characterized by even several times the concentration of cadmium than light soils (Alloway 1995).

Soils in uncontaminated regions contain less than 1 mg Cd kg^{-1}, while in polluted areas the level of Cd ranges between ten to hundreds of mg kg^{-1} (Table 14.2).

Table 14.1 The content of cadmium (mg kg^{-1}) in selected biolites

Fossil fuel	Country	Mean	Range	References
Hard coal	Bulgaria	8.60	ND	Kortenski and Sotirov (2002)
	Poland	0.20	<0.20–7.70	Bojakowska (2009)
	Spain	0.30	ND	Querol et al. (1996)
	USA	0.47	0.07–0.14	Finkelman (1993)
Brown coal	Bulgaria	3.30	ND	Kortenski and Sotirov (2002)
	Poland	2.00	<0.2–2.00	Bojakowska (2009)
	USA	ND	0.04–0.07	Stricker et al. (2007)
Peat	Poland	0.20	<0.20–1.80	Bojakowska (2009)
	Russia	0.56	0.20–1.33	Stepanova et al. (2015)

ND no data, *DL* detection limit

Table 14.2 The concentration of cadmium in various soils

Country	Concentration (mg kg^{-1} dry wt)	Remarks	References
		Background level	
North Europe	0.13		Reimann et al. (2012)
South Europe	0.22		Reimann et al. (2012)
USA	0.36		Bradford et al. (1996)
China	0.119		Chen et al. (2004)
		Industrial area	
France	44.6 (15.3–8.6)	Area directly adjacent to a Pb and Zn smelter	Tête et al. (2015)
Italy	1.0–4.16	Home garden on areas near ferroalloy activity	Ferri et al. (2015)
Poland	34.1 (5.24–51.91)	Area directly adjacent to mine and metallurgical plant	Baran et al. (2015)
Slovenia	73.4 (53.6–86.0)	Area surrounding the former lead smelter	Al Sayegh Petkovšek et al. (2014)
Spain	5.0–218	Near a mineral dressing plant	Álvarez-Ayuso et al. (2013)
		Agricultural area	
Croatia	0.66		Romic and Romic (2003)
Serbia	1.4		Dragović et al. (2008)
Spain	0.34 (0.10–0.88)		Micó et al. (2006)
USA	0.27		Holmgren et al. (1993)
China	0.27 (0.01–152.95)		Zhang et al. (2015)
		Urban area	
Norway	0.17		Reimann and de Caritat (1998)
Spain	0.32		Tume et al. (2011)
USA	0.87		McBride et al. (2014)

The main anthropogenic sources include metal mining and smelting, metallurgic and electronic industries, use of fossil fuels, fertilizing with mineral, and sewage sludge especially including phosphates, as well as municipal and industrial waste. To a certain extent, it also includes warfare and military training. Cadmium penetrates soils in rainwater containing dusts emitted by power plants, local heating plants, road transport, and industrial factories, as well as through direct introduction via fertilizers and pesticides in the past. The physical erosion and chemical decay of mining wastes produced by the exploitation of Zn ores may be a severe threat for ecosystems endangered by the mobilization and emission of toxic elements, including Cd. As noted by Álvarez-Ayuso et al. (2013) in soils of a mining area, the total level of Cd in the soil profile ranged from 5 to 218 mg kg^{-1}, while nearby the mining

wastes in the superficial layer of the soil, the concentration of cadmium was 0.10–11.0 mg kg^{-1}. In most of the studied locations, the amount of Cd was higher than dangerous levels in the biosphere, exceeding 3–8 mg kg^{-1} (Kabata-Pendias and Pendias 1999).

In Europe, the most frequent range of mean Cd levels in superficial soil layers is between 0.1 and 1 mg kg^{-1}. Levels below 0.1 mg Cd kg^{-1} had been found in Denmark, Finland, Norway, Sweden, and Portugal, with the highest concentrations found in Switzerland, Greece, Slovenia, and Ireland (Pan et al. 2010). In rural soils it was noted that the background Cd level was <1 mg kg^{-1} and the mean concentration was usually between 0.2 and 0.8 mg kg^{-1} (Adriano 2001). Similar levels of Cd (0.1–0.3 mg kg^{-1}) were detected in uncontaminated rural and agricultural areas of NE USA (Holmgren et al. 1993; US EPA 2005). In this matter the situation in some industrialized regions of China seems to be much worse, as the Cd concentration in some areas of agricultural soils exceeded 3 mg kg^{-1}, even though the mean concentration of Cd in rural areas of China is the same as in the USA at 0.27 mg kg^{-1} (Zhang et al. 2015).

Phosphate-based fertilizers may contain Cd as a contaminant at levels varying from trace amounts to as much as 300 mg Cd kg^{-1} of dry product and therefore can be considered the main source of cadmium contamination in rural regions (Grant and Sheppard 2008; Six and Smolders 2014). It is estimated that 0.3–10 g Cd ha^{-1} $year^{-1}$ on average is introduced in this manner (Kabata-Pendias and Szteke 2012). An important source of Cd in the soil is sewage sludge used as organic fertilizer. The estimated Cd content in sewage sludges in the UE-27 is 1.8 mg kg^{-1}. In the USA, the Cd concentrations ranged from 0.21 to 11.8 mg kg^{-1} (ECB 2005; EPA 2009; Six and Smolders 2014).

Atmospheric transport is probably the most significant vector of Cd distribution in the environment. Once released into the atmosphere, it is diffused, transported by winds, and finally deposited onto the ground and water bodies. This deposition may occur locally (close to the source), regionally, or in distant places from the sources of emission. In some cases, Cd may be transported with air masses for hundreds or thousands of kilometers. The level of atmospheric dispersion and the distance of embedding of this element depend on many factors, including the size of the molecules, height of the emitter (chimney), and meteorological conditions (UNEP 2006). Cadmium present in the atmosphere is adsorbed on the surface of dust particles of different diameter, from <0.1 to 1 μm (Molnár et al. 1995).

The removal of Cd and other dangerous substances on dust particulates happens through wet and dry deposition. Atmospheric deposition of Cd provides increased content in soil in areas located close to the sources of emission, such as power and incineration plants, traffic emitting Cd from combusted fuels, and mechanic attrition of the road surface and building components, but mostly by tire erosion (Fergusson and Kim 1991). For this reason an increased concentration of not only Cd but also other heavy metals is observed next to the roadways. The concentration of Cd in road dust may equal a few to even 11 mg kg^{-1} (Faiz et al. 2009).

The concentration of Cd in the air is strongly diversified. As noted by Reimann and de Caritat (1998), in areas at a distance from the emission sources, the level of Cd

ranges from 0.002 to 2.2 ng m^{-3}, but in industrialized regions it ranges from 0.5 to even 620 ng m^{-3}. Such a great diversity in Cd in the air is mostly the result of the type of activity undertaken in a particular area, the type of installations (including de-dusting modules) and the distance between the point of measure and the source of emission. In urbanized areas, the background levels of Cd ranged from 0.2 to 3 ng m^{-3} (WHO 2007).

In Europe, depending on the region, the concentration of Cd in ambient air is from 0.05 to 0.60 ng m^{-3}, reaching the lowest levels in the northern parts (Ilyin et al. 2015). In North America, the concentrations of Cd in ambient air are 1 ng m^{-3} in nonindustrialized areas and 40 ng m^{-3} in urban areas, whereas in Asia the concentration of Cd in ambient air is below the detection range in rural regions up to 12.9 ng m^{-3} in urbanized areas (ATSDR 2012; Shridhar et al. 2010; Islam et al. 2015).

Atmospheric deposition plays an important role in urbanized areas, mostly due to the high concentration of low-height emission sources, car transport and industry. The atmospheric deposition flux of Cd in different regions of the world is strongly diversified, and it is estimated that the dry and wet atmospheric depositions to the soil are <1 and <10 g ha^{-1} $year^{-1}$, respectively (Kabata-Pendias 2001).

Acid rains and soil acidification cause an increase in the geochemical mobility of Cd, which in turn results in an increased concentration of this element in surface and groundwater (Campbell 2006). The range of average concentrations of Cd in the seas and oceans is 0.07–0.11 μg L^{-1} (Kabata-Pendias and Szteke 2012), but some sweetened water bodies with poor connection to oceans, for example, the Baltic Sea, have a concentration reaching 2 μg L^{-1} (Szefer 2002). Much higher concentrations of this element are noted in watercourses, especially in river estuaries (Table 14.3).

The inflow of Cd into rivers includes direct municipal and industrial wastewater discharges, runoff from agricultural areas (anthropogenic sources), and Cd from atmospheric precipitation (natural and anthropogenic sources). Probably about 900 and 3600 tonnes of Cd are deposited into aquatic environments throughout the world through atmospheric deposition of emissions originating from anthropogenic and natural sources. From weathering and erosion, large quantities of Cd (about 15,000 tones) are transported by rivers into the world's oceans (UNEP 2010). Total waterborne Cd input into the Greater North Sea from eight European

Table 14.3 Cadmium concentrations in river water

Country	Range (mean) μg L^{-1}	References
Norway	<0.05–0.09	Reimann et al. (2009)
Belgium	(0.07)	Crévecoeur et al. (2011)
France	(0.03)	Idlafkih et al. (1995)
Hungary	<0.10–0.60 (0.4)	Bird et al. (2003)
Italy	0.001–0.091 (0.03)	Protano et al. (2014)
Latvia	(0.02)	Klavinš et al. (2000)
Poland	0.002–1.090	Helios-Rybicka et al. (2005)
Romania	0.30–3.00 (1.20)	ICPDR (2002)
USA	1.00–75.0	Angelo et al. (2007)

countries, the UK, Sweden, Norway, the Netherlands, Germany, France, Denmark, and Belgium, was evaluated at 23 tonnes year^{-1}, with main source of this element from agricultural activity (UNEP 2010).

In water ecosystems, ionic Cd is relatively quickly assimilated by hydrobionts. However the bioavailability may be reduced by the amount of suspended particulate matter (SPM), which is considered as the most important carrier of Cd and other trace metals, and is responsible for the introduction of elements into coastal systems and for the incorporation into sediments. Bottom sediments that are formed as a result of the sedimentation of solid particles become both the reservoir and the source of many pollutants.

4 Cadmium Production and Uses

Cadmium is produced as a by-product of processing zinc-bearing ores (80% of production) and refining of lead and copper from sulfide ores (Morrow 2001). This element is collected in the pyrometallurgical recovery and during the recycling of batteries. Recycled Cd is about 18% of the total amount of world Cd supplies (UNEP 2010).

Until the 1980s, the production of Cd in the world was systematically growing, and in 1988 it exceeded 20,000 tonnes year^{-1} and currently is oscillating around this level (Fig. 14.1). Today, China is the world leader in this area and provides about 1/3 of global Cd production. It is estimated that more than 60% of refined Cd production

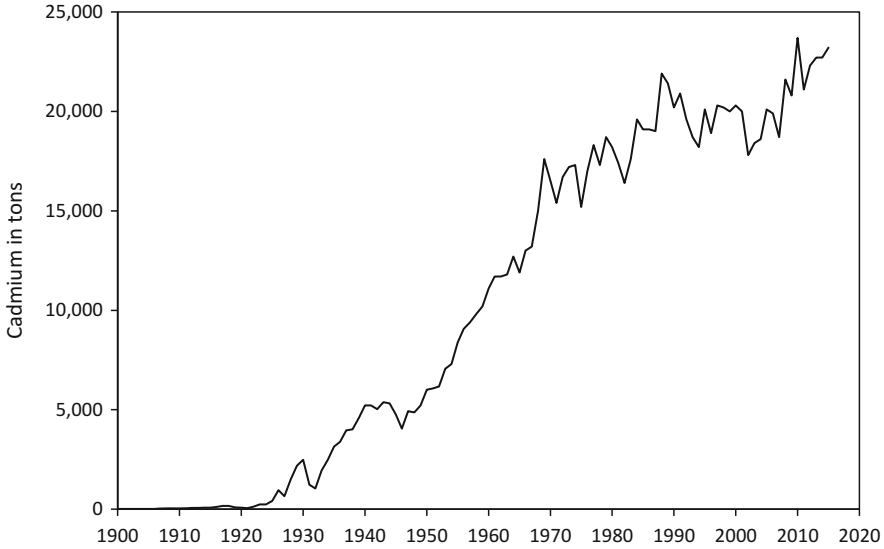

Fig. 14.1 World production of cadmium (USGS 2014)

is located in Asia and just over a dozen percent in North America (MCS 201CHAPTER 144). Cadmium is used for many purposes, including metal and alloy plating processes due to its anticorrosive properties. Cadmium can also absorb neutrons, so for this reason is used in nuclear reactors (AMAP 2005; UNEP 2006).

Cadmium is used in the production of nickel-cadmium batteries (Ni-Cd), chain reaction controlling rods, and filters to absorb thermal neutrons and pigments (e.g., cadmium yellow) for plastics. The usage of Ni-Cd batteries in consumer electronics has shown a decreasing trend in recent years as a consequence of legal regulations that limit the use of traditional batteries in preference to lithium-ion batteries (Li-Ion) which dominate in laptops, mobile phones, and other small electronic devices due to their better properties. However, the demand for Cd may increase because of a few new possibilities in the use of nickel-cadmium batteries, especially in industry, for storing the energy obtained by some photovoltaic systems (Tolcin 2011).

4.1 *Cadmium in Nature: Geogenic and Anthropogenic Sources*

Cadmium is emitted into the environment from natural and anthropogenic sources, which mostly have points of distribution. Volcanoes, airborne soil particles, fires, and biogenic release are the main natural sources of Cd emission. The anthropogenic sources include industrial processes, e.g., nonferrous metal production (mining and smelting), stationary fossil fuel combustion, waste incineration, iron and steel production, cement production, and wear of the tread on motor vehicle tires (Fig. 14.2).

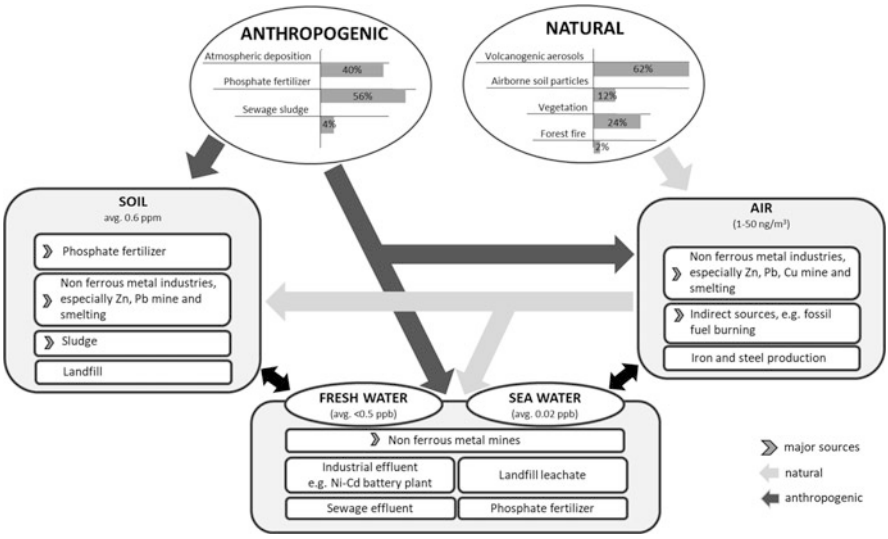

Fig. 14.2 Natural and anthropogenic sources of cadmium emission

As noted by Henley and Berger (2013), "trace elements in a complex particle—gas mixtures in atmospheric plumes above active volcanoes are enriched by up to several hundred times relative to their parent magmas." The studies on volcanic materials (lava and gases) performed during the Tolbachik (Kamchatka) eruption in February, April, and May 2013 showed that the concentration of Cd in lava reached about 0.056 ppm, while in emitted gases, it reached 0.60 ppm (Zelenski et al. 2014). Moreover, volcanic gases and dust contributed to significant physicochemical changes in rainwater following eruptions, in the neighborhood of the volcanoes and nearby water reservoirs—they, for example, induced a decrease in the pH and an increase in the level of heavy metals, including Cd (Eriksson et al. 2003).

Forest and peat bog fires are another relevant natural source of Cd and other elements. During such incidents, large amounts of dust transport different organic and inorganic substances, including the toxic metals, into the atmosphere. It was shown that the percentage of metals in the total mass concentration of PM 2.5, emitted during the fire, may range from 1% to 30%, which is subjected mostly to the amount of carbonaceous matter in the dust (See et al. 2007). This fraction of dust coming from the natural fires may contain even about 40 ng Cd m^{-3}. It is estimated that the concentration of Cd in such dust may increase by 2–16 times compared to the background (Betha et al. 2013).

It is also estimated that anthropogenic emissions of Cd are a factor of two to three times higher than natural emissions (Pacyna and Pacyna 2001). In 28 EU countries, as reported by the European Environmental Agency (EEA 2015), the 1990–2013 emission of Cd into atmosphere decreased by 75% (from 253 to 63 tonnes $year^{-1}$). Today, China plays the biggest role in global Cd emission from anthropogenic sources. During 1990–2010 the total Cd emission in China increased by about 360% (from 474 tonnes to 2186 tonnes) due to rapid economic growth (Fig. 14.3).

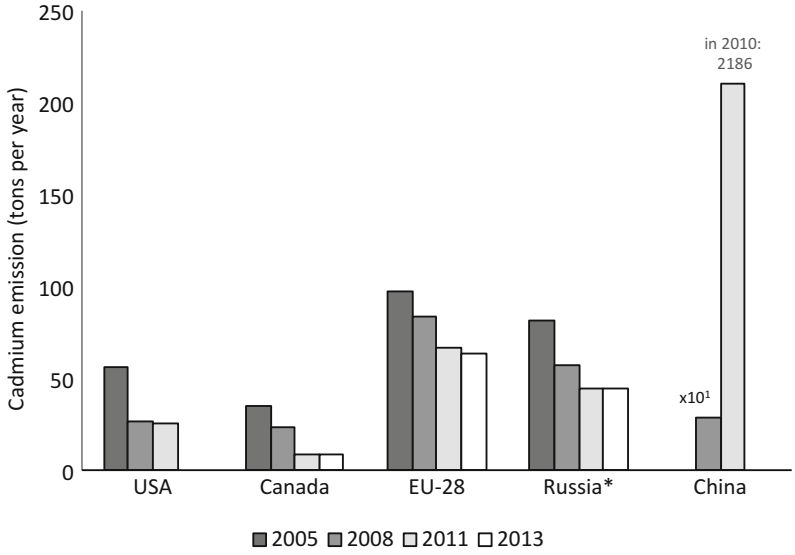

Fig. 14.3 Total cadmium emission from anthropogenic sources in different countries (asterisk including Asian and European parts of Russia) (Shao et al. 2013; CEIP 2015)

The total atmospheric emission of Cd evaluated for China in 2010 was about 77% and 14% from nonferrous metal smelting and coal combustion, respectively (Shao et al. 2013). Similarly in Canada, the production of nonferrous metals is the main source of atmospheric Cd emission while in the USA fossil fuel combustion (UNEP 2010).

5 Biological Status of Cadmium

Bioavailable Cd located in the soil, absorbed by plants and soil invertebrates, continues to appear in the food chain (Fig. 14.4). The invertebrates collect Cd directly from the soil or plants by ingestion, while some are also able to absorb it over the entire surface of the body. Heikens et al. (2001) noted that in most invertebrate taxonomic groups, the concentrations of Cd in the body increased with increasing soil concentrations and could be organized in the order: Lumbricidae > Arachnida > Diplura > Diplopoda > Collembola > Coleoptera. The taxonomic groups for which Cd accumulation is independent of the total soil concentration follow the order: Isopoda > Formicidae > Chilopoda. The authors also observed that internal Cd concentrations were high in Isopoda and low in Coleoptera and Chilopoda. The observed differences in Cd bioaccumulation between the invertebrate species result from differences in morphology, physiology (e.g., regulation capabilities), behavior, habitat, and food preferences. In general, invertebrates that have direct contact with the soil as well as those that consume organic matter rich in Cd accumulate more of this element.

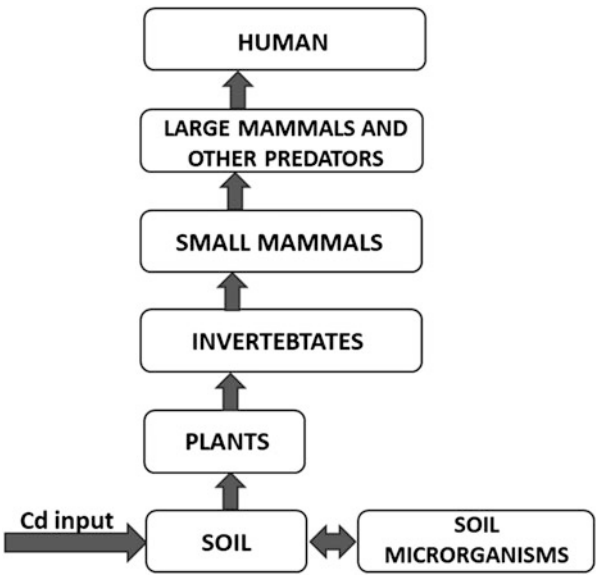

Fig. 14.4 Translocation of cadmium in the food chain

The amount of Cd accumulated in invertebrates depends also on the effectiveness of detoxification mechanisms. Such detoxification may proceed with the excretion of Cd and/or via storage of Cd in the form of neutral compounds (e.g., metallothionein complexes) and/or by storage in special structures that prevent the transport of Cd to crucial places where it may cause disturbances in biochemical processes (Lindqvist et al. 1995). Earthworms and other invertebrates that are an important link in the food chain accumulate considerable amounts of Cd and mediate its transfer to carnivores, mammals, and birds (Roodbergen et al. 2008; Schipper et al. 2012).

5.1 Toxicity of Cadmium

Cadmium and its compounds move to the homeothermic organisms of vertebrates via inhalation and ingestion. Via the respiratory system, about 5–50% of inhaled Cd is absorbed, of which 10% (as CdO) accumulates in the lungs, with the remainder entering the bloodstream. Via the digestive system about 1%–10% of Cd is absorbed (ATSDR 2012). Cadmium, an element without any proven biological role, does not have any transporters to facilitate its absorption and distribution in the organism. By using the phenomenon of "ionic mimicry," the absorbed Cd connects with transporters specific for other divalent ions such as Fe^{2+}, Zn^{2+}, and Ca^{2+}. Moreover, Cd can pass through the membranes of erythrocytes with thiol group complexes, including L-cysteine and glutathione, GSH (Bridges and Zalups 2005).

In the distribution of Cd, an important role is played by albumin and metallothionein (MT). Four types of MT are defined, by which MT-1 and MT2 are induced by Cd and other metal ions or stress. In turn, MT-3 and MT-4 are not inducible by Cd (see review by Nordberg 2009). Cadmium complexes with serum proteins are transported to the liver, where the Cd induces the synthesis of new molecules of MT. In hepatocytes, the bigger share of MT binds Cd, and some is released into the bloodstream where it complexes with Cd (CdMT) and in this form moves to the kidneys. CdMT is easily filtered in the renal glomeruli and reabsorbed in the proximal channels. After degradation of CdMT, the Cd^{2+} ions are released and start to act toxically to this organ, leading to disorders (Klassen et al. 1999).

In the case of respiratory exposure, the target organs for Cd are the kidneys and the lungs, while for digestive exposure—the kidneys and the bones (ATSDR 2012). However, it has been shown that the form of this element and its dose also play a role in the transport and deposition of Cd. For instance, Groten et al. (1994) have found that in the oral administration of Cd as $CdCl_2$ and CdMT to rats at a dose of 30 and 90 mg kg^{-1} body weight (mg kg^{-1} bw), higher concentrations of $CdCl_2$ were noted in the liver, while in the kidneys, CdMT accumulated to a higher extent. At smaller doses (0.3 and 3 mg kg^{-1} bw), no such differences were observed.

Cadmium is an element identified with carcinogenic and teratogenic activity. It is found to be a modulator of endocrinal activity, negatively affecting the reproductive process. Also, the cardiotoxicity, hepatotoxicity, and neurotoxicity of Cd have been

demonstrated (Limaye and Shaikh 1999; Kim et al. 2013; Xu et al. 2013; Wang et al. 2015). One of the most important aspects of cadmium toxicity is its ability to induce (indirectly) oxidative stress in cells (Stohs et al. 2001; Wang et al. 2015).

In 1993, the International Agency for Research on Cancer (IARC) defined Cd as a carcinogenic substance and qualified it to category I (IARC 1993). The carcinogenic activity of Cd is more related to the oxidative stress this element causes than to its mutagenic activity. Joseph (2009) defined four main mechanisms of Cd activity in the process of carcinogenesis: (1) induction of oxidative stress, (2) aberrant gene expression, (3) blocking DNA repair mechanisms, and (4) blocking apoptosis. The other features of Cd that affect the carcinogenic potential include the ability to cause the aberrant DNA methylation, cell proliferation, and endocrine disruptions. The mechanism of carcinogenic activity of Cd may also concern the disruption of intercellular communication causing changes in protein adhesion, which directly translates into the growth, differentiation, and migration of cells. Between the other tumors caused by the exposure to different Cd compounds, we can include adenocarcinomas of the lung, tumors of the pancreas and the testes, sarcomas, and mammary gland tumors in rats and mice (Garcia-Morales et al. 1994; Waalkes et al. 2000; Goyer et al. 2004; Murphy et al. 2012).

Experimental studies on animals have shown that Cd directly acts on bone cells to decrease bone formation and increase bone resorption. The exposure to even environmental levels of Cd causes a decrease in mineral bone density (demineralization, osteomalation, and osteoporosis) and extends the risk of bone fractures. This results from disturbances in calcium (Ca) metabolism, as well as other bioelements including copper (Cu). It has been demonstrated that oral administration of Cd to laboratory mammals causes a release of Ca from the bones and an increase in Ca in urinary excretion (Wilson and Bhattacharyya 1997). However, in other studies, no changes in the concentrations of circulating $1.25(OH)_2$ vitamin D, parathormone, nor calcitonin were found, although Cd causes hormonal disturbances (Sacco-Gibson et al. 1992). Bone mechanical strength depends not only on the level of bone mineralization but also on the organic matrix, constructed mostly from collagen. Iguchi and Sano (1982) showed that Cd disturbs the maturation of collagen via inhibiting the Cu-dependent enzyme—lysyl oxidase—that catalyzes the collagen cross-linking.

Cadmium was also defined as an endocrine activity modulator that shows estrogenic and antiandrogenic potential. By disturbing the functions of the hypothalamus-pituitary-gonad axis, Cd disrupts the work of the reproductive system and normal development (Lafuente et al. 2001).

On the basis of former studies, Cd has been defined as a gonadotoxin responsible for decreasing fertility in men and other mammals. Experiments by Haffor and Abou-Tarboush (2004) showed that Cd was a testicular toxicant in mice, causing damage in the endothelium and Sertoli cells. In studies on rats, impairments in spermato- and spermiogenesis were also observed (Hew et al. 1993) as well as a decrease in sperm motility to a total decay in the group with the biggest exposure (0.8 mg kg^{-1} bw) (Xu et al. 2001). In rat females under Cd treatment, a disrupted ovarian histoarchitecture, an extended estrous cycle, and delayed pubertal onset were noted (Samuel et al. 2011).

Studies of the embryotoxicity of Cd in Wistar rats (administration: 20 mg Cd kg^{-1} bw) have demonstrated the occurrence of external malformations and an increase in the number of different anomalies in fetuses with reduced metacarpus ossification, cleft palate, and right or left renal cavitation (Salvatori et al. 2004). Also Aprioku et al. (2014) found many abnormalities in Cd-exposed pregnant female Wistar rats and their offspring. The females had received 4 and 8 mg of Cd kg^{-1} day^{-1} (from conception to gestation), which resulted in a disturbance in the growth and developments of the fetuses, as an effect of improper functioning of the ovaries and placenta. Moreover the authors noted reductions in fetal body weights and limb bone lengths, inhibition of weight gain, and miscarriages. At 4 mg kg^{-1} day^{-1}, the number of fetuses in the uterus was significantly lower in comparison to the control group, and at 8 mg kg^{-1} day^{-1}, all pregnancies were aborted.

In birds, exposure to Cd causes similar morphological and physiological changes as in mammals. Li et al. (2010), studying testicular toxicity induced by dietary Cd (150 mg kg^{-1} diet/60 days) in cocks, noted a decrease in antioxidative enzyme activity (SOD and GSHPx) in the testicular tissue and a decrease in serum testosterone levels, with a simultaneous increase in the amount of lipid peroxidation and the number of apoptotic cells in the testes. Also, testicular damage was noted, such as edematous testes, severe necrosis, and degeneration of seminiferous tubules, as well as spermatogenesis inhibition. Dietary treatment with Cd resulted in reduced egg production and eggshell thickness in laying hens fed diets supplemented with 3, 12, and 48 mg kg^{-1} of Cd for 12 weeks (Leach et al. 1979).

5.2 *Toxicokinetics and the Effects of Cadmium in Wildlife*

Cadmium, in both metallic and saline forms, is poorly absorbed in mammals. It is estimated that via the respiratory, ingestive, and dermal paths, about 25%, 1–10%, and <1% of a dose are absorbed (ATSDR 2012). After absorption, Cd is widely distributed throughout the body and accumulates in many organs, including the liver, kidneys, pancreas, testes, and intestines with the highest concentration found in the liver and kidneys. Although the kidneys are pointed out as the main target for Cd, sometimes the liver shows higher concentrations of Cd. This depends on the form in which the cadmium occurs. Studies by Cherian (1983), aiming to assess the absorption and tissue distribution of Cd in mice (C57BL/6J) repeatedly fed with $^{109}CdCl_2$ or ^{109}Cd-MT (20 μg Cd once a week for 5 weeks), have shown differences in the distribution of this element in the organs. In the group of mice treated with $^{109}CdCl_2$, the location of Cd between the organs was as follows: liver (73.63%) > kidney (15.62%) > stomach (2.92%) > pancreas (2.52%) > small intestine (2.04%) > cecum (0.41%) > lung (0.41%) > heart (0.39%) > spleen (0.28%) > blood (0.23%) > testes (0.14%) > bone (0.10%). In the group treated with ^{109}Cd-MT, the ratios were kidney (69.8%) > liver (18.01%) > small intestine (4.24%) > cecum (1.76%) > stomach (1.07%) > pancreas (0.81%) > spleen (0.35%) > lung (0.28%) > heart, blood (0.24%) > testes (0.22%) > bone (0.11%). Moreover these studies revealed a

similar body retention of $^{109}CdCl_2$ and ^{109}Cd-Mt for just the first 3 weeks. In the following weeks, the mice treated with $^{109}CdCl_2$ continued to retain more Cd. In rats it was demonstrated that if fodder contained low levels of Cd (0.11 and 1.1 ppm), its concentration in the liver increased throughout all the experiment (until the eighth month), while in greater concentrations (5–40 ppm) it reached a plateau in the liver in the fourth month. However, in the kidneys, regardless of the dose, the level of Cd constantly increased until the end of the experiment (Hiratsuka et al. 1999).

Studies on birds by García-Fernandez et al. (1995) indicated that bird kidneys are the primary organ for Cd accumulation (61%), followed by the liver (31%), brain (4%), bones (3.5%), and blood (0.5%). Also the amount of absorbed Cd affects the distribution of Cd in the organs of the birds. It was shown that in lower doses, Cd accumulates mostly in the kidneys and, in higher doses, in the liver (Lehman and Klaassen 1986).

In homeothermic vertebrates, exposure to Cd runs in many ways, but the digestive tract has the biggest meaning for environmental exposure to this element. Once absorbed, Cd remains in the organism for a very long time. The biological half-life ($T_{1/2}$) of this metal is very diversified in particular tissues and organs. Based on the Nordberg-Kjellström model, $T_{1/2}$ of Cd was estimated in the human liver and kidneys at 4–19 years and 6–38 years, respectively. For the other tissues, this period has been assessed at 9–47 years (ATSDR 2012). In mouse organs, $T_{1/2}$ is 1.2 years for the liver, 11.8 years for the kidneys, ~1 year for the spleen, and 58 days for the gonads (Matsubara-Khan 1974). Such a long $T_{1/2}$ is caused by the fact that the absorbed Cd is excreted very slowly. It is removed from the organism mainly through the wall of the gastrointestinal tract and to some extent by the hepatobiliary system (Cikrt and Tichý 1974). When Cd enters the organism through ingestion, then the fecal and urinary excretions are approximately equal, and daily excretion is estimated to be 0.007% and 0.009% of body burden, respectively (Kjellström and Nordberg 1985). With respiratory exposure, Cd is excreted mostly with feces and to a lesser extent with urine (Rusch et al. 1986).

In birds, it is considered that they can eliminate Cd and other metals through excretion and depositing Cd in the feathers and eggshell. The most discussed is the role of the eggs in the deposition and elimination of Cd. Eggs, especially their shells, provide an effective method of excretion of Cd. Depending on the species of the bird, the eggshell may contain different amounts of Cd, for example, only 5% of the body burden in roseate terns (*Sterna dougallii*) and 29% for herring gulls (*Larus argentatus*) (Burger 1994). However, other studies suggest that the transfer of Cd to the eggshell is very low and the share in the excretion of Cd from the organism of female birds is low (Leach et al. 1979). Comparative studies by Burger and Gochfeld (1991) on the content of Cd in the feathers and eggs of the common tern (*Sterna hirundo*) have shown that the feathers may contain even more than 12 times more Cd than eggs (0.05 and 0.004 mg kg^{-1}, respectively). Due to the relatively low content of Cd in the feathers, the cited authors suppose that during the molting period, the share of feathers in Cd elimination is significant.

Environmental exposure to Cd produces a wide variety of chronic and less frequent acute effects in wildlife species, including mammals and birds, which are

often similar to those seen in humans. To estimate the ecological risk for terrestrial wildlife, a toxicity reference value (TRV) is used, which indicates the exposure dose/concentration above which ecologically significant effects may occur in wildlife species and below which it is expected that such effects will not occur. In the USA, in 2009, the Biological Technical Assistance Group (BTAG) updated the avian cadmium TRV-low (NOAEL, no-observed-adverse-effect level) from 0.08 to 0.07 mg kg^{-1} bw day^{-1}, based mainly on data concerning the renal effects of Cd in wood ducks *Aix sponsa* described in the work by Mayack et al. (1981) (DTSC 2009). On the other hand, the lowest-observed-adverse-effect level (LOAEL) was established at 1.0 mg kg^{-1} bw day^{-1} (based on kidney nephrosis in mallards *Anas platyrhynchos*, Cain et al. 1983). The TRV-high as a mid-range adverse effect level was established at 10.43 mg kg^{-1} bw day^{-1} based on reproductive and multiple systemic effects observed in Japanese quail *Coturnix japonica*, described by Richardson and Fox (1974). In reference to mammals, the low and high TRV for Cd were established at 0.06 and 2.64 mg kg^{-1} bw day^{-1}) (DTSC 2009). To establish these values, data on the influence of Cd exposure to the reproductive potential of mice were used, as cited in the papers by Webster (1988) and Schroeder and Mitchener (1971).

In ecotoxicological studies on homoeothermic mammals, Cd is primarily measured in the liver and kidneys and less often in muscles (mostly in game animals due to the potential risk of human intoxication). The other tissues are occasionally analyzed in this matter. Scheuhammer (1987) suggested that Cd levels below 3 mg kg^{-1} dw in the liver and 8 mg kg^{-1} dw in the kidneys of adult nonaquatic birds reflect the background levels and above those values indicate an increase in environmental exposure to the element. Adverse effects are expected when Cd concentrations in the liver and kidney of the birds exceed 40 and 100 mg kg^{-1} ww, respectively (Furness 1996). In the case of mammals, acceptable Cd concentrations in the whole kidney were established at <100 mg kg^{-1} ww (or <350 mg kg^{-1} dw) and in the kidney cortex at 150 mg kg^{-1} ww. Adverse effects on the kidney such as cellular damage are expected at 105 mg Cd kg^{-1} dw and above (Shore and Douben 1994).

5.3 Cadmium Bioaccumulation

The process of heavy metal accumulation is affected by factors dependent on both the organism (mostly physiological) and the environment. Cadmium is characterized by a high potential of accumulation due to the relatively high mobility and bioavailability for plant and soil invertebrates, mostly earthworms. Al Sayegh Petkovšek et al. (2015) showed that the bio-concentration factor (BCF) of cadmium in soil earthworms ranged from 1.8 to over 29, which indicates that earthworms could be an important source of Cd exposure for animals placed higher in the food chain, such as some mammals (rodents, insectivores, wild boar *Sus scrofa*, badger *Meles meles*) and birds. Despite data indicating an increased concentration of Cd in the tissues of

animals from the higher trophic levels (Lazarus et al. 2008; Durkalec et al. 2015), it has not been unambiguously proven if Cd undergoes biomagnification or not (Mann et al. 2011).

5.3.1 Cadmium Bioaccumulation in Small- and Medium-Sized Mammals

Small mammals (or micromammals, mainly insectivores like shrews, moles, and rodents), due to the small size of the body and high metabolic rate, are more exposed to the accumulation of environmental pollutants than large mammals. They assimilate Cd mostly through ingestion and to a smaller extent through inhalation or the skin. In the case of fetuses, Cd transfers to their organisms via the placenta and the maternal blood. Similarly, the assimilation of Cd by small mammals depends primarily on the pollution level—mostly of the soil and the type of diet, the way of feeding, trophic level, season, age, and sex. The average concentrations of Cd in this group of mammals, in the case of the liver and kidneys, range from <0.05 to 163.2 and <0.50–99.6 mg kg^{-1} dw (Table 14.4). Analysis of the type of diet and trophic level in relation to the level of Cd in micromammal tissues has shown that omnivorous mammals and carnivores accumulate more Cd in their tissues than herbivores. Hamers et al. (2006) have demonstrated that an estimated daily dietary intake of Cd in the predatory common shrew *Sorex araneus* was about three orders of magnitude higher than in the herbivorous bank vole *Myodes glareolus* (4.6–5.9 vs 0.006–0.007 mg Cd kg^{-1} bw day^{-1}, respectively). This reflects in the accumulation of Cd in the kidneys of these animals as the common shrew presented from 5 to even 10 times higher concentrations of Cd than the bank vole. As was presented in the studies by Smith and Rongstad (1982), omnivorous mammal like deer mice *Peromyscus maniculatus* contained more Cd than the herbivorous meadow vole *Microtus pennsylvanicus*. The common shrew, in a diet of which earthworms constituted a significant part, was characterized by a higher concentration of Cd than the bank vole (Veltman et al. 2007a).

Fritsch et al. (2010) in his studies on a multispecific group of small mammals (Rodentia, wood mouse *Apodemus sylvaticus*, bank vole *Myodes glareolus*, European pine vole *Microtus subterraneus*, field vole *Microtus agrestis*; Insectivora, common shrew *Sorex araneus*, pygmy shrew *Sorex minutus*, greater white-toothed shrew *Crocidura russula*) living at diverse distances from a former French smelter have concluded that Cd accumulation in both the liver and the kidneys followed in the animals in the descending order: common and pygmy shrew > wood mouse > voles. It also should be mentioned that in mammals from an area of low metal contamination, the median values of hepatic Cd concentration in insectivorous species ranged from 126 to 163 mg kg^{-1} dw (with a maximum level of 274 mg kg^{-1} dw), and in herbivorous rodents from the same area, medians were between 1.3 and 3.6 mg kg^{-1} dw (with maximum level of 23 mg kg^{-1} dw). The mentioned authors have demonstrated statistically significant differences in the concentration of Cd among rodent species and between rodents and shrews. An analogical regularity in

Table 14.4 Cadmium concentration (mg kg^{-1} dw) in tissues of small and medium size mammals

Species	Localization	Concentration	References
Liver			
Yellow-necked mouse *Apodemus flavicollis*	Slovenia		Al Sayegh Petkovšek et al. (2014)
	Control site	0.17 (0.03–0.36)	
	Former lead smelter	17.9 (0.89–57.1)	
	Thermal power plant	0.37 (0.03–1.80)	
	Slovakia	0.10 (0.03–0.20)	Kramárová et al. (2005)
Wood mouse *Apodemus sylvaticus*	Slovakia	0.23 (0.10–0.30)	Kramárová et al. (2005)
	France		Tête et al. (2015)
	Control site	1.4 (0.3–4.3)	
	Former Pb/Zn smelter	5.6 (1.4–18.6)	
	Portugal		Lourenço et al. (2013)
	Control site	0.30 ± 0.08 (±SD)	
	Uranium mining site	0.44 ± 0.15 (±SD)	
Bank vole *Myodes glareolus*	Slovenia		Al Sayegh Petkovšek et al. (2014)
	Lead smelter	162.7 (12.5–445.5)	
	Thermal power plant	0.56 (0.30–0.86)	
	The reference area	0.63 (0.10–1.82)	
	France		Fritsch et al. (2011)
	Smelter-impacted area	11 (0.13–16)	
	Poland		Włostowski et al. (2009)
	Spring	3.42	
	Autumn	1.98	
	UK, Wales		Milton et al. (2003)
	Reference area	0.10 ± 0.03 (±SE)	
	Former lead mine	0.30 ± 0.10 (±SE)	
Wild rat *Rattus rattus*	Portugal		Pereira et al. (2006)
	Sulfur mill (SM)	0.320 ± 0.140 (±SE)	
	~5 km from the SM	0.381 ± 0.025 (±SE)	
Greater white-toothed shrew *Crocidura russula*	France		Fritsch et al. (2011)
	Smelter-impacted area	72 (3–741)	

(continued)

Table 14.4 (continued)

Species	Localization	Concentration	References
Common shrew *Sorex araneus*	France		Fritsch et al. (2010)
	Low contaminated area near former smelter	163.2 (18.6–267)	
Brown hare *Lepus europaeus*	Croatia		Linšak et al. (2014)
	Reference area	2.52 (1.70–2.98)	
	Agricultural area	3.48 (1.48–8.10)	
	Serbia	0.43 (0.03–1.35)	Petrović et al. (2014)
Arctic hare *Lepus arcticus*	Canada		Pedersen and Lierhagen (2006)
	Adult	4.48 (1.68–10.90)	
	Juvenile	0.196 (0.02–0.44)	
	Portugal	0.23 (0.10–0.73)	Eira et al. (2005)
European polecat *Mustela putorius*	Italy	0.26	Alleva et al. (2006)
American mink *Neovison vison*	USA	0.33 (0.20–0.71) GM	Mayack (2012)
Stone marten *Martes foina*	Italy	3.17 (<DL–30.06)	Alleva et al. (2006)
Kidney			
Yellow-necked mouse *Apodemus flavicollis*	Slovakia	0.84 (0.28–1.68)	Kramárová et al. (2005)
Wood mouse *Apodemus sylvaticus*	Slovakia	2.08 (0.60–3.88)	Kramárová et al. (2005)
	France		Tête et al. (2015)
	Control site	5.1 (0.3–17.8)	
	Former Pb/Zn smelter	16.5 (4.3–40.1)	
	Netherland		van den Brink et al. (2010)
	Floodplain area	0.18 (0.06–1.81)	
	Sandy soil	9.85 (0.82–86.6)	
	Portugal		Lourenço et al. (2013)
	Control site	0.7 ± 0.27 (±SD)	
	Uranium mining site	1.35 ± 0.49 (±SD)	

(continued)

Table 14.4 (continued)

Species	Localization	Concentration	References
Bank vole *Myodes glareolus*	Poland		Włostowski et al. (2009)
	Spring	3.36	
	Autumn	1.88	
	UK, Wales		Milton et al. (2003)
	Reference area	0.3 ± 0.1 (±SE)	
	Former lead mine	1.9 ± 0.6 (±SE)	
	Netherlands	1.7	Hamers et al. (2002)
Wild rat *Rattus rattus*	Portugal		Pereira et al. (2006)
	Sulfur mill (SM)	1.28	
	~5 km from the SM	0.41	
Common shrew *Sorex araneus*	Netherlands	7.2	Hamers et al. (2002)
Common shrew *Sorex araneus*	France		Fritsch et al. (2010)
	Low contaminated area near former smelter	99.6 (4.2–325.7)	
Pygmy shrew *Sorex minutus*	France		Fritsch et al. (2010)
	Low contaminated area near former smelter	42.1 (22.6–626.5)	
Brown hare *Lepus europaeus*	Croatia		Linšak et al. (2014)
	Reference area	12.4 (11.8–20.2)	
	Agricultural area	66.4 (44.8–160.2)	
	Slovakia	5.18 (<DL–15.58)	Kramárová et al. (2005)
	Poland	15.9 (median)	Mysłek and Kalisińska (2006)
	Serbia	4.19 (0.20–17.69)	Petrović et al. (2014)
European rabbit *Oryctolagus cuniculus*	Portugal	3.37 (0.76–12.54)	Eira et al. (2005)
Arctic hare *Lepus arcticus*	Canada		Pedersen and Lierhagen (2006)
	Adult	106.6 (52.2–219.9)	
	Juvenile	1.73 (0.29–4.41)	
Pine marten *Martes martes*	Croatia	4.24 (1.14–19.32) GM	Bilandžić et al. (2012a)
Eurasian otters *Lutra lutra*	Korea	0.339	Kang et al. (2015)
Mink *Neovison vison*	Canada, Yukon	0.81	Gamberg et al. (2005)

(continued)

Table 14.4 (continued)

Species	Localization	Concentration	References
Muscle			
Bank vole *Myodes glareolus*	UK, Wales		Milton et al. (2003)
	Reference area	0.03 ± 0.01	
	Former lead mine	0.04 ± 0.01	
Wild rat *Rattus rattus*	Spain, Canary Archipelago	0.0032	Torres et al. (2011)
Brown hare *Lepus europaeus*	Slovakia	0.16	Kottferová and Koréneková (2000)
	Croatia		Linšak et al. (2014)
	Reference area	0.13 (0.07–0.19)	
	Agricultural area	0.15 (0.09–1.04)	
Arctic hare *Lepus arcticus*	Canada		Pedersen and Lierhagen (2006)
	Adult	0.082 (0.035–0.201)	
	Juvenile	0.005 (0.002–0.009)	
	Canada	0.20	Mallory et al. (2004)
	Baffin Island		
European rabbit *Oryctolagus cuniculus*	Portugal	0.16 (0.12–0.16)	Eira et al. (2005)

Mean and range in parentheses
GM geometric mean, *SD* standard deviation, *SE* standard error

the diversification of Cd level in the tissues of micromammals with a different diet (shrews > voles > wood mouse) was noted also by other researchers (Gall et al. 2015). The interspecific differences observed in the concentration of Cd in tissues may also have a physiological ground. Hunter et al. (1987) suggest that the field vole and wood mouse appeared to regulate metal accumulation, while common shrew showed considerable accumulation of Cd. The examples of concentration of Cd in the tissues of small and medium size are shown in Table 14.4.

In the case of insectivorous shrews, it was found that the concentration of Cd in the liver and in the whole organism is closely correlated to the content of Cd in the soil, while in the case of herbivorous voles, no such relation was noted (Veltman et al. 2007b). Van den Brink et al. (2011), in studies concerning not only soil properties on Cd accumulation in small mammals but also species traits and habitat, found that Cd accumulation patterns differed between habitats and were affected by species traits. The authors indicated that local soil properties were most important for predicting Cd accumulation in the specific feeding nonmobile species like the common vole. In the case of the mobile species (wood mice) with a variable diet, the most important factor was diet composition. And for intermediately mobile species (bank vole) with a variable diet, both diet and soil properties were of significance.

Studies on Cd bioaccumulation concerning both sex and age of the micro-Mammalia do not always confirm a connection between the concentration of this metal in tissues and diet and soil properties or even results opposite to each other. For instance, Sánchez-Chardi et al. (2007) concluded that in insectivorous shrews, the content of Cd was rising with age. Similarly, Hunter et al. (1989) noted that between three species of micromammals, wood mouse, field vole, and common shrew, only in the shrew did Cd accumulate significantly positively with age, which corresponds to the results of Hunter et al. (1989). However Fritsch et al. (2010) stated that Cd concentrations in the liver and kidneys increased with age in herbivorous (wood mouse, bank vole, field vole, European pine vole) and insectivorous (common shrew, pygmy shrew, greater white-toothed shrew) micromammals. Blagojević et al. (2012) noted that in the black-striped field mouse *Apodemus agrarius* from Lešnica, Serbia (unpolluted area), the highest accumulations of Cd were characteristic for the young individuals, and not the adults. These authors explain these findings twofold: (1) the higher Cd accumulation rate may be caused by the higher metabolic rate of the juveniles, which translates into a higher uptake of food and accordingly Cd, and (2) in adult individuals a decrease in intestinal absorption of Cd takes place. Due to the fact that the authors have not found any differences between Cd accumulation in young individuals from polluted and not polluted areas, they suggest that in neonates and juveniles, the bioaccumulation of Cd and other heavy metals is more likely related to the high rate of metabolism than the degree of pollution of the environment. In carnivores like the American mink *Neovision vision*, European otter *Lutra lutra*, and polecat *Mustela putorius*, Cd concentrations usually increased with age (Hyvärinen et al. 2003; Grove and Henny 2008; Mayack 2012). Also in herbivorous species of the Leporidae family, an analogical regularity was observed, where in brown hares *Lepus europaeus* aged 3–6 months, the concentration of Cd in the kidneys was 0.39 mg kg^{-1} ww and was about one order of magnitude lower than in individuals aged 24–36 months (2.37 mg kg^{-1} ww). In the case of the liver, the oldest brown hare individuals had about five times higher concentrations of Cd than the youngest (Petrović et al. 2014).

The relations between sex and Cd bioaccumulation in small mammals are rarely analyzed, and studies in this area usually do not confirm any differences between males and females (Hyvärinen et al. 2003; Lemarchand et al. 2010). If they are found, usually females have higher levels of Cd than males (Scheirs et al. 2006). Mayack (2012) explained these with gender differences in relative growth.

Another factor that may affect the accumulation of Cd in animal organisms is the seasonal rhythm of changes and the diversity in diet composition related to it. Hunter et al. (1987) observed differences in the level of Cd in the field vole, wood mouse, and common shrew, which were the effect of seasonal changes in the diet of each. These results correspond to an analysis by Włostowski et al. (2009), who found that the accumulation of Cd in the liver and kidneys was about 70% higher in the bank voles caught in March than in November.

Fernández et al. (2012) in studies on the variability in the transfer and bioaccumulation of heavy metals, including Cd, in trophic compartments of terrestrial ecosystems in Spain, observed a common accumulation pattern: secondary

consumers (shrews) > detritivores (slugs) > primary consumers (wood mouse) > productors (oaks), yet without biomagnification of Cd in the woodlands.

Among the semiaquatic carnivore species, some differences in the concentration of Cd were found that were due to different compositions in diet. As noted by Mayack (2012), Cd accumulation in American mink was greater than in the river otter *Lontra canadensis*. The typical terrestrial prey of the mink are small mammals, especially those dependent on detritus-based food chains that may contain increased Cd levels, synonymous with transferring a higher Cd load to the organism of the mink. In contrast to the mink, the river otter feeds mainly on fish. The author suggests that biomagnification of Cd in land trophic chains may affect the higher and more diversified concentrations of Cd in minks than otters.

The accumulation of Cd in particular organs of animals depends on their level of exposure. Hunter et al. (1989) have observed that in the common shrew, with low exposure, accumulation was located in the kidneys and liver, while with higher exposure (at ingestion rates of 25 mg kg^{-1} day^{-1}), Cd accumulated mostly in the liver. In studies on Cd in the brown hare, it was demonstrated that the main organs of accumulation in both the contaminated and reference areas were the kidneys. However, the ratio between Cd levels in the kidneys and the concentration in the liver (Cd_{kidney}:Cd_{liver}) of hares from the polluted area was a few times higher than in individuals from the reference area, at 15.7 and 4, respectively. Moreover, differences in the accumulation of Cd in the muscles and brain between the studied animals were found. In the polluted area, the concentration of Cd in the brain of the hare was higher than in the muscles, while in the reference area, more Cd was found in the muscles than in the brain (Linšak et al. 2014). High values of the ratio Cd_{kidney}:Cd_{liver} (from 9 to 30) in hares were also reported by Petrović et al. (2014), wherein they indicated that this ratio was highest in older individuals.

5.3.2 Bioaccumulation in Large Mammals

In Europe and North America, among the herbivorous ungulates, most data concerns the concentration of Cd in cervids like roe deer *Capreolus capreolus*, red deer *Cervus elaphus*, moose *Alces alces*, white-tailed deer *Odocoileus virginianus*, and reindeer *Rangifer tarandus* (reindeer in Europe, caribou in North America). Omnivorous and carnivorous animals are less intensively studied in this respect. In the liver and kidneys of large herbivorous mammals (cervids) from different regions of the world, mean concentrations of Cd ranged from 0.19 to 32 and from 3 to 172 mg kg^{-1}, respectively, and in Leporidae from 0.2 to 4.5 and from 1.5 to 107 mg kg^{-1} dw (Tables 14.4 and 14.5), respectively.

In omnivores and carnivores, their hepatic and renal concentrations ranged from <DL to 20 and from <0.8 to almost 200 mg kg^{-1} dw, respectively (Tables 14.6 and 14.7). The degree of environmental contamination had a significant effect on Cd bioaccumulation in cervids from polluted areas that lived in close proximity to mines or ironworks—those animals had a few or even dozens of times higher concentrations of Cd in comparison to individuals of the same species from uncontaminated reference areas. For example, studies in Poland have demonstrated that mean

Table 14.5 Cadmium concentration (mean and range in parentheses; mg kg^{-1} dw) in tissues of large herbivores

Species	Localization	Concentration	References
Liver			
Red deer *Cervus elaphus*	Croatia	0.54	Lazarus et al. (2014)
	Poland	0.42	Wieczorek-Dąbrowska et al. (2013)
	Slovakia	0.93 (0.25–3.11)	Kramárová et al. (2005)
	Spain		Rodríguez-Estival et al. (2011)
	Reference area	0.197 (0.066–0.616)	
	Mines	0.275 (0.099–1.162)	
Reindeer *Rangifer tarandus*	Norway	2.33 (0.621–7.804)	Hassan et al. (2012)
Caribou *Rangifer tarandus*	Canada, Québec		Robillard et al. (2002)
		3.57 immature	
		3.78 adult	
Moose *Alces alces*	Canada, Yukon	17.49	Gamberg et al. (2005)
	Canada, Nova Scotia	5.8 (<0.05–51.9)	Pollock (2005)
	USA, Alaska	3.64 (0.21–32.13)	Arnold et al. (2006)
	Sweden	5.93 (0.86–21.96)	Frank et al. (2000)
Roe deer *Capreolus capreolus*	Croatia	1.824	Lazarus et al. (2014)
	Poland		Durkalec et al. (2015)
	Polluted area	22.97 (3.35–73.58)	
	Control area	0.41 (0.05–1.83)	
	Czech	0.79	Čelechovská et al. (2008)
	Slovakia	0.96	Kottferová and Koréneková (2000)
Fallow deer *Dama dama*	Croatia	0.45	Lazarus et al. (2014)
	Czech	0.25	Čelechovská et al. (2008)
White-tailed deer *Odocoileus virginianus*	Canada, Nova Scotia	1.1 (0.05–28.1)	Pollock (2005)
European bison *Bison bonasus*	Poland	1.61 (1.11–2.07)	Włostowski et al. (2006)
	Poland	2.96	Kośla et al. (2008)
Kidney			
Red deer *Cervus elaphus*	Croatia	Whole kidney, 9.44	Lazarus et al. (2008)
		Cortex, 21.57	

(continued)

Table 14.5 (continued)

Species	Localization	Concentration	References
	Slovakia	10.40 (1.40–25.06)	Kramárová et al. (2005)
Roe deer *Capreolus capreolus*	Poland		Durkalec et al. (2015)
	Polluted area	172 (0.05–390.98)	
	Control area	6.88 (1.01–39.26)	
	Czech	2.99	Čelechovská et al. (2008)
	Slovakia	8.09	Kottferová and Koréneková (2000)
Moose *Alces alces*	Canada, Yukon	122.24	Gamberg et al. (2005)
	Canada, Nova Scotia	60.4 (14.3–346.1)	Pollock (2005)
	Alaska	Cortex: 38.19	Arnold et al. (2006)
		(0.435–285.80)	
	Sweden	41.76 (3.74–107.88)	Frank et al. (2000)
Caribou *Rangifer tarandus*	Canada, Québec		Robillard et al. (2002)
		23.19 immature	
		30.80 adult	
	Canada	28.28 (6.53–191.4) GM	Pollock et al. (2009)
Fallow deer *Dama dama*	Czech	3.01	Čelechovská et al. (2008)
European bison *Bison bonasus*	Poland	Cortex: 12.14	Włostowski et al. (2006)
		(8.48–15.31)	
	Poland	6.28	Kośla et al. (2008)
Muscle			
Red deer *Cervus elaphus*	Spain		Taggart et al. (2011)
	Control area	0.119 (0.007–0.867)	
	Mined area	0.112 (0.007–1.211)	
Red deer	Croatia	0.21	Lazarus et al. (2014)
Reindeer *Rangifer tarandus*	Norway	0.007 (0.004–0.025)	Hassan et al. (2012)
Caribou *Rangifer tarandus*	Canada, Québec		Robillard et al. (2002)
		0.046 immature	
		0.046 adult	
Roe deer *Capreolus capreolus*	Croatia	0.039	Lazarus et al. (2014)
	Poland		Durkalec et al. (2015)
	Polluted area	0.15 (0.011–0.539)	
	Control area	0.025 (<DL–0.142)	
	Czech	0.028	Čelechovská et al. (2008)
	Slovakia	0.143	Kottferová and Koréneková (2000)

(continued)

Table 14.5 (continued)

Species	Localization	Concentration	References
Fallow deer *Dama dama*	Croatia	0.086	Lazarus et al. (2014)
	Czech	0.021	Čelechovská et al. (2008)
Moose *Alces alces*	Canada, Yukon	0.107	Gamberg et al. (2005)

GM geometric mean, *DL* detection limit

Table 14.6 Cadmium concentration (mean and range in parentheses; mg kg^{-1} dw) in different tissues of carnivorous mammals

Species	Localization	Concentration	References
Liver			
Red fox *Vulpes vulpes*	Switzerland	1.72	Dip et al. (2001)
	Italy	0.33 (<DL–2.54)	Alleva et al. (2006)
	Spain	0.113 (<DL–1.425) GM	Millán et al. (2008)
	Slovakia	0.69 (0.40–1.25)	Piskorová et al. (2003)
Iberian wolf *Canis lupus signatus*	Spain	0.53 (<DL–1.55)	Hernández-Moreno et al. (2013)
Gray wolf *Canis lupus*	Croatia	0.055 Med	Vihnanek Lazarus et al. (2013)
	Russia	<DL	Shore et al. (2001)
	Canada	1.42	Gamberg and Braune (1999)
Iberian lynx *Lynx pardinus*	Spain	0.09 (0.037–0.254) GM	Millán et al. (2008)
Eurasian lynx *Lynx lynx*	Croatia	1.07 (0.828–1.393) GM	Bilandžić et al. (2012a)
Kidneys			
Red fox *Vulpes vulpes*	Switzerland	5.37	Dip et al. (2001)
	Slovakia	0.925 (0.74–1.776)	Piskorová et al. (2003)
Iberian wolf *Canis lupus signatus*	Spain	2.69 (0.079–5.14)	Hernández-Moreno et al. (2013)
Gray wolf *Canis lupus*	Canada	5.93	Gamberg and Braune (1999)
	Croatia	0.925 (0.033–4.477) GM	Bilandžić et al. (2012a)
Muscle			
Gray wolf *Canis lupus*	Croatia	0.037 (0.011–0.525) GM	Bilandžić et al. (2012a)
Red fox *Vulpes vulpes*	Spain	0.007 (<DL–0.047) GM	Millán et al. (2008)
	Slovakia	0.111 (0.074–0.259)	Piskorová et al. (2003)
Iberian lynx *Lynx pardinus*	Spain	0.004 (<DL–0.009) GM	Millán et al. (2008)
Eurasian lynx *Lynx lynx*	Croatia	0.011 (0.007–0.015) GM	Bilandžić et al. (2012a)

DL detection limit, *GM* geometric mean, *Med* median

Table 14.7 Cadmium concentration (mean and range in parentheses; mg kg^{-1} dw) in tissues of omnivorous mammals

Species	Localization	Concentration	References
Liver			
Wild boar *Sus scrofa*	Croatia	1.40	Lazarus et al. (2014)
		1.17	Bilandžić et al. (2012b)
	Poland		Durkalec et al. (2015)
	Polluted area	19.90 (2.74–141.37)	
	Control area	0.67 (0.104–3.37)	
	Spain		Taggart et al. (2011)
	Control area	0.119 (0.007–0.867)	
	Mined area	0.112 (0.007–1.211)	
	Italy	0.303 (0.029–1.360)	Amici et al. (2012)
	Slovakia	1.00 (0.43–3.36)	Piskorová et al. (2003)
European badger *Meles meles*	Croatia	1.92 (1.107–3.713) GM	Bilandžić et al. (2012a)
	Italy	2.39 (<DL–17.32)	Alleva et al. (2006)
	Czech	3.89	Bukovjan et al. (2014)
	Spain	0.017 GM	Millán et al. (2008)
Brown bear *Ursus arctos*	Croatia	1.239 (1.035–1.499) GM	Bilandžić et al. (2012a)
	Croatia	3.891	Lazarus et al. (2014)
	Slovakia	2.959 (0.893–4.427)	Čelechovská et al. (2006)
Muscle			
Wild boar *Sus scrofa*	Croatia	0.208	Lazarus et al. (2014)
	Poland		Durkalec et al. (2015)
	Polluted area	0.16 (0.032–0.560)	
	Control area	0.016 (<0.001–0.088)	
	Spain		Taggart et al. (2011)
	Mined area	0.41 (<DL–1.566)	
	Control area	0.11 (<DL–0.456)	
	Italy	0.316 (0.124–1.524)	Amici et al. (2012)
	Slovakia	0.16 (0.08–0.68)	Piskorová et al. (2003)
Eurasian badger *Meles meles*	Spain	0.003 GM	Millán et al. (2008)
European badger *Meles meles*	Croatia	0.036 (0.024–0.08) GM	Bilandžić et al. (2012a)
	Czech	0.40	Bukovjan et al. (2014)
Brown bear *Ursus arctos*	Croatia	0.032	Lazarus et al. (2014)
	Croatia	0.016 (0.012–0.020) GM	Bilandžić et al. (2012a)
	Slovakia	0.068 (0.036–0.0.168)	Čelechovská et al. (2006)
Kidney			
Wild boar *Sus scrofa*	Italy	4.208 (0.064–12.32)	Amici et al. (2012)
	Slovakia	2.24 (0.56–109.28)	Piskorová et al. (2003)
Brown bear *Ursus arctos*	Slovakia	69.44 (33.60–4.588)	Čelechovská et al. (2006)
	Croatia	Cortex, 66.0	Lazarus et al. (2014)
European badger *Meles meles*	Croatia	11.285 (6.475–30.44) GM	Bilandžić et al. (2012a)
	Czech	8.24	Bukovjan et al. (2014)

DL detection limit, *GM* geometric mean

concentrations of Cd in the kidneys of roe deer from highly industrialized and from uncontaminated areas were 172 and less than 7 mg kg^{-1} dw, respectively. An analogous difference was found in the kidneys of the omnivorous wild boar *Sus scrofa* 198 vs ~8 mg kg^{-1} dw (Durkalec et al. 2015). In large carnivorous mammals like the wolf *Canis lupus*, a high diversity in tissue bioaccumulation of Cd was observed, but still not as high as in ungulates. The highest concentration of this metal was found in the livers of wolves from Yukon, Canada (1.42 mg kg^{-1} dw), and the lowest in the European wolves from Spain and Croatia, respectively, 0.53 and 0.05 mg kg^{-1} dw (Gamberg and Braune 1999; Bilandžić et al. 2012a; Hernández-Moreno et al. 2013). At the same time, no Cd at all was found in the livers of wolves from Northwest Russia. Differences in the presented data regarding the high hepatic Cd concentration in the wolves from Yukon are probably brought about by the abundance of Cd in the geological base. Cadmium penetrates plants, including the *Salix* type, characterized by a high ability to accumulate Cd, and an important ingredient in the diets of caribou and moose, the main prey of wolves in that area (Elkin and Bethke 1995; Gamberg et al. 2005).

As in present studies, the interspecific diversification in Cd content in analogous tissues of animals located in the same area results from their food preferences to a high extent (Alleva et al. 2006; Bilandžić et al. 2012a; Mayack 2012; Durkalec et al. 2015). Among carnivores living near Pesaro (Italy), the highest Cd levels in the liver were found in the omnivorous badger *Meles meles* and stone marten *Martes foina*, at 9 and 6 times more than in the red fox *Vulpes vulpes* with a diet consisting mainly of small mammals (Alleva et al. 2006).

Many researchers have indicated that a higher position in a trophic chain is not necessarily related to the level of Cd in the organism. Metcheva et al. (2003) observed that the contamination observed in the examined mammalian species depended not only on the trophic chain position but also on the food composition and lifestyle. The highest concentrations of Cd were found in the tissues of large and small mammals with a diet rich in earthworms, as these accumulate the highest amounts of Cd and other metals (Scheifler et al. 2006; Roodbergen et al. 2008).

Due to the slow elimination of Cd from the organism and its long half-life, a higher concentration of this element is usually observed in older animals in comparison to young individuals. Dip et al. (2001) demonstrated that in the red fox from urban and suburban areas, the concentration of Cd in the kidneys was significantly higher in older animals than in younger ones (e.g., in adult and young animals from suburban areas, the median concentrations of Cd were 1.82 and 0.73 mg kg^{-1} ww, respectively). An age-dependent accumulation of Cd was also found in the liver of the fox. In turn, in wolves, this relation was observed only in the kidneys (Gamberg and Braune 1999). A positive relation between the concentration of Cd in the kidneys and the age of the animals was also found in wild ruminants (Arnold et al. 2006; Lazarus et al. 2008).

The bioaccumulation of Cd in large- and medium-sized mammals depends on many biological factors, such as the quality and amount of consumed food, size of the body, and age of the organism. Sometimes differences in Cd accumulation between males and females have been observed, which may have resulted from

the different metabolic rates of the gender, as well as the hormonal and physiological status of the body (Burger et al. 2007). Sex-related differences could also be associated with differential feeding habits and feeding areas between males and females. However, diversity in Cd accumulation between the sexes is rarely described and is usually, as in small mammals, not confirmed statistically, as presented in the moose, red fox, and Egyptian mongoose *Herpestes ichneumon* by Custer et al. (2004) and Millán et al. (2008), or a higher concentration is found in females, as was shown in the wolf by Gamberg and Braune (1999) and Hernández-Moreno et al. (2013).

In herbivores, an important role in Cd bioaccumulation is played by the season, which is related not only to the availability of particular species of plants in the foraging area but also to changes in Cd assimilation by plants and translocation, which both directly affect the Cd level in particular parts of the plant. As was reported by Brekken and Steinnes (2004), the annual fluctuations of Cd concentration in plants may range from 2% to 82%. In general, the highest Cd concentration in plants is noted in spring and then in autumn and the lowest in summer. The drop in Cd level in plants in summer was explained by the so-called dilution effect (Brekken and Steinnes, 2004).

From an ecotoxicological point of view, as well as human health, the evaluation of Cd bioaccumulation is particularly relevant in the consumable parts of game animals. In the European Union, the maximum acceptable concentrations of this metal in the muscles, liver, and kidneys are 0.05, 0.5, and 1.0 mg kg^{-1} ww, respectively (EC 1881/2006). As noted by Piskorová et al. (2003), wild boar from Slovakia exceeded the norms for Cd content in 13.3% of muscle samples, 20% of liver samples, and 26.6% of kidney samples in this omnivorous mammal. Such over maximal Cd levels were also found in typically herbivorous cervids (roe deer, red deer), European hares, and wild boar in Eastern Slovakia (Kottferová and Koréneková 2000). It is worth indicating that free-living ruminants assimilate more cadmium in their tissues than domesticated ruminants (Kramárová et al. 2005). Włostowski et al. (2006) have also observed that free-ranging European bison accumulate more Cd in the liver and kidneys than domestic animals. For example, mean concentrations of this element in the liver of European bison and cattle were 0.45 and 0.20 mg kg^{-1} ww, respectively.

5.4 Bioaccumulation in Birds

According to the trophic position, age, environment, and Cd content in the diet, very diverse concentrations of Cd have been observed in the tissues of wild birds (Table 14.8). From recently published data about hepatic and nephric Cd concentrations in terrestrial birds, values range widely, from <DL to 17.8 and from <DL to >56.5 mg kg^{-1} dw, respectively (Levengood 2003; Alleva et al. 2006; Orłowski et al. 2012; Carneiro et al. 2014; Binkowski and Sawicka-Kapusta 2015). The concentrations of Cd in the livers of birds indicate elevated values to the background level (>3 mg kg^{-1} dw) (Dauwe et al. 2005; Orłowski et al. 2012). They can occur,

Table 14.8 Concentration of cadmium (mean and range in parentheses; mg kg^{-1} dw) in the tissues of bird species representing different taxonomic and trophic groups

Species and trophic group		Localization	Concentration	References
Liver				
House sparrow *Passer domesticus*	G	Italy	0.27	Alleva et al. (2006)
		Kosovo	1.318 (0.075)	Millaku et al. (2015)
Great tit *Parus major*	I	Belgium	2.72 (0.56–11.8)	Dauwe et al. (2005)
		China	0.68 ± 0.10	Deng et al. (2007)
Red crossbill *Loxia curvirostra*	G	Italy	0.58 (0.30–0.91)	Alleva et al. (2006)
Greenfinch *Carduelis chloris*	G	Italy	0.55 (0.30–0.91)	Alleva et al. (2006)
		China	0.56 ± 0.09	Deng et al. (2007)
European blackbird *Turdus merula*	O	Italy	0.58 (<DL–1.49)	Alleva et al. (2006)
Rook *Corvus frugilegus*	O	Poland	17.2 (16.3–17.8)	Orłowski et al. (2012)
Common pheasant *Phasianus colchicus*	O	Italy	1.03	Alleva et al. (2006)
		Czech	1.00 ± 0.024	Čelechovská et al. (2008)
Greater sage-grouse *Centrocercus urophasianus*	H	USA, Wyoming and Montana	4.75 (0.20–48.5)	Dailey et al. (2008)
Eurasian sparrow hawk *Accipiter nisus*	C	Italy	0.52 (<DL–2.33)	Alleva et al. (2006)
Common buzzard *Buteo buteo*	C	Italy	0.49 (<DL–1.58)	Alleva et al. (2006)
Common kestrel *Falco tinnunculus*	C	Italy	0.09 (<DL–0.33)	Alleva et al. (2006)
		Poland/Czech	0.3	Kalisińska et al. (2009)
Bald eagle *Haliaeetus leucocephalus*	P	USA, Maine	0.35 (0.04–1.95)	Mierzykowski and Todd (2012)
Brown owl *Strix aluco*	C	Italy	1.30 (0.18–2.49)	Alleva et al. (2006)
		Spain	5.52 ± 8.33	Pérez-López et al. (2008)
		Poland/Czech	0.04	Kalisińska et al. (2009)
Barn owl *Tyto alba*	C	Italy	0.18 (<DL–1.67)	Alleva et al. (2006)
Little owl *Athene noctua*	I	Italy	0.66 (<DL–5.36)	Alleva et al. (2006)
		Spain	0.60 ± 0.57	Pérez-López et al. (2008)
		Spain	1.39 ± 0.87	Pérez-López et al. (2008)
		Italy	0.64	Naccari et al. (2009)
		Poland/Czech	0.9	Kalisińska et al. (2009)
		Portugal	0.184 (<DL–1.801)	Carneiro et al. (2014)

(continued)

Table 14.8 (continued)

Species and trophic group		Localization	Concentration	References
Long-eared owl *Asio otus*	C	Italy	0.82 (<DL–6.48)	Alleva et al. (2006)
		Spain	1.24 ± 0.75	Pérez-López et al. (2008)
Canada geese *Branta canadensis*	H	USA	0.60	Tsipoura et al. (2011)
Mallard *Anas platyrhynchos*	H	USA	<2.54–2.94	Levengood (2003)
		Poland	0.85	Kalisińska et al. (2004)
		Japan	4.82 (0.94–14.45)	Mochizuki et al. (2002)
Wood duck *Aix sponsa*	H	USA	<2.54–6.06	Levengood (2003)
Gray heron *Ardea cinerea*	P	Italy	0.06 (<DL–0.21)	Alleva et al. (2006)
		Korea	0.24 (0.19–0.29)	Kim and Oh (2015)
Black-crowned night herons	P	Korea	0.22 (0.15–0.30)	Kim and Oh (2015)
		Italy	0.17 (<DL–0.37)	Alleva et al. (2006)
Kidney				
House sparrow *Passer domesticus*	G	Kosovo	1.318 ± 0.075	Millaku et al. (2015)
Great tit *Parus major*	I–G	China	1.32 ± 0.25	Deng et al. (2007)
		Belgium	14.1 (4.1–28.3)	Dauwe et al. (2005)
Rooks *Corvus frugilegus*	O	Poland	17.0 (15.5–17.7)	Orłowski et al. (2012)
Common pheasant *Phasianus colchicus*	O	Czech	0.42	Čelechovská et al. (2008)
Brown owl *Strix aluco*	C	Poland/Czech	14	Kalisińska et al. (2009)
Common buzzard *Buteo buteo*	C	Netherlands	7.41 ± 0.90	Jager et al. (1996)
		Spain	0.27	García-Fernandez et al. (1995)
		Italy	2.09	Naccari et al. (2009)
		Poland/Czech	1.2	Kalisińska et al. (2009)
		Portugal	0.865 (0.033–8.344)	Carneiro et al. (2014)
Mallard *Anas platyrhynchos*		Poland	2.588 ± 1.819	Kalisińska et al. (2004)
		Japan	15.4 (4.68–38.07)	Mochizuki et al. (2002)
Muscle				
Canada geese *Branta canadensis*	H	USA	0.020	Tsipoura et al. (2011)

(continued)

Table 14.8 (continued)

Species and trophic group		Localization	Concentration	References
Mallard *Anas platyrhynchos*	H	Poland	0.27 (0.08–0.0.71)	Szymczyk and Zalewski (2003)
Rook *Corvus frugilegus*	O	Poland	17.2 (15.6–17.8)	Orłowski et al. (2012)
		Italy	0.09 (0.03–0.18)	Naccari et al. (2009)
Common pheasant *Phasianus colchicus*	O	Czech	0.010	Čelechovská et al. (2008)
Feathers				
Great tit *Parus major*	I–G	Belgium	11.6 ± 1.5[a]	Dauwe et al. (2002)
		Belgium	0.93 ± 0.07	Dauwe et al. (2002)
		China	0.11 ± 0.09	Deng et al. (2007)
		Portugal	0.10 ± 0.03	Costa et al. (2013)
		Slovenia	0.07 ± 0.11	Al Sayegh Petkovšek et al. (2015)
Blue tit *Cyanistes caeruleus*	I–G	Belgium	8.0 ± 1.4[a]	Dauwe et al. (2002)
		Belgium	1.4 ± 0.4	Dauwe et al. (2002)
Greenfinch *Carduelis chloris*	H	China	0.001	Deng et al. (2007)
Canada geese *Branta canadensis*	H	USA	0.086 ± 0.010	Tsipoura et al. (2011)
Mallard *Anas platyrhynchos*	H	Poland	<DL–0.04	Binkowski and Sawicka-Kapusta (2015)
Common buzzard *Buteo buteo*	C	Italy	0.11 (0.04–0.18)	Naccari et al. (2009)

G granivores, *I* insectivores, *H* herbivores, *C* carnivores, *P* piscivores, *O* omnivores, *DL* detection limit

[a]Polluted area

for example, in birds from rural areas in which phosphate and organic (manure and slurry) fertilizers containing large amounts of Cd are used (Orłowski et al. 2012).

One of the most important factors regulating the bioaccumulation of Cd in birds is the level of contamination of the bird habitat by this metal. Moreover, other important roles are played by factors affecting the bioavailability and transfer of Cd, such as the characteristics of the soil and landscape composition. Fritsch et al. (2012), in studies on trace metal transfer to European blackbirds *Turdus merula*, observed that Cd in the blood was weak correlated with soil pollution. For this reason the authors think that in this case, ecological processes like prey availability like feeding behavior are major indicators of metal transfer than the availability of

Cd in the soil. Moreover, Fritsch et al. (2012) suggest that "food chain effects" of Cd transfer result more from the preferential use of selected types of habitats by birds than from their general heterogeneity. In studies on the impact of the diversified diet of the small owl *Athene noctua* on the level of Cd accumulation, it was shown that it is strongly and positively correlated with the number of earthworms in the diet. Also it was concluded that the affinity of the common vole to a diet of earthworms assists in lowering the exposure of this bird species to Cd (Schipper et al. 2012). Extremely high concentrations of Cd were noted in the kidneys and bones of a particular type of ptarmigan (white-tailed ptarmigan *Lagopus leucurus*) living in the Colorado Rocky Mountains (USA) (Larison 2002), the diet of which included the willow, assimilating Cd in an order of magnitude higher amounts than other plants.

Interspecies differences in Cd bioaccumulation are explained mostly by the qualitative and quantitative differences in the diets of the birds (Berglund et al. 2011). For this reason exposure to Cd can differ between different bird species in the same habitat. For example, birds whose diet includes mostly arthropods (such as the pied flycatcher *Ficedula hypoleuca*) accumulate higher amounts of Cd in their tissues than birds that feed on seeds, fruits, and other plant elements, like the great tit *Parus major* (Berglund et al. 2011). Alleva et al. (2006) have also made a comparison of Cd concentrations between particular trophic groups, which demonstrated that the highest concentrations of Cd were typical in the liver for omnivorous birds (0.46 mg kg^{-1} ww) and for herbivorous birds (0.01 mg kg^{-1} ww). In general, the order of particular trophic groups according to the hepatic Cd concentration is as follows: omnivorous > frugivorous > insectivorous, granivorous > carnivorous (small mammals) > carnivorous (aquatic invertebrates) > piscivorous > carnivorous (bird-eating) > herbivorous. Moreover, the interspecies differences in Cd accumulation in avian bodies may also be the result of different genetic and biochemical features, including the ability to synthesize specific types and amounts of metallothionein (MT), which take part in Cd detoxification, which is most intensive in the liver and kidneys. In studies in this area, it was shown that at the same level of exposure to Cd in different types of ducks, the highest concentration of Cd is usually found in mallard *Anas platyrhynchos* (Levengood 2003; Szymczyk and Zalewski 2003; Lucia et al. 2010). The results of studies by Lucia et al. (2010) indicate that mallards are characterized by higher basal MT protein levels in the liver and kidneys than the Muscovy duck *Cairina moschata*, which is why a higher accumulation of Cd is found in mallard organs than in the Muscovy duck. Moreover, they observed that in the case of mallards exposed to greater doses of Cd, induction of the MT gene arose after 10 days and at lower doses after 40 days, while in Muscovy duck, induction of the MT gene appeared after 40 days for both levels of exposure to Cd.

Usually, in birds, no differences in tissue concentration of Cd are observed (Kalisińska et al. 2004; Deng et al. 2007; Carneiro et al. 2014; Binkowski and Sawicka-Kapusta 2015). Such differences do however occur between birds from different age categories, while usually higher concentrations of Cd are noted in the

tissues of older individuals (García-Fernández et al. 1996; Larison 2002; Kalisińska et al. 2004; Berglund et al. 2011; Carneiro et al. 2014). For example, in the Portuguese common buzzard *Buteo buteo*, Carneiro et al. (2014) showed that young individuals were characterized by twice lower concentrations of Cd in the liver (0.209 vs 0.409 mg kg^{-1} dw) and a three times lower level of Cd in the kidneys (0.698 vs 2.165 mg kg^{-1} dw) than adult individuals. Still, Naccari et al. (2009), in studies on the same species in Sicily, found a higher concentration of Cd in the kidneys of adult animals in comparison to young. Also in the case of the white-tailed ptarmigan *Lagopus leucurus*, the concentration of Cd in the kidneys increases with age at a rate of approximately 0.5 μg Cd day^{-1} of exposure (Larison 2002).

However, there are also some reports indicating that higher concentrations of Cd in most of the internal organs are noted for immature birds, especially chicks (Fritsch et al. 2012). This phenomenon may be related to diversity between the diet of the adult and young birds as well as the quicker rate of metabolic change in the intensively growing chicks, which strongly affects Cd absorption from the food. It was shown that the young individuals of both granivorous and omnivorous bird species feeding by parents with mostly soil invertebrates such as the ground-dwelling Coleoptera and earthworms accumulate considerable amounts of Cd. With such a diet, chicks assimilate large amounts of this element, which accumulate in their organisms (Fritsch et al. 2012; Orłowski et al. 2012).

5.5 *Bioindicators and Biomarkers in Ecotoxicological Studies*

One of the most commonly used methods for monitoring contamination of the environment by heavy metals is evaluation of their bioaccumulation in the tissues of different species of animals used as bioindicators. In biomonitoring and ecotoxicological studies, wild (including micromammals and game animals) and domesticated mammals and birds from the human neighborhood are used.

Small land mammals are found to be very good bioindicators, mostly due to the widespread occurrence, limited home range, generalized feeding habits, short life, high reproductive indexes and metabolic rate, as well as simplicity in obtaining them for research. They are an important part of the ecosystems as they are part of many trophic chains and for this reason play a great role in the circulation and transfer of many elements, including Cd. Ecotoxicological studies are usually performed with wood mice (Sánchez-Chardi et al. 2007; van den Brink et al. 2010; Lourenço et al. 2013; Tête et al. 2015), field mice, yellow-necked mice, voles, moles, and shrews (Damek-Poprawa and Sawicka-Kapusta 2003; Veltman et al. 2007a; Fritsch et al. 2011; Nesterkova et al. 2014) and the slightly bigger wild rat (Pereira et al. 2006). Many researchers consider mice and rats to be particularly useful in bioindication, as

they pass many of the important criteria for good indicators: (1) their populations are properly large; (2) they have a wide geographic distribution; (3) they occur in both polluted and nonpolluted areas; (4) they can live in human neighborhoods and consume human food, which make mice and rats good indicators of human exposure; (5) they have a small home range, so they may be treated as site-specific indicators; and finally (6) they are located in a mid-position in many trophic chains (Pereira et al. 2006).

Some researchers in studies on rodents indicate that some species are particularly sensitive and useful in ecotoxicological evaluations. Martiniakova et al. (2012), based on studies of the accumulation of Cd and other elements in the kidney, liver, testis, uterus, and bones of free-living wild rodents from a polluted area in Slovakia, indicate that bank voles are more sensitive heavy metal-loaded bioindicators than yellow-necked mice. In turn Braeuer et al. (2015) observed that between four examined species of small mammals (*Apodemus sylvaticus*, *Microtus arvalis*, *Myodes glareolus*, and *Sorex araneus*), the most sensitive bioindicator was the common shrew.

Another important group in biomonitoring and ecotoxicological studies is the herbivorous Leporidae, wild rabbits and hares, as they are an important edible game species, and moreover they are important prey for several predator species (Lazarus et al. 2014). The concentration of Cd measured in their tissues gives indirect information not only of the degree of pollution in the environment they live in but also about the risks of consuming them. Eira et al. (2005) reported that the mean Cd concentration in wild rabbit kidneys from Portugal was 1.02 mg kg^{-1} ww and that, in 30% of kidney samples, Cd levels exceeded the threshold value (1.0 mg kg^{-1} ww, the maximum value set for the kidneys of cattle and domestic poultry for human consumption in the EU).

In ecotoxicological studies on Cd, carnivores are also considered, mostly from the Canidae, Mustelidae, and Procyonidae families. The diverse food preferences of the particular species allow them to provide information on the level of contamination in the different habitats. Among the mostly used species, the polecat (*Mustela putorius*) and marten (*Martes martes* and *M. foina*) seem to be the best bioindicators of land ecosystem pollution, as their diet is less related to water ecosystems and, as cited by Ryšavá-Nováková and Koubek (2009), is dominated by mammals and birds. Also, the American mink (*Neovison vison*), which is a subject of numerous ecotoxicological and biomonitoring studies, is used as a sensitive bioindicator of pollution of terrestrial ecosystems, even though the proportion of fish in their diet is considerable (Krawczyk et al. 2013). Thereby, the load of Cd in the organism of a mink in part comes from a water habitat. Otters in turn are mostly connected with water ecosystems, and for this reason, their role as a bioindicator of pollution of land ecosystems is low.

Game animals are good bioindicators as they provide information not only about the quality of the ecosystem of which they are part of but also about the potential threat to venison consumers. The most common studies are on wild ruminants, such as roe deer, red deer, fallow deer, and in northern countries the moose and reindeer.

The wild boar also plays a significant role in ecotoxicological studies, whose role as an indicator of environmental pollution is largely in relation to xenobiotics, which are accumulated in the soil. Also animals that live in human neighborhoods (e.g., the fox) are relevant for delivering information about the level of contamination of the human habitat. Dip et al. (2001) indicate that foxes living in urban and suburban areas may be valuable bioindicators of Cd contamination of urbanized areas.

Widely spread species of birds and mammals may also be considered especially valuable biomonitors, allowing comparisons of the level of Cd accumulation within a single continent or between them (Eurasia and North America), as well as species with similar biology, for example, the erne *Haliaeetus albicilla* vs American erne *H. leucocephalus* or reindeer vs caribou.

Usually the concentration of Cd in the organs of mammals follows the descending sequence, kidney > liver > muscle, caused by the fact that the kidneys are the most important organ in the accumulation of this element. According to the fact that the affinity of Cd to the bones is much less than, for example, Pb, cadmium is measured in bone tissue less often. Such studies were undertaken by Łanocha et al. (2013), who observed similar concentrations of Cd in the bones of Canidae (foxes, dogs) and humans, which indicate the usefulness of these animals to evaluate the human threat of exposure to this element. As noted by Herber (2004), only in large exposures to Cd is this element stored in the liver, while in small doses, Cd accumulates mostly in the kidneys.

The concentration of Cd is most frequently evaluated in the kidneys and liver; however the research material is diverse and may differ in particular groups of animals. In murine, the concentration of Cd is measured in the tissues and organs (mostly in the blood, liver, and kidneys and occasionally in the spleen, brain, and muscles) as well as in the whole body. Also the tail of these animals is used (Ferreira et al. 2015). In bigger mammals, studies are performed usually on the liver, kidneys, muscles, as well as fur and bones. Blood may be used as an indicator of current exposure to Cd while hair and bones as indicators of long-term exposure.

Wild birds are often used in biomonitoring and ecotoxicological studies. Usually these studies focus on predatory birds, located at the top of the trophic chains. Pérez-López et al. (2008) indicated that the local- and upper-trophic-level species are believed to be especially vulnerable to metals which explains their important role as environmental contamination indicators. Diurnal species, e.g., the common buzzard (*Buteo buteo*), northern goshawk (*Accipiter gentilis*), common kestrel (*Falco tinnunculus*), Eurasian sparrow hawk (*Accipiter nisus*), as well as nocturnal species, e.g., the long-eared owl (*Asio otus*), tawny owl (*Strix aluco*), and barn owl (*Tyto alba*), are found to be useful species for the biomonitoring of metals and local monitors of contaminant levels (Pérez-López et al. 2008). These birds are usually sedentary, and their wide diet includes small mammals, birds, amphibians, reptiles, and insects.

Many works have concerned smaller birds from other trophic levels and typical for particular ecosystems, as well as those living in human neighborhoods. Although Cd and other metals accumulate better in the organs of longer-lived animals, it seems that relatively short-living passerines, e.g., the house sparrow, great tit, and blue tit, are good biomonitors of Cd levels (Markowski et al. 2014). In studies on the level of

Cd in tissues of the house sparrow (*Passer domesticus*) from locations with different degrees of contamination, Millaku et al. (2015) stated that the concentration of Cd was significantly higher in the tissues of sparrows from polluted areas in comparison to those living in the reference region. This indicates that the house sparrow could be considered as an indicator for environmental contamination. Moreover, passerines are numerous, have a wide range of presence and a small home range, and are relatively highly located in the food chain. Another advantage of these animals is the fact that the biology of this species is well known (which simplifies the interpretation of results) as is their ecotoxicological use (which in turn simplifies comparisons of results from different research teams, regions, and countries). Additionally in the case of the great tit and blue tit, it is easy to monitor their population especially during the breeding season, as they often use nesting boxes made by people. This favors noninvasive sample collections, for example, in the case of studies on the natural mortality of chicks, as well as in observations of possible reproductive or behavioral aberrances in the polluted areas. A particularly important feature of passerines in their use in biomonitoring and ecotoxicological studies is their foraging in small home ranges, making them suitable as biomonitors for point source contamination (Markowski et al. 2014).

The pied flycatcher (*Ficedula hypoleuca*) is commonly used in ecotoxicological studies, and especially the breeding population (Berglund et al. 2011; Eeva and Lehikoinen 2015), even though it is a migratory bird. This species spends winter in Central Africa and visits its breeding areas from the middle of April. Nevertheless it is a species sensitive to environmental pollution (reductions in the hatchability of eggs, increases in nesting mortality) (Berglund and Nyholm 2011), which predisposes it for ecotoxicology. Also, soil invertebrate-feeding birds, like the rook (*Corvus frugilegus*), seem to be good biomonitors, which similar to predators from the top levels of trophic levels are vulnerable to high doses of heavy metals in their diet. Until now this species had been frequently passed by in biomonitoring and ecotoxicological studies. Only a few works about the levels of environmental contamination in the tissues of this bird are available (Orłowski et al. 2012, 2014), with most dated in the 1960s and 1970s.

Costa et al. (2013) suggest the use of chicks in nesting boxes in the evaluation of local environmental contamination. The authors explain that this may simplify material and data collection for a defined area and time period. Additionally, the chicks in nesting boxes are exposed to a lesser extent than the adult individuals to external airborne deposition from industrial sources. This allows assessment of the effects of diet in the concentration of Cd in the tissues of chicks.

In biomonitoring and ecotoxicological studies in birds, Cd is mostly measured in the liver, kidneys, and pectoral muscle, rarely in the blood, and only occasionally in other types of sample. The content of Cd in the liver and kidneys is a reflection of the temporal exposure, while blood levels illustrate the current exposure. The ratio of Cd concentration in the liver to the kidney may be used to evaluate the length and dose of exposure. A factor lower than 1 suggests long exposure to small doses (Scheuhammer 1987). Data about the concentration of Cd in the liver and kidneys may also be used to settle regression lines in the CSRL (Cd standard regression line)

model developed by Mochizuki et al. (2008), which allows the definition of whether animals are intoxicated with Cd.

More and more often, researchers decide to use material which may be obtained in a noninvasive way, such as feathers, eggs, or eggshells (Deng et al. 2007; Costa et al. 2013; Markowski et al. 2014); however in some studies, a low usefulness in the assessment of Cd environmental pollution has been demonstrated with those sources (Binkowski and Sawicka-Kapusta 2015). This is caused by the fact that the content of Cd in feathers is not always correlated with the level of this element in the blood and organs nor with the pollution of the environment (e.g., in the soil) (Tsipoura et al. 2011). Due to the fact that during the molting season birds are able to eliminate large amounts of metals, in such studies, feathers formed during or just after the breeding period should be chosen. Additionally Costa et al. (2013) have observed that the feathers of chicks differ in the content of metals from the feathers of fully grown birds, which in part is related to the constant growth of the feathers in chicks. For this reason, they suggest that during interpretation of the results, the stage of feather development should be taken into account.

It seems that the use of eggshells in biomonitoring is controversial, as the location of the habitat (e.g., big and small cities, countryside) did not affect the Cd content in them, as was shown by Orłowski et al. (2014). This observation concerns also whole eggs, in which the concentration of Cd did not always reflects the environmental levels of contamination by Cd and was often below the detection limit (Roodbergen et al. 2008). This indicates that the concentration of Cd, in contrast to the other heavy metals, is probably physiologically regulated in eggs.

Despite the fact that feces are more often used as an object of studies on the evaluation of environmental contamination and Cd exposure (Berglund and Nyholm 2011; Berglund et al. 2011), Binkowski and Sawicka-Kapusta (2015) have stated that feces do not seem to be a useful material to study as they do not present internally accumulated concentrations.

In ecotoxicological studies, *biomarkers* are widely used as biological indicators, allowing for qualitative or quantitative evaluation of interactions between an organism and chemical, physical, and biological factors of the environment. Biomarkers have been divided into three groups—biomarkers of (1) exposure, (2) effect, and (3) susceptibility (Mussali-Galante et al. 2013)—of which the first two play the biggest role in the assessment of the risk of Cd exposure. Among the exposure biomarkers, the most often used are the biomarkers of the internal dose that show the presence of a particular toxic factor in the organism, with the tissues and organs treated as internal dosimeters. To a lesser extent, the biomarkers of an effective biological dose are used. The biomarkers of the effects are DNA single- and double-strand break (earthworms; Fourie et al. 2007), chromosome aberrations (dipterans; Michailova et al. 2000), micronuclei (wood mouse; Sánchez-Chardi et al. 2007), and sister chromatid exchange (Algerian mice; Tapisso et al. 2009). Among the biochemical biomarkers of the effects of Cd exposure, the most often used are metallothionein which increase in concentration at the moment of a direct threat (great tit, Vanparys et al. 2008). There are also some studies that confirm the

usefulness of *N*-acetyl-β-D-glucosaminidase activity (NAG) as a biomarker of the effects of exposure (pheasants; Zielińska et al. 2015).

6 Conclusions

Cadmium is a toxic element, which naturally occurs in the environment. Despite that the global Cd emission is decreasing in the last few decades, its presence in the environment is still a severe ecological problem. Animals that live in polluted areas may contain extremely high concentrations of Cd in their tissues. Long exposure even to low doses of Cd leads not only to many disorders within the organism itself but may also result in changes in the whole ecosystem.

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Chapter 15
Fluorine, F

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Abstract We summarize literature data on the concentrations of fluorine (F) in various tissues of terrestrial mammals and birds. The results of various studies indicate the usefulness of the determination of fluoride in hard tissues of wildlife for monitoring the environmental F contamination, as well as its role in the assessment of the effectiveness of measures taken to reduce F emissions, e.g., from industrial sources.

1 Introduction

Atmospheric air is contaminated with fluorine compounds not only as the result of various human economic activities but also by natural factors such as aeolian dust, volcanic emissions, evaporation of chemical components from sea and ocean surfaces, cosmic dust, and natural disasters (Francisca and Carro Perez 2009; Kabata-Pendias 2011). Changes in the chemical composition of the environment disrupt the homeostasis of ecosystems, an essential factor for their natural existence (Kabata-Pendias 2011). The accumulation of fluoride in soils is particularly dangerous, as the soil is the first barrier regulating its transfer into the food chain, and any changes in the natural fluoride concentration in the soil, such as an increase in levels or changes in quantitative proportions, cause adverse ecological and nutritional effects (Flueck and Smith-Flueck 2013; Kabata-Pendias 2011).

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2 General Properties

At room temperature, fluorine is a pale yellow-green gas (Kabata-Pendias 2011) with a penetrating odor, strongly affecting the mucous membrane. As one of the most electronegative and reactive of all elements (Kolditz 1994), at room or elevated temperatures, fluorine binds directly to all elements apart from oxygen and nitrogen and therefore readily reacts with the most organic compounds. Fluorine ions have a high ability to form complexes with heavy metal ions in aqueous solutions (Kabata-Pendias 2011). Fluorine also creates compounds with nonmetallic elements, comprising covalent bonds (Kabata-Pendias 2011). Thanks to its high electronegativity, fluorine oxidizes many elements to the highest degrees, and the small size of its atom leads to high coordination numbers (Kolditz 1994).

Assessments of exposure to fluorine and its compounds can be made by determinations in different parts of the environment. The maximum allowable fluoride level in the air at workplaces is 0.05 mg m^{-3}, with an allowable momentary level of 0.4 mg m^{-3}. Acceptable concentrations of fluorine in air emissions are 0.03 mg m^{-3} (for 30 min), 0.01 mg m^{-3} (average daily concentration), and 0.0016 mg m^{-3} (average annual concentration) (Węglarz and Michalski 1998).

3 Fluorine Minerals, Production, and Uses

Fluorine constitutes about 0.06–0.09% of elements in the earth's crust, i.e., 625 mg kg^{-1} on average (Kabata-Pendias 2011). Due to the fact that fluorine is one of the most reactive elements, in the environment, it creates common and poorly soluble mineral complexes (WHO, 2006), which include fluorspar, rock phosphate, cryolite, apatite, mica, hornblende, and others (Murray 1986). Igneous and sedimentary rocks are the richest in the poorly soluble calcium fluoride (fluorite, CaF_2). The highest F levels are found in alkaline to acidic igneous rocks, while the lowest levels are found in ultra-alkaline rocks (Kabata-Pendias 2011). The average F level in rocks ranges from 0.1 to 1.0 g kg^{-1} (Indulski 1989). Fluorine exhibits lipophilic and oxyphilic tendencies (Kabata-Pendias 2011).

Fluorspar is the most common commercial source of F. Global mining production of fluorspar, apart from the United States (data not available), was estimated in 2008 at about 5840 kt and rose in 2014 to about 6850 kt (US Geological Survey 2015).

Other minerals used in the industry include phosphate rock applied in the manufacture of phosphate fertilizers and cryolite used in the production of aluminum (Murray 1986) and as a pesticide. The by-products of the conversion of phosphate rock into phosphate fertilizers are fluorosilicates, which after purification are a source of fluoride added to drinking water in various countries in the past or currently to assist in preventing dental caries (Reeves 1986).

4 Fluorine in Nature: Geogenic and Anthropogenic Sources

4.1 Water

Fluoride is naturally present in various water bodies, ranging from 1 mg L^{-1} in the sea to approx. 0.5 mg L^{-1} (or less) in rivers and lakes. The concentration in groundwater depends mainly on the structure of the mineral rock and the degree of solubility of fluorine compounds (Hem 1989). In addition, calcium and sodium ions can reduce or increase the content of fluoride in water: the more calcium, the lower the concentration of fluoride; the reverse is true for sodium (Edmunds and Smedley 1996).

High concentrations of fluoride in groundwater resulting from the construction of mineral substrates have been noted in areas of India, Pakistan, West and South Africa, Sri Lanka, Thailand, in all provinces and autonomous regions of China, and in South America (WHO 2006). Central European countries that have elevated levels of fluoride in groundwater include Ukraine, Moldova, Hungary, and Slovakia (Fordyce et al. 2007).

Particularly high concentrations of fluorine compounds in water can be observed in areas of high volcanic activity (Allibone et al. 2012; Edmunds and Smedley 1996). Therefore, thermal waters—especially those with a high pH—are rich in fluorine compounds (Edmunds and Smedley 1996). Many lakes in Sudan, Ethiopia, Uganda, Kenya, and Tanzania have a very high content of fluorine ranging from 690 mg L^{-1} in Tanzania to 2800 mg L^{-1} in Kenya. Also groundwaters in those areas are characterized by high levels of fluoride ranging from 30 to 50 mg L^{-1}. Samples of groundwater from bores drilled to source drinking water exceeded the safety threshold of 1–1.5 mg L^{-1} (WHO 2006), which correlated with a high rate of fluorosis in those areas (Manji and Kapila 1986). Many scholars have also indicated a relationship between volcanic activity and the increased incidence of fluorosis among people and animals, even at large distances from the sources of emissions (Allibone et al. 2012; Cronin and Sharp 2002; Flueck and Smith-Flueck 2013; Francisca and Carro Perez 2009).

The countries of South America, especially Chile, Peru, Argentina, and Paraguay, are particularly susceptible to high concentrations of fluoride in the groundwater because of the geographical location of those countries, bordering the Ring of Fire, a seismically active region. Research conducted by Francisca and Carro Perez (2009) showed elevated concentrations of fluoride in groundwater samples in Argentina (0–13.5 mg F L^{-1}) and directly linked to recent volcanic eruptions. After the eruption of the Puyehue-Cordon Caulle in 2011 (PCCVE, June 2011), Argentina and Chile saw an increase in the incidence of fluorosis in humans, confirming the impact of the eruption on the content of fluoride in the environment (Flueck and Smith-Flueck 2013). Similar observations were made by Oruc (2008) after analyzing data from areas located near Tendurek Volcano in Eastern Turkey.

4.2 Air

Many researchers believe that only the areas around industrial plants are environmentally contaminated, endangering only local fauna and flora. However, research in areas located far from the emitters has shown that these are also ecologically threatened. The spread of pollutants greatly depends on the directions of winds. The distribution of winds, climatic conditions, and the level of emissions are factors determining the extent and spread of industrial emissions (Machoy et al. 2001, 2002).

Fluorine does not occur in the atmosphere in a free state. Fluoride is emitted into the air in the form of gas and solids. The greatest spread of fluoride in the air can be observed close to active volcanoes (Edmunds and Smedley 1996). Another natural source of atmospheric fluoride in the soil is in seawater spray carried by the wind. In urban areas, most of the fluoride found in the air is the result of human activity. The aluminum industry is responsible for the emission of 10% of the total amount of atmospheric fluoride. Ironworks, superphosphate factories, brickyards, glassworks, coal-fired power plants, and petroleum refineries also pollute the atmosphere with fluoride (Machoy et al. 2002).

5 Biological Status of Fluorine

Fluoride may be present in inorganic and organic compounds. Individual forms are soluble to varying degrees and then absorbed by plants, animals, and humans, exhibiting diverse levels of toxicity (Kabata-Pendias 2011). This is significant in the case of fluoride—an element that acts slowly, not giving symptoms for many years. In particular, this applies to the skeletal system because the physiological role of fluorine is mainly related to the processes of bone mineralization (Machoy-Mokrzyńska 2000).

The affinity of fluorine to metals, in particular divalent ones (Ca, Mg, Mn, Fe, Cu, Zn), promotes the formation of different compounds, which change the physiological effects of these cations. Precipitated magnesium and calcium fluorides are deposited in different, mainly hard, tissues (Gutowska et al. 2005). Fluorine, when ingested in large quantities, can be harmful to human health and animals, particularly taking into account the very narrow margin of safety between a tolerable and a toxic dose (Giżewska and Machoy 1988; Machoy-Mokrzyńska 2000).

Acute fluoride poisoning affects virtually all organs in the human or animal body and can be fatal due to blockages in cell metabolism. Fluoride inhibits enzymatic processes and may even halt them. In particular, this applies to metalloenzymes. Also significant is the disruption of calcium-dependent essential functions of the body. Other metal ions may also be bound by fluoride, which then causes blockages of various biochemical reactions (Barbier et al. 2010). The toxicity of fluoride may be enhanced by the reaction of the environment. The acidic pH of the stomach, the

oral cavity, and the final sections of the urinary tract favors the formation of highly toxic hydrogen fluoride (Giżewska and Machoy 1988; Jędrzejuk and Milewicz 1996).

The main route of gaseous and particulate fluoride absorption is the respiratory system (Barbier et al. 2010). In the gastrointestinal tract, fluorine is easily absorbed by simple diffusion (Giżewska and Machoy 1988). It permeates rapidly through cell membranes and is fed to all tissues (Barbier et al. 2010). In direct contact, fluoride can also be absorbed through the skin (Giżewska and Machoy 1988) and penetrates skin appendages—for example, both the organic and inorganic parts of nails. In addition to transepidermal absorption, fluorine exhibits a potential for transfollicular absorption via hair follicles and sebaceous glands. However, this route is less effective due to the small area of absorption (Giżewska and Machoy 1988).

Absorbed fluoride spreads throughout the human or animal body (Barbier et al. 2010; Giżewska and Machoy 1988). It can be found in all tissues, with the greatest accumulation in bones and teeth (Giżewska and Machoy 1988; Kabata-Pendias 2011). Fluoride ions are rapidly taken up by the bone, which results in the replacement of hydroxyl ions included in hydroxyapatite and creation of fluorhydroxyapatite or fluorapatite (Machoy 1990; Gutowska et al. 2005).

Fluoride retained in skeletal bone may be gradually released to the blood and urine. Blood acts as a means of fluoride transport in the body. Approximately 75% of fluoride in the blood is located in the plasma; the remainder is inside the red blood cells or on their surface. Unlike in bones, soft tissue concentrations do not increase with age or the duration of exposure (Indulski 1989).

The major route of excretion of fluoride is the urinary tract, although small amounts may also be excreted in sweat, feces, and saliva. Elimination of fluoride takes place in two phases: a rapid phase taking place over a matter of weeks and probably related to the ion exchange in the hydration shell, followed by a second slower phase with an average half-life lasting about 8 years, resulting from the resorption by osteoclast cells. Fluoride is excreted faster from trabecular bone than from compact bone. Approximately half of the absorbed fluoride is excreted in the urine via glomerular filtration. Fluoride may undergo resorption in the renal tubules, depending on the pH of the urine. In urine, fluoride is mainly present as F^- and in small amounts as HF (Indulski 1989).

6 Toxicity of Fluorine in Homeothermic Animals

6.1 Effect on Bones and Teeth

In the case of long-term absorption of fluoride into the body, a negative two-way action can be observed. Fluoride damages bone matrix, affecting biosynthesis of collagen by cells producing intercellular substance, via alteration of their activity, damage, or destruction (Yan et al. 2015). Secondly, it can form sparingly soluble calcium and magnesium fluorides, which lead to hypermineralization (Yan et al.

2015). The excessive accumulation of fluoride in bones can interrupt the formation of the crystal nucleation process. Crystallization occurs continuously toward the c-axis at the peripheral area, while the central area remains amorphous, resulting in crystal defects (Kakei et al. 2007). In addition, in trabecular bone, excessive accumulation of fluoride may increase bone volume and trabecular thickness without a concomitant increase in trabecular connectivity, which may reduce bone quality despite the increase in bone mass (Aaron et al. 1991). In addition, severe fluorosis leads to chronic osteomyelitis (Schultz et al. 1998).

Teeth with fluorosis are characterized by varying degrees of discoloration of the enamel, hypoplasia, and posteruptive surface defects. Subsurface layers of enamel exhibit hypomineralization, accentuated striae of Retzius, and wide hypomineralized incremental ranges of abnormal enamel structures, which may result from the negative effect of fluoride on the secretory activity of ameloblasts and enamel maturation (Kierdorf et al. 1996c, 2000b; Richter et al. 2010). Chronic exposure to fluoride also causes defects in the mineralization of the dentine, manifested by hypomineralization or interglobular dentin. However, according to one of the hypotheses, in certain stages of life, this structure includes mechanisms that protect it from exposure to high doses of fluorine. Those mechanisms include the placental barrier in the fetal period and the blood-milk barrier in the breast-feeding period; the uptake of most serum fluoride by the developing skeletal system occurs in this period of rapid growth of young individuals (Richter et al. 2010).

Severe fluorosis causes pathologically increased wear and fracture of teeth and periodontal bone lesions caused by inflammation of the periosteum. The result of the strong abrasion of the occlusal surface of teeth is opening of the pulp chamber, formation of periapical ulcers, and—eventually—tooth loss (Schultz et al. 1998).

6.2 Neurotoxicity of Fluorine Compounds

Fluoride has a negative effect on many metabolic processes in the human body. It is also a potent neurotoxin, resulting in the degeneration of structures such as the hippocampus, cerebral cortex, and cerebellum (Shivarajashankara et al. 2002). Exposure to fluoride inhibits receptors in the brain and reduces the production of neurotransmitters (Yu et al. 2008). Moreover, chronic intake of fluoride during the development of the brain may lead to reduced intelligence and disorders of the processes associated with memory and learning (Xiang et al. 2003), which may be related to changes in the structure and function of synapses (Celio and Blümcke 1994; Ziemiańska et al. 2012). At high concentrations, fluorine is an inhibitor of the metalloproteinases MMP2 and MMP9 (Kato et al. 2014), enzymes responsible for proteolysis in the perineuronal network that perform a protective function against inflammatory lesions and degeneration of nerve cells and participate in the stabilization of synapses and matured neurons (Celio and Blümcke 1994).

Research conducted by Basha et al. (2011) in rats dosed with 100 and 200 mg L^{-1} NaF in drinking water showed histopathological changes in discrete brain regions

and decreased learning and memory abilities in multigenerational rats. The presence of eosinophilic Purkinje cells, degenerating neurons, decreased granular cells, and vacuolations was noted in discrete brain regions of the fluoride-treated group. In the T-maze experiments, rats treated with fluoride showed worse results in comparison to the control group (poor acquisition and retention and higher latency), and the observed changes deepened in the subsequent generations of the rats (Basha et al. 2011), which may indicate a negative cumulative impact of fluorine on the developing brain. The observed changes may be caused by a growing oxidative stress induced by both the increase in the concentration of free oxygen radicals (Eisenbrandt and Nitschke 1989) and inhibited action of antioxidant enzymes by fluorine (Wang et al. 2004). At the same time, abnormal production of thyroid hormones induced by fluorine compounds also contributed to the antioxidant imbalance (Basha et al. 2011).

Piscivorous birds are particularly vulnerable to fluoride compounds. Their brain fluoride concentrations are significantly higher than in mammals, which results from the cumulative properties of fluorine originating from their prey (Kalisińska et al. 2014).

6.3 *Effects of Fluorine on Glucose Metabolism*

There exist only a few studies on the effects of fluoride on the muscle metabolism of glycogen, a very important source of glucose and energy for muscles (McGown and Suttie 1977; Dost et al. 1977; Shashi et al. 1988). Waldbott et al. (1978), after examining about 500 people with chronic fluorosis, compiled a list of clinical features, which included chronic fatigue that is not relieved by rest, weakness, and involuntary muscle contractions. Their observations were later confirmed by Susheela (2001).

The regulation of blood glucose levels is dependent on the concentration of insulin in the blood. Diurnal variation in the concentration of this hormone depends on melatonin secretion by the pineal gland (Peschke et al. 2013). Studies on birds (Kalisińska et al. 2014) show that this gland accumulates large amounts of fluorine, compared to the brain and bone, which significantly interferes with the metabolism of glucose in the pineal gland, leading to the formation of paracrystalline structures containing large amounts of glycogen. Deficiency of this hormone can have significant consequences on the metabolism of birds and seasonal migrations (Kalisińska et al. 2014).

6.4 *The Role of Fluorine in the Development of Inflammation*

The role of fluorine in the development of the inflammatory process is poorly defined (Schamschula and Barmes 1981). It is known that prolonged exposure to fluoride

stimulates oxidative stress, accelerating pathological changes within cells (Das et al. 2006; Guan et al. 2000). NaF increases the formation of ROS in macrophages (Goldman et al. 1995) and activates a signaling cascade in response to stress, which involves the activation of MAP kinase in vascular endothelial cells. In addition, fluoride lowers the activity of antioxidant enzymes (glutathione peroxidase, superoxide dismutase, glutathione reductase, and catalase) in macrophages, which can indirectly contribute to an increase in ROS levels observed in these cells. Higher production of ROS increases lipid peroxidation, which in turn leads to apoptosis (Gutowska et al. 2010).

NaF in in vitro cultures reduces the intracellular concentration of ATP and the loss of mitochondrial transmembrane potential (Gutowska et al. 2010), suggesting that the multidirectional effect of NaF on cells can be caused by limiting the availability of ATP in these cells, a substance necessary for protein phosphorylation rather than by G protein activation (Goldman et al. 1995).

Prolonged exposure to fluoride leads to changes in the efficiency and catalytic activity of enzymes involved in the metabolism of eicosanoids, inflammatory processes, vascular remodeling, coronary heart disease, myocardial infarction, etc. (Goldman et al. 1995, 1997; Gutowska et al. 2012; Wessel et al. 1989). Eicosanoid synthesis in macrophages is controlled by the availability of free arachidonic acid. Fluoride increases arachidonic acid release in the cell membranes of macrophages, which increases the activity of cytosolic phospholipase A2 ($cPLA_2$) and the synthesis of prostaglandins in macrophages (Gutowska et al. 2011, 2012; Schulze-Specking et al. 1991; Wessel et al. 1989). It is believed that by stimulating G protein (guanine nucleotide binding), fluoride increases the amount of thromboxane B_2 (TXB_2), 6-ketoprostaglandin F1 alpha, and prostaglandin F2 alpha (PGF2α) in the serum of people exposed to NaF (Dodam and Olson 1995), which has been confirmed by in vitro studies (Coffee et al. 1992).

By changing the intracellular calcium concentration (Murao et al. 2000; Xu et al. 2007), fluoride can cause translocation of protein kinase C (PKC) from the cytosol to the membrane, where the increase in PKC activity has a positive effect on the release of arachidonic acid from the membrane and its availability for the synthesis of prostaglandins (Garcia et al. 1992). In addition, the increase in intracellular calcium concentration and an increase in PKC activity are factors stimulating PLA_2 and PLC (Garcia et al. 1992). cAMP plays an important role in regulating many processes in macrophages, i.e., phagocytosis or migration. High intracellular concentrations of cAMP are negatively correlated with the activity of these processes, and incubation of macrophages with sodium fluoride ions increases the levels of intracellular cAMP (Houdijk et al. 1991).

Chronic fluorosis also leads to a change in the composition and structure of cell membranes (Wang et al. 2000). These changes include changing the content of neutral lipids and phospholipids (Guan et al. 2000). In studies on macrophages, an increase in diacylglycerol synthesis was observed following exposure to fluoride (Dieter and Fitzke 1993; Wessel et al. 1989), which may have taken place via the hydrolysis of other phospholipids (Dieter and Fitzke 1993). Literature data suggest

that activation of PLA_2 and increased eicosanoid synthesis are caused by fluoride-induced synthesis of diacylglycerols (Wessel et al. 1989).

7 Fluoride in Mammals

Ecotoxicological research designed to indirectly evaluate environmental pollution by various substances, for example, by fluorine compounds, is focused on the determination of concentrations in the bodies of wild animals. Primarily, concentrations are determined in the organs responsible for detoxification in mammals and birds, namely, the liver and kidneys. However, some elements, including fluorine, accumulate in increasing quantities in hard tissues. Therefore, determinations for long-term pollution and exposure of living organisms to fluoride are much more frequently based on levels in the hard tissues building bones, teeth, and antlers (Bezerra de Menezes et al. 2003).

7.1 Farm Animals

The first alarming symptoms of the negative impact of pollution with fluoride on living organisms were observed in farm animals, such as cattle (Burns, 1969; Dale and Crampton 1955; Filippovskiĭ 1969; Green 1946; Gründer 1972; Murray 1967; Obel and Erne 1971; Schmid 1956; Udall and Keller 1952) and sheep (Burns 1969). Research conducted over many years and in many countries has shown a link between emissions from certain industries and fluorosis in cattle (Gründer 1972; Krook and Maylin 1979; Choubisa 2015). It was noted that cattle grazing on pastures near aluminum smelters or heat and power plants ate grasses growing in the contaminated area and thus accumulated fluoride in their bodies, negatively affecting their health and thus farm productivity and profits (Bunce 1985; Krook and Maylin 1979).

However, not only atmospheric emissions may increase fluoride levels in the body. Long-term (30 years) fertilization of soil with phosphorus fertilizers contaminated with fluorine compounds may result in increased consumption of this element by animals (Grace et al. 2008). Areas that naturally contain high concentrations of fluoride in the soil and waters (India, China) also demonstrate the occurrence of fluorosis and numerous disturbances in the normal functioning of the body and the retention of a number of elements in farm animals in numerous studies (Wang et al. 1995; Choubisa et al. 2012; Narwaria and Saksena 2012; Choubisa 2014; Khandare et al. 2015; Choubisa and Choubisa 2016).

7.2 Ungulates

The most common materials in research on environmental pollution with fluorine compounds are the antlers and mandibles of deer, due to the cumulative capacity of F in hard tissues of the body (Shupe et al. 1984; Jelenko and Pokorny 2010). However, some studies have also used hair and hooves (Zakrzewska et al. 2004). Antlers have a well-known annual growth cycle and therefore enable the determination of fluoride pollution in the previous year. The rapid growth of antlers results in the accumulation of particularly large amount of fluoride during antlerogenesis and allows using antlers as a model to study the impact of large amounts of fluoride on bone formation. Furthermore, analysis of antler samples and pedicle bone permits a noninvasive monitoring of environmental pollution with fluoride (Kierdorf et al. 1997, 2000a, b). The mandible accumulates fluoride during the entire life of the organism and thus reflects the cumulative effect of fluoride on the body (Kierdorf et al. 1989; Gutowska et al. 2004). Fluoride is captured faster during the growth of the bone than later in life, when accumulation occurs during normal bone remodeling (Kierdorf et al. 1995). Both tissues are easily accessible. Mandibles are often systematically collected by hunting associations in order to control the number and health of wild game, while antlers (as hunting trophies) can come from private collections (Jelenko and Pokorny 2010).

Antlers and bones of deer are excellent materials from which to study large-scale environmental contamination with fluorides in areas inhabited by these animals, due to the large numbers of animals and the high degree of adaptation to the conditions in a given area (Shupe et al. 1984; Vikøren and Stuve 1996b; Machoy et al. 1991; Kierdorf et al. 2000a, b, 2012; Piotrowska et al. 2006). In addition, antlers are highly useful in the analysis of the direction and extent of contamination with fluoride from emission sources such as aluminum smelters (Kierdorf and Kierdorf 2002; Kierdorf et al. 2012) and iron and steel smelters (Kierdorf and Kierdorf 2003).

Jelenko and Pokorny (2010), after examining 141 antlers and 220 mandibles of roe deer (*Capreolus capreolus*) derived from animals hunted between 1960 and 2007 (antlers) and 1997 and 2009 (mandibles) in the area of the largest Slovene thermal power plant of Šoštanj (STPP), showed a high correlation between annual emissions from the plant and the average annual contents of fluoride in the antlers and mandibles. In addition, by comparing the results obtained for samples from different years, they noted a significant reduction in the emission of pollutants containing fluorine compounds from the plant after 1995 and 2000, which was connected with the introduction of equipment purifying exhaust gases. Kierdorf and Kierdorf (2000), after examining roe deer (*Capreolus capreolus*) antlers between 1932 and 1998 also showed seasonal changes in the emissions of pollutants containing fluoride in the eastern suburbs of Cologne (an area of 800 km^2, Germany). The fluoride content in the antlers dropped significantly in the 1980s and 1990s, which indicated a reduction in fluoride emissions (Kierdorf and Kierdorf 2000). Also, research conducted by the same researchers (Kierdorf and Kierdorf 2001) in the period of 1951–1999 in the industrialized Ruhr area (Western Germany)

showed a correlation between the concentration of fluoride in the environment and its content in the tested antlers.

The results showed a gradual reduction in the amount of fluoride in the atmosphere in the study area after 1980, which probably resulted from the use of effective measures to control emissions in Germany and neighboring countries (Kierdorf and Kierdorf 2001).

Research conducted by Newman and Yu (1976) on the black-tailed deer (*Odocoileus hemionus columbianus*) from an industrial area northwest of Washington showed dental abnormalities and abnormal patterns of tooth wear associated with the occurrence of fluorosis in these animals. The levels of fluoride in the bones were 10–30 times higher than the concentration of this element in the bones of animals from reference areas (Newman and Yu 1976). Shupe et al. (1984), after examining the bones and teeth of deer (*Odocoileus hemionus columbianus*), moose (*Alces alces*), and bison (*Bison bison*), from Utah, Idaho, Montana, and Wyoming, observed changes in the bones and teeth of those animals, correlating with the amount of fluoride pollution in their habitats (industry and water with high fluoride levels).

Zakrzewska et al. (2005) conducted a study on F in the bones of red deer (*Cervus elaphus*) from an area of northwestern Poland in the 1990s, a period covering the opening of the Police chemical plant near the city of Szczecin (Poland) (Zakrzewska et al. 2005). Bone samples collected from animals in the area more exposed to F compounds (areas of Szczecin and Police) contained an average of 50% more F compared to samples from areas distant from the source of emission. Similar conclusions were reached by other authors who examined the mandibles of deer coming from areas exposed to the emissions of fluorine compounds and in the areas without any major industrial plants (Poland) (Machoy et al. 1995; Gutowska et al. 2004). Dąbkowska et al. (1995a, b) examined animal bones collected between 1982 and 1990 and showed that the reduction in production volume and modernization of the chemical plant in Police resulted in a reduction of emissions into the environment, which in turn resulted in lower fluoride content in the bones of animals in 1990 compared to samples from 1982 (Dąbkowska et al. 1995a, b).

Teeth are also recommended as an excellent material to study the level of intake of fluoride and a very good indicator of chronic exposure to this element (Kierdorf et al. 1993, 1996b, 1999; Vikøren and Stuve 1996a, b; Richter et al. 2011). In addition, damage to the teeth significantly correlates with the degree of damage to forests in which the tested animals dwelled (Zemek et al. 2006). The teeth with fluorosis were characterized by an opaque enamel, and in cases of severe fluorosis, the enamel became damaged or its surface reduced, and occlusal surfaces were subject to greater wear. This led to hypermineralization and ameloblast dysfunction and throughout the enamel striae of Retzius became strengthened (Schultz et al. 1998; Appleton et al. 2000; Kierdorf et al. 1993, 1996b, 2000a, b). Studies on the teeth of wild boar (*Sus scrofa*) originating from areas of the Czech Republic (Bohemia) and Germany (Saxony) showed a significantly higher content of fluoride in comparison with samples taken from animals originating from areas of western Germany (Kierdorf et al. 2000a, b). Also, teeth of the red and roe deer (*Capreolus*

capreolus) proved to be an excellent material for the analysis of environmental exposure to fluoride. Extending the research to teeth with dentine enabled a more precise determination of specific periods of exposure to fluoride during the life of the individual (Kierdorf et al. 1999; Richter et al. 2010). Schultz et al. (1998), after examining 545 red deer mandibles, showed the occurrence of severe fluorosis in more than 11% of the animals, accompanied by pathologically increased wear and fractures of the teeth, periodontal bone lesions caused by inflammation of the periosteum, and chronic osteomyelitis in the mandible. The strong occlusal abrasions resulted in the opening of the pulp chamber, forming periapical ulcers and eventually tooth loss, which according to the authors is an important factor reducing the lifespan of the animals (Schultz et al. 1998).

In addition to human activities, volcanic eruptions are a significant factor introducing fluorine compounds to the environment. This source of fluorine may affect organisms over much larger areas and at larger distances. Flueck and Smith-Flueck (2013) decided to examine the impact of these emissions using animals as bioindicators. The study involved red deer from areas about 100 km from the Puyehue-Cordon Caulle volcano a year after an eruption. The researchers recorded a level of fluoride in bones exceeding 5000 mg kg^{-1} and the occurrence of severe dental fluorosis, manifested in enamel hypoplasia, breakages, pitting, mottling, and extremely rapid ablation of entire crowns down to the underlying pulp cavities. Tooth loss reduced the physical condition of animals, and although a preliminary analysis of the water and volcanic ash showed no danger for living organisms, a study on ruminants as indicators of the contaminated ecosystem clearly demonstrated a 38-fold increase in the level of fluoride in bones during the first 15 months of exposure after the volcano eruption (Flueck and Smith-Flueck 2013) (Table 1).

7.3 Canids

Biomonitoring of environmental risks associated with fluoride pollution is usually based on samples of bones, teeth, and antlers from ungulates. However, medium-sized omnivorous mammals seem to be more suitable for this type of research, because their type of diet and longevity make them more similar to humans (Kay et al. 1975). Such animals include the red fox (*Vulpes vulpes*) and raccoon dog (*Nyctereutes procyonoides*). The red fox fulfills the conditions established for good bioindicators (Ellenberg 1991), which include large geographical coverage, but not a too large range, stable local population, fixed position in the food chain, and the ease of specimen collection via hunting. For these reasons, this species is often used in studies of various types of environmental pollution, including fluorine compounds (Palczewska-Komsa et al. 2014). Although both red fox and raccoon dog have many features that make them potentially ideal bioindicators (Apostoli 1992), there is little data on the concentration of F in the hard tissues of red foxes (Kalisińska and Palczewska 2007; Kalisińska and Palczewska-Komsa 2011; Palczewska-Komsa et al. 2014) and raccoon dogs (Palczewska-Komsa et al. 2014).

Table 1 Concentrations of fluoride in hard tissues of ungulates

Species	Tissue	Year	Fluoride (mg kg^{-1})	Place of collection	Reference
Roe deer *Capreolus capreolus*	Mandible $n = 112$	1986	43–901	5 localities in England and Scotland	Walton and Ackroyd (1988)
	Antler $n = 10$		1220–2010		
	Mandible $n = 39$	1985–1993	208–1026 (dw)	Harz mountains (Germany)	Kierdorf et al. (1995)
Moose *Alces alces*	Mandible $n = 1104$	1990–1993	>8000	The vicinity of seven Norwegian aluminum smelters (Norway)	Vikøren and Stuve (1996b)
Roe deer *Capreolus capreolus*	Mandible $n = 147$	1990–1993	>8000	Vicinity of seven Norwegian aluminum smelters (Norway)	Vikøren and Stuve (1996b)
Red deer *Cervus elaphus*	Mandible $n = 24$ (examined group)	1985–1993	(dw) 948–4680	N-Bohemian brown coal belt (the vicinity of the two towns: Karlovy Vary and Chomutov—examined group; Harz mountains, State of Lower Saxony—control group)	Kierdorf et al. (1996a)
	$n = 39$ (control)		208–1026		
Red deer (*Cervus elaphus*)	Mandible			The North-Bohemian brown coal belt (the vicinity of the two towns (Karlovy Vary and Chomutov) and Nejdek and forest district Eibenstock—examined groups; Harz mountains, State of Lower Saxony—control group)	Kierdorf et al. (1996b)
	$n = 27$, Karlovy Vary $n = 18$, Nejdek $n = 15$, forest district Eibenstock $n = 39$, control	1986–1993 1982–1990 1988, 1989 1985–1993	2754 ± 1088 1244 ± 523 883 ± 444 540 ± 227		
Red deer (*Cervus elaphus*)	Antler and pedicle $n = 18$		Antler (ba): Bohemia 845 ± 257 Control 206 ± 124 Pedicle (ba): Bohemia 1448 ± 461 Control 322 ± 157	North Bohemia (Czech Republic) and two uncontaminated areas in West Germany	Kierdorf et al. (1997)
Red deer *Cervus elaphus*	Mandible $n = 61$	1985–1993	>4000 (dw)	Ore mountains and their southern foreland, Czech-German border region	Schultz et al. (1998)

(continued)

Table 1 (continued)

Species	Tissue	Year	Fluoride (mg kg^{-1})	Place of collection	Reference
Roe deer *Capreolus capreolus*	Mandible Ruhr area $n = 76$	1955–1998	(dw) 150 (2-year-old specimen taken in 1997) 5724 (10-year-old specimen taken in 1957)	The federal state of North Rhine-Westphalia, Germany	Kierdorf and Kierdorf (2000b)
	Cologne area $n = 81$ Age range 1–11 years	1983–1998			
Roe deer (*Capreolus capreolus*)	Antlers	1932–1998	158–3713 dw	The eastern suburbs of Cologne, Germany	Kierdorf and Kierdorf (2000)
Wild boars *Sus scrofa*	Mandible and teeth $n = 47$	1995–1997	Mandible (dw): Bohemia 754.3 ± 149.6 Saxony 490.8 ± 135.1 Control 304.7 ± 91.0 Teeth (dw): Bohemia 382.1 ± 165.2 Saxony 125.0 ± 38.3 Control 33.6 ± 26.7	Fluoride-polluted areas in Bohemia (Czech Republic) and Saxony, Germany	Kierdorf et al. (2000a)
Roe deer *Capreolus capreolus*	Antlers $n = 167$	1951–1999	110–8178 (ba)	Industrialized Ruhr area, W Germany	Kierdorf and Kierdorf (2001)
Roe deer (*Capreolus capreolus*)	Antlers $n = 188$	1990–1999	113–11, 995 (ba)	14 areas of North Rhine-Westphalia, Germany	Kierdorf and Kierdorf (2002)
Roe deer *Capreolus capreolus*	Antlers $n = 116$	1948–2000	118–5428 (ba)	Industrialized area of Siegen, W Germany	Kierdorf and Kierdorf (2003)
Red deer *Cervus elaphus* Roe deer *Capreolus capreolus*	Mandible $n = 51$ $n = 175$	Hunting season 1998/1999	55–273 171–430	NW Poland	Gutowska et al. (2004)
Roe deer *Capreolus capreolus*	Mandible $n = 7$ $n = 7$	Early 1990s	(dw) 1374–3790 1719–3411	Fluoride-polluted area along Czech-German border	Richter et al. (2010)

(continued)

Table 1 (continued)

Species	Tissue	Year	Fluoride (mg kg^{-1})	Place of collection	Reference
Red deer *Cervus elaphus*					
Roe deer *Capreolus capreolus*	Antler $n = 141$	1960–2007	110–1210 (yearlings) 130–2340 (young adults) 250–2590 (older adults)	Area of Slovene thermal power plant of Šoštanj (Slovenia)	Jelenko and Pokorny (2010)
	Mandible $n = 220$	1997–2009	30.0–227 (fawns) 33.8–383 (yearlings) 61.5–1020 (adults)		
Roe deer *Capreolus capreolus*	Mandible $n = 157$ $n = 117$	1996–1997, 2009	Median (dw) 3147 350	Five counties in the northwestern part of the Czech Republic	Kierdorf et al. (2012)
Red deer *Cervus elaphus*	$n = 127$ $n = 72$	1996–1997, 2009	1263 288		
Red deer *Cervus elaphus*	Bone $n = 26$	2012	>5175 (dw)	100 km from the volcano: the Puyehue-Cordon Caulle (Chile)	Flueck and Smith-Flueck (2013)

dw dry weight, *ba* bone ash

One such study is the work of Kay et al. (1975), in which the analysis of the bones of coyotes (*Canis latrans*) from uncontaminated areas of North America showed an almost two times lower content of fluoride in samples when compared to those from femoral wild canids (32 red foxes and 18 raccoon dogs) from contaminated sites in northwestern Poland (Palczewska-Komsa et al. 2014). These studies confirm the results obtained by other authors pointing to increased accumulation of fluoride in the hard tissues of red foxes (Walton 1984) living in areas surrounding industrial plants emitting fluorine compounds into the atmosphere (Table 2).

7.4 Small Wild Mammals

A large number of biomonitoring studies on small mammals have demonstrated the importance of eating habits in selecting species for this type of research (Talmage and Walton 1991). Environmental studies on exposure to fluorine compounds have

Table 2 Concentrations of fluoride in hard tissues of selected canid species

Species	Tissue	Year	Fluoride (mg kg^{-1})	Place of collection	Reference
Coyote *Canis latrans*	Bone $n = 2$	1975	321 (dry weight)	Montana (USA)	Kay et al. (1975)
Red fox *Vulpes vulpes*	Mandible $n = 230$	–	283 (Aberdeen in Scotland) 1650 (aluminum plant, Anglesey) (dry weight)	Several areas within the United Kingdom (areas not contaminated and areas near aluminum plant, Anglesey)	Walton (1984)
Red fox (*Vulpes vulpes*)	–	Hunting seasons 2004/2005	514 (group I) 389 (group II)	West (group I) and north (group II) of Szczecin, Western Pomerania (Poland)	Kalisińska and Palczewska (2007)
		2005/2006	(dry weight)		
Red fox (*Vulpes vulpes*)	Teeth (first molars of the permanent teeth) $n = 35$	The hunting seasons 2004/2005 2005/2006	297 (6–12 months, $n = 11$), 385 (12–20 months, $n = 10$), 654 (>20 months, $n = 14$) (bone ash)	West Pomeranian and Pomeranian Voivodeships (Poland)	Kalisińska and Palczewska-Komsa (2011)
Red fox *Vulpes vulpes*	Femur bone $n = 32$	The hunting seasons 2008/2009, 2011/2012, 2012/2013	175.9–3668.1 (dry weight)	Area of the north-western Poland	Palczewska-Komsa et al. (2014)
Raccoon dog *Nyctereutes procyonoides*	$n = 18$	2009/2010, 2011/2012, 2012/2013	83.7–1190.3 (dry weight)	Area of Warta Mouth National Park	

Concentrations in mg kg^{-1} bone ash or dry weight, maximum value or range reported in respective references

been carried out on small wild mammals such as wood mice (*Apodemus sylvaticus*), shrew (*Sorex araneus*), and field vole (*Microtus agrestis*) (Shore 1995).

Boulton et al. (1997) conducted a study on the impact of fluoride on the appearance of the teeth of the short-tailed field vole from fields affected by different levels of industrial fluoride pollution. On the incisors of the voles consuming relatively low doses of fluoride, the changes were largely limited to the distortion of enamel pigmentation, as in the case of molars. In areas with a high degree of fluoride pollution, changes were observed in the composition and strength of both the enamel and dentin; incisors showed hypoplasia and enamel pigmentation, while the occlusal surfaces of the molars exhibited severe erosion and exposed dentin (Boulton et al. 1997). Also in this case, the amount and rate of accumulation of

fluorine in hard tissue were dependent on the age of the tested animals. After birth, the young did not show any change in the construction of the incisors, but after weaning, teeth showed significant morphological changes and serious damage. The rate of accumulation of fluoride in bones showed age-related changes rapidly in young individuals, whereas in adults, it reached a relative equilibrium, due to the slowdown in the animal's growth (Boulton et al. 1994).

8 Fluoride in Wild and Domestic Birds

Due to increasing anthropogenic pollution, it is very important to be able to identify areas contaminated with fluoride through biomonitoring based on bird bones. This type of research reflects the natural geochemical background and the effects of human activity. However, as most birds are migratory animals, living in different environments and with different feeding behaviors, it is difficult to use these species as indicators. The concentrations of fluoride in the bones of wild birds are characterized by a very large interindividual and interspecies variability.

About 99% of fluorine present in the bird's body is stored in the bones. The amount of fluorine deposited in bones is age and diet dependent. In the skeleton of domestic ducks (*Anas platyrhynchos f. dom.*), 28.7% of fluorine is deposited in the skull and 69.8% in other bones. Birds seem to be able to tolerate fairly high doses of fluoride, which has been proven experimentally in American kestrel's (*Falco sparverius*) fed doses of 1120 and 2240 mg kg^{-1} F^{-}. Those doses did not interfere with the development of internal organs, including the brain, although decreased bone resistance to fractures (Bird et al. 1992). For this reason, the birds could be suitable for the biomonitoring of fluoride contamination.

Fluoride absorption and incorporation into the bone are strongest during the rapid growth phase of the birds. The normal concentration of fluoride in the bones of chickens (*Gallus gallus f. dom.*) and other birds can range from 500 to 1000 mg F^{-} kg^{-1} dry weight (Xie and Sun 2003; Committee on toxicology 1993). Higher concentrations induce bone fluorosis. However, studies on the bones of the black heron (*Egretta ardesiaca*) living in the vicinity of a phosphate processing complex in the United States showed a level of 1700 mg F^{-} kg^{-1} dw (Henny and Burke 1990). Gulls (Larinae) are vulnerable to exposure from high doses of fluoride when they reside in the vicinity of aluminum smelters. A study on migratory species of gulls has shown that measurements of F concentration in eggshells are useful for monitoring the local exposure of wild birds to fluoride. In contrast, the volume of eggs, shell thickness, and percentage of fertilized eggs are not good indicators of the exposure of seagulls to fluorine compounds (Vikøren and Stuve 1996a, b). Interestingly, a study on the tissues of the Adélie penguin (*Pygoscelis adeliae*) living on an island in Ardley Maxwell Bay showed an extremely high content of F^{-} in the range from 832 to 7187 mg kg^{-1}, while radiographs provided no evidence of skeletal fluorosis. Very high concentrations of fluoride in the bones of penguins can be explained by the diet of these birds, with an 80% share of krill in which the average fluoride

concentration in soft tissue is more than 1200 mg kg^{-1}, while in the shell, it is even higher than 3800 mg kg^{-1}. It is likely that penguins and other seabirds that live in the waters of Antarctica are extremely resistant to high concentrations of fluoride in their tissues, as part of the adaptation of these animals to an environment with a high concentration of fluoride (Xie and Sun 2003). Moreover, in the white-faced heron (*Egretta novaehollandiae*) and in different species of cormorants (*Phalacrocoracidae*) living in industrially uncontaminated regions of New Zealand, the average fluoride concentration is up to 35 mg kg^{-1} of ash (670–1580 mg kg^{-1} dw) (Robertson and Lock 1994).

Studies show that treating chickens with sodium fluoride containing water for several weeks at doses ranging from a few to several mmol L^{-1} increases their rate of bone maturation and secondary mineralization. Such changes can have a significant impact on bone density and fragility (Lundy et al. 1992). A postmortem study showed that the supplementation of drinking water with fluoride at a concentration of 6–20 mg L^{-1} for 17 weeks of growth, and then for 57 further weeks, resulted in a linear increase in weight gain and a fluoride content in the femur of laying hens. In that study, the addition of fluoride to drinking water had a significant effect on the production of eggs, but not the strength of the eggshell. Histopathological examination showed no changes in the liver or kidneys. Data from that study indicated that laying hens tolerated a fluoride intake of 4.453 mg day^{-1} for up to 74 weeks (Coetzee et al. 1997). Other authors have demonstrated that a long-term intake of fluorine at up to 300 mg kg^{-1} body weight had no negative effects on the morphology nor mechanical properties of bones (Suttie et al. 1984) and that fluorine had a positive effect on bone strength at lower doses, with an adverse influence only at higher doses (Turner et al. 1992).

There is an interesting study showing that in chickens fed F for 50 days at a concentration of 110 mg kg^{-1} body weight, there were significant and strongly age-related differences between the content of fluoride in the bone tissues. The compact bone fluorine level was 0.192 mg g^{-1} and increased with age up to 0.336 mg g^{-1}. Cancellous bone fluoride levels rose with age, from 0.174 to 0.224 mg g^{-1}. Bone marrow fluorine remained between 0.009 and 0.012 mg g^{-1}, with the lowest concentrations in the cartilage; at 0.005 mg g^{-1}, this value was decreasing during the study. The authors noted that the concentration of fluoride in the cartilage negatively correlated with the level in the cancellous bone and marrow (Dołegowska 2002; Dołegowska et al. 2003). In summary, the increase in the content of fluorine in both cortical and cancellous bone correlated with intensive processes of bone formation and remodeling in young chickens. The slow decline of the fluorine content in the articular cartilage is probably due to an age-related decrease in intensity and specificity of calcification processes within the cartilage.

The main problem in cage poultry breeding is the development of dyschondroplasia, which greatly reduces the economic results of farms. Tibial dyschondroplasia changes the cartilage at the base of the tibia of fast-growing broilers. Soft bones can thicken at the base, deform, and break up. Inflammation of the tibia can lead to problems with mobility, dehydration, and death. Prevention of

the disease consists in slowing down the growth of chickens at the beginning of breeding.

Treatment with sodium fluoride increases the strength of the humeral bones and in tibial fractures, which is a consequence of the increase in the marrow ash fluoride levels. At the same time, this supplementation did not result in a decreased quality and efficiency of egg laying (Merkley 1981). Even small concentrations of F (e.g., 0.46 mg kg^{-1} dw) are likely to increase the hardness of the bone, and in addition the chicks grow better if a feed containing sodium fluoride is also added with the appropriate proportions of calcium phosphate (Shim et al. 2011). On the other hand, the toxic effects of fluoride in the diet lead to the inhibition of growth of chickens due to a decreased appetite and reduced feed intake, which has a potential impact on the growth and health of the animals (Choubisa 2010). It has been found that doses of 1000 and 1300 mg kg^{-1} dw fluoride decreased feed intake, weight gain, and efficiency of egg production. Long-term administration of high doses of sodium fluoride, however, does not lead to a permanent loss of value of production, because the changes related to the lack of appetite subside within 6 months of cessation of exposure. An increase in fluoride in the diet is accompanied by a reduction in the volume of eggs with a tendency for a better quality eggshell (resistance to deformation and fracture) and also a drop in the retention of phosphorus, magnesium, and calcium levels, resulting in less calcium available for bone formation. There is also a slowdown in yolk synthesis (Guenter and Hahn 1986).

Experimental studies show that differences in the content of fluoride in the bones of poultry are gender related due to physiological factors associated with the production of eggs. Bone fluoride levels are higher in hens than cocks, due to an increased metabolism of minerals in the bones of females during egg production. Calcium is removed from bones to create eggshells. The increased absorption of calcium is also accompanied by increased fluoride absorption. Probably, fluoride moves with calcium to the bone, but when the calcium is removed from bones to form the eggshell, fluoride remains, and the concentration proportionally increases with each cycle of egg production.

A 2-year experiment proved that the concentration of fluoride in the bones of chickens is significantly higher after puberty in relation to young chickens (Michel et al., 1984). Higher concentrations of fluoride were recorded in the bones of females of other birds, e.g., owls, in the breeding season with a diet containing 200 mg F^- kg^{-1} dw (Pattee et al. 1988), and gulls during the breeding season living near an aluminum smelter (Vikøren and Stuve 1996a, b). Such dependences were not observed in free-living urban pigeons (Salicki and Kalisinska 2006).

There are significant differences in bone fluoride levels in birds depending on the type of the bone. It was shown that in spinal and cranial bones, fluoride concentrations are higher than in the long bones and higher in the compact bone than in cancellous bone (Xie and Sun 2003). One should not forget that the amount of fluoride accumulation in the bones of birds is also a function of age (Henny and Burke 1990).

Most fluoride accumulated in the body of the birds is found in the bones. However, fluorides are also present in the blood and soft tissues and then excreted

in the feces and to a lesser extent in the mucus of salt glands located above the eyes of certain birds, especially in seabirds (Culik 1987).

In total, there are two ways to eliminate fluoride from circulation: excretion by the kidneys and deposition in the bones and eggshells. Interestingly, in chickens, even at a concentration of F^- in the diet reaching 1300 mg kg^{-1}, the amount of fluoride in the egg white did not exceed 1 mg kg^{-1}.

The addition of aluminum salts in the diet causes a reduction in fluoride levels in the liver and kidney, but not in the pectoral and tibial muscle in birds (Hahn and Guenter 1986). The results of studies on impaired reproductive efficiency of owls (*Otus asio*) in areas contaminated with fluoride showed that despite having no significant differences in the hematocrit value, hemoglobin, plasma calcium levels, nor alkaline phosphatase, between control and treatment groups, the addition of 200 mg kg^{-1} of sodium fluoride to the diet of the birds produced a significant reduction in the volume and weight of the eggs. One-day-old owls weighed 10% less, and their tibiotarsus was significantly shorter in comparison to the control group. In addition, in the group of owls fed with sodium fluoride at 40 mg kg^{-1}, there were significantly higher serum phosphate levels compared to the control group (Hoffman et al. 1985).

In another study on 7-day-old chicks of American kestrels (*Falco sparverius*) fed daily with fluoride supplementation at concentration of 0 (control), 1120, and 2240 mg kg^{-1}, there were no significant differences between the three groups in the length of the duodenum, the lengths of the jejunum and the ileum, and the weight of the adrenal glands, brain, stomach, spleen, heart, kidney, liver, pancreas, and pectoral muscle. Treatment with NaF resulted in a significant reduction in the resistance of bones to fractures (Bird et al. 1992). On the other hand, other authors report pathological effects of fluoride intake on the renal function (Bai et al. 2010) and thymus (Chen et al. 2010) in chickens.

In China, chicken farms suffered considerable economic losses due to fluorosis associated with the use of a feed additive containing about 300 mg kg^{-1} fluorine and in some cases up to 2000 mg kg^{-1} (Liu et al. 2003). This has resulted in numerous reports by local researchers to help in understanding the cellular mechanism of fluoride toxicity. Some authors indicated a decrease in the percentage of T lymphocytes caused by oxidative damage and apoptosis resulting from the toxic effects of fluoride on the lymphoid tissue in the avian caecum (Chen et al. 2009; Liu et al. 2012). Others showed that feeding broilers with feed containing NaF at 800 and 1200 mg kg^{-1} induce apoptosis of lymphocytes via DNA damage mechanisms and also decrease the synthesis of Bcl-2, an integral membrane protein on the outer membrane of mitochondria. An overexpression protects cells from apoptosis in response to different stimuli, since the role of Bcl-2 is to block the release of cytochrome c from mitochondria (Liu et al. 2013).

The results of yet another work proved that high doses of fluoride caused severe oxidative stress and damage to the spleen cells of broiler chickens on a diet containing 800 and 1200 mg F^- kg^{-1} for 42 days. Those chickens experienced an increase in plasma concentrations of fluoride and damage to the mitochondria, a decrease in superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px), and

an increased level of malondialdehyde as a product of lipid peroxidation in the spleen (Chen et al. 2011). In contrast to those results, other experiments showed that a 3-week diet containing fluoride at 300 mg kg^{-1} had no effect on the activity of L-gulonolactone oxidase, the resources of ascorbic acid in the selected tissues of chickens (plasma, kidney, liver, muscle, and adrenal gland), and the resistance to stressors (Maurice et al. 2002).

Birds have an incomplete blood-brain barrier, which increases the likelihood of penetration of various substances into the brain (Kuenzel et al. 1997). It appears that an excess of fluoride is deposited in soft tissues, especially in the brain of birds; it constitutes a permanent biologically inactive deposit that the body is not able to remove.

There are no known adaptive mechanisms to prevent or reduce the toxicity of fluoride in birds. One can only presume the important role of calcium ions, which may bind F and form insoluble salts, such as CaF_2 (Monsour and Kruger 1985). This was confirmed by studies that found a surprisingly high concentration of F in the brains of common merganser (*Mergus merganser*) in northwestern Poland. The highest mean concentration of fluoride in this species was observed in bones (430 mg kg^{-1} dw) and the pineal gland (780 mg kg^{-1} dw) and the lowest in the brain (170 mg kg^{-1} dw), in both adult and young mergansers living in areas located between a fertilizer production plant and a power plant (Kalisińska et al. 2014).

Pathological changes caused by the toxic effects of fluoride on the brains of migratory birds may have serious consequences for their populations. Experiments have shown that fluoride has neurotoxic properties and adversely affects the functioning of the brain. Even at low doses, fluoride contributes to the induction of apoptosis of neurons and formation of oxidative stress, increasing the amount of free radicals and lipid peroxidation in the brain (Choi et al. 2012). On the other hand, in laying hens, phenylmethylsulfonyl fluoride (PMSF)—an inhibitor of serine proteases—reduces the risk of organophosphorus neuropathy which leads to severe paralysis of the peripheral nerves induced by toxic effects of tricresyl phosphate (TOCP), a pesticide that may be present in feed (Song et al. 2009; Mangas et al. 2014). In addition, using a feed with a combination of fluoride at a concentration of 10 mg kg^{-1} accompanied by vitamin K and calcium also helped to achieve a 20% reduction in the loss of bone structures, thus preventing osteoporosis in laying hens (Fleming et al. 2003).

9 Summary

Fluoride is ubiquitous in the environment as a particulate in the air and in ionic forms in surface and groundwaters, soil, and sediments. Its natural circulation in nature is accompanied by processes related to the economic activities of man (Shaw 2012). In light of the data we have presented in this chapter, it seems necessary to monitor the presence of fluoride in the environment, as its uncontrolled intake may pose a serious risk for human and animal health (Machoy et al. 2002). The results of various studies

indicate the usefulness of the determination of F in hard tissues of wildlife for monitoring the environmental F contamination, as well as its role in the assessment of the effectiveness of measures taken to reduce F emissions, e.g., from industrial sources (Kierdorf and Kierdorf 2000b).

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Chapter 16
Lead, Pb

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Abstract We present literature data on the concentrations of lead (Pb) in various organs of terrestrial mammals and birds. The presented data have been summarized in terms of animal species, organs, and the approximate year of sampling and area. Studies on Pb in the muscles of various mammalian species indicate that Pb levels in the environment are not as high as 25 years ago, and in most of the non-contaminated areas they do not exceed 1 mg kg^{-1} dw in the muscle of herbivorous or predatory mammals. Bioindication research helps to determine not only the history and the present state of lead pollution but also allows an understanding of the phenomenon of the circulation of lead in nature, as well as in prediction of the risk of its presence in the trophic chain. Long-term bioindication research conducted on the bones and soft tissues of mammals and birds, as well as the eggs and feathers, indicates the usefulness of this type of material for evaluating the state of the environment.

1 Introduction

Lead (Lat. plumbum, Pb) is believed to be the first metal smelted by humans (Lessler 1988). From the very beginnings of lead smelting, anthropogenic lead dust has spread in the atmosphere by air currents, reaching areas as distant as Greenland and leaving clear traces in the environment. The isotopic composition of lead particles preserved under the layers of ice in Greenland confirms their anthropogenic nature and indicates their place of origin, thanks to the unique combinations of lead isotopes in each lead ore (Gale and Stos-Gale 1981). Only the first of the isotopes, ^{204}

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Pb, is always present in the same amount, while the levels of the remaining three isotopes vary: ^{206}Pb (1.35–1.5%), ^{207}Pb (23.5–27%), and ^{208}Pb (20.5–23%) (ATSDR 2013).

After the introduction of silver coin minting in the Mediterranean region (approximately 680 BC), relying on the use of litharge (lead oxide) in silver smelting (cupellation), the levels of anthropogenic lead began to clearly rise in the successive ice layers of Greenland (Nriagu 1983; Rosman et al. 1997). Lead also became commonly used in various areas of daily life. For centuries, lead acetate served as a sweetener, wine preservative, an inhibitor of cider fermentation, an anti-inflammatory agent, and an abortifacient. Other lead compounds, such as galena (lead sulfide), cerussite (lead carbonate), and litharge, were used as drug ingredients. Metallic lead, thanks to its plasticity and softness, was used for making pipes, roofs (lead sheets are still being used for this purpose), pots, coins, bullets, weights, and many other common objects.

The toxic effects of lead have been known for centuries, with the first description of lead poisoning found in "Alexipharmaca," a poem by Nikander from the second century BC (Waldron 1973). Despite the accumulated knowledge about its harmful effects, lead was responsible for the longest-lasting environmental poisoning epidemic in human history. In the twentieth century, the discovery of anti-knock properties of tetraethyl lead and the use of leaded petrol-fueled engines resulted in a rapid increase in the concentration of lead in the atmosphere. Although leaded petrol has been removed from use in many countries (e.g., in 1976–1986 in the United States, in 2005 in the European Union (EU)), lead compounds are still being used in aviation fuels. In addition, although the sale of lead paints was banned in the United States in the late 1970s, and in the EU in 1992, they are still used in the restoration and preservation of historic buildings (including the interiors) and art (Directive EP 1998; Statutory Instruments 2005, 2009; European Commission 2008).

The current presence and toxicity of lead makes it the second most dangerous environmental poison according to ATSDR Priority Substance List (2013). No lowest safe concentration exists for lead, which contributes to 0.6% of the global burden of disease (WHO 2009). Although the carcinogenic action of lead compounds has not yet been fully proven (Mccabe et al. 2001), it has been shown that lead can contribute to the induction of neoplastic processes by the inhibition of DNA repair enzymes (Rajaraman et al. 2006). The International Agency for Research on Cancer (IARC) has classified inorganic lead compounds to Group 2A: Probably carcinogenic to humans and lead to Group 2B: Possibly carcinogenic to humans (IARC 2016).

2 General Properties of Lead

Lead is a carbon group element with atomic number 82, group IVa, atomic weight 207.19, density 11.340 g cm^{-3} at 20°C, and melting point 327.46°C. This element can occur in oxidation states II and IV. It is a soft metal (hardness 1.5 Mohs), with a bluish-white color and easily oxidizes in the air, which results in its surface being coated with hydroxide and carbonate that prevent further oxidation (US DHHS 1999).

3 Lead in Nature

Environmental lead can be divided into primary and secondary deposits. The former became the component of rocks at the time of their formation, while the secondary lead (or radiogenic) derived from the radioactive decay of uranium and thorium (Kabata-Pendias and Pendias 1999). Lead occurs naturally in igneous rocks and clay (at 10–40 mg kg^{-1} (or ppm, part per million)) and at much lower levels in alkaline igneous rocks and carbonate sediments (0.1–10 ppm) (Kabata-Pendias and Pendias 1999). Feldspar and mica are richest in this element, due to lead's ability to replace potassium in those formations. The most important minerals of lead include galena (PbS), anglesite ($PbSO_4$), cerussite ($PbCO_3$), pyromorphite ($Pb_5(PO_4)_3Cl$), and mimetite ($Pb_5(AsO_4)_3Cl$). Lead can be found in the deposits of many metals, including zinc, silver, and gold. Most commonly, it is derived from lead sulfide.

Lead has potent chalcophilic properties. The average lead concentration in coal is 25 ppm, with the maximum content in ash following combustion exceeds 2000 ppm. Ash from oil may contain 500 ppm of lead on average (Kabata-Pendias and Pendias 1999). Lead exhibits low migration into soils; hence its distribution there reflects its content in rocks and anthropogenic influences in surface layers (Adriano 2001; Hettiarachchi and Pierzynski 2004). The common occurrence of zinc and lead ores, as well as their sulfides and galena, have resulted in the formation of joint deposits via post-magmatic processes. Metasomatic deposits found in limestone and dolomite are the most important category of zinc and lead deposits. These include mesothermal deposits whose galena is often argentiferous and may also contain gold. Many of these fields are substantial and contain significant resources (from 10 to 15 million tons), including those found in Leadville, Colorado (USA), Broken Hill in Northern Rhodesia (Africa), and Nerchinsky District in Zabaykalsky Krai (Russia). Telethermal deposits are characterized by ore mineralization occurring usually in certain layers that are themselves layered. The largest deposits of this kind in the world can be found in the mainly zinc-containing "Joplin District" in the USA (parts of Missouri, Oklahoma, and Kansas) and the mainly lead-containing deposits in southeastern Missouri. The largest European deposits are found in Poland, in the Silesian-Cracow area (US Geological Survey 2015).

In 2014, the global mine production of lead was expected to be about 5.50 million tons, with production increases in Australia, China, and the United States. The International Lead and Zinc Study Group (ILZSG) forecast global refined lead production to increase slightly from that in 2013, to 11.3 million tons, primarily driven by increases in Australia, Belgium, China, India, Italy, and South Korea. ILZSG projected global lead consumption to increase slightly in 2014 from that in 2013, to 11.3 million tons, partially owing to an increase in China, and that global refined lead production would exceed consumption by 38,000 tons (U.S. Geological Survey 2015).

The lead-acid battery industry accounted for about 90% of the reported US lead consumption during 2014. Lead-acid batteries were primarily used as starting-lighting-ignition (SLI) batteries for automobiles and trucks and as industrial-type batteries for standby power for computer and telecommunications networks and for motive power. During the first 9 months of 2014, 93.5 million lead-acid automotive batteries were shipped by North American producers (U.S. Geological Survey 2015).

Atmospheric lead is a result of industrial and traffic-related emissions of dust, including significant quantities from coal combustion (WHO 1995; Marcus and McBratney 2011). According to WHO (2000), the average concentration of lead in the air in and around crop fields reaches 0.1–0.3 μg m^{-3} and about 0.5 μg m^{-3} in the vicinity of villages and towns. Near large European cities, it ranges from 0.5 to 3.0 μg m^{-3}. The most lead-polluted air is found around mines and metal smelters, where it can reach a dozen or so μg m^{-3} (WHO 2000). Although the use of tetraethyl lead—the most prevalent compound of this metal in the atmosphere—had been eliminated from fuels with the introduction of the US ban on the sale of leaded petrol in 1986, the concentration of this element in the atmosphere continues to grow, particularly in countries with developed metallurgical and mining industries, as well as from the related recycling of various products, e.g., batteries (Statutory Instruments 2005, 2009). In Europe, the ban on the sale of lead-containing fuel has been in force since 2005, based on the Directive of the European Parliament relating to the quality of petrol and diesel fuels (Directive EP 1998). An additional source of lead in the atmosphere is secondary dust coming from asphalted streets, parking lots, and sports fields with surfaces made of polyvinyl chloride.

Lead is also released from natural sources as a result of natural mobilization during volcanic activity and the weathering of rocks. The major natural sources of emissions into the air are volcanoes, airborne soil particles, sea spray, biogenic material, and forest fires. A recent study estimates emissions from natural sources between 0.22 and 4.9 million tons per year (UNEP 2010). The total emissions and distribution by sources vary considerably among countries. Overall emissions of lead decreased by about 95% over the 21-year period from 1982 to 2002, falling from about 54,500 tons per year in 1982 to about 1550 tons in 2002. The significant reduction in lead emissions was mainly due to restrictions and bans on the use of leaded petrol for vehicles and also implementation of improved air pollution controls (UNEP 2010).

Along with other air pollutants, lead falls on the surface layer of the ground and from there is absorbed into the deeper layers together with rainwater. It accumulates in soils, and due to the lack of biodegradation, this is where it reaches the highest environmental concentrations. Lead-contaminated soil becomes an indirect source of lead for humans, via plants growing near roads with heavy traffic or in the vicinity of current or former mines and smelters (Marcus and McBratney 2011). The bioavailability of lead in the soil depends on its pH; acidic soil increases the bioavailability of lead and its penetration into plants, while neutral soil pH reduces the absorption of heavy metals by flora. In addition, the bioavailability of lead is raised by high zinc concentrations, triggered by low soil pH (Alvarenga et al. 2014; Wuana and Okieimen 2011).

The major source of direct lead release to soils is the use of ammunition. In 2003 the total global consumption of lead for ammunition was about 120,000 tons. Ammunition is partly used for hunting and partly in shooting ranges, where the lead is either accumulated at the range or collected for recycling. Moreover, lost lead shots may poison waterfowl and other birds ingesting the shots. Terrestrial environments in various countries are also exposed to lead present in paints, balancing weights for vehicles, sheathing of cables left in the ground, and lead batteries. Large amounts of lead are directed to landfills and waste dumps with discarded products and residues from mining and base metal production (UNEP 2010).

Lead may be present on the surfaces of leaves and other plant parts due to deposition from the atmosphere. Plants can also take up lead from contaminated soils and retain most of it in the roots or transport it to other parts. The bioavailability of lead in soils is limited due to the strong adsorption of lead by soil organic matter; however, this availability may increase with a decrease in pH and organic matter. It also depends on soil moisture and type of soil amendments. For example, the addition of calcium and phosphorus to the soil reduces the bioavailability of lead, while the addition of K_2EDTA may increase lead uptake. Finally, some plant species have a high sensitivity to lead, while others exhibit a high tolerance. The potential use of plants to remediate contaminated soil has recently received a great deal of interest, since heavy metal contamination of soil is a serious problem in industrial and postindustrial areas (Henry 2000).

Lichens and funghi are excellent bioacumulators of trace elements, since the concentrations found in their thalli can be directly correlated with those in the environment. Some of them are able to accumulate heavy metals at very high concentrations without showing visible pathological symptoms (Baranowska-Bosiacka et al. 2001).

Plants can accumulate lead in those parts considered edible for herbivores and humans, which is a serious problem in many parts of the world. Dietary exposure to lead for adult consumers in 19 European countries ranges from 0.36 to 1.24 μg kg^{-1} body weight (bw) per day (lower bound for a country with lowest average exposure—upper bound for a country with highest average exposure) and from 0.73 to 2.43 μg kg^{-1} bw per day for high consumers, respectively. Overall, cereals and vegetables (potatoes) are the most significant sources of lead exposure in the general European population (EFSA 2010).

Water, both on the surface and in the ground, is a source of lead mainly as a result of human industrial activities. Surface waters may accumulate lead from precipitation in air-polluted areas or when it is washed out with rain from the soil, but the most lead-contaminated waters are found near industrial plants releasing polluted wastewater or in areas of crops fertilized with nitrogen agents contaminated with lead (WHO 1995). Drinking water also may contain trace amounts of lead due to outdated water supply systems, where pipes of internal water supply systems, welds, valves, and house connections may contain lead (WHO 1995). In many European countries, lead systems are used in many buildings, especially in the older districts of large cities (Hayes and Skubala 2009). In recent years, numerous studies have shown that exposure to even relatively low concentrations of lead in the water, within the limits of 25–50 μg L^{-1}, previously regarded as harmless to human health, do increase the concentration of lead in the blood. As a result, the experts of the World Health Organization have concluded that concentrations of lead in water intended for drinking should not exceed 10 μg L^{-1} (WHO 2011).

4 Lead Accumulation and Toxicity in Humans

Lead enters the human body primarily through the gastrointestinal tract and respiratory system and is then transported to all tissues via the blood. For this reason, lead poisoning and determination of exposure in general and occupationally exposed populations are measured by the whole blood lead levels (Pb-B) (WHO 1995). However, this good indicator of current exposure to lead does not directly reflect levels in the brain (Lidsky and Schneider 2003; White et al. 2007; Baranowska-Bosiacka et al. 2011). Lead easily penetrates the blood-brain barrier, reaching much higher concentrations in the cerebrospinal fluid than in the whole blood. This is due to difference in half-life period between the places of deposition; in the blood it is about 35 days, while in the brain it is about 2 years, and in bones from 1 to 30 years (Conti et al. 2012a). In addition to the skeletal system, background levels of lead accumulate in the liver (1 mg kg^{-1}), kidney (0.8 mg kg^{-1} in the cortex and 0.5 mg kg^{-1} in the core), and then in the ovaries and pancreas (0.4 mg kg^{-1}), spleen (0.3 mg kg^{-1}), prostate and adrenal glands (0.2 mg kg^{-1}), brain and adipose tissues (0.1 mg kg^{-1}), testes (0.08 mg kg^{-1}), heart (0.07 mg kg^{-1}) and skeletal muscle (0.05 mg kg^{-1}) (Giel-Pietraszuk et al. 2012).

Inorganic lead is not transformed in the body, while tetraalkyl compounds are dealkylated in the liver. Two thirds of inorganic lead is excreted with urine and in 1/3 via bile into the intestine and further excreted in the feces. Small amounts, physiologically irrelevant for the body, are excreted in sweat, milk, and saliva and accumulate in the hair and nails. Di- and mono-alkyl derivatives, resulting from the dealkylation of tetraalkyl lead compounds, are excreted primarily in the urine. Inhaled lead is either exhaled or moved with discharge into the gastrointestinal tract, where the particles not absorbed in the intestines are excreted in the feces (Baranowska-Bosiacka and Chlubek 2006).

Currently, researchers focus particularly on the neurotoxic actions of lead (Rao Barkur and Bairy 2015; Sanders et al. 2015). These studies tend to propose an ever lower "safe threshold concentration" of this element. Although in 1991 the American Center for Disease Control (CDC, United States Department of Health and Human Services) lowered the safe threshold concentration of Pb-B to 10 μg dL^{-1} (WHO 1995), followed by 5 μg dL^{-1} for children and pregnant women (CDC 2012), a lot of data indicates that even lower concentrations pose a threat to health (CDC 2004, 2005, 2007). Some researchers argue that there is no such thing as "the safe level of lead." This means that at each concentration of lead in the body, we may expect irregularities in the biochemical processes in many organs, particularly in the nervous tissue (Koller et al. 2004). In addition, this metal has been found to accumulate in some tissues/organs from which it may be released under certain conditions (pregnancy, osteoporosis, hormonal disorders). This may lead to increased blood lead levels and consequently higher brain levels. Even the bone pool of lead, previously considered a permanent place of deposition, can be mobilized according to a recent study (Conti et al. 2012b; CDC 2004).

For lead risk assessment and follow-up of time trends, there is a need for adequate information on exposure. The neurotoxic impact of very low levels of prenatal lead exposure (below 5 μg dL^{-1}) has been observed in infants and very young children, which suggests a revision of established health guidelines for prenatal exposure to lead (CDC 2012).

Acute lead poisonings, such as those resulting in encephalopathy (70–100 μg dL^{-1}), are rare nowadays. However, as recently as 2009–2010, 400 children died from lead poisoning in two villages in the province of Zamfara in northwestern Nigeria in Africa. Thousands of local children and adults are still seriously ill due to lead contamination from illegal gold mining, undertaken with the simplest primitive methods, with no safety precautions against the relatively high proportion of lead in gold ores (Moszynski 2010; Dooyema et al. 2012; Plumlee et al. 2013).

The toxicity of lead affects many organs, the most sensitive being the brain, blood, and kidneys (Baranowska-Bosiacka and Chlubek 2006). Its hematoxicity is associated with the inhibition of heme synthesis, leading to anemia; here, lead inhibits the activity of δ-aminolevulinic acid dehydratase (ALAD) and ferrochelatase, which catalyzes the insertion of ferrous iron into protoporphyrin IX, yielding heme. A reduction in their activity leads to the accumulation of δ-aminolevulinic acid (ALA) and erythrocyte protoporphyrin in the blood and an increase in the level of porphyrins in the urine and feces (Giel-Pietraszuk et al. 2012). The blood lead level, which triggers ALAD inhibition and an increase in the concentration of free erythrocyte protoporphyrin, is about 20–30 μg dL^{-1}. The first symptoms of anemia occur at concentrations higher than 50 μg dL^{-1}. Nephropathy, with a typical atherosclerosis, glomerular atrophy, and interstitial fibrosis, develops at a concentration greater than 60 μg dL^{-1} (Giel-Pietraszuk et al. 2012).

5 Lead Accumulation and Toxicity in Birds and Mammals

Many factors, such as age, sex, physiological status, diet, dose, and exposure time, affect the absorption of lead in birds. Lead levels in tissues causing physiological dysfunction, the clinical symptoms of poisoning, and death vary between species. A comprehensive study on interpreting tissue concentration of environmental contaminants (Nelson Beyer and Meador 2011) indicates the background concentration of lead in birds to be <20 μg dL^{-1} in blood, <2 mg kg^{-1} wet weight (ww) in the liver and kidneys, and <10 mg kg^{-1} dry weight (dw) of the bone in birds.

For birds in general, liver lead concentrations within the clinical poisoning range (≥ 6 mg kg^{-1} ww) suggest lead poisoning. Bone lead concentrations of ≥ 20 mg kg^{-1} dw are considered to suggest excessive exposure. Because of the rapid uptake and slow release of lead from the bone, bone concentration can be used to determine the geographical patterns of poisoning in populations. The suggested threshold of increasing severity of effects for Anseriformes are 20–50 μg dL^{-1} in blood and two <6 mg kg^{-1} ww in the liver and kidney (subclinical poisoning); 50–100 μg dL^{-1} in blood, 6–10 mg kg^{-1} ww in the liver, and 6–15 mg kg^{-1} ww in the kidneys (clinical poisoning); and >100 μg dL^{-1} in blood, 10 mg kg^{-1} ww in the liver, and >5 mg kg^{-1} ww in the kidneys (severe clinical poisoning). Suggested thresholds for pigeons and doves (ordo Columbiformes) are $20 < 200$ μg dL^{-1} in blood, two <6 mg kg^{-1} ww in the liver, and two <15 mg kg^{-1} ww in the kidneys (subclinical poisoning); 200–300 μg dL^{-1} in blood, 6–15 mg kg^{-1} ww in the liver, and 15–30 mg kg^{-1} ww in the kidneys (clinical poisoning); and >300 μg dL^{-1} in blood, >15 mg kg^{-1} ww in the liver, and >30 mg kg^{-1} ww in the kidneys (severe clinical poisoning). Lead concentrations in mammalian blood and soft tissue are useful as a biomarker of acute lead poisoning, whereas lead in the bone is more relevant for evaluating health effects over a long period. Tables 1 and 2 present

Table 1 Toxic and nontoxic levels of lead in the blood and urine of various animals according to the Normal Range Values for WVDL Toxicology (μg dL^{-1}) (WVDL 2015)

Animal group	Normal	High	Toxic
Blood			
Avian	0.02–0.2	>0.6	1–30
Canine	0.01–0.1	0.3–0.8	0.6–7.4
Caprine	<0.2	0.5–0.9	>0.9
Equine	0.04–0.25	0.3–0.6	0.33–2.5
Feline	<0.1	0.7	>1
Lapine	0.02–0.3	0.3–1.4	
Ovine	0.02–0.25	0.7–0.9	1-5
Porcine	0.04–0.1	0.3–3.0	>1.2
Urine			
Bovine	<0.05		0.2–1.0
Canine	<0.05		>0.075
Feline	0.05–0.2		0.5–1.8
Bovine	<0.05		0.2–1.0

Table 2 Toxic and nontoxic lead levels (mg kg^{-1} ww) in the soft tissues of various animals, according to the Normal Range Values for WVDL Toxicology (WVDL 2015)

Animal group	Normal	High	Toxic
Brain			
Bovine	0.25–0.50	1.5–4.5	3.5–7.0
Kidney			
Avian	0.4–4.0	4–48	32–6400
Bovine	0.08–8.0	12–80	20–2800
Camelid	<8		
Canine	0.4–10.0	20–40	40–200
Caprine	2.0–4.0	15–20	>40
Cervid	<4		
Equine	0.12–5.2	12–20	20–800
Feline	<4.0		
Lapine	0.4–4.0		>40
Ovine	0.4–3.2	20–400	20–800
Porcine	<2.8	20–100	
Ursine	0.8–8.0		
Liver			
Avian	0.3–1.6	3–33	20–466
Bovine	0.3–3.3	7–33	16–1000
Camelid	<7		
Canine	0.3–11.7	12–17	167–667
Caprine	1.7–3.3	10–17	>33
Cervid	<3		
Equine	0.27–4.7	10–17	13–1667
Feline	<3		33–243
Lapine	0.7–2.0	10–19.0	>33
Mammals	<3	7–17	>17
Ovine	0.10–2.7	17–83	33–333
Porcine	<2.3	16–83	
Ursine	0.20–6.7		

nontoxic and toxic Pb levels in the blood, urine, and tissues of various animals (WVDL 2015).

There is no evidence of a difference in susceptibility between mammals and humans, suggesting a predictiveness of their lead dose-effect relations. Blood lead levels >5 μg dL^{-1} are associated with neurobehavioral deficits and neurotoxicic effects. Levels >20 μg Pb dL^{-1} are associated with adverse reproductive effects, and levels >40 μg dL^{-1} result in nephrotoxic and hematological changes. Blood lead levels >80 μg dL^{-1} cause death (Nelson Beyer and Meador 2011).

6 Bioaccumulation of Lead in Wildlife

Lead found in wild animals can come from both natural and anthropogenic sources. Anthropogenic pollution contributes to an increase in the concentration of Pb in the air, water, and food chain (Fig. 1). Ingestion and inhalation are the most significant routes of exposure to Pb in terrestrial animals. Currently, there exist two major anthropogenic sources of this toxic metal—ammunition and non-ammunition-based lead. Ecotoxicological studies on Pb are usually performed on bones (from recently caught or dead animals or those stored in museums) and in the liver and kidneys (as organs responsible for the detoxification of the body). Many studies also analyze Pb levels in the meat of hunted animals, due to its possible effects on human health. In contrast, much less frequently studied are animal nervous system tissues, including the brain, even though the central nervous system is the target destination of Pb toxicity in warm-blooded vertebrates. This clearly smaller group of works (compared to studies on the bone, liver, and kidney) is partly due to the difficulty and time required to perform trepanation (Scheuhammer and Norris 1996; Hunt et al. 2009a; Lazarus et al. 2014; Legagneux et al. 2014).

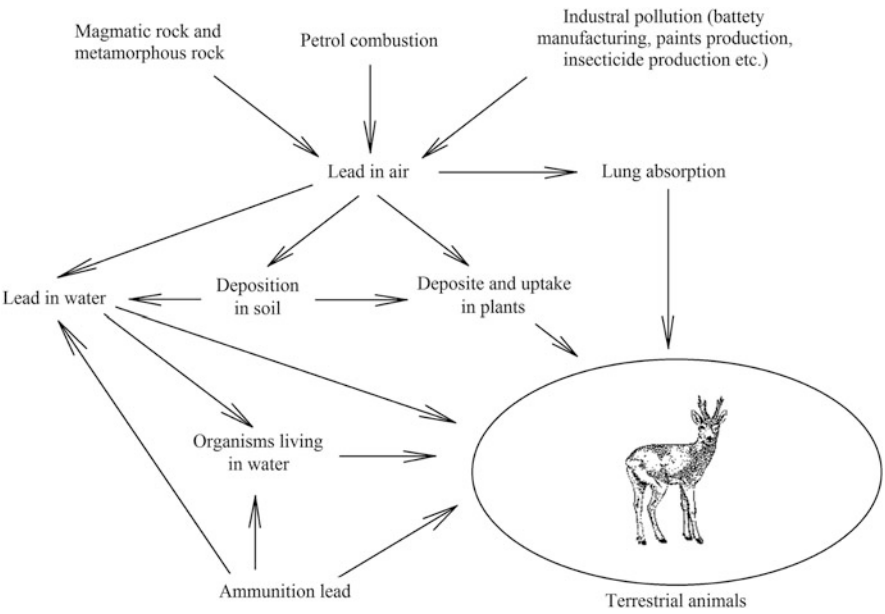

Fig. 1 Routes of exposure of terrestrial mammals to lead

6.1 Lead in Mammalian Tissues

Animals intake lead primarily orally, with approximately 40% of lead being absorbed from the gastrointestinal tract into the bloodstream (Smith et al. 2008). Studies in rats, orally given lead acetate (PbAc), at 5 mg kg^{-1} of body weight per day for 6 weeks, show that Pb accumulated in all tissues, although most abundantly in the long bones (Senapati et al. 2001). After 6 weeks of exposure, Pb increased five times from 15.52 to 80.2 mg kg^{-1} dw. However, in the soft tissues, such as the liver and kidneys, the increase in Pb was much lower: three times in the liver (from 3.05 to 9.80 mg kg^{-1} dw), more in the kidneys (from 4.97 to 19.1 mg kg^{-1} dw), and considerably less in the whole blood (0.31–0.96 mg kg^{-1} dw). In the brain there was a near twofold increase in Pb (from 2.89 to 5.09 mg kg^{-1} dw) (Senapati et al. 2001), although Pb levels in different brain structures varied depending on the brain structure and exposure period (Klein and Koch 1981).

6.1.1 Industrial Activities of Man and Lead in Mammalian Tissues

Pb pollution is a major problem in industrialized countries, with the highest levels observed near mines, metal smelters, industrial areas, and large cities. Lead levels in bones and soft tissues of small mammals are a good indicator of Pb contamination in these areas. A UK study conducted in the 1990s at a site close to a lead mine showed that the concentration of this element in the femur of the bank vole (*Clethrionomys glareolus*) was more than 60 times higher than in the bones of the same species from not-polluted areas, 203.0 ± 13.0 vs. 3.2 ± 0.8 mg kg^{-1} dw (Milton et al. 2003). In specimens living in the vicinity of the mine, muscle Pb was 36 times higher than in those trapped in uncontaminated areas (3.6 ± 0.6 vs. 0.10 ± 0.02 mg kg^{-1} dw), 13 times higher in the liver, and 50 times higher in the kidneys.

Research on bone Pb in roe deer found near defunct lead mines in other European regions conducted in 2004–2006 (Sierra Madrona Mountains and the valley of Alcudia in Southern Spain) also showed a significantly higher content of Pb (averaging 3.53 ± 0.92 mg kg^{-1} dw) than in roe deer living in non-polluted areas of southern Spain and forest areas in Europe in the 1970s (0.93 ± 0.10 mg kg^{-1} dw on average) (Fig. 2) (Kierdorf and Kierdorf 2000; Reglero et al. 2008).

Comparative test results on Pb in the tissues of the European hare (*Lepus europaeus*) living in Finland also provided evidence of the relationship between human industrial activity and increased levels of Pb in the soft tissues of the animals (Venäläinen et al. 1996). In the early 1980s, liver Pb concentrations in the European hare living in the industrial areas of southern Finland (3.4 ± 2.9 mg kg^{-1} dw) were significantly higher than in non-polluted areas of Finland where they did not exceed 1.60 mg kg^{-1} dw (1.57 ± 0.47 mg kg^{-1} dw) (Fig. 3).

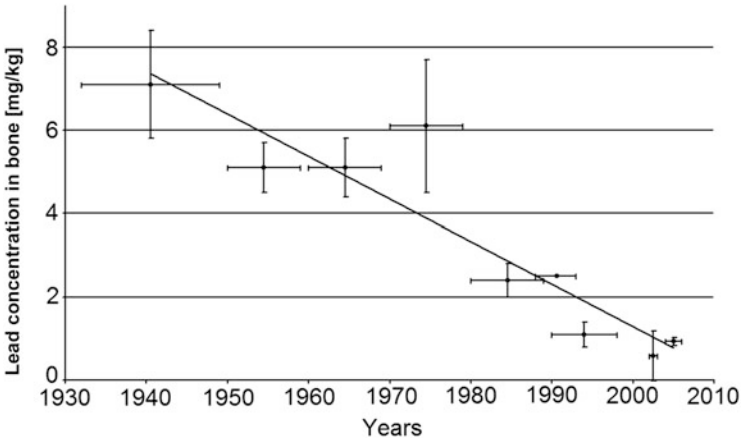

Fig. 2 Lead levels in cervids 1930–2005

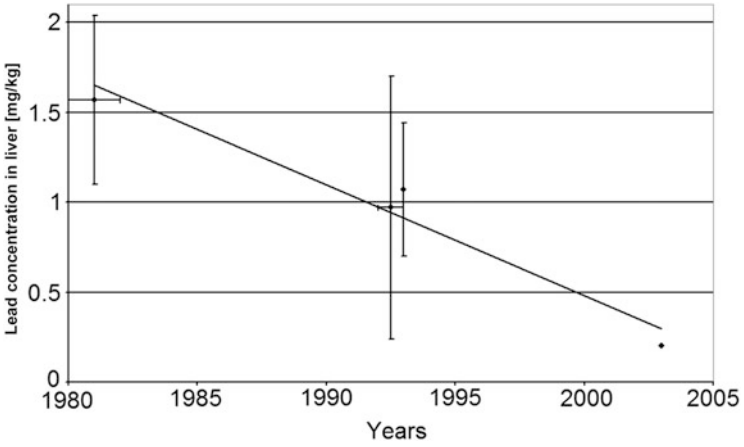

Fig. 3 Lead levels in the liver of rabbits over the years 1980–2003

6.1.2 Combustion of Leaded Gasoline and Lead in Mammalian Tissues

Long-term use of gasoline with tetraethyl lead has strongly influenced the levels of Pb near busy roads, which is reflected in levels in the tissues of small mammals living in the vicinity. An example of this research is the bank vole, carried out in the UK in 1972. In the kidneys of the animals living in the nearby roadsides, Pb levels were several times higher (an average of 13.0 mg kg^{-1} dw) than in specimens captured 0.5 mile from the road (an average of 5 mg kg^{-1} dw) (Williamson and Evans 1972). Also, studies conducted in the United States on the tissues of the

Norway rat (*Rattus norvegicus*) caught near roads in the city have shown several times higher liver Pb concentrations than in specimens caught in suburban areas away from busy roads (3.34 ± 0.45 vs. 0.44 ± 0.09 mg kg^{-1} dw) (Mouw et al. 1975). Another study conducted in Texas in the late 1970s showed that in all the tissues of urban Norway rats, Pb concentrations were significantly elevated compared to individuals caught in non-contaminated suburban areas. In the bones of urban rats from Houston (USA), Pb concentrations were dozens of times higher than in individuals living in the outer suburbs, 146.0 vs. 8.8 mg kg^{-1} dw (Way and Schroder 1982), and their liver and kidney Pb levels were about three times higher compared to rats from the outer suburbs. Research conducted in the early 1990s in Europe (Vienna, Austria) also showed elevated concentrations of Pb in the femur of the European mole (*Talpa europaea*) living near busy roads, averaging 29.8 ± 11.6 mg kg^{-1} dw (Komarnicki 2000).

6.1.3 Ammunition and Fishing Sinkers as Sources of Lead Poisoning in Wildlife

At first, studies of exposure of wildlife to lead were mainly ascribed to industrial activities, such as metallurgy, the use of lead paint and gasoline with tetraethyl lead (Blus et al. 1999; Hernberg 2000; Finkelstein et al. 2003). More recent papers also mention contamination caused by ammunition and fishing sinkers because of their widespread recreational and subsistence use in wildlife habitats (Haig et al. 2014). Currently, larger mammals and birds are hunted to control the number of wild animals and as a hobby. In the northern hemisphere, in particular, this refers to deer, lagomorphs, wild boar, foxes, and birds such as pheasants, partridges, and ducks. Lead ammunition (bullets and pellets) often remains in the environment and pollute woodlands and meadows. This poses a direct threat to birds, which find and consume the lead pellets (Pain 1990). It is estimated that this causes Pb poisoning in approximately 4% of all large birds (Pain et al. 2015). Birds are also an important link in the food chain, which results in elevated levels of Pb in the bodies of carnivores (Pain et al. 2010; Rogers et al. 2012). Lead can also enter the body directly, if the hunted animal is not killed during a hunt and the ammunition remains in the body for a long time. Lead poisoning related to lead pellets was observed in 24% of bald eagles (*Haliaeetus leucocephalus*) in the state of Wyoming, USA (Bedrosian et al. 2012). In addition, in the state of Iowa (USA), more than 50% of bald eagles had high Pb levels in the body due to the presence of lead pellets in their bodies (Neumann 2009). Lead pellets and bullets remain in the flesh of many hunted animals (Hunt et al. 2009b; Pain et al. 2010). Consumption of that meat and offal by people increases the risk of increased blood Pb levels. According to the Regulation of the European Commission in 2006, the permissible Pb concentration in consumed meat must not exceed 0.10 and 0.50 mg kg^{-1} ww in offal (Commission Regulation EC 2006).

Fishing results in the pollution of waterway beds due to lost lead sinkers. Small lead weights can be eaten by fish and shellfish feeding on the bottom, and thus Pb from this source becomes included in the trophic chain. Such weights may also be swallowed by waterfowl, including dabbling and diving ducks, swans, and other birds feeding at the bottom (Haig et al. 2014). As shown by a recent study, among the toxicologically significant sources, Pb-based paints, mining, metallurgy, leaded gasoline, lead pellet, and fishing sinker are primary exposure pathways for birds in terrestrial and aquatic systems (Beyer et al. 2013; Haig et al. 2014). For this reason, regulators worldwide have introduced proposals to ban lead ammunition and hardware in hunting and fishing (Haig et al. 2014).

6.1.4 Lead in the Muscles of Mammals

In the next section, we present literature data on the concentrations of lead in various organs of terrestrial mammals, including muscle (Table 3). To facilitate comparison, the presented data have been summarized in terms of animal species, organs, and the approximate year of sampling. Primarily, we cite literature data on the concentrations of lead in the muscles of mammals, an important component of the diet for carnivorous animals and humans. Therefore, this is an important indicator of exposure to lead for animals at the apex of the trophic chain, indicating the accumulation of lead in the entire food chain.

Studies on Pb in the muscles of various mammalian species indicate that Pb levels in the environment are not as high as 25 years ago, and in most of the non-contaminated areas they do not exceed 1 mg kg^{-1} dw in the muscle of herbivorous or predatory mammals. Pb in the muscle of moose (*Alces alces*) inhabiting the forests of Canada, conducted in 2000, averaged 0.1 ± 0.3 mg kg^{-1} dw (Gamberg et al. 2005). Muscle Pb in this species caught in the forests of Finland was very low and amounted to 0.066 mg kg^{-1} dw (Venäläinen et al. 2005). In reindeer (*Rangifer tarandus*) caught in Norway in 2005, muscle Pb was 0.026 mg kg^{-1} dw (Hassan et al. 2012). In red deer (*Cervus elaphus*) from the forests of Slovakia and Poland, investigated in the late 1990s and 2000s, muscle Pb was 0.30 ± 0.07 and 0.6 ± 1.1 mg kg^{-1} dw, respectively (Kottferová and Koréneková 1998; Jarzyńska and Falandysz 2011). In the Arctic hare (*Lepus arcticus*) living in non-polluted forest areas of Canada, it was 0.011 mg kg^{-1} dw (Pedersen and Lierhagen 2006). Muscle Pb in European hares (*Lepus europaeus*) harvested in the early 1980s in Finland averaged 0.43 mg kg^{-1} dw, while in a study conducted in the early 1990s it had dropped to 0.166 mg kg^{-1} dw, indicating a significant improvement in the environmental Pb contamination (Venäläinen et al. 1996). However, muscle Pb in European hares inhabiting non-polluted forests in Slovakia examined in the early 1990s were significantly higher with an average 1.2 ± 1.6 mg kg^{-1} dw (Kottferová and Koréneková 1998).

Studies on carnivorous mammals show significantly more diverse concentrations of Pb, depending on the location and species. In a Croatian population of gray wolf (*Canis lupus*) hunted in 2009–2010, muscle Pb concentrations averaged

Table 3 Arithmetic mean lead levels (mg Pb kg^{-1} dw) in the muscles of various mammalian species

Trophic group and species	Mean level	SD	Years	Country	References
Herbivores					
Micromammals					
Bank vole *Clethrionomys glareolus*	0.100	0.020	1995	Britain	Milton et al. (2003)
Wood mouse *Apodemus sylvaticus*	0.051	0.043	2001	Spain	Torres et al. (2004)
Medium and large size					
European hare *Lepus europaeus*	0.167		1992–1993	Finland	Venäläinen et al. (1996)
European hare *Lepus europaeus*	1.12	1.20	1998–2001	Poland	Mysłek and Kalisińska (2006)
European hare *Lepus europaeus*	1.170	1.600	1993	Slovakia	Kottferová and Koréneková (1998)
Arctic hare *Lepus arcticus*	0.011		2003	Canada	Pedersen and Lierhagen (2006)
Red deer *Cervus elaphus*	0.030	0.070	1993	Slovakia	Kottferová and Koréneková, (1998)
Moose *Alces alces*	0.100	0.300	1994–2001	Canada	Gamberg et al. (2005)
Reindeer *Rangifer tarandus*	0.033	0.013	1990–1991	Finland	Rintala et al. (1995)
Omnivores					
Wild boar *Sus scrofa*	0.410	0.090	2005–2006	Italy	Danieli et al. (2012)
Insectivore					
Mouse-eared bat *Myotis myotis*	0.670	0.030	2007	Czech Rep.	Pikula et al. (2010)
Carnivores					
Brown bear *Ursus arctos*	0.010		2009–2010	Croatia	Bilandžić et al. (2012)
Eurasian badger *Meles meles*	0.260		2009–2010	Croatia	Bilandžić et al. (2012)
Eurasian lynx *Lynx lynx*	0.017		2009–2010	Croatia	Bilandžić et al. (2012)
Gray wolf *Canis lupus*	0.070		2009–2010	Croatia	Bilandžić et al. (2012)
Red fox *Vulpes vulpes*	0.133	0.030	2010	Italy	Naccari et al. (2013)
Pine marten *Martes martes*	0.013		2009–2010	Croatia	Bilandžić et al. (2012)
Stone marten *Martes foina*	0.100	0.260	2008–2009	Croatia	Bilandžić et al. (2010)

SD standard deviation

0.133 ± 0.830 mg kg^{-1} dw (Bilandžić et al. 2010, 2012), like in foxes (*Vulpes vulpes*) from Italian forests examined at the same time, 0.133 ± 0.03 mg kg^{-1} dw (Naccari et al. 2013).

In the muscles of large omnivorous mammals, e.g., brown bears (*Ursus arctos*), hunted in the forests of Croatia in 2010, Pb concentrations were very low at 0.01 mg kg^{-1} dw (Bilandžić et al. 2012). In wild boar coming from forested areas in Italy at the same time, muscle Pb was 0.414 ± 0.093 mg kg^{-1} dw (Danieli et al. 2012). In the muscles of smaller predators, such as the stone marten (*Martes foina*) caught in forested areas in Croatia in 2008–2009, Pb level was 0.10 ± 0.26 mg kg^{-1} dw (Bilandžić et al. 2010). Although in a study conducted in Croatia, muscle Pb in Eurasian lynx (*Lynx lynx*) was much lower, at 0.0166 mg kg^{-1} dw (Bilandžić et al. 2012), similar to pine marten (*Martes martes*) 0.013 mg kg^{-1} dw (Bilandžić et al. 2012), Eurasian badgers (*Meles meles*) from Croatia studied in 2009–2010 had muscle Pb of 0.25 mg kg^{-1} dw (Bilandžić et al. 2012).

In a recent study in the Czech Republic, muscle Pb in very small mammals, such as mouse-eared bat (*Myotis myotis*) and pipistrelle bats (*Pipistrellus pipistrellus*), were 0.67 ± 0.03 and 0.67 ± 0.07 mg kg^{-1} dw, respectively (Pikula et al. 2010). In a research conducted in 2001, the content of Pb in the muscles of wood mice (*Apodemus sylvaticus*) living in non-polluted areas of Spain was much lower (0.051 ± 0.043 mg kg^{-1} dw, Torres et al. 2004) than in mentioned insectivorous bats from polluted Czech Republic.

6.1.5 Lead in Mammalian Bones

Animals may periodically experience lead poisoning associated with the ingestion of lead shot or fishing sinkers or after being shot by hunters. Such periodic fluctuations in the concentration of lead in the blood are reflected in the concentration of lead in soft tissues. In contrast, an animal's liftetime exposure to lead can be shown by bone lead levels. Hence, data presented later in this section can be used for a relatively thorough analysis of environmental pollution by lead in the investigated area.

Over the last 10 years, research on the bones of herbivorous mammals, such as the red deer (*Cervus elaphus*) living in the forests of Spain and Croatia, showed Pb concentrations at 0.93 ± 0.10 and 0.58 ± 0.60 mg kg^{-1} dw, respectively (Reglero et al. 2008; Lazarus et al. 2005). Deers belong to the most significant group of game animals and therefore are a good material for bioindicative research. Long-term studies show that Pb concentrations in the tissues of these animals continue to decline. This is primarily related to the prohibition on leaded gasoline and paints containing lead and also to a growing use of non-lead bullets and pellets. A long-term study on the bones of deer living in the forests bordering the eastern suburbs of Cologne (Germany) showed that in roe deer (*Capreolus capreolus*) hunted between 1932 and 1949 (including World War II), bone Pb (average of 7.1 ± 1.3 mg kg^{-1} dw) was high compared to animals living in the same area but examined in the following decades. From 1950 to 1969 and 1970 to 1979, the average bone Pb levels were 6.1 ± 1.6 and 5.1 ± 0.6 mg kg^{-1} dw, respectively (Kierdorf and Kierdorf 2000).

After the ban on the use of Pb in gasoline and paints in many European countries, by as early as the 1980s–1990s, bone Pb had fallen steadily in the deer. In the period 1980–1989 and in the early 1990s, bone Pb in cervids in Germany and the Netherlands had dropped by half compared to the 1970s, 2.4 ± 0.4 and 2.5 mg kg^{-1} dw, respectively (Kuiters 1996; Kierdorf and Kierdorf 2000). At present, the concentration of Pb in the bones of roe deer inhabiting Germany and the Netherlands has fallen below 1.0 mg kg^{-1} dw.

In carnivorous mammals Pb content in the bones is varied. In foxes (*Vulpes vulpes*) living in non-polluted regions of Poland in the late 2000s, it was 0.98 ± 1.15 mg kg^{-1} dw (Lanocha et al. 2012). In the 1990s, bone Pb in the gray wolf (*Canis lupus*) from the forests of North America (Canada) was 0.40 ± 0.86 mg kg^{-1} dw (Gamberg and Braune 1999). In the Dutch omnivorous wild boars (*Sus scrofa*) examined in the late 1980s and 1990s, bone Pb averaged 4.8 mg kg^{-1} dw (Kuiters 1996), and this value is much higher than in mentioned carnivorous and herbivorous species.

6.1.6 Lead in the Mammalian Brain

Little is known about the subclinical signs, biochemical and behavioral changes and corresponding concentrations of brain Pb in animals (ATSDR 2007). In control mammalian groups used in laboratory experiments and small mammals from reference area in field studies, brain Pb levels generally ranged from <0.10 to 0.50 mg kg^{-1} dw (Stowe et al. 1973; Mierau and Favara 1975; Yoo et al. 2002; Mari et al. 2014; Kalisinska et al. 2016). A concentration of <0.50 mg Pb kg^{-1} dw in the brain can therefore be considered as reflecting the background level.

6.2 Lead in Tissues in Birds

Birds are sensitive to Pb exposure, leading to apparent sublethal or lethal toxic responses, with exposure documented in 20 species (reviewed by Tranel and Kimmel 2009). Lead shot pellets or bullet fragments are commonly ingested by many avian species and may cause lethal poisoning and sublethal effects, with population level implication for conservation of some species (Bellinger et al. 2013).

After permeating the bird's body, Pb is transported by the blood to all tissues. A high concentration of this metal in the blood and soft tissues indicates a recent exposure to Pb prior to sampling. In contrast, increased bone Pb concentrations indicate chronic exposure or short-term exposure to high concentrations of lead. Importantly, bone Pb may be released to the blood due to bone remodeling. Nevertheless, this process takes a long time and bone Pb is generally assumed to reflect the average lifelong exposure. Levels greater than 5 mg kg^{-1} in the bone are thought to indicate increased environmental pollution with lead (Orłowski et al. 2012). In Table 4 are gathered data on lead in urban pigeons.

Table 4 Arithmetic mean lead levels (mg Pb kg^{-1} dw) in the bones of pigeons living in urban areas

Species	Mean level	SD	Years	Country	Notice	References
Pigeon	42	21	1970s	Japan	Tokyo, central city	Ohi et al. (1974)
Pigeon	2.67	4.00	1970s	Japan	Tokyo, suburban city	Ohi et al. (1974)
Feral pigeon *Columba livia f. domestica*	40.9	25.6	1983–1985	Slovakia	Bratislava	Janiga and Zemberyová (1998)
Feral pigeon	29.9	10.4	1983–1985	Slovakia	Bratislava	Janiga and Zemberyová (1998)
Feral pigeon	39.3	28.1	2000–2001	Korea	Seoul, urban area	Nam and Lee (2006a)
Feral pigeon	14.0	6.3	2000–2001	Korea	Ansan, industrial area	Nam and Lee (2006a)
Feral pigeon	31.7	18.3	2000–2001	Korea	Busan, industrial area	Nam and Lee (2006a)
Feral pigeon	2.40	1.15	2000–2001	Korea	Duckjuk Island, rural	Nam and Lee (2006a)

SD standard deviation

In contrast, feathers are low in Pb compared to the soft tissues and bones (Ek et al. 2004). This is due to the fact that Pb is transported from the blood to the feathers only during the short period of their formation. As a result, Pb does not accumulate in the feathers. Eggs also contain little Pb (Ek et al. 2004). Similar to feathers, this is related to the fact that Pb penetrates in the short period of egg development in the breeding season. Bioindication research sometimes uses bird droppings, which have been shown to have 3× higher Pb levels than soft tissues (Ek et al. 2004).

6.2.1 The Impact of Environmental Pollution on Pb Concentration in the Avian Eggs

Eggshells are good bioindicative material due to the relative ease of sampling and the noninvasive character, as well as their ability to accumulate Pb and relative durability. This makes it possible to perform comparative studies of Pb pollution in the area over many years. Bird eggs are also an important object of environmental studies due to the strictly defined time and place of nesting. Pb from the blood of a female bird reaches the eggs during their development in the period preceding the laying of eggs in a nest. Therefore, the amount of Pb in eggs correlates with the level of Pb in the blood of birds during the breeding season. This, in turn, correlates with the content of Pb in the diet of the birds near the nesting site (Ek et al. 2004).

Due to their position in the food chain, birds of prey play an important part in research on the bioindication of environmental pollution with heavy metals. An example of this is the american kestrel (*Falco sparverius*), whose eggshells collected in the area of New York (USA) in the early 1970s showed average Pb levels of 0.908 ± 0.073 mg kg^{-1} dw (Lincer and McDuffie 1974). In the eggshells of double-crested cormorant (*Phalacrocorax auritus*) in Minnesota (USA), Pb concentrations in the eggs were 0.128 ± 0.390 mg kg^{-1} dw (Burger and Gochfeld 1996). However, in the eggs of osprey (*Pandion haliaetus*) collected in New Jersey, USA, concentrations of Pb in 1989 averaged 0.03 mg kg^{-1} dw (Clark et al. 2001) and had increased in studies conducted 10 years later, to 0.87 mg kg^{-1} dw (Clark et al. 2001).

Pb pollution in cities may also be indicated by the levels determined in the eggshells of birds that live permanently in cities, e.g., doves. In Seoul and Ansan (Korea), eggshells of doves (*Columba livia*) showed very high Pb levels. In Seoul, eggshell Pb in the early twenty-first century averaged 4.8 ± 0.6 mg kg^{-1} dw (Nam and Lee 2006b), while in Ansan it was 3.3 ± 0.3 mg kg^{-1} dw. In a study conducted at the same time in Europe, in a highly industrialized area in Antwerp (Belgium), the eggshells and egg contents of the great tit (*Parus major*) also showed high concentrations of Pb, 1.505 ± 0.597 and 2.18 ± 0.72 mg kg^{-1} dw, respectively (Dauwe et al. 2005).

6.2.2 Lead in Bird Feathers

Feathers are an important bioindicative material because of the possibility of intravital sampling, which is important in the study of birds threatened with extinction. Due to the high content of keratin, rich in sulfur amino acids, feathers easily bind Pb, which has a high affinity for –SH groups in the protein. Although air pollution does not directly affect Pb levels in feathers, lead dust can cover the outer surface of feathers. Pb is incorporated in the feathers via the blood during their formation (Lodenius and Solonen 2013). Therefore, feathers are a valuable indicator of Pb contamination in the breeding and wintering areas, and this biological material is often used in ecotoxicology (Table 5). It is understood that a Pb concentration greater than 4 mg kg^{-1} dw indicates sublethal poisoning, which negatively affects the reproductive functions of birds (Norouzi et al. 2012).

Due to the accumulation of Pb in the food chain, research on birds of prey gives valuable information about lead contamination over large areas. Studies conducted in the late 1990s in common buzzards (*Buteo buteo*) from non-contaminated areas of Italy showed feather Pb to average 1.48 mg kg^{-1} dw (Battaglia et al. 2005). In southeastern Spain, common buzzard feathers from environmentally clean areas had lower Pb levels, averaging 1.01 ± 0.20 mg kg^{-1} dw (Martínez-López et al. 2004). Feather Pb in the booted eagle (*Hieraaetus pennatus*), also from southeastern Spain, and the Spanish imperial eagle (*Aquila adalberti*) from the south-central part of the country caught in recent years (Martínez-López et al. 2004; Rodriguez-Ramos Fernandez et al. 2011) were 0.72 ± 0.31 and 0.043 ± 0.078 mg kg^{-1} dw. In northern goshawk (*Accipiter gentilis*), caught in the same area of southeastern Spain, feather

Table 5 Arithmetic mean lead levels (mg Pb kg^{-1} dw) in the feathers of diurnal and nocturnal avian predators

Species	Sex	Mean level	SD	Years	Country	References
Common buzzard *Buteo buteo*		1.48		1998–1999	Italy	Battaglia et al. (2005)
Common buzzard		1.01	0.20	1999–2000	Spain	Martínez-López et al. (2004)
Common buzzard	M	0.95	1.00	1997–2007	Spain	Castro et al. (2011)
	F	1.75	1.19	1997–2008	Spain	Castro et al. (2011)
Booted eagle *Hieraaetus pennatus*		0.72	0.31	1999–2000	Spain	Martínez-López et al. (2004)
Spanish imperial eagle *Aquila adalberti*		0.043	0.078	1997–2008	Spain	Rodriguez-Ramos Fernandez et al. (2011)
Golden eagle *Aquila chrysaetos*		0.68	0.09	2008–2010	USA, Montana	Harmata and Restani (2013)
Northern goshawk *Accipiter gentilis*		0.98	0.29	1999–2000	Spain	Martínez-López et al. (2004)
Northern goshawk	M	1.55	0.77	1997–2005	Spain	Castro et al. (2011)
	F	2.24	1.86	1997–2006	Spain	
Osprey *Pandion haliaetus*		0.80	2.20	2000–2001	USA, Florida	Lounsbury-Billie et al. (2008)
Tawny owl *Strix aluco*		0.38 0.024		1986 2005	Norway	Bustnes et al. (2013)
Little owl *Athene noctua*		2		1998–1999	Italy	Battaglia et al. (2005)
Brown owl *Strix aluco*	M	1.84	8.38	1997–2009	Spain	Castro et al. (2011)
	F	3.47	14.45	1997–2010		

SD standard deviation, *F* female, *M* male

Pb was 0.98 ± 0.29 mg kg^{-1} dw. In North America (USA, Montana), feather Pb in golden eagles (*Aquila chrysaetos*) from ecologically clean areas was 0.68 ± 0.09 mg kg^{-1} dw (Harmata and Restani 2013). Feather Pb in osprey from the cleaner areas of Florida Bay (USA) did not differ from the content in feathers of other birds of prey, at 0.80 ± 2.20 mg kg^{-1} dw (Lounsbury-Billie et al. 2008).

Feather Pb levels in tawny owls (*Strix aluco*) have shown that Pb contamination in Norway has significantly reduced over the last 25 years. In 1986, feather Pb in this species was 0.36 mg kg^{-1} dw, while in 2005 it was only 0.024 mg kg^{-1} dw (Bustnes et al. 2013). In contrast, recent studies on feather Pb levels in the little owl (*Athene noctua*) living in the woods in northern Italy point to a persistent

contamination of the environment with lead, showing levels as high as 2 mg kg^{-1} dw (Battaglia et al. 2005).

In lead biomonitoring of urban ecosystems, feathers of some species are used. Due to the constant presence of pigeons in large cities, these birds are an important indicator of urban pollution by heavy metals. Research on pigeon feathers shows very high pollution in urban areas and indicates a high tolerance of this species to Pb poisoning. In studies conducted in recent years in Greater Paris (France), Pb concentrations in the feathers of feral pigeons were as high as 13.82 mg kg^{-1} dw (Frantz et al. 2012). In Iraq, in the Hormod Protected Area, feather Pb in the rock dove was 7.7 mg kg^{-1} dw (Norouzi et al. 2012). Similarly, high concentrations of Pb were found in the feathers of feral pigeons living in the cities of Seoul and Ansan, Korea, 4.99 $\pm$ 1.21 and 9.01 $\pm$ 3.00 mg kg^{-1} dw (Nam et al. 2004). In comparison, in the late 1990s the concentration of Pb in the feathers of the mourning dove (*Zenaida macroura*) from the nuclear reservation Savannah River Site in Par Pond, South Carolina, USA, were much lower, at 0.466 $\pm$ 0.132 mg kg^{-1} dw (Burger et al. 1997).

6.2.3 Lead in the Liver of Birds

The liver is involved in many physiological functions, including blood plasma protein synthesis or metabolism of glucose. Therefore, studies on the concentrations of harmful substances in this organ allow to assess the health status of birds in areas contaminated with lead. It is understood that liver Pb $<$ 2 mg kg^{-1} dw is the concentration resulting from the natural occurrence of Pb in nature (Kim and Oh 2013), not affecting its normal functions. The range of 6.0–30.0 mg kg^{-1} dw is considered toxic, disturbing normal function of the body and indicating lead poisoning. The concentration of Pb in the liver of birds above 30.0 mg kg^{-1} dw reflects acute poisoning which leads to death.

The following literature data show the concentration of lead in the liver of birds of prey, situated top of the food chain and therefore at a higher risk of Pb accumulation in the liver than other birds. Because of the rapid elimination of lead from soft tissues, the collected data show only the general condition of the biota in a specific area within a specified time. Results vary significantly due to the randomness of serious lead poisoning associated with swallowing lead pellets or ingestion of a shot animal.

According to a recent study, in the white-tailed eagle (*Haliaeetus albicilla*) from Korea, liver Pb was 4 mg kg^{-1} dw (Nam and Lee 2011). The moderate pollution with Pb in the south Baltic coast in Poland is indicated by liver Pb levels in the white-tailed eagles averaging 1.10 $\pm$ 0.60 mg kg^{-1} dw (Falandysz et al. 2001).

Studies on another group of predators, owls (*Strigiformes*), living in industrial areas in Korea, confirmed the contamination of those areas with Pb. Liver Pb levels of the Eurasian eagle-owl (*Bubo bubo*) averaged 3.6 mg kg^{-1} dw (Nam and Lee 2011). In Europe, increased levels of pollution with Pb were recorded in northern Italy, and accordingly, liver Pb in little owls from Bologna and Parma Pb were 0.667 ± 0.037 and 0.773 ± 1.267 mg kg^{-1} dw (Zaccaroni et al. 2003). In Galicia (Spain) Pb concentrations in the liver of the barn owl (*Tyto alba*) and the little owl were 3.12 ± 2.21 and 4.00 ± 0.26 mg kg^{-1} dw, respectively (Pérez-López et al. 2008). In the long-eared owl (*Asio otus*) and tawny owl, respectively, liver Pb levels were 4.09 ± 2.56 and 2.75 ± 2.65 mg kg^{-1} dw (Pérez-López et al. 2008). In Sicily, southern Italy, the livers of common buzzard had very high concentrations of Pb, on average 48.4 ± 12.5 mg kg^{-1} dw (Naccari et al. 2009).

Passerine birds commonly occur on all continents of the northern hemisphere and constitute a valuable reference for lead pollution. Due to the similar location of passerines in the food chain, the literature data presented below allow to compare the state of the environment between the selected areas. The levels of this heavy metal in the liver of these birds in non-contaminated areas are less than 1 mg kg^{-1} dw. An example of this is the recent study of the northern cardinal population (*Cardinalis cardinalis*) from the state of Missouri in the United States, in which the level of Pb in the liver equaled 0.45 ± 0.16 mg kg^{-1} dw (Beyer et al. 2013). In the hooded crow (*Corvus cornix*) from the province of Cuneo in Italy, liver Pb was 0.3 ± 0.9 mg kg^{-1} dw (Giammarino et al. 2014). In the great tit from Belgium, Pb levels in the liver were also low and averaged 0.81 mg kg^{-1} dw (Dauwe et al. 2005).

Liver Pb levels in industrial areas related to the extraction of metals, can significantly exceed 1 mg kg^{-1} dw (Table 6). In the vicinity of Southeast Missouri (USA) Lead Mining District, liver Pb levels in northern cardinal (*Cardinalis cardinalis*) and the American robin (*Turdus migratorius*) were 10.5 ± 2.3 and 33.6 ± 10.0 mg kg^{-1} dw, respectively (Beyer et al. 2013). In China, in the province of Beijing in the vicinity of the Capital Steel Company, Pb level in the Eurasian tree sparrow (*Passer montanus*) was 10.68 ± 5.27 mg kg^{-1} dw in females and 13.26 ± 1.67 mg kg^{-1} dw in males (Pan et al. 2008). Some areas of India are also highly polluted with lead, and in the industrial Nilgiris District, Pb concentrations in the liver of jungle babbler (*Turdoides striatus*) and common myna (*Acridotheres tristis*) were as high as 14.77 ± 4.93 and 11.233 ± 0.867 mg kg^{-1} dw, respectively (Jayakumar and Muralidharan 2011). Some areas of Europe, which are not associated with the ore mining, can also be heavily contaminated with lead. As demonstrated in a study on rural areas in northeastern Poland, in rook chicks (*Corvus frugilegus*) Pb levels in the liver were as high as 5.0 ± 0.8 mg kg^{-1} dw (Orłowski et al. 2012).

Table 6 Arithmetic mean lead levels (mg Pb kg^{-1} dw) in passerine livers

Species	Mean level	SD	Years	Place	Notice	References
American robin *Turdus migratorius*	3.41	1.10	2009–2010	USA, Missouri		Beyer et al. (2013)
American robin *Turdus migratorius*	33.6	10.0	2009–2010	USA, Missouri	Mining area	Beyer et al. (2013)
Common myna *Acridotheres tristis*	1.23	0.87	1998–1999	India		Jayakumar and Muralidharan (2011)
Eurasian tree sparrow *Passer montanus*	7.25	8.90	2002	China, Beijing	Adult	Pan et al. (2008)
Great tit *Parus major*	0.81		2000	Belgium	Female	Dauwe et al. (2005)
Great tit *Parus major*	0.64	0.15	2004	China, Beijing		Deng et al. (2007)
Greenfinch *Chloris chloris*	0.45	0.06	2004	China, Beijing		Deng et al. (2007)
Hooded crow *Corvus cornix*	0.30	0.90	2005–2006	Italy		Giammarino et al. (2014)
Jungle babbler *Turdoides striatus*	14.77	4.93	1998–1999	India		Jayakumar and Muralidharan (2011)
Northern cardinal *Cardinalis cardinalis*	0.45	0.16	2009–2010	USA, Missouri		Beyer et al. (2013)
Northern cardinal *Cardinalis cardinalis*	10.50	2.33	2009–2010	USA, Missouri	Mining area	Beyer et al. (2013)
Northern cardinal *Cardinalis cardinalis*	8.40		1999	USA, Georgia	Firearms training facility	Lewis et al. (2001)
Rook *Corvus frugilegus*	5.0	0.8	2005	Poland		Orłowski et al. (2012)

SD standard deviation, *F* female

7 Conclusions

Over the last several decades, there has been increased awareness of the dangers to living organisms and ecosystems from lead pollution. Gradual understanding of the mechanisms of lead toxicity has helped to reduce its use. These actions have been taken largely in economically developed countries, yet the global anthropogenic emissions of lead into the atmosphere still remains at a high level. Bioindication research helps to determine not only the history and the present state of lead pollution but also allows an understanding of the phenomenon of the circulation of lead in nature, as well as in prediction of the risk of its presence in the trophic chain.

Long-term bioindication research conducted on the bones and soft tissues of mammals and birds, as well as the eggs and feathers, indicates the usefulness of this type of material for evaluating the state of the environment.

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Chapter 17
Mercury, Hg

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Abstract In nature, mercury (Hg) occurs in the elemental form (Hg^0), as well as in inorganic (InHg) and organic (OrgHg) compounds. It is the only heavy metal that is liquid at room temperature and easily turns into a gas. Mercury vapours can be transported with air masses for hundreds and thousands of kilometres and—after falling down—contribute to the pollution of land and waters. In aquatic environments biogeochemical processes promote the natural microbial conversion of InHg to methylmercury (MeHg), the most bioavailable form of Hg.

Human activities have increased atmospheric Hg concentrations 3–5 times over the past 150 years, mainly as a result of the combustion of fossil fuels. It is believed that all forms of Hg are toxic to endothermic animals and humans, but MeHg is particularly dangerous because of its neurotoxic and teratogenic effects as well as negative influence on reproduction. Moreover, in nature MeHg is biomagnified, and its concentration reaches the highest levels in top predators, especially piscivorous species. For several decades, there have also been reports documenting the local occurrence of dangerously high concentrations of Hg in organisms living in terrestrial ecosystems (including spiders, insects and songbirds feeding on them) in areas, which had been subject to anthropogenic Hg pollution many decades ago. Studies on inland aquatic and terrestrial ecosystems have indicated the long-term persistence of Hg introduced into the environment and the complexity of its transformations and circulation in nature. A better understanding of these processes requires further research, including the issue of bioaccumulation and biomagnification of MeHg in various ecosystems.

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1 Introduction

Mercury causes many environmental and health problems. Together with lead and cadmium, it belongs to the group of particularly toxic metals, which do not have any physiological functions in warm-blooded vertebrates (including humans), and therefore even small amounts of absorbed mercury result in the disruption of biochemical processes in the body. Its elevated concentrations in birds and mammals lead to the development of many diseases (mainly in the nervous and excretory systems) and death (Clarkson and Magos 2006).

2 General Properties

Mercury (Hg from "hydrargyrum", i.e. "liquid silver" from Greek "hydr-" for water and "argyros" for silver) is a heavy metal with a density of 13.55 g cm^{-3}. It is the only metal which occurs in a liquid form at room temperature; its freezing point is –38.83°C and boiling point is 356.73°C. It has good electrical conductivity and high volatility, reaching a vapour pressure of 1.22×10^{-3} mm at 20°C (2.8×10^{-3} mm at 30°C). Its solubility in water is 6×10^{-6} g^{-1} 100 ml (25°C). In the atomic table of elements, mercury is located in the group IIB, with atomic number 80 and atomic mass 200.59. There are 33 known isotopes of Hg, of which 7 are stable. The general pool of Hg is dominated by three isotopes: ^{199}Hg, ^{200}Hg and ^{202}Hg. at 16.9%, 23.1% and 29.7%, respectively (Blum 2011). In the environment, mercury exists in the elemental form (Hg^0) and in compounds with I (mercurous or Hg^+) and II oxidation states (mercuric or Hg^{2+}). Elemental mercury is an extremely good "solvent" for gold, silver and many other metals (except iron) via the formation of amalgams (alloys). It forms both inorganic and organic compounds, with the latter known as organomercurials. Common mercury salts contain halides (fluorine, chlorine, bromine and iodine) and sulphur (HgS). Organic compounds occur as R_2Hg and RHgX, where R represents a simple alkyl group such as methyl (CH_3^-) and X represents atoms or groups such as chlorine, bromine, iodine, cyanide and hydroxyl. Two of the organic compounds are monomethyl mercury CH_3HgX (methylmercury, MeHg) and dimethyl mercury $(CH_3)_2Hg$, the most important chemical forms of Hg with respect to environmental impact assessments (National Research Council 2000; Scoullos et al. 2001).

3 Mercury in Nature

Mercury is a natural component of the Earth's crust, occurring in soil, water and air where it penetrates into living organisms. In the environment it is found in an elemental form or in inorganic and organic compounds with varying degrees of toxicity to plants and animals, including vertebrates.

3.1 Mercury in the Abiotic Environment

It is estimated that Hg constitutes only 0.083×10^{-4}% of the Earth's crust and is in the 63rd position in terms of percentage share in the lithosphere. Mercury is present in the Earth's upper crust at a mean concentration of ~0.05 mg kg^{-1} (ppm). Its abundance in igneous rocks is lower than in sedimentary rocks (0.004–0.08 and 0.01–0.40 ppm, respectively) and is mainly concentrated in argillaceous sediments. As a chalcophile element, this metal exhibits high affinity for sulphur and low to oxygen. Mercury occurs mainly in minerals containing sulphides and sulpho-salts and accompanies the ores of many metals (including copper, silver, zinc and lead). Generally, Hg is considered to be a rare element and extensively dispersed in the lithosphere (Yaroshevsky 2006; Kabata-Pendias and Mukherjee 2007; Kabata-Pendias 2011).

About 90 Hg minerals have been described, including cinnabar (HgS) and calomel (Hg_2Cl_2). Various ores generally contain from 0.1 to 2.5% Hg and occasionally >7% Hg. In some parts of the world there are geological anomalies with very high accumulations of minerals rich in Hg. Geologists have described more than 2200 sites where ores not only contain significant amounts of mercury but where also the soil, deposits of coal and oil and inland waters are characterized by elevated Hg content. Most of these sites are located within three transcontinental belts, usually with significant volcanic activity. The first belt (Mediterraneo-Himalayan) runs from the Iberian Peninsula in Europe to the Himalayas in Asia, the second covers the area lying along the west coast of the Pacific, and the third runs through the western areas of the Americas, together with the Pacific Ocean adjoining them; therefore, the Pacific is surrounded by the zone naturally high in mercury (Rytuba 2003; AMAP/UNEP 2013). Ores containing cinnabar, the most widespread of natural mercury-containing minerals, are present in approximately 60 countries. Five of the richest deposits of Hg include three European sites (Almaden in Spain, Monte Amiata in Central Italy, Idrija in Slovenia) and one located in North America (including New Almaden and New Idria in California, USA) and in South America (Huancavelica in Peru). These deposits were exploited for hundreds of years but eventually were closed in the period 1982–2002 (Ferrara et al. 1999; Gnamuš and Horvat 1999; US GS 2016a). In addition to those already mentioned, areas particularly rich in mercury can be found in China and Kyrgyzstan (Scoullos et al. 2001; Hylander and Meili 2003; Gómez et al. 2007).

The concentration of Hg in environmental samples is generally low outside of these geological anomalies and areas anthropogenically contaminated by this element. Hg levels in the air in Greenland range between 0.01 and 0.06 ng m^{-3} and in snow and rainwater do not normally exceed 0.2 μg L^{-1}. In inland surface waters, the concentration of Hg ranges from 0.2 to 1.0 μg L^{-1}, and it is typically lower in rivers than in lakes (Adriano 2001). Globally, the average concentration of mercury in soils assumes is about 0.16 mg kg^{-1} dry weight, (range 0.06–0.20 mg kg^{-1} dw), but in European agricultural soils, it is markedly less and does not exceed 0.04 mg kg^{-1} dw (Adriano 2001; De Vos et al. 2006). Much higher values are listed in soils of

volcanic origin, where the concentration of Hg can exceed 7 mg kg^{-1} (Kabata-Pendias 2011). From the environmental and economic points of view, the mercury content in mined and processed raw materials is most essential. These are mainly ores of mercury and other metals, which are accompanied by mercury, rocks used in the cement industry and fossil fuels (Table 17.1). To obtain mercury on an industrial scale, ore with an average content of 0.6–3.2% is exploited, while there are also deposits in Almaden (Spain) which comprise 8% Hg or 80,000 ppm. In addition, some local rocks there contain small drops of native mercury (Kim et al. 2004; Gómez et al. 2007). Most mercury mines in the world have been closed, with those remaining open are located mainly in Asia.

3.2 Mercury Production and Uses

Due to its unique properties, mercury and its compounds have been used in a variety of applications since ancient times. Over the centuries, cinnabar (vermilion) with a characteristic vivid red colour was widely used as a pigment in art, wall decorations, cosmetics and some medicines in Rome, mediaeval Europe, Egypt, India and China. Even in the twenty-first century, it is used in some ritualistic and spiritual practices. Up to now mercury was extracted in poor countries by heating cinnabar in a current of air and condensing the vapour. By 500 BC, mercury was used to make amalgams with other metals. This property of mercury to form alloys is still widely used, particularly in obtaining precious metals and the preparation of dental amalgams ("silver fillings"). Such cheap and permanent fillings have been used in dentistry since the nineteenth century. Since the last century, mercury has been used on a large scale in the chemical and electrochemical industries for electrical and electronic applications (among others in switches, batteries, fluorescent lamps and energy-saving light bulbs). It is also found in some control devices (thermometers, barometers and manometers) and some pesticides, although developed countries significantly reduced the use of mercury in various products and processes due to its high toxicity and environmental hazard (Caley 1928; Parsons and Percival 2005; Masur 2011; Teaf and Garber 2012).

The world's richest source of cinnabar and quicksilver in Almaden (Spain) was operated for over 2000 years, with about 7 million tons of Hg extracted (Tejero et al. 2015). For comparison, from 1500 to 2000, the entire world production of Hg was less than 1 million tons, of which Almaden accounted for ~33% (Gómez et al. 2007; Hylander and Meili 2003; Tejero et al. 2015). As late as in 1971–1980, world production of Hg was very large, with an estimated production of 81,925 tons Hg, of which the former Soviet Union (including Ukraine, Russia, Kyrgyzstan and Tajikistan) accounted for 26%, Spain (Almaden) for 18% and the United States (California and Nevada) for 10.2% (Hylander and Meili 2003). Since then, the global excavation of Hg has dropped more than five times, and in the decade from 2001 to 2010, it amounted to a total of 16,310 tons (US GS 2001–2011). Table 17.2

Table 17.1 Mercury concentrations in raw materials for industry (dw, dry weight)

Material	Mean value	Range	Source
Rocks			
Raw materials for metallurgy, mg kg^{-1}			
Mercury ores		188–22310	Kim et al. (2004)
Zinc and lead ores		27–1198	Rytuba (2003)
Raw materials for cement industry, μg kg^{-1} dw			
Limestone	17	<1–391	Hills and Stevenson (2006)
Sand	29	<1–556	Hills and Stevenson (2006)
Clay	52	2–270	Hills and Stevenson (2006)
Shale	57	2–436	Hills and Stevenson (2006)
Fossil fuels			
Peat, μg kg^{-1} dw			
World		60–300	Adriano (2001)
Brown coal, μg kg^{-1} dw			
North America	130	7–1200	Toole-O'Neil et al. (1999)
Europe		20–1500	Glodek and Pacyna (2009)
Coal, μg kg^{-1} dw			
World	217	10–1780	Pye et al. (2006)
United States	170		Mukherjee et al. (2008)
Canada	60–140		Pye et al. (2006)
Europe		10–1500	Glodek and Pacyna (2009)
Ukraine	390		Pye et al. (2006)
China	30–340	20–1590	Pye et al. (2006)
India		110–800	Mukherjee et al. (2008)
Crude oil, μg kg^{-1} dw			
World	7.3	0.5–600	Wilhelm et al. (2007)
North America	5.3		Wilhelm et al. (2007)
Asia	220		Wilhelm et al. (2007)
Thailand	593		Wilhelm et al. (2007)
Near East	0.8		Wilhelm et al. (2007)
Europe	8.7		Wilhelm et al. (2007)
Russia		3.6–19.5	Lang et al. (2012)
Natural gas, μg Nm^{-3}			
World		1–1000	Visvanathan (2003)
North America		1–20	Eckersley (2010)
Europe		1–50	Eckersley (2010)
East Europe		1–2000	Lang et al. (2012)
Asia SE		10–2000	Eckersley (2010)
Near East		1–10	Eckersley (2010)
Biomass, μg kg^{-1} dw			
		30–80	Pye et al. (2006)

Table 17.2 Three countries with the highest mercury production in selected years (metric tons)

Year	Three countries with the highest mercury production	Source
1980	USSR (2139), Spain (1697), Yugoslavia (1058)	US Bureau of Mines (1981)
1985	USSR (2240), Spain (1554), Algeria (793)	US Bureau of Mines (1986)
1990	USSR (2100), China (800), Mexico (735)	US Bureau of Mines (1991)
1995	Spain (1700), China (500), Algeria (450)	US GS (1996)
2000	Spain (600), Kyrgyzstan (600), Algeria (200)	US GS (2001)
2005	China (500), Kyrgyzstan (300), Spain (150)	US GS (2006)
2010	China (1400), Kyrgyzstan (250), Chile (150, Hg as a by-product)	US GS (2011)
2015	China (1600), Mexico—exports (500), Kyrgyzstan (70), Russia (50)	US GS (2016b)

shows the three countries with the highest production of Hg in the period 1980–2015.

By the end of 1970, mining mercury in European mines in Almaden, Monte Amiata, Idrija and North America, and Hg use in various sectors of the economy in those parts of the world, was significantly higher compared to developing countries in Europe and Asia. Over time, it changed significantly, and since 2005 China has been the world leader in extraction (Table 17.2). In 2015, 1600 tons Hg was excavated in China, accounting for nearly 70% of global production (US GS 2016b). It is estimated that 80% of the world's mercury reserves have already been processed through human products (Meinert et al. 2016).

Before 1980 metallic mercury had been used in significant quantities, mainly for the extraction of gold and silver (for centuries), in dental amalgam fillings, as a catalyst in the chlor-alkali industry (where liquid Hg is the cathode, and this is one of three chlorine production technologies) and production of vinyl chloride monomer (VCM) used to synthesize polyvinyl chloride, PVC, to produce tubes, bottles, window frames and many articles. Moreover, metallic Hg is used in measuring devices, in electrical and electronic switches as well as in fluorescent lamps. Inorganic mercury compounds were used, among others, in Hg-oxide batteries, as pigments and dyes and as antiseptics in pharmaceuticals, while organic compounds of Hg (including alkyl forms) were used mainly as effective biocides in the paper industry and were added as an antifouling agent to paints and as fungicide to protect seeds and plants from fungal diseases (Hylander and Meili 2003). Due to the strong toxicity of mercury, already well documented in medical and ecotoxicological studies from 1950 to 1980, and focusing on the protection of health and care for the quality of the environment, regulations limiting economic exploitation, mining and trade of mercury have been gradually introduced in the European Union (EU) and North America. In those parts of the world, mercury mines had been shut before 2002. The consequence of the aforementioned actions was a drastic reduction in demand for mercury and a drop in its prices (Hylander and Meili 2003; Parsons and Percival 2005; Mohapatra and Mitchell 2009; UNEP 2013).

World mercury mining in 1980 was still relatively high at 6811 tons, but in 2005 it fell to 1520 tons. At that time, production and consumption of mercury shifted significantly from Europe and North America to Asia (US GS 1981, 2006). In 2005, including in Asia, Europe and North America, various sectors of the economy consumed 3188 tons Hg, of which Asia accounted for almost 67%, Europe (EU25 + CIS and other European countries) for 22.5% and North America 10.8% (AMAP/UNEP 2008). In Asia, most mercury is used in VCM and battery production (750 and 280 tons, respectively), in EU25 in mercury-cell chlor-alkali production (175 tons) and dental amalgam production (95 tons) and in North America in mercury-cell chlor-alkali production (60 tons) and production of measuring and control devices (48 tons). Several years later (in 2011), the global demand for mercury had dropped to 1930 tons, and the dominant recipient of this metal was chemical manufacturing (including 15% of the chlor-alkali industry and 21% of vinyl chloride monomer production) and artisanal and small-scale gold mining ASGM (24%) and batteries (13%), and further positions were dental amalgams 8%, measuring and control devices 7%, electrical and electronic devices 7% and fluorescent lighting 4% (UNEP 2013). According to a report by the United Nations Environmental Programme (UNEP) Global Mercury Partnership and its mercury-cell chlor-alkali production partnership area, this industry saw a very noticeable reduction in global demand for mercury. Between the base year 2005 and 2015, the consumption of mercury in the chlor-alkali industry fell by 50%, from 500 to 250 tons, resulting from the reduction in the number of plants that uses mercury in the production of chlorine and alkalis, through their closure or a shift into mercury-free technology (UNEP 2016), especially in this regard in the EU, where the use of mercury in chlor-alkali industry will have ceased in 2017 (Eurochlor 2016).

Although between 1980 and 2007 the global demand for mercury fell dramatically, and its production decreased almost six times (from 6811 to 1170 tons according to US GS in 1981, 2008), in recent years this downward trend has unfortunately changed, caused by the global economic crisis in 2008. For comparison, in 2008 and 2015, the global production of mercury was, respectively, 1320 and 2340 tons, significantly higher than in 2007 (US GS 2010, 2016b). The current increase in demand for mercury is significantly associated with an increased demand for gold, as its acquisition by the inexpensive method of amalgamation requires Hg. This method is mainly used in ASGM in developing countries (UNEP 2013).

3.2.1 Emission Sources of Mercury

Hg is released from natural (geogenic) and anthropogenic sources, including intentional (Hg acquisition from its ores, meeting the needs of certain sectors of the economy) and unintentional, that accompany various production and energy processes. Geogenic sources of mercury in nature include volcanic eruptions, weathering of rocks, natural forest fires and steppes and evaporation of the seas and oceans. Partially, these also include areas around active and abandoned Hg mines (with the deposited waste), often with significant levels of that element.

Terrestrial sources and the oceans are credited with 48 and 52% of total annual emissions of mercury into the air. Researchers that from 80 to 600 tons of Hg reach from the land to the air, with the geogenic emissions mainly caused by mass burning (13%) and metal release from the desert, metalliferous and non-vegetated zones (10%), as well as some biomes such as tundra, grassland, savannah, prairie and chaparral (9%) (Pirrone et al. 2010; AMAP/UNEP 2013). In 2010 oceanic sources accounted for up to 2900 tons of Hg released into the global atmosphere, including the contribution from re-emission processes, which are emissions of previously deposited Hg originating from anthropogenic and natural sources, and primary emissions from natural reservoirs (AMAP/UNEP 2013).

Over the past few decades, the major sources of anthropogenic mercury unintentionally released into the air are the combustion of fossil fuels, mining and the processing of non-ferrous ores, cement production, natural gas cleaning, recycling and government stockpiles and incineration of sludge from biological treatment (Mohapatra and Mitchell 2009). Fossil fuels and various industrial raw materials usually contain small quantities of Hg (Table 17.1), but given the huge amounts used by man, their contribution to environmental pollution with Hg is a key position in its biogeochemical cycle. However, in 2010 it was recognized that global anthropogenic emissions of mercury to the air are mainly based on artisanal and small-scale gold mining (ASGM), before the process of burning coal for the needs of electro-energy (AMAP/UNEP 2013). It is estimated that in 2010, Hg from anthropogenic sources amounted to about 2000 tons, and another 1000 tons was released into waters, wherein the emission of water is much less recognized and evaluated in comparison to the atmospheric release. It is believed that chlor-alkali plants, paper pulp factories and mine wastes have been the major industrial sources that discharge mercury waste into water bodies (Mohapatra and Mitchell 2009; AMAP/UNEP 2013; UNEP 2013). In 2010, global atmospheric mercury emissions totalled 8900 tons, of which the current emissions from natural and anthropogenic sources account for 80–600 tons and about 2000 tons. The remaining amount of Hg (60%) in the annual amount came from re-emission, with the terrestrial and oceanic volumes estimated to be 1700–2800 and 2000–2950 tons, respectively (AMAP/UNEP 2013).

For about 200 years, we have seen a significant increase in the quantity of mercury circulating in nature. This is indicated by comparative studies of lake bottom sediments, peat deposits and core glaciers (Schuster et al. 2002; Allan et al. 2013). It is estimated that, compared to pre-industrial times, the concentration of Hg in the atmosphere and in the geochemical background has increased at least three times and probably 5–10 times in relation to the natural level (Mason et al. 2012; Horowitz et al. 2014). On a global scale, in the period 1850–2010, unintentional anthropogenic sources (from "by-product" sectors including fossil fuel combustion) issued to the atmosphere 215,000 tons of mercury. During that time, a further 540,000 tons of mercury was introduced into the environment from intentional commercial Hg uses and nonatmospheric releases from chlor-alkali plants and mining processes. From this very large pool, 20% reached the air, 30% waters, 30% soils and 20% landfill wastes. Some of this mercury remains in landfills

or is associated with bottom sediments, but a significant quantity (310,000 tons) actively participates in the geochemical cycle (Horowitz et al. 2014).

Emissions of mercury into the environment have clearly differed between the Northern and Southern Hemispheres, where human economic activity releases 70% and 30% Hg, respectively (Pacyna et al. 2006; Selin et al. 2008; Pirrone et al. 2010; AMAP/UNEP 2013). This disparity in the emissions of Hg between the two hemispheres has historical, economic and demographic reasons.

Mercury released from natural and anthropogenic sources circulates in nature for a long time and is transmitted over long distances by strong atmospheric and ocean currents. Probably, it will take about a thousand years before mercury is released from stable formations in the lithosphere and circulating in the air-water-soil system, settles on the ocean floor and is permanently bound by mineral deposits in the rock formation processes (Mason et al. 2012; Horowitz et al. 2014).

Between 1980 and 2007, the mining of mercury decreased almost six times, which was driven by the results of numerous studies and regulations for the protection of health and the environment. Scientific studies provide ample evidence of the strong toxicity of Hg (especially MeHg) on humans and other warm-blooded vertebrates and document a dramatic increase in the amount of anthropogenic environment (Hylander and Meili 2003; Clarkson and Magos 2006; Horowitz et al. 2014). Out of many disasters caused by environmental Hg poisoning, the best known are the tragic events from the Japanese Minamata Bay from the 1950s, with the mass Hg poisoning of residents, their cats and wild birds, via the fish and seafood consumed. The primary source of mercury was wastewater from chemical plants discharging into the bay. The increasing awareness of risks arising from the increase in the amount of anthropogenic Hg in the environment has led to the introduction of regulations aimed at limiting the extraction, use and trade of Hg and consequently a reduction in the release of mercury into the air, water and soil from anthropogenic sources. Such pro-health and pro-environmental legislative action were taken earliest in the well-developed countries of the EU, North America and Japan, but globally more important will be the implementation of the provisions of the Minamata Convention, adopted on 10 October 2013 at a diplomatic conference held in Kumamoto, Japan. The convention entered into force on 16 August 2017 (www.mercuryconvention.org).

3.3 Biological Status of Mercury

According to current knowledge, mercury does not have any physiological function in eukaryotic and in most prokaryotic organisms. Its accumulation results in various life-threatening disorders and can lead to fatal poisoning (Clarkson 1992; Barkay and Wagner-Döbler 2005; Scheuhammer et al. 2015). Recently, Gregoire and Poulain (2016) showed a peculiar exception among prokaryotes: photosynthetic microorganisms from the group of purple non-sulphur bacteria (representing genera

Rhodobacter and *Rhodopseudomonas*) are able to use Hg as an electron acceptor during photosynthesis.

Mercury was identified thousands of years ago and is one of the oldest toxicants known. The three forms of Hg, i.e. elemental, inorganic and organic mercury (especially CH_3Hg-R; methyl-Hg or MeHg), have different toxicological properties. Mercury can occur in compounds either in +1 or +2 oxidation state, i.e. in mercurous (I) and mercuric(II) compounds, respectively. In nature, inorganic divalent Hg (II) compounds predominate, with relatively few monovalent Hg(I) compounds. Monovalent Hg compounds are less toxic than Hg(II) compounds as they are less soluble in water (WHO 2003; Park and Zheng 2012).

The biogeochemical cycle of Hg and toxicity involve bacteria that produce MeHg. In the environment some anaerobic sulphate- and iron-reducing bacteria can methylate oxidized mercury (Hg^{2+}) and to a smaller degree Hg^0, thus generating MeHg (Hu et al. 2013; Li and Cai 2013). Biologically mediated production of MeHg predominantly occurs under anaerobic conditions in sediments of inland waters, nearshore and oceanic sea floors, as well as in peatlands, wetland soils and some rice paddy fields, for example, in China (Zhang et al. 2010; Gu et al. 2011; Windham-Myers et al. 2014; Zhao et al. 2016). MeHg is also present in most if not all aquatic organisms. Methylation of InHg to MeHg and demethylation of MeHg are the two most important processes in the cycling of MeHg, determining the levels of MeHg in aquatic and terrestrial ecosystems. Aerobic bacteria have evolved an efficient strategy of eliminating mercuric (Hg^{2+}) and organic mercury compounds (including MeHg) from the environment through the reduction of Hg^{2+} to Hg^0 (Li and Cai 2013).

Methylation and biomagnification of Hg have been well researched in aquatic ecosystems due to the consumption of Hg-contaminated fish, crayfish and molluscs, which may lead to poisoning of humans and other warm-blooded vertebrates. By contrast, studies on Hg and especially MeHg in terrestrial ecosystems are few (Clarkson 1992; Larosa and Allen-Gil 1995; Wolfe et al. 1998; Jackson et al. 2011; Douglas et al. 2012; Kalisinska et al. 2012a; Rieder et al. 2013; Scheuhammer et al. 2015). Since MeHg in aquatic ecosystems is subject to biomagnification, Hg reaches its highest levels in predatory fish, piscivorous birds and marine and semiaquatic mammals. Mercury concentrations in those biotas can be many millions of times greater than in the waters which serve as their aquatic habitat or food source (Lavoie et al. 2013; Finley et al. 2016). The greatest increase in MeHg concentration occurs in the trophic step between water and algae. It is estimated that the biomagnification factor (BMF) between water and seston often ranges from $\sim 10^5$ to $\sim 10^6$ with the BMF of MeHg concentrations between successive trophic levels above algae generally less than 10^1 (Wolfe et al. 2007). In terrestrial ecosystems, biomagnification of MeHg also occurs, yet this phenomenon has been much less researched (Rimmer et al. 2010; Rieder et al. 2013; Osborn et al. 2011; Jackson et al. 2015; Abeysinghe et al. 2017).

3.4 Mercury Toxicity

In the 1950s, dramatic events took place in the Japanese Bay of Minamata with many lethal mercury poisonings in humans, cats and wild birds. Over 3000 brain-damaged victims were diagnosed with "Minamata disease", and veterinary medicine introduced the term "dancing cats" to describe the neurological symptoms observed in cats. Both "Minamata disease" and "dancing cats" were the result of Hg poisoning accompanied by other contaminants spilled into the gulf from a nearby chemical factory. In the gulf's sediments, bacteria transformed inorganic mercury into MeHg, whose levels progressively increased in organisms from successive trophic levels. Large amounts of MeHg in fish, crustaceans and mussels were consumed by humans and animals inhabiting those areas, resulting in diseases and fatal poisonings (D'Itri 1991; Aronson 2005; Hachiya 2006; Ekino et al. 2007; Grandjean et al. 2010). Also in the 1950s, MeHg toxicity in the developing brain was first recognized in cases of congenital Minamata disease among newborns and children. At the same time, it was noted that the mothers had no symptoms of Hg toxicity or were minimal (Clarkson and Magos 2006; Ekino et al. 2007).

A few later studies from the 1960s to 1970s were conducted by Swedish naturalists on birds and rodents feeding on grains and on predators feeding on these granivores. They showed that Hg poisoning can also occur in terrestrial environments, not just aquatic environments. Inorganic and organic Hg compounds (including MeHg) were then common components of pesticides (fungicides) serving as seed dressing. Large quantities of Hg from the fungicides were detected in granivores and even larger levels in predatory birds and mammals preying on the passerines and rodents (Borg et al. 1969; Johnles and Westermark 1969). From 1960 to 1990, Hg-containing fungicides had been banned in Northern Hemisphere countries with highly developed agriculture (UNEP 2002). After all those years, it is very difficult to determine how much of the Hg pesticides has been introduced into the environment since the usage (launched in the first quarter of the twentieth century) lasted dozens of years. In the United States, Sweden and Japan, it is estimated that 800, 600 and 1600 tons of Hg fungicides were sprayed each year in rural areas of those countries (with Japan being more than 20 times smaller in area than in the United States) (Smart 1968; Kiesling and Lloyd 1971). Currently, agricultural soils are also being contaminated with anthropogenic Hg due to fertilization with sewage sludge, but this process is much less intense. It is estimated that in the EU, the Hg concentrations in sewage sludge recycled to agriculture vary among its member states from 0.2 to 4.6 mg kg^{-1} dw (Milieu Ltd. WRc and RPA 2010). In the 2000s the amount of mercury introduced into agricultural soils in the 27 EU countries probably exceeded 4 tons per year (AMAP/UNEP 2013). Total Hg from atmospheric deposition (derived from natural and anthropogenic sources) of agricultural origin and released from soil rocks contributes to pollution of the terrestrial environment. Mercury is washed away from these areas and is transported to various waters bodies where it is methylated and (partly as Hg^0) is released into the atmosphere and transported over considerable distances. In addition, soils in river valleys are

exposed to various forms of Hg during periodic inundations. However, in aquatic environments, as compared to land, Hg is to a much greater degree integrated into food chains, and aquatic food can be a significant threat to the health of humans and wildlife. Generally free-living terrestrial animals are chronically exposed to low concentrations of Hg contained in food, water and ambient air. Mercury toxicity has been studied at the levels of molecules, cells, tissues, organisms, species and ecosystems (Borg et al. 1969; Wren 1984; Scheuhammer et al. 1998a, b; Aschner 2000; Schurz et al. 2000; Silva-Pereira et al. 2005; Wolfe et al. 2007).

The toxicity of mercury has been attributed to its high affinity to protein-containing sulfhydryl (thiol) groups (–SH). These groups are especially abundant in proteins containing cysteine and methionine, which are sulphur amino acids. Proteins rich in cysteine include glutathione peroxidase (GSH-Px), metallothioneins (MTs) and keratins. GSH-Px belongs to the family of very important antioxidant enzymes, which also contain selenium (Se) (Clarkson and Magos 2006). MTs and keratin structures (including hair and feathers) may contain up to 30% and 26% of cysteine, respectively (Clarkson and Magos 2006; Agarwal and Behari 2007; Greenwold and Sawyer 2013). The MTs are low-molecular-weight proteins and are present in various cells (especially in the liver and kidneys) and serum of vertebrates, but they were also discovered in invertebrates. MTs have a few main hypothesized functions: homeostasis of essential metals such as zinc (Zn) and copper (Cu), detoxification of non-essential Hg and cadmium (Cd), protection against oxidative damage and free radical scavenging (Isani and Carpenè 2014).

All mercury species are accumulated by eukaryotic organisms. Vertebrates can uptake toxic mercury from the environment through the lungs, gills, skin and from the digestive tract. In wildlife the alimentary tract plays the most important route. From avian and mammalian gastrointestinal tracts, MeHg is most effectively absorbed at a rate over 90%. InHg is absorbed from the diet, at most at a rate of a few to a dozen percent, and Hg^0 at <0.01% (Serafin 1984; Clarkson and Magos 2006; Park and Zheng 2012; Ye et al. 2016). Inhaled Hg^0 vapour in the lungs of mammals is absorbed at up to 85%, as demonstrated by experimental research on mammals and epidemiological studies of humans occupationally exposed to mercury vapour (Pendergrass et al. 1997; Falnoga et al. 2000; Bose-O'Reilly et al. 2010; Bernhoft 2012).

Mercury toxicity studies have taken into account many factors, including the physico-chemical properties of this element. Mercury is classified as a chalcophile element (alongside Se, Cd and Pb), with a typically higher affinity to sulphur (S) and a lower affinity to oxygen (O) than iron (Fe). In living organisms, Hg is highly competitive in relation to essential metals, mainly Zn and Cu, which are displaced from the S binding sites in cysteine to be replaced by Hg^{+2} and/or $MeHg^+$. Sulphur amino acids (cysteine, Cys, and methionine, Met) are constituents of enzyme, transport and structural proteins, which after binding to Hg change their properties and structure (Grosicki and Kowalski 2002; Fraga 2005; García-Barrera et al. 2012; Dobrakowski et al. 2013). In the case of Cys, over the course of evolution, S has been replaced by Se to form the 21st amino acid, selenocysteine (SeCys). It is a natural component of selenoproteins in all animal kingdoms including vertebrates

(Lu and Holmgren 2009). From this group of proteins, the most important are enzymes such as GSH-Px, thioredoxin reductase and iodothyronine deiodinase. These proteins participate in the antioxidant protection of cells and the metabolism of thyroid hormones and of immunological processes. Selenoproteins may contain from 1 to 15 SeCys per protein subunit (Ralston et al. 2008; Mehdi et al. 2013). $MeHg^{+}$ ions possess electrophilic properties, and they interact with and oxidize nucleophilic groups of various biomolecules, especially those containing sulfhydryl groups. Besides proteins (i.e. antioxidant enzymes, neurotransmitter receptors, transporters), sulphydryl groups contain nonprotein thiols such as cysteine and glutathione, GSH (Farina et al. 2013). GSH is an important antioxidant in animals, preventing damage to cellular components caused by reactive oxygen species and other factors including Hg^{+2} and $MeHg^{+}$ (Schurz et al. 2000; Pompella et al. 2003; Clarkson and Magos 2006; Wolfe et al. 2007).

As the binding affinity of Hg for Se is up to a million times higher than for S, Hg (especially Hg^{2+} and $MeHg^{+}$) inexorably sequesters Se, directly impairing selenoenzyme activity and synthesis. At the same time, Se compounds are able to decrease the toxicity of Hg, which has been established in all investigated species of mammals, birds and fish (Dietz et al. 2000; Belzile et al. 2009; Ralston and Raymond 2010).

3.4.1 Mercury Cytotoxicity, Genotoxicity, Cancerogenicity and Teratogenicity

The cytotoxicity and genotoxicity of the various forms of Hg are evaluated mainly in vitro assays on human and non-human cell lines (De Flora et al. 1994; Silva-Pereira et al. 2005; Robinson et al. 2010; Polunas et al. 2011; Fernandes Azevedo et al. 2012; Roy et al. 2013; Wang et al. 2013, 2016). The results of in vivo Hg genotoxicity tests (based mostly on leucocytes) that assessed the damage of nuclear genetic material (comet assay, micronucleus test, chromosome aberration tests) do not always confirm differences between the material obtained from warm-blooded vertebrates exposed to Hg and from control/comparison groups (Hansteen et al. 1993; Rozgaj et al. 2005; Kenow et al. 2008; Crespo-López et al. 2009). Various ions of Hg exhibit a high ability to bind –SH groups of protein and nonprotein compounds, and on this ground a number of hypotheses have been formulated about molecular mechanisms of Hg genotoxicity. In this respect, the most commonly mentioned are four mechanisms: oxidative stress connected with generation of free radicals, effect on microtubules, influence on DNA repair mechanisms and direct interaction with DNA molecules (De Flora et al. 1994; Myers and Davidson 1998; Burbacher et al. 1990; Crespo-López et al. 2009).

In vitro cytotoxicity studies have shown that in various human and animal cell lines, both InHg and MeHg induce numerous adverse changes. These changes mainly rely on altering mitochondrial function and raising oxidative stress by generating free radicals or by interacting with sulfhydryl groups (Polunas et al. 2011; Farina et al. 2013; Agrawal et al. 2015; Wang et al. 2013, 2016). Additionally,

in human embryonic neural progenitor cells, MeHg induces oxidative damage to mitochondrial DNA (Wang et al. 2016).

The carcinogenetic potential of InHg is still being debated. In the 1990s the International Agency for Research on Cancer (IARC 1993) classified MeHg compounds as possibly carcinogenic to humans (Group 2B), but metallic mercury and InHg compounds were not classifiable as carcinogenic to humans (Group 3). The classifications of MeHg, Hg^0 and InHg are still in use by the IARC (2017). Drasch et al. (2004) reviewed papers concerning the influence of Hg on laboratory rats and mice and revealed that male rats receiving extremely high oral doses of $HgCl_2$ or MeHgCl had an increased number of renal tubule tumours. These compounds caused severe nephropathy in the rodents. It is likely that dietary MeHgCl may act in mice as a tumour promoter. However, the connection between Hg exposure and carcinogenesis remains controversial (Drasch et al. 2004; Crespo-López et al. 2009).

Methylmercury is known as an embryotoxic and teratogenic agent. The teratogenicity of MeHg is well documented in fish, birds, mammals and humans. This compound especially affects normal development of the central nervous system (Domingo 1994; Samson and Shenker 2000; Schurz et al. 2000; Heinz et al. 2011; Gandhi et al. 2013). In addition to the already mentioned adverse effects of Hg on wildlife, its effects on endocrine and immune systems are also important (Zhu et al. 2000; Kenow et al. 2007; Tan et al. 2009). Tan et al. (2009) listed five main endocrine-related mechanisms of Hg across these systems: (a) accumulation in the endocrine system, (b) specific cytotoxicity in endocrine tissues, (c) changes in hormone concentrations, (d) interactions with sex hormones and (e) upregulation or downregulation of enzymes within the steroidogenesis pathway. However, disorder and impairment of endocrine and immune systems by Hg and the net effects on the demography of wild animals are poorly understood (Kenow et al. 2007; Frederick and Jayasena 2011).

3.4.2 Mercury Neurotoxicity and Lethal Levels of Total Mercury in Soft Tissues

All three Hg species may occur in the brain, including elemental Hg. A certain part of inhaled Hg^0 is deposited in the brain as demonstrated in humans and laboratory animals (Warfvinge et al. 1992; Tjälve and Henriksson 1999; Bose-O'Reilly et al. 2010; Park and Zheng 2012). Also Hg^0 can be transported through the olfactory pathway to the olfactory bulbs and later into other brain areas (Galić et al. 1999; Tjälve and Henriksson 1999; Park and Zheng 2012). As Hg^0 is lipid soluble and highly diffusible, it can cross the blood-brain barrier and other cellular and intracellular membranes (Park and Zheng 2012). In humans inhalation of Hg^0 vapour can cause acute and chronic intoxication. Typical symptoms connecting with this include airway symptoms and many neurological problems (tremor, ataxia, coordination disturbances, abnormal reflexes, polyneuropathy with sensation difficulties, loss of memory, neurocognitive disorders) as well as kidney problems such as proteinuria (Bose-O'Reilly et al. 2010). In laboratory animals, the neurological symptoms

following exposure to Hg^0 are poorly understood, but in rats a significant increase in Hg concentrations in different parts of the brain (primarily in the neocortex, in the basal nuclei and in the cerebellar granule cells) and in the kidneys were shown in comparison to the control group (Warfvinge et al. 1992; Galić et al. 1999). Unlike elemental and organic mercury species, the oxidized Hg forms (Hg^{2+}) are not able to effectively cross the blood-brain barrier, but such process could not be excluded (Park and Zheng 2012). Organic Hg compounds, especially MeHg, can easy cross the blood-brain barrier (however, less efficiently as Hg^0) and are accumulated in vertebrate brains. The probable active transport of MeHg (via neutral amino acid transporters) into the brain is preceded by the formation of MeHg-cysteine complexes (ADSTR 1999; Clarkson and Magos 2006). MeHg does not uniformly affect the nervous system, and Hg concentration in the brain varies between the compartments (Eto et al. 1999, 2010; Farina et al. 2013).

Speciation analyses of brain Hg in vertebrates show that a much larger proportion of THg is present in the form of MeHg (typically >80%) and a small fraction as InHg. Depending on the degree and duration of exposure to MeHg, the percentage of brain THg may change over time and varies greatly between individuals of the same species and between various species. In extreme cases in some people exposed to MeHg in childhood and for more than 20 years, up to 80% of brain THg may be InHg (Farina et al. 2013). Most wildlife is exposed to long-term exposure to small amounts of MeHg contained in the diet, with the exception of long-living piscivorous species. MeHg, which has penetrated into the brain, is gradually demethylated and transformed into InHg. The demethylation of MeHg has been found in the brain of humans and several wild species of birds and mammals from inland environments (Eto et al. 1999; Gnamuš and Horvat 1999; Scheuhammer et al. 2008; Strom 2008; Eagles-Smith et al. 2009; Haines et al. 2010; Basu 2012; Kalisinska et al. 2014a; Jo et al. 2015). Presumably, the remaining part of brain InHg can occur in insoluble and biologically inert compounds with selenium such as tiemannite (HgSe) (Whanger 2001; Nakazawa et al. 2011). In long-lived animals and humans, the half-life for MeHg in the brain is determined in days or months, but for InHg it is many years (Vahter et al. 1994; ADSTR 1999; Rice et al. 2014). Until recently it had been assumed that MeHg that gets into the brain did not leave, similar to InHg produced by MeHg demethylation or oxidation of Hg^0. However, works by Lohren et al. (2015, 2016), investigating MeHg and InHg transfer across the blood-brain barrier in a primary in vitro porcine model, may lead to the revision of this view. In the latter paper, Lohren et al. (2016), the researchers documented the transport of MeHg via the barrier in both directions, with diffusion as the transfer mechanism. Additionally for $HgCl_2$, their data delivered evidence that the blood-brain barrier transfers InHg out of the brain.

Lethal brain levels of Hg have not yet been established for most mammals and birds. In literature, in the brains of piscivorous mammals experimentally intoxicated with MeHg, river otter *Lontra canadensis* and American mink *Neovison vison* (previously *Mustela vison*), Hg levels were 23.7 and 19.9 mg kg^{-1} ww and 11.9 mg kg^{-1} ww, respectively (Aulerich et al. 1974; Wobeser et al. 1976; O'Connor and Nielsen 1981). In field studies in North America, brain Hg in single dead or

dying river otter and mink were ~30 and 13.4 mg kg^{-1} ww, respectively (Wren 1985; Sleeman et al. 2010; Wobeser and Swift 1976). A lower range was shown by THg concentrations (8.1–18.6 mg kg^{-1} ww) in experimentally and non-intentionally intoxicated domestic cats from Japan and Northwestern Ontario Reserve (Canada), which revealed neurological symptoms typical for Minamata disease (Takeuchi et al. 1977). Shore et al. (2011) defined >10 mg THg kg^{-1} ww as a lower indicative value in mammalian brains, which may be associated with adverse effects on survival and resulting in death. Krey et al. (2015) analysed a large number of reports on mammalian brain Hg concentrations and proposed a THg threshold concentrations for toxic endpoints: clinical symptoms >6.75 mg kg^{-1} ww (29 mg kg^{-1} dw), neuropathological signs >4 mg kg^{-1} ww (17.2 mg kg^{-1} dw), neurochemical changes >0.4 mg kg^{-1} ww (1.72 mg kg^{-1} dw) and neurobehavioral changes >0.1 mg kg^{-1} ww (0.43 mg kg^{-1} dw).

In adult passerines (starling *Sturnus vulgaris*, grackle *Quiscalus quiscula*, red-winged blackbird *Agelaius phoeniceus*, brown-headed cowbird *Molothrus ater*, zebra finch *Poephila guttata* and piscivorous great egret *Ardea albus*), which were experimentally intoxicated with MeHg, the concentration of brain THg was in the range of 20–45 mg kg^{-1} ww (Finley et al. 1979; Scheuhammer 1988; Spalding et al. 2000). The highest THg residues in brains among wild birds found dead in fields were within the range of 13–14 mg kg^{-1} ww: in tawny owl *Strix aluco* from Norway feeding on small rodents, piscivorous white-tailed eagle *Haliaeetus albicilla* from Sweden and common loon *Gavia immer* from Canada (Jensen et al. 1972; Holt et al. 1979; Scheuhammer et al. 2008). The values found in wild birds were clearly smaller than in experimental studies, but free-living animals are more exposed to various adverse environmental factors, including food shortages, than captive ones (Van der Molen et al. 1982; Wiener et al. 2003). A combination of the environmental factors can cause premature death before brain THg levels in birds reach ≥20 mg kg^{-1} ww, established as lethal in laboratory conditions. In addition, dead animals are quickly eaten by scavengers, which is why they are rarely obtained for analysis. It has been experimentally shown that chicks are more sensitive to the toxic effects of Hg than adult birds. Data presented by Heinz and Locke (1976) indicate that lethal brain THg levels can be as low as 3–7 ppm in mallard ducklings. Shore et al. (2011) suggested indicative values of THg concentrations for avian brains of non-marine species, which may be associated with bird deaths at >15 mg kg^{-1} ww and >3 mg kg^{-1} ww in adults and developing youngs, respectively, and correspond well to data from Jensen et al. (1972), Holt et al. (1979), Scheuhammer et al. (2008) and Heinz and Locke (1976). Neurological symptoms (e.g. trembling) have been observed in 1 hatch-year osprey with 1.2 mg kg^{-1} ww THg in the brain (or 6.2 mg kg^{-1} dw) (Hopkins et al. 2007). However, THg threshold concentrations for toxic endpoints analogous to those proposed for mammals have not been developed, i.e. ones that would include subclinical, neuropathological, neurochemical and neurobehavioral changes, although some attempts have been made in this regard (Scheuhammer et al. 2008; Rutkiewicz et al. 2011; Rutkiewicz 2012).

Mercury is not only neurotoxic but also nephrotoxic for elemental and inorganic mercury species. The kidney is a major repository of InHg in warm-blooded

vertebrates. Within the kidney divalent Hg accumulates primarily in the cortex and outer stripe of the outer medulla (Aschner and Aschner 1990; Wolfe et al. 1998; Bridges and Zalups 2010). It should be underlined that birds differ from mammals in having a renal portal system. In birds the venous blood from the terminal portion of the digestive tract flows to the kidney rather than the liver, as in mammals. This may make the avian kidney more vulnerable than the mammalian (Wolfe et al. 1998). Indicative values of THg concentrations in mammalian kidney associated with death, as proposed by Shore et al. (2011), are lower than in avian species, >25–30 mg kg^{-1} ww compared to >40 mg kg^{-1} ww. Also THg indicative value estimated for the adult mammalian brain are lower than in the analogous avian organ. However, in the case of the liver, the indicative value is higher in mammals than birds: >25–30 THg kg^{-1} versus >20 mg THg kg^{-1} (Shore et al. 2011).

Lethal concentrations of THg in the soft tissues of mammals and birds are most commonly determined in the liver and kidney, followed by the brain. Muscles are rarely taken into consideration, although they constitute a large part of the body weight of the animals, and the collection of muscle samples is easy when compared to the brain (Finley et al. 1979; O'Connor and Nielsen 1981; Wren et al. 1987; Farrar et al. 1994; Thompson 1996; Shore et al. 2011; WVDL 2015). In addition, the efficient functioning and coordination of skeletal muscles play a key role, especially in predators, because they co-determine the effectiveness of hunting. Based on relatively scarce data concerning THg concentrations in tissue pairs: liver (L)–muscle (M) and muscle–brain (B) in adult individuals of wild animals and birds, and those experimentally intoxicated with organomercury, correlation coefficients (r) and the values of two indices M_{THg}/L_{THg} and B_{THg}/M_{THg} were calculated, and potentially lethal muscle THg concentrations were estimated. In both animal groups, an increasing hepatic THg concentration was initially accompanied by a marked increase in muscle levels (Fig. 17.1, panels a and b). After exceeding ~10 mg kg^{-1} ww in the muscle, the increase in THg slowed down and stabilized at 25–35 and 25–40 mg kg^{-1} ww in mammals and birds, respectively, while the hepatic THg significantly exceeded 100 mg kg^{-1} ww over time in some cases. Among inland mammalian and avian species, the highest hepatic THg levels were detected in river otter (96 mg kg^{-1} ww) and common loon (200 mg kg^{-1} and 370 mg kg^{-1} ww) (Wren 1985; Stone and Okoniewski 2001; Scheuhammer et al. 2008). In the livers of marine mammals and birds, levels exceeding 1000 and 200 mg THg kg^{-1} ww, respectively, were found in some cases (Kim et al. 1996; Storelli et al. 1999; Pompe-Gotal et al. 2009).

In the multispecies groups of mammals and birds, the correlation coefficient between the concentration of THg in the liver and muscle exceeded 0.95, and the values of r were, respectively, 0.928 and 0.964 (Fig. 17.1, panels a and b). Using the appropriate equations from panels A and B, we calculated THg concentrations for avian and mammalian muscle when the concentration of hepatic THg reached the lower limit values of the estimated lethal range (25 and 20 mg kg^{-1} ww, respectively) (Shore et al. 2011). At these hepatic THg concentrations in mammalian and avian muscle, potentially lethal values were 9.8 and 7.3 mg kg^{-1} ww. Other researchers had also found a significant correlation (r ranging from 0.60 to 0.98) between muscle

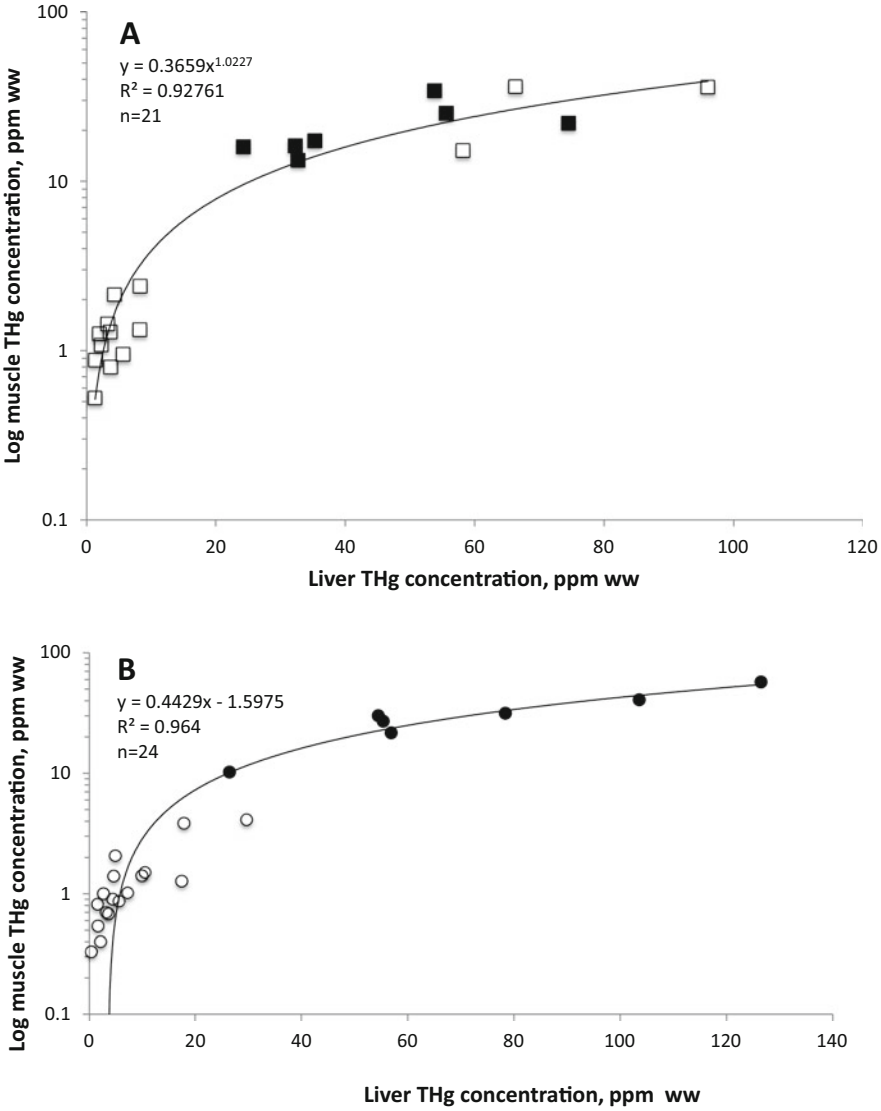

Fig. 17.1 Relationship between total mercury (THg) concentrations (mg kg^{-1} = ppm ww, wet weight) in liver and muscle, muscle and brain in terrestrial mammals and birds. Panel (**A**) Used data of intoxicated mammals such as river otter *Lontra canadensis* (O'Connor and Nielsen 1981), American mink *Neovison vison* (Aulerich et al. 1974; Wobeser et al. 1976), cat *Felis catus* (Charbonneau et al. 1974), ferret *Mustela putorius furo* (Hanko et al. 1970) and wild animals such as river otter (Sheffy and St Amant 1982; Wren 1985; Langlois and Langis 1995; Fortin et al. 2001; Strom 2008; Sellers 2010; Sleeman et al. 2010; Dornbos et al. 2013), Eurasian otter *Lutra lutra* (Hernández et al. 1985; Hyvärinen et al. 2003; Lodenius et al. 2014), American mink *Neovison vison* (Sheffy and St Amant 1982; Langlois and Langis 1995; Fortin et al. 2001; Wobeser and Swift 1976). Panel (**B**) Used data of intoxicated birds such as cowbird *Molothrus ater* (Finley et al. 1979), redwing *Agelaius phoeniceus* (Finley et al. 1979), starling *Sturnus vulgaris*

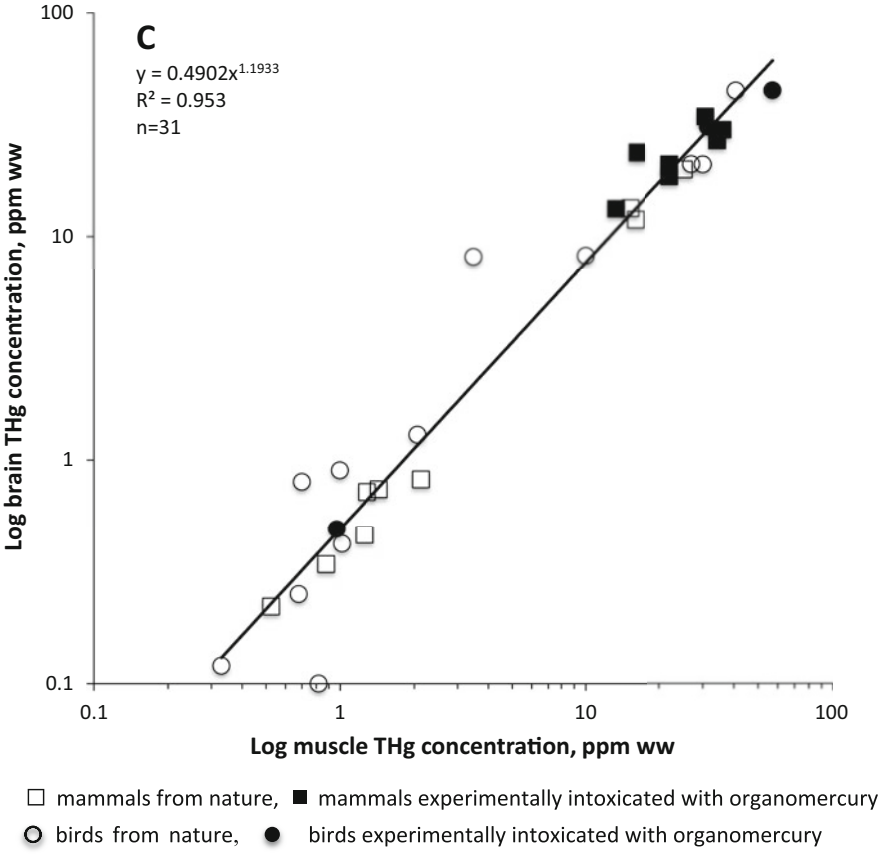

Fig. 17.1 (continued) (Finley et al. 1979), grackle *Quiscalus quiscula* (Finley et al. 1979), American kestrel *Falco sparverius* (Bennett et al. 2009), mallard *Anas platyrhynchos* (Hough and Zabik 1972) and wild birds from nature such as osprey *Pandion haliaetus* (Holt et al. 1979; Norheim and Frøslie 1978; Evers et al. 2005; Hopkins et al. 2007; Kalisinska et al. 2014a), bald eagle *Haliaeetus leucocephalus* (Evers et al. 2005; Evans 1993), white-tailed eagle *H. albicilla* (Norheim and Frøslie 1978; Kalisinska et al. 2014a; Henriksson et al. 1966; Falandysz et al. 2000), common loon *Gavia immer* (Evers et al. 2005; Scheuhammer et al. 1998b), common merganser *Mergus merganser* (Langlois and Langis 1995; Scheuhammer et al. 1998b; Kalisinska et al. 2010). Panel (**C**) Used data of intoxicated mammals: river otter (O'Connor and Nielsen 1981), American mink (Aulerich et al. 1974; Wobeser et al. 1976), cat (Charbonneau et al. 1974), ferret (Hanko et al. 1970) and wild mammals from nature such as river otter (Sheffy and St Amant 1982; Wren 1985; Fortin et al. 2001; Strom 2008; Sleeman et al. 2010; Dornbos et al. 2013), American mink (Sheffy and St Amant 1982; Fortin et al. 2001; Wobeser and Swift 1976), Eurasian otter (Kalisinska et al. 2016, 2017); intoxicated birds, cowbird (Finley et al. 1979), redwing (Finley et al. 1979), starling (Finley et al. 1979), grackle (Finley et al. 1979), mallard (Hough and Zabik 1972); and wild birds from nature, osprey (Holt et al. 1979; Hopkins et al. 2007; Kalisinska et al. 2014a), bald eagle (Evans 1993), white-tailed eagle (Holt et al. 1979; Kalisinska et al. 2014a; Henriksson et al. 1966; Jensen et al. 1972), common merganser (Kalisinska et al. 2010)

and hepatic THg concentrations in inland mammals (Lord et al. 2002; Millan et al. 2008; Strom 2008; Kalisinska et al. 2009; Lodenius et al. 2014) and birds (Hopkins et al. 2007; Eagles-Smith et al. 2008), although not always (Halbrook et al. 1994; Kalisinska et al. 2010; Lanocha et al. 2014). These ambiguous results may be related to the large variations of hepatic THg concentration and M_{THg}/L_{THg} index in endothermic animals exposed to Hg. The mean value of the index is statistically higher in mammals than birds (0.42 versus 0.31, $t = 2.34$; $p < 0.03$). Wolfe et al. (2007) emphasized a poor correlation between liver THg concentration and its effects. Unlike the liver, the muscle THg concentration is more representative of brain THg concentration and correlates better with its effect. Moreover, MeHg is a dominant species of Hg in the brain and muscle tissues. These suggestions are supported by our analysis of data on THg concentration in the muscle and brain of mammals and birds combined into one group (Fig. 17.1, panel c). The correlation coefficient for this relationship exceeded 0.97, and values of the index B_{THg}/M_{THg} for mammals and birds were close, at 0.73 and 0.82, respectively. In another study, Shore et al. (2011) suggested that the lethal concentrations of THg in the brain of mammals and birds are >10 and >15 mg kg^{-1} ww, respectively. Taking into consideration the equation from panel c, it may be assumed that the lethal THg level in muscle is about 13 mg kg^{-1} ww for mammals and 18 mg kg^{-1} ww for birds. On the basis of equations from Fig. 17.1, it can be assumed that the lethal concentration of THg in the muscles of mammals and birds is in the range 10–13 mg kg^{-1} ww and 7–18 mg kg^{-1} ww, respectively. Heinz (1996), based on literature data, estimated that muscle Hg concentrations associated with harmful Hg exposure in adult birds ranged from 15 to 30 mg kg^{-1} ww. In the context of our analysis of avian muscle, it seems that the lower value suggested by Heinz (1996) is more likely.

3.4.3 Inorganic and Organic Mercury Distribution in Bodies of Mammals and Birds

The three forms of Hg (elemental, inorganic and organic) that penetrate the organisms of vertebrates differ with respect to their toxicokinetics regarding absorption, distribution and accumulation. In laboratory studies, the influence of MeHg (in MeHgCl form) and mercury compounds of Hg(II) (especially $HgCl_2$) are most frequently investigated. Mercurous mercury Hg(I), for example, in the form of mercurous chloride (Hg_2Cl_2), is little absorbed in the body. This compound readily dissociates in body fluids where, from Hg_2Cl_2, double atom cations of Hg_2^{2+} are realized and from this is formed one atom of divalent Hg^{2+} and another of elemental mercury (Hg^0). Elemental mercury from this unimportant source and the vapour of this metal from inhaled air are oxidized into the mercuric form (Hg^{2+}) in erythrocytes and tissues. Both inorganic and organic Hg species are excreted primarily in faeces. Absorption of MeHg from the digestive tract in warm-blooded vertebrates is very high (about 90%), with a great amount of it excreted in faeces (about 85–90%) and 5% with urine. Scientists have estimated that only up to 15% of absorbed MeHg is incorporated in various tissues and organs. Fur or hair in mammals as well as feather

in birds are also an important route of excretion, especially MeHg (Farris et al. 1993; Clarkson and Magos 2006; Wolfe et al. 2007).

Mammalian pelt and avian plumage sometimes incorporates even >80% of THg in the body. MeHg is permanently built into hair and feathers during their growth. It is a dominant species of Hg in these tissues and becomes biologically inactive there, as confirmed in studies on experimental animals and wildlife from inland ecosystems. After long exposure to MeHg in laboratory experiments and chronic exposure of wildlife, MeHg and/or THg concentrations in these keratin skin structures usually reach the highest values in comparison to liver, kidney, brain and muscle THg (Thomas et al. 1988; Farris et al. 1993; Wood et al. 1996; DesGranges et al. 1998; Mierle et al. 2000; Hyvärinen et al. 2003; Bennett et al. 2009; Lieske et al. 2011; Nam et al. 2012; Wang et al. 2014). However, THg and/or MeHg are rarely assayed in all of the mentioned tissues in the same individuals. Eventually, MeHg is removed from mammalian and avian bodies during moulting, and therefore hair and feathers are also an important additional route of Hg excretion (Honda et al. 1986; Farris et al. 1993; Clarkson and Magos 2006; Wolfe et al. 2007; Wang et al. 2014; Evans et al. 2016). After Hg in fur and feathers, the second largest Hg pool can be found in skeletal muscles, with up to 50% of the remaining MeHg in the body (Farris et al. 1993; DesGranges et al. 1998; Saeki et al. 2000; Nam et al. 2005) from the large proportion of skeletal muscles in the body mass of vertebrates and their vasculature. For example, in the body of predatory mammals and birds, these muscles represent on average 50–55% and 30–40% of body mass, respectively (Honda et al. 1986; Biewener 2011; Muchlinski et al. 2012), and in the case of fish, it is up to 70% of their body weight (Kisia 1996). In the muscles of warm-blooded vertebrates from inland ecosystems, Hg occurs mainly in the form of MeHg (70–95% of THg), and the concentration is usually low (<0.50 mg kg^{-1} ww), with the exception of the muscles of fish species near the top of a food web and piscivorous wildlife (Wren et al. 1980; Mason et al. 1986; Rothschild and Duffy 2005; Kinghorn et al. 2007; Strom 2008; Ruelas-Inzunza et al. 2009; Chumchal et al. 2011; Burger et al. 2013; Hall et al. 2014; Kalisinska et al. 2014a, b, 2017; Wentz et al. 2014). Observed transient storage of large amounts of MeHg in the muscle may protect other tissues against MeHg toxicity.

Because of the large proportion of muscles in body weight and easily digestible MeHg contained in them, they play an important role in the transfer of this substance from freshwater invertebrates and fish to semiaquatic piscivores and benthophages and from carrion of these animals to terrestrial scavengers (Sheffy and St Amant 1982; Halbrook et al. 1994; Langlois and Langis 1995; Fortin et al. 2001; Evers et al. 2005; Chumchal et al. 2011; Kalisinska et al. 2009, 2016). However, mercury, especially MeHg, is rarely assayed in the muscles of warm-blooded vertebrates. Among the tissues of terrestrial vertebrates, Hg achieves the highest concentration in the liver and kidneys, so THg is most frequently analysed in these organs, although in total they account for no more than 4–6% of the body weight of mammals and birds (Fischer and Bartlett 1957; Holliday et al. 1967; Hughes 1970; Kruska and Schreiber 1999; Lanszki et al. 2008; Balk et al. 2009; Kalisinska et al. 2010). In the kidney and livers of many fish-eating mammalian and avian species, the percentage

of MeHg decreases as THg concentration increases in the organs (Norheim and Frøslie 1978; Wiener et al. 2003; Gamberg et al. 2005a). The liver and kidney have been suggested as one of the major sites of MeHg demethylation in mammals and birds. Above the threshold value of 10 mg THg kg^{-1} dw (~3 mg THg kg^{-1} ww), hepatic %MeHg declines rapidly from a high value (~90%) (Eagles-Smith et al. 2009). However, interspecies differences are observed in this respect, and hepatic intensification of MeHg demethylation in birds can occur already in the range of 5–7 mg THg kg^{-1} dw, because then %MeHg in THg falls below 70% (Scheuhammer et al. 1998b; Dietz et al. 2013; Kalisinska et al. 2014c). Some researchers (Gamberg et al. 2005a; Martin et al. 2011) suggest that in piscivorous mammals (such as mink), the demethylation process of hepatic MeHg is activated well below the 30 mg THg kg^{-1} dw threshold (10 mg kg^{-1} ww) suggested by Wiener et al. (2003). Energy costs of MeHg demethylation in avian and mammalian livers are probably high but to date have not been estimated (Eagles-Smith et al. 2009; Dietz et al. 2013; Kalisinska et al. 2014c). Methylmercury demethylation is observed in tissues other than the liver and kidney but at a lower intensity and efficiency. This process is well documented in the brain of a number of mammals and birds, including terrestrial species. However, species of endothermic animals differ in the proportion of brain MeHg to THg (Vahter et al. 1994; Farina et al. 2003; Scheuhammer et al. 2008, 2015). It is generally assumed that demethylation of MeHg in fish and other vertebrate muscles does not occur or is negligible, with the percentage of MeHg in THg usually exceeding 80–90% (O'Connor and Nielsen 1981; Houserova et al. 2006; Strom 2008; George et al. 2011; Kalisinska et al. 2014b; Harley et al. 2015; Scheuhammer et al. 2015). However, in a few papers concerning the muscle of fish, birds and mammals, we can find data indicating that %MeHg can be $\leq$70%, especially in cases where THg $<$ 0.5 mg kg^{-1} ww. Pal et al. (2012) and Park et al. (2010) found in 8 out of 13 (8/13) and 5/13 investigated Asian freshwater fish species (generally with muscle THg 0.05–0.45 mg kg^{-1} ww) mean values of % MeHg were in the range 50–69%. Sometimes in predatory freshwater fish (such as *Elops machnata* and *Pelates quadrilineatus* from Taiwan), whose muscles contained $>$1 mg THg kg^{-1} ww, MeHg did not exceed 70% of THg (Huang et al. 2008). In three aquatic birds species from Mexico THg muscle levels varied from 0.32 to 0.45 mg kg^{-1} ww, and the %MeHg was in the range of 26–61% (Ruelas-Inzunza et al. 2009). In two populations of white-tailed eagle from Europe, the share of MeHg reached 45 and 58% when the mean THg in the eagle muscle was just 4.8 and 0.46 mg kg^{-1} ww, respectively (Norheim and Frøslie 1978; Kalisinska et al. 2014a). In the muscle of the piscivorous river otter mean, 72% MeHg of THg was sporadically revealed (THg = 0.89 mg kg^{-1} ww, Wren et al. 1980), but in marine cetaceans a value $<$70% was very often noticed. In 11 out of 16 studied species, the means were in the range 36–67%, and THg concentrations varied from 1.0 to 39.5 mg kg^{-1} ww (Endo et al. 2005). The data quoted above may indicate that MeHg demethylation in vertebrate muscles does occur, although this process requires further investigation and collection of more data. On the basis of comparative studies of two populations of blue shark (*Prionace glauca*) from the Azores and the Canary Islands, Branco et al. (2004) speculated that the diet of migrating animals may differ

significantly in MeHg content due to differences in exposure to Hg at different locations. Periodic stays in areas where prey contains less MeHg promote gradual demethylation and elimination of MeHg already accumulated in the muscles of sharks, and at the same time the supply of new portions of MeHg with food to their organisms is then lower. Branco et al. (2004) found in the shark's muscle from the Canaries %MeHg much lower than in sharks from the Azores 55–70% and >80%, respectively, although muscle THg concentrations were similar.

3.5 Mercury in Elements of Inland Food Chains

Food is the main source of Hg for humans and wildlife, but its absorption from digestive tract is strictly dependent on the chemical form and amount of Hg in various diets. Mercury concentrations increased from autotrophic organisms to herbivores < detritivores < omnivores < carnivores (Rimmer et al. 2010). For terrestrial herbivorous and omnivorous animals, plant, fungi and invertebrates are the most important components of their food. Soil invertebrates, insects, spiders and other arthropods or small- and medium-sized birds and mammals are eaten by different predators depending on their body size and food preferences. Some carnivore mammals and aquatic birds of inland habitats are highly specialized in catching fish. Below are presented some aspects of Hg transfer between different environmental components, including soil and plants, plants and warm-blooded herbivores as well as preys and predators.

3.5.1 Mercury in Plants and Mushrooms

The amount of MeHg in soils is low relative to THg, and the dominant form in soils is InHg (Burton et al. 2006). Bioavailability of soil InHg for plants is very low. A significant part of the InHg taken from the soil is retained in the roots, which are a barrier to mercury uptake. There is a positive correlation between the concentration of InHg in the soil and roots, but it does not occur between soil Hg and its content in shoots and leaves, which are about ten times lower than in the roots, and probably the transport of Hg from the roots to the stems either does not occur or is a very slow process (Wang and Greger 2004; Tomiyasu et al. 2005). The main soil factors affecting the collection of this toxic metal by plants include organic matter, oxygen and carbon, redox potential, Hg species and their concentrations and the presence of other metals in the soil solution (Tomiyasu et al. 2005; Patra and Sharma 2000; Azevedo and Rodriguez 2012). In plants, the dominant form is InHg, which is >97% THg (Mailman and Bodaly 2005; Dombaiová 2005). In unpolluted areas, THg concentration in leaves is negligible and is characterized by considerable variability, ranging from several to several dozen micrograms per kilogram of dry matter ($\mu g\ kg^{-1}$ dw). In addition to the species diversity of plants, it is related to seasonal variation. In young leaves, compared to older ones, at the end of the growing season, the

concentration of mercury is an order of magnitude smaller. The mercury detected in the leaves basically comes from the surrounding air, most likely Hg^0, entering through the stomata, and probably leaf uptake of Hg is irreversible (Bushey et al. 2008; Laacouri et al. 2013). In areas where Hg was mined (e.g. Almaden zone in Spain), Hg concentration in soils is many thousand mg kg^{-1} dw, and in some herbal plant species, it reaches 7–23 mg THg kg^{-1} dw (or 7000–23,000 μg kg^{-1} dw), thousands of times greater than in plants in uncontaminated areas (Moreno-Jimenez et al. 2006; Laacouri et al. 2013). In contrast to InHg, which is absorbed by the root system and kept there, in wetlands MeHg enters more efficiently both to water plants and through the roots to the aerial parts of plants (Patra and Sharma 2000; Windham-Myers et al. 2014). This organic species of mercury in plants from paddy fields may reach levels up to 63 μg kg^{-1} dw in rice grain and pose a significant health risk to people, as has been demonstrated for rice grown on soils with a high concentration of Hg in Asia (Qiu et al. 2012; Rothenberg et al. 2014). Probably, due to the consumption of rice grain from such areas, not only humans but also grain-feeding animals (especially granivorous birds) are at risk of MeHg intoxication.

Of the nonanimal inland organisms, fungi are considered the greatest accumulator of Hg from the soil (Falandysz and Borovička 2013). Usually, higher Hg concentrations are detected in these than in their substrates, and fungi accumulate especially high levels in the areas of geochemical anomalies such as the mercuriferous Eurasian belt (including Almaden in Spain, Monte Amiata in Italy and Chinese Yunnan Province). In the mushrooms found there, the average concentration of THg varies from 1 to 100 mg kg^{-1} dw (Bargali and Baldi 1984; Esbri et al. 2011; Falandysz et al. 2015). The concentration of MeHg in mushrooms is generally low and ranges between 0.01 and 3.7 mg kg^{-1} dw, with the proportion of MeHg in THg not exceeding 5% (Bargali and Baldi 1984; Rieder et al. 2011).

3.5.2 Mercury in Earthworms

For some terrestrial invertebrates and vertebrates, the source of mercury may be soil contaminated with Hg. It is the essential food of earthworms or is an admixture for the intaken plant and animal foods of soil invertebrates, birds and mammals (Hargreaves et al. 2011; Rieder et al. 2013). In soils, over 90% of the invertebrate biomass may consists of earthworms. That is why, they are a significant object in ecotoxicological studies on Hg (Zhang et al. 2009; Teršič and Gosar 2012; Rieder et al. 2011; Abeysinghe et al. 2017). Concentrations of Hg in earthworm bodies depend on animal species and various soil conditions such as Hg forms and their amount, content of organic matter, pH and oxygen availability (Zhang et al. 2009; Rieder et al. 2013; Abeysinghe et al. 2017). Additionally, Rieder et al. (2011) demonstrated that earthworms inhabiting topsoils (endogenic) contained the highest concentrations THg and MeHg, followed by deep-burrowing earthworms (anecic) and litter-inhabiting organisms (epigeic). Methylated organic Hg species bioaccumulate more readily, and much higher bioconcentration factors (BCFs) from soil to earthworms are reported for MeHg than for THg (BCFs are calculated as THg or MeHg

concentrations in the organisms divided by the corresponding concentrations in the soils). For example, in earthworms from Swiss forest, soils non-contaminated with Hg (mean THg level at 0.18 mg kg^{-1} dw) mean THg and MeHg in all investigated earthworm groups were 1.04 and 0.09 mg kg^{-1} dw, respectively. The share of MeHg in THg did not exceed 9%. BCF for THg and MeHg differed significantly: 7.2 vs. 83.1 (Rieder et al. 2011).

Analogical data has also been presented for earthworms living in rice paddy soils (Abeysinghe et al. 2017) sampled at various distances from abandoned mercury mines in Guizhou (China) and at control sites without a history of Hg mining. The highest mean THg concentrations were detected in the soil near the mines (80–125 mg kg^{-1} dw). However, even at sites distant from a mine (7–8 km) and in control samples THg levels were quite high (~20 and ~0.6 mg kg^{-1} dw, respectively). On the other hand, in those samples the concentration of MeHg was negligible and did not exceed 0.001 mg kg^{-1} dw, with the proportion of MeHg in THg estimated at $\leq$0.01%. In earthworm bodies, mean concentrations of THg and MeHg decreased with the increasing distance from the mine. In the animal samples at sites distant 7–8 km from the mine and at control areas, the average THg concentrations were approximately 10 and 0.60 mg kg^{-1} dw and for MeHg 0.10 and 0.05 mg kg^{-1} dw, respectively. Share of MeHg in THg in the two group of earthworms was ~8 and ~2%, similar to levels reported by other researchers (Zhang et al. 2009; Rieder et al. 2011). In the study, BCFs for THg and especially for MeHg increased with distance from the mine. In earthworms sampled at 7–8 km from mines and at reference sites mean values of BCFs for THg were in the range 0.5–1.0 and almost three orders of magnitude lower than BCFs calculated for MeHg. Mean values of BCF for MeHg at control sites and 7–8 km from mines were about 900 and 300, respectively. Abeysinghe et al. (2017) suggested that specific soil conditions in rice paddies may make the earthworms important biomagnifiers of MeHg. Such large differences observed between the BCF for THg and BCF for MeHg in the case of earthworms and soils (even with negligible Hg contamination) are influenced by very high absorption of lipophilic MeHg from their intestine compared to InHg. This is probably due to the methylation of InHg occurring in their digestive tract due to the activity of the microbiota. At least two arguments for this are given by Rieder et al. (2013) on the basis of their experimental studies. Firstly, earthworms contained about six times higher concentrations of MeHg if they grew in soils treated with InHg than in soils without Hg. Secondly, the concentrations of MeHg in earthworm casts and in the soils were similar and did not change over time.

3.5.3 Mercury in Spiders and Insects

Studies of MeHg contamination of food webs have historically focused on aquatic organisms including those inhabiting inland reservoirs. However, recent reports have shown that terrestrial organisms such as songbirds, bats and reptiles can exhibit elevated Hg burden by feeding on MeHg-contaminated spiders and insects (Cristol et al. 2008; Jackson et al. 2011; Drewett et al. 2013; Yates et al. 2014; Gann et al.

2015). Studies in this field are mainly conducted in floodplains, riparian and wetland ecosystems of North America, which have documented historical influence of Hg pollutants. It has been shown that in such areas (especially not too distant from Hg point sources) MeHg in terrestrial predatory spiders from the Lycosidae family reach high concentrations, in the range 0.60–1.29 mg kg^{-1} dw, which may be comparable or greater than in fish from neighbouring waters (Cristol et al. 2008; Speir et al. 2014; Gann et al. 2015; Standish 2016). In areas with negligible contamination or unpolluted with Hg, average concentration of MeHg in Lycosidae varies from 0.06 to 0.15 mg kg^{-1} dw (Bartrons et al. 2015; Gann et al. 2015; Tavshunsky et al. 2017). Depending on trophic position (which can be derived from $\delta^{15}N$), other arthropods in the areas with the historically proven exposure to Hg may exhibit MeHg concentrations from 0.02 mg kg^{-1} dw in herbivorous leafhoppers to 1.18 mg kg^{-1} dw in detritofagous isopods (Cristol et al. 2008; Standish 2016).

Long-lived cicadas are another example of increased concentrations of MeHg in arthropods. The larvae of these insects live in the ground (2–17 years) and feed on root juice. In the Hg-contaminated soils, the effective absorption of MeHg occurs through the roots from where it can be taken up by cicadas. In Huludao City (NE China), with a chlor-alkali plant and two zinc smelters (industrial sources of Hg), its soils contained on average 4.08 mg THg kg^{-1} dw and 0.009 mg MeHg kg^{-1} dw. Cicadas *Cryptotympana atrata* from such soils accumulated in their bodies on average 0.124 mg MeHg kg^{-1} dw, in a range from 0.021 to 0.319 mg MeHg kg^{-1} dw (Zheng et al. 2010). Thus, these insects, although not associated with aquatic food chains, may constitute an important local source of MeHg intoxication for predatory arthropods, insectivorous birds, bats and other animals. The number of studies on bioaccumulation and biomagnification of MeHg in terrestrial food webs is gradually increasing, which should result in a better understanding and explanation of these processes. Importantly, this requires close cooperation between specialists in various fields, including zoology, ecology, toxicology of animals, plants and soils.

3.5.4 Transfer of Mercury from Inland Aquatic Ecosystems to Terrestrial Vertebrates

Compared to the Hg transfer between the links of the aforementioned food chains, much more data has been gathered on predatory warm-blooded vertebrates (including semiaquatic mammals and aquatic birds) that inhabit inland areas and feed on aquatic food, especially fish. Studies on the relationships between these organisms, taking into account Hg forms and their concentration levels, have been conducted at least since the mid-twentieth century. Their initiation was closely related to the dramatic events in the Gulf of Minamata and documented the neurotoxic and disruptive effects of Hg on reproductive processes in humans and other homeothermic animals. Fish (and in less degree shellfish) are considered most significant source of MeHg exposure for humans and wildlife. Therefore, many countries have set standards to protect humans from Hg in food. For example, in the EU the limit for Hg in freshwater fish for humans is 0.5 mg kg^{-1} ww or 500 μg kg^{-1} ww

(1000 μg kg^{-1} ww for pike *Esox lucius* and eel *Anguilla anguilla*) (Commission Regulation, EC 2006), and in the United States 300 μg MeHg kg^{-1} ww is recommended (US EPA 2001, 2010). According to the EU Water Framework Directive, Environmental Quality Standards (EQS) for some chemicals in biota have been set, with mercury being defined as a priority hazardous substance (Directive 2008/105/EC). EQS are intended to protect top predators against secondary poisoning and refer to THg; for freshwater fish, the EQS for Hg (EQS/Hg) is at 20 μg kg^{-1} ww. Apart from the EU, only Canada has a standard designed of Hg (MeHg) to protect fish-eating animals at 33 μg kg^{-1} ww (Canadian Environmental Quality Guidelines 2000). The Canadian standard concerning Hg in freshwater fish is 65% higher than the European EQS/Hg. In North America the value of 100 μg kg^{-1} ww in fish is of concern for the protection of piscivorous mammals, including mink and otters (Scudder et al. 2009). However, robust data on the dietary Hg exposure thresholds that result in deleterious effects, including disturbances in reproduction, exist only for very few bird species. Typical range of Hg effect thresholds are approximately from 200 to over 1400 μg kg^{-1} ww in natural and/or experimental diets (Fuchsman et al. 2017). In North America, the piscivorous common loon has been intensively studied in field and laboratory settings (Evers et al. 2003; Kenow et al. 2008; Scheuhammer et al. 2008; Kenow et al. 2011). The dietary screening benchmark of 180 μg Hg kg^{-1} ww in whole body prey fish was established for this species, characterized as moderately sensitive to Hg intoxication (Heinz et al. 2009; Depew et al. 2012).

The concentration of Hg in fish depends on the degree of environmental pollution with this metal, the intensity of Hg methylation, the size of fish (closely correlated with their age) and their trophic level (Depew et al. 2013a; Eagles-Smith et al. 2014). Because of the higher cost of MeHg analysis (2–3 times greater than that for Hg analysis), THg in various animal tissues is assayed in the most investigations, including monitoring studies. It is generally accepted that the Hg in fish muscle occurs in the form of MeHg, which accounts for ~90% of THg (US EPA 2010). Concentration of Hg in freshwater fish in various parts of the world varies considerably. The United States and Canada have very large databases on Hg concentration in many species of fish. These data (after appropriate selection, standardization and statistical processing) allow an estimate of Hg concentrations in prey (Hg_{PREY}) of piscivorous fish and wildlife and evaluate their potential. In North America ecological monitoring of Hg depends crucially on top piscivorous fish such as walleye *Sander vitreus* and northern pike *Esox lucius* and among fish from lower trophic levels—yellow perch *Perca flavescens* and largemouth bass *Micropterus salmoides*. Among piscivorous wildlife, Hg monitoring uses common loon, bald eagle (to a smaller extent), mink and river otter (Evers and Clair 2005; Evers et al. 2007; Depew et al. 2013a). The United States Geological Survey (USGS) developed the National Descriptive Model for Mercury in Fish (NDMMF, http://emmma.usgs.gov; Wente 2004), which was later adopted in Canadian reports (Depew et al. 2013b). For example, in standardized fish (collected in 1998–2005) coming from streams across the United States, fish Hg concentrations at 27% of sampled sites exceeded the US EPA human health criterion (300 μg kg^{-1} ww). However, THg concentrations in fish

from >66% of the sites exceeded the value of 100 μg kg^{-1} ww that is of concern for the protection of piscivorous mammals. The highest mean Hg concentrations (between 1800 and 1950 μg kg^{-1} ww) were noticed in fish from blackwater coastal-plain streams draining forests or wetlands in eastern and south-eastern part of the United States as well as from streams draining gold- or Hg-mined basins in the Western United States (Scudder et al. 2009). Clearly lower concentrations of Hg were found in fish living in 21 national parks in the Western United States, with average value at ~78 μg kg^{-1} ww (Eagles-Smith et al. 2014). According to Depew et al. (2013b) Hg concentration in Canadian fish (gathered in years 1967–2010) averaged 370 μg kg^{-1} ww (from below detection to 10,430 μg kg^{-1} ww). In fish from years 1990–2010 estimated Hg_{PREY} ranged from 10 to 960 μg kg^{-1} ww with a mean of 90 μg kg^{-1} ww, decreasing westwards. This is consistent with spatio-temporal tendency in the United States of a decrease in Hg_{PREY} from east to west (Evers et al. 2007). This situation is closely related to the strong industrialization of the south-eastern regions of Canada and the Northeastern United States, where winds carry air masses anthropogenically contaminated with Hg. Mercury contamination is gradually deposited westwards, but the influence of mercury from bedrocks cannot be ruled out either (Page and Murphy 2005; Evers et al. 2007; Wentz et al. 2014).

The European Union as a whole lacks a common database on Hg concentration in fish that could be comparable to the North American one. In Scandinavian countries Hg concentrations in freshwater fish have been reported regularly since the late 1960s and early 1970s. The most data was collected for top predator northern pike followed by Eurasian perch *Perca fluviatilis*, which represents a lower trophic level (Munthe et al. 2007; Danielsson et al. 2011; Akerblom et al. 2014). Munthe et al. (2007) took into account all lacustrine data for Sweden, Norway and Finland from 1965 to 2004. In a standardized size of pike and perch, they found mean Hg concentrations of 730 and 400 μg kg^{-1} ww, respectively, in the three Scandinavian countries. Importantly, mean value of Hg in "standard fish" (1 kg pike or 0.3 kg perch or 3.2 kg brown trout *Salmo trutta* or 1.4 kg Arctic char *Salvelinus alpinus*) was estimated to be as high as 690 μg kg^{-1} ww (Munthe et al. 2007). The authors of that report stated that the data from Scandinavia show some similarity with data from a large survey in NE North America, when considering the mean values for various fish species. In the recent past in both regions, similar levels of atmospheric Hg pollution were noticed, and the geographic characteristics of bedrock and soils exhibit many analogies. For Eurasian perch and North American yellow perch, the mean concentrations were comparable: 400 versus 440 μg kg^{-1} ww. However, an important difference was observed between these two regions, with Hg concentration in the pike from Scandinavia higher than in NE North America: 730 vs. 640 μg kg^{-1} ww (Munthe et al. 2007). Miller et al. (2013) analysed data concerning Eurasian perch from Sweden and Finland covering the period 1974–2005. Swedish data from a later period (post-1996) show that in the fish from 22 and 72% lakes Hg concentrations were as high as >500 μg kg^{-1} ww and between 200 and 500 μg kg^{-1} ww, respectively. By contrast, after 1996 more lakes in Finland showed Hg concentrations in fish greater than 500 μg kg^{-1} ww (31%), while fewer lakes had fish Hg concentrations below 500 μg kg^{-1} ww (68%). Despite considerable reductions in Hg

use and production as well as lower Hg atmospheric deposition in these countries, Miller et al. (2013) indicated that Hg concentrations in the fish exceeded the EQS/Hg (and EQS/Hg for the Nordic region was 200–250 μg kg^{-1} ww). Moreover, in both Finland and Sweden, the perch from over 90% lakes exhibited Hg concentration exceeding 100 μg kg^{-1} ww, which in North America is a level of concern for the protection of piscivorous mammals. One of the probable reasons for the persistence of elevated Hg concentrations in fish may be significantly lower selenium concentration in the Scandinavian environment (similar to Poland and eastern Germany). The deficiency of this element in the diet of vertebrates is accompanied by an increased accumulation of Hg, and in the case of fish from Scandinavia and Poland, this was indicated by Julshamn et al. (1986), Lindqvist et al. (1991), Hultberg (2002) and Kalisinska et al. (2017). In addition to the aforementioned species, bream *Abramis brama* is used to assess the quality of the aquatic environments in Europe, a common benthofagous species sampled in the German Environmental Specimen Bank (Wellmitz 2010). German biomonitoring research from the years 1994–2009 showed that on average Hg concentrations changed from ~100 to 350 μg kg^{-1} ww and exceeded the EQS/Hg in all analysed years and all 17 sites from which breams came from: rivers Rhine, Danube, Saar, Elbe and its tributaries Saale and Mulde (Wellmitz 2010). Between 2007 and 2013, Hg levels were analysed in breams from five riverine places in France, Netherlands, Sweden and United Kingdom and one German lake as reference site (Nguetseng et al. 2015). Means of Hg concentration ranged from 18 to 246 μg kg^{-1} ww. However, the EQS/Hg was exceeded in all years and at all riverine sites including the reference site except for the year 2012. The available data show that in Europe, the areas with not exceeded EQS/Hg in various fish species (even in non-piscivorous breams) are not very often reported; exceptions include some freshwater aquifers in Poland and Croatia (Zrncic et al. 2013; Szkoda et al. 2014).

In Asia, several year-long and systematic biomonitoring of Hg in freshwater fish has only been conducted in South Korea. In other countries occasional research has usually concerned individual species and reservoirs (Jin et al. 2006; Kim et al. 2012; Pal et al. 2012; Zhu et al. 2012). In 2006–2008 in Korea, analysis covered 55 species of wild freshwater fish, among which seven species predominated. The most numerous of them were two piscivores (largemouth bass *Micropterus salmoides* and Far Eastern catfish *Silurus asotus*) and five omnivores (steed barbell *Hemibarbus labeo*, Korean bullhead *Pseudobagrus fulvidraco*, pale chub *Zacco platypus*, crucian carp *Carassius auratus*, carp *Cyprinus carpio*). Each freshwater fish species was assigned to an appropriate trophic level (piscivore, carnivore, omnivore, planktivore). The piscivores had the highest median Hg concentration (148 μg kg^{-1} ww) than carnivores and omnivores (83 μg kg^{-1} ww and 68 μg kg^{-1} ww, respectively). The median in planktivores was the lowest, at 30 μg kg^{-1} ww. In most piscivorous species (including largemouth bass) from 12 sites Hg level exceeded 500 μg kg^{-1} ww, which is recommended by the Korea Food and Drug Administration and the World Health Organization to protect human health (Kim et al. 2012).

The fish bioaccumulation factor (BAF), which expresses the ratio of THg (or MeHg) concentration in fish to the concentration in ambient water, depends on

many factors including trophic position and fish size (US EPA 2000; Yu et al. 2011). BAF is mainly presented in a logarithmic form (log10), and in freshwater prey fish and larger predatory fish, it is usually in the range from 5.9 to 6.6 (Yu et al. 2011; Scudder Eikenberry et al. 2015; Wu 2017). In ecotoxicological studies, analysis of MeHg biomagnification is very important, including indicators of changes in concentration between different trophic levels (TMF, trophic magnification factor). Extensive analysis of Lavoie et al. (2013) shows that in freshwater food webs MeHg levels increase by a factor of 8.1 per trophic level. In addition, they stated that TMF is higher in lentic than lotic waters (7.6 vs. 9.8), and values of this factor increase from tropical via temperate to polar climatic zones (TMF, 3.9, 7.5 and 12, respectively). Finally, biomagnification factors (BMFs) are also estimated within food web, and the factor concerning MeHg (or THg) is expressed as the ratio of concentration in animal bodies to the concentration in their food (in ppm or ppb) (Rolfhus et al. 2011). BAF and BMF are very seldom presented in piscivorous inland birds and mammals, which participate in transport of Hg from aquatic to terrestrial environments. BAF and BMF calculated for piscivorous birds take into account Hg concentrations in water, fish and avian blood, feathers or eggs but rarely in soft tissues including muscle (Henny et al. 2009; Yu et al. 2011; Falkowska et al. 2013). In the transmission of Hg (especially MeHg) from freshwater fish to piscivorous wildlife of inland ecosystems muscle tissue plays important role for at least two reasons. Firstly, among soft digestible tissues, skeletal muscles represent the largest percentage of body weight, and secondly Hg present in them is almost all in MeHg form, which is easily absorbed. Therefore, it seems reasonable to analyse BMF using Hg concentrations in fish and wildlife muscle (not fish muscle and indigestible fur or feathers). For example (based on muscle tissue), in two pairs American mink—fish and Eurasian otter—fish from Western Poland BMFs were 27.3 and 10.9, respectively (Kalisinska et al. 2017). In addition, they found that these mammals quite often die on the roads and are later eaten by scavengers, thus contributing to the further transmission of Hg in the local terrestrial food web.

3.6 Mercury Concentrations in Soft Tissues in Various Groups of Inland Wildlife

The literature available in English includes many publications on the concentration of THg and much fewer investigate MeHg in soft and hard tissues of wild animals, especially in North America and Europe. In spite of this, there are basically no studies which estimate the average concentrations of THg representing the main ecotrophic groups. In order to characterize and compare the concentration of THg in wild terrestrial mammals and birds of the Northern Hemisphere, 140 studies from the years 1973–2017 were selected, including data on at least one of four soft tissues: liver, kidney, muscle and brain. The average concentrations of THg (mainly arithmetic means) from these reports concerned a minimum of three specimens of an

individual species. If several groups of animals of the same species were included in the study (due to sex, age, temporal or territorial division), mean THg concentrations selected for the analysis referred to the largest number of individuals, preferring adults. Since the concentrations in soft tissues were given in mg kg^{-1} in dry or wet weight, we made appropriate calculations, and the final results are presented in mg kg^{-1} ww. Mammalian livers, kidneys, muscles and brains contain on average 70%, 75%, 75% and 80% of water, respectively, as calculated on the basis of several works (Weiner 1973, Blus and Henny 1990, Reinoso et al. 1997; Gamberg et al. 2005a, b; Sleeman et al. 2010; Kalisinska et al. 2012a, b). In the case of birds, it was assumed that their liver, kidney, muscle and brain contain 70%, 75%, 70% and 80% water, respectively (mean values were calculated based on the work of Cosson et al. 1988; Cosson 1989; Binkowski et al. 2013; Kalisinska et al. 2010, 2014a).

Data on mammals and birds were grouped according to their ecotrophic category. Among mammals, three groups were identified: Herb-M (predominantly herbivorous), Carn-M (terrestrial carnivores) and SemCarn-M (semiaquatic carnivores). Four groups were distinguished among the birds: TerrOmn-B (terrestrial omnivores and herbivores), TerrPred-B (diurnal and nocturnal predators), W-B (non-piscivorous waterfowl) and Pisc-B (piscivores). Groups, names of species and data sources are given in Table 17.3.

The analysis excluded cases indicating very high THg concentrations in the liver and kidneys, which were recorded in warm-blooded vertebrates living in areas heavily contaminated with mercury. For carnivorous mammals and those who prefer a different diet, excessive concentrations of mercury in liver and/or kidney were assumed to be above 16.5 and 12.5 mg kg^{-1} ww, respectively, i.e. two-thirds and one-half of the value associated with mortality of mammals (lower value of the range: <25–30 mg kg^{-1} ww), which was reported by Shore et al. (2011). The data of piscivorous birds and other ecotrophic groups that indicated very high Hg exposure were not included in this analysis. The threshold levels in the livers and kidneys in Pisc-B were over 2/3 of the levels, shown by Shore et al. (2011) to be associated with the death of non-marine birds (20 mg kg^{-1} ww and >40 mg kg^{-1} ww, respectively). Therefore, cases were excluded from statistical calculations when hepatic and nephric THg concentrations were higher than 13.2 and 26.4 mg kg^{-1} ww. In relation to other ecotrophic bird groups, the exclusion limit was 1/2 of the levels indicated for avian liver and kidney by Shore et al. (2011), i.e. 10 and 20 mg kg^{-1} ww.

Figure 17.2 shows the mean concentrations of THg in soft tissues of the various ecotrophic groups of birds and mammals inhabiting the inland areas in the Northern Hemisphere. Many species included in Table 17.3 occur in both Eurasia and North America. Some of them are native species on both continents (such as common loon, mallard, osprey, Eurasian elk/moose, reindeer/caribou), but some of them have been introduced, for example, fallow deer from Europe to North America and American mink and raccoon from North America to Europe (Genovesi et al. 2012; Bradley et al. 2014). Belonging to the same species and/or genus, occurrence on both continents and the large biological similarity (e.g. bald eagle and white-tailed eagle) are a justification for using their THg data in joint analyses.

Table 17.3 Analysed ecotrophic groups of mammals and birds, species names and source of data

Group	Species	Source of data
Mammals		
Herb-M, predominantly herbivore	Ungulates Red deer *Cervus elaphus*, roe deer *Capreolus capreolus*, fallow deer *Dama dama*, Japanese serow *Capricornis crispus*, mule deer *Odocoileus hemionus*, white-tailed deer *O. virginianus*, Eurasian elk/moose *Alces alces*, reindeer/caribou *Rangifer tarandus*, wild boar *Sus scrofa* Others European hare *Lepus europaeus*, snowshoe hare *L. americanus*, common rabbit *Oryctolagus cuniculus*, Eurasian beaver *Castor fiber*, American beaver *C. canadensis*, muskrat *Ondatra zibethicus*	Europe Aastrup et al. (2000); Albinska et al. (2011); Berzas Nevado et al. (2012); Bilandžić et al. (2010a); Celechovska et al. (2008); Dobrowolska and Melosik (2002); Eira et al. (2005); Falandysz (1994); Gasparik et al. (2012); Giżejewska et al. (2014); Gnamuš and Horvat (1999); Kalas et al. (1995); Krynski et al. (1982); Lazarus et al. (2008); Piskorova et al. (2003); Rudy (2010); Sobanska (2005); Spiric et al. (2012); Srebocan et al. (2011); Suran et al. (2013); Szkoda et al. (2012); Zarski et al. (1995) North America Gamberg et al. (2005b, c); Keeyask Hyd Ltd (2012); Khan and Forester (1995); Langlois and Langis (1995); Robillard et al. (2002); Smith and Armstrong (1975); Wren (1986); Wren et al. (1980) Asia Honda et al. (1987)
Carn-M, terrestrial carnivore	Canids red fox *Vulpes vulpes*, Arctic fox *Alopex lagopus*, raccoon dog *Nyctereutes procyonoides*, wolf *Canis lupus* Others Pine marten *Martes martes*, beech marten *M. foina*, American marten *M. americana*, European polecat *Mustela putorius*, Egyptian mongoose *Herpestes ichneumon*, common ganet *Ganetta ganetta*, Iberian lynx *Lynx pardinus*, brown bear *Ursus arctos*	Europe Alleva et al. (2006); Bilandžić et al. (2010b); Corsolini et al. (1999); Kalisinska et al. (2009, 2012a); Komov et al. (2016); Lodenius et al. (2014); Millan et al. (2008); Piskorova et al. (2003); Prestrud et al. (1994); Zilincar et al. (1992) North America Dehn et al. (2006); Gamberg and Braune (1999); Hoekstra et al. (2003); Langlois and Langis (1995); Sheffy and St Amant (1982)
SemCarn-M, semiaquatic carnivore	Eurasian otter *Lutra lutra*, river otter *Lontra canadensis*, American mink *Neovison vison* (previously *Mustela* vison), raccoon *Procyon lotor*	Europe Brzezinski et al. (2014); Gutleb et al. (1998); Hyvärinen et al. (2003); Kalisinska et al. (2012b, 2016); Kalisinska unpbl. data; Kruuk et al. (1997); Lanocha et al. (2014); Lanszki et al. (2009); Lemarchand et al. (2010); Ljungvall et al. (2017); Lodenius et al. (2014); Mason and Madsen (1992); Mason et al. (1986);

(continued)

Table 17.3 (continued)

Group	Species	Source of data
		Norheim et al. (1984) North America Bank et al. (2007); Bowman et al. (2012); Carmichael and Baker (1989); Dornbos et al. (2013); Evans et al. (2000); Fortin et al. (2001); Gamberg et al. (2005a); Halbrook et al. (1994); Harding et al. (1998); Hernandez et al. (2017); Keeyask Hyd Ltd (2012); Khan et al. (1995); Klenavic et al. (2008); Kucera (1983); Langlois and Langis (1995); Lord et al. (2002); Martin et al. (2011); Mayack (2012); Mierle et al. (2000); Poole and Elkin (1992); Poole et al. (1995); Ropek and Neely (1993); Sellers (2010); Sheffy and St Amant (1982); Souza et al. (2013); Stansley et al. (2010); Strom (2008); Wren (1986); Wren et al. (1980); Yates et al. (2005)
Birds		
TerrOmn–B, terrestrial herbivore and omnivore	Galliformes willow ptarmigan *Lagopus lagopus*, rock ptarmigan *L. muta*, ring-necked pheasant *Phasianus colchicus* Passeriformes Black-capped chickade *Poecile atricapillus*, House Wren *Troglodytes aedon*, great tit *Parus major*, song thrush *Turdus philomelos*, hooded raven *Corvus cornix* Others Song thrush *Gallinago gallinago*	Europe Celechovska et al. (2008); Dauwe et al. (2005); Holt et al. (1979); Kalas et al. (1995); Zarski et al. (2015) North America Ackerman et al. (2016); Braune and Malone (2006a)
TerrPred–B, diurnal and nocturnal predators	Falconiformes Eurasian sparrowhawk *Accipiter nisus*, Eurasian sparrowhawk *A. gentilis*, red kite *Milvus migrans*, golden eagle *Aquila chrysaetos* Strigiformes Eurasian eagle-owl *Bubo bubo*, tawny owl *Strix aluco*	Europe Holt et al. (1979); Houserova et al. (2005); Kenntner et al. (2003); Kenntner et al. (2007); Kitowski et al. (2015); Norheim and Frøslie (1978); Walker et al. (2016) Asia Honda et al. (1986)
W–B, non-piscivore waterfowl	Anseriformes Mallard *Anas platyrhynchos*, gadwall *A. strepera*, green-winged teal *A. crecca*, American black duck *A. rubripes*, northern pintail *A. acuta*, northern shoveler *A. clypeata*, wood duck *Aix sponsa*, canvasback *Aythya*	Europe Falandysz et al. (1988); Florijančić et al. (2016); Kalisinska et al. (2013); Kitowski et al. (2015); Parslow et al. (1982) North America Ackerman et al. (2016); Braune and

(continued)

Table 17.3 (continued)

Group	Species	Source of data
	valisineria, lesser scaup *A. affinis*, Canada goose *Branta canadensis*, brant *B. bernicla*, white-fronted goose *Anser albifrons*, mute swan *Cygnus olor*	Malone 2006b; Burger and Gochfeld (1985); Champoux et al. (1999); Cristol et al. (2012); Gerstenberger (2004); Hughes et al. (2014); Lindsay and Dimmick (1983); Petrie et al. (2007); Pollock and Machin (2008); Rothschild and Duffy (2005); Stickel et al. (1977); Tsipoura et al. (2011) Asia Saeki et al. (2000); Zamani-Ahmadmahmoodi et al. (2010)
Pisc–B, piscivore	Falconiformes Osprey *Pandion haliaetus*, white-tailed eagle *Haliaeetus albicilla*, bald eagle *H. leucocephalus*, Anseriformes common merganser *Mergus merganser* Suliformes Great cormorant *Phalacrocorax carbo*, double-crested cormorant *P. auritus* Podicipediformes Great crested grebe *Podiceps cristatus* Gaviiformes common loon *Gavia immer* Pelecaniformes Grey heron *Ardea cinerea*, great blue heron *A. herodias*, American white pelican *Pelecanus erythrorhynchos*	Europe Falandysz et al. (2000); Holt et al. (1979); Houserova et al. (2007); Kalisinska et al. (2010, 2014a); Kenntner et al. (2001); Kitowski et al. (2015); Krone et al. (2004, 2006); Lemarchand et al. (2012); Norheim and Frøslie (1978) North America Evers et al. (2005); Greichus et al. (1973); Hopkins et al. (2007); Langlois and Langis (1995); Mierzykowski et al. (2011, 2013); Rutkiewicz et al. (2011); Scheuhammer et al. (1998b); Sepúlveda et al. (1998); Stone and Okoniewski (2001); Stout and Trust (2002); Weech et al. (2003); Wolfe and Norman (1998); Wood et al. (1996) Asia Mazloomi et al. (2008); Nam et al. (2005)

3.6.1 Mercury Concentrations in Mammalian Soft Tissues

The low concentration of THg in the aboveground parts of plants (with the predominant share of InHg poorly absorbed in the gastrointestinal tracts of mammals and birds) results in a negligible exposure of most herbivorous animals to this toxic metal. In the three groups of mammals we distinguished above, THg concentrations were the smallest in Herb-M, but they can be arranged in the following ascending order: muscle < brain < liver < kidney (0.015, 0.026, 0.056 and 0.173 mg kg^{-1} ww). According to Wisconsin Veterinary Diagnostic Laboratory (WVDL 2015), normal THg concentration in cervid kidney and liver does not exceed 0.1 mg kg^{-1} ww, which only in the case of liver is consistent with the level established for the

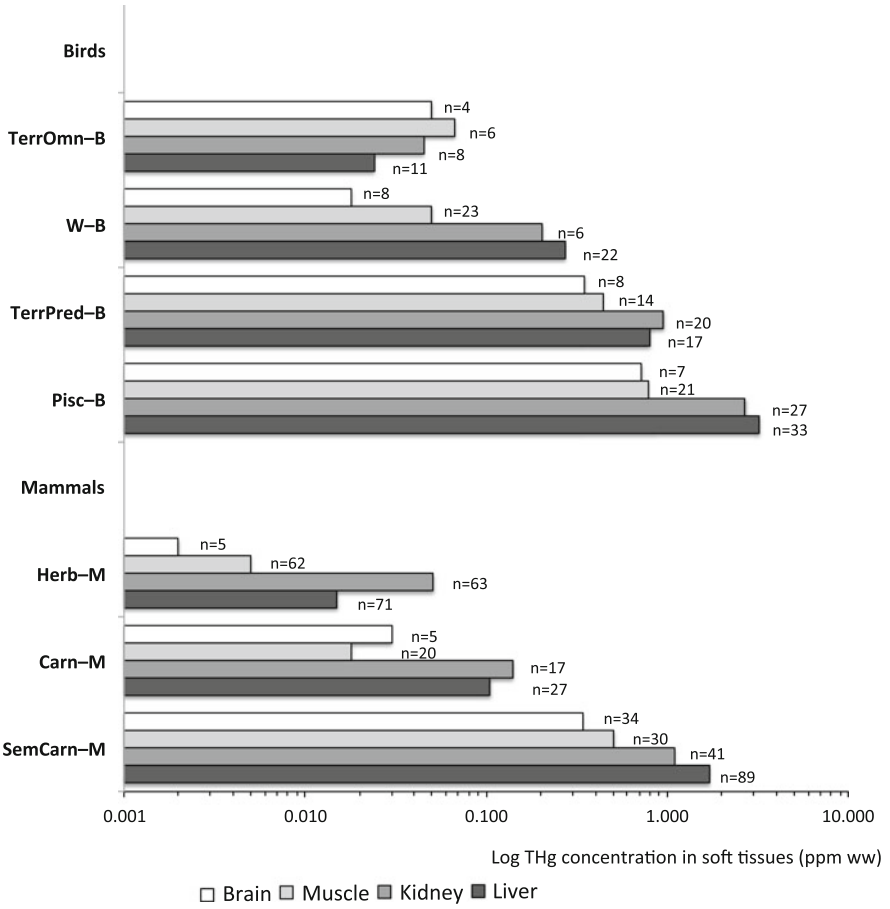

Fig. 17.2 Medians of total mercury concentrations (ppm = mg kg^{-1}; ww, wet weight) in soft tissues of inland mammals (Herb–M, predominantly herbivore; Carn–M, terrestrial carnivore; SemCarn–M, semiaquatic carnivore) and birds (TerrOmn–B, terrestrial omnivore and herbivore; TerrPred–B, diurnal and nocturnal predators; W–B, non-piscivore waterfowl; Pisc–B, piscivore birds) from the Northern Hemisphere (for more details see Table 17.3)

multispecies group of Herb-M. Two reports on special cases were excluded from this group, which indicated that increased concentrations of THg may be found even among herbivores. In the early 1990s among herbivorous ungulate mammals, there were exceptions such as roe deer from zones of a mercury mine in Idrija (Slovenia), which was active in the 1990s, and caribou from Canadian Arctic, Northwest Territories and Nunavut (Gnamuš and Horvat 1999; Gamberg et al. 2005b). In the roe deer, liver and kidney Hg levels were 0.64 and 15.56 mg kg^{-1} ww. Hepatic and nephric tissues of the caribou contained 2.04 and 12.80 mg Hg kg^{-1} ww, respectively. In both cases, the main reason for such a high concentration of Hg was the specific diet of these animals, containing large amounts of Hg. In the aboveground

parts of plants from a smelter area of Idrija, average Hg was ~50 mg kg^{-1} dw. Leaves of plants in those areas intensively absorbed Hg^0 released during the roasting of ores containing this metal (Gnamuš and Horvat 1999). Caribou in the far north, on the other hand, mainly feeds on mosses and lichens, perennial plants which lack root systems and absorb contaminants (including Hg), along with their nutrients, from atmospheric deposition. In addition, high Hg levels in detoxification organs were related to the caribou weight loss in spring, resulting in lower absolute organ weights (Gamberg et al. 2005b).

The diet of carnivores (Carn-M) is very diverse. Their prey consists mostly of rodents, lagomorphs and birds, with the admixture of carrion, reptiles, frogs, insects, fruits and other parts of plants. In these predators, the average THg concentration in the liver and kidneys was similar and amounted to 0.105 mg kg^{-1} ww and 0.140 mg kg^{-1} ww, respectively. Farrar et al. (1994) argue that in the liver and kidneys of the dog, the concentration of THg usually does not exceed 0.1 mg kg^{-1} ww, and in the WVDL list for canids from 2015 (including domestic dog), the normal Hg concentration in tissues is <0.1 mg kg^{-1} ww and <0.200 mg kg^{-1} ww, respectively. In both cases, these values do not differ from those calculated by us for the multispecies Carn-M group. In their muscles and brain, the THg concentration was an order of magnitude lower than in the liver and kidneys, and they did not exceed 0.018 mg kg^{-1} ww and 0.030 mg kg^{-1} ww, respectively (Fig. 17.2).

SemCarn-M group represents four species of the superfamily Musteloidea, including piscivorous mustelids. Among them, the diet of otters is 90% fish, American mink 60%, and raccoon 30% (Table 17.3; Kalisinska et al. 2017). This mammalian group is characterized by the largest body of data (especially with regard to the liver and kidney). Median THg concentration in the liver, kidney, muscle and brain of SemCarn-M were, respectively, 1.70, 1.09, 0.51 and 0.34 mg kg^{-1} ww. Comparisons of median hepatic and nephric THg concentrations between Eurasian otter (liver $n = 12$, 2.57 mg kg^{-1} ww; kidney $n = 7$, 1.30 mg kg^{-1} ww) and river otter from North America (liver $n = 25$, 1.78 mg kg^{-1} ww; kidney $n = 11$, 1.42 mg kg^{-1} ww) showed no significant differences.

According to WVDL (2015), normal THg concentrations in the liver and kidneys of mustelids are <0.20–0.70 mg kg^{-1} ww and <1.0 mg kg^{-1} ww, respectively, much lower than our results. In North American studies from the 1980s, when Hg intoxication of otters and minks was much more frequent, background hepatic THg in those piscivorous species was indicated as <4–5 mg kg^{-1} ww and ~2 mg kg^{-1} ww, respectively (Wren 1986; O'Connor and Nielsen 1981; Carmichael and Baker 1989). In the light of the quoted papers from 1980s and our statistical analysis (taking into account European and North American reports from 1981 to 2017), it can be assumed that currently the values of hepatic background level for otters and American mink are <3.0 mg kg^{-1} ww and <1.5 mg kg^{-1} ww, respectively. According to our analysis, THg levels in the kidney, muscle and brain of the piscivorous mammals are <1.5, 1.0–1.3 and 0.3–0.6 mg kg^{-1} ww, respectively.

Comparisons of hepatic THg concentration showed statistically confirmed differences between all three ecotrophic groups, and their values can be arranged in a decreasing series of SemCarn-M > Carn-M > Herb-M (1.700 > 0.105 >

0.015 mg kg^{-1} ww). In relation to SemCarn-M, the concentrations of THg in the kidneys, muscles and brain of Carn-M were about an order of magnitude lower, and in the Herb-M groups, it was two orders of magnitude lower. No significant differences were found in kidney and brain THg between Carn-M and Herb-M (Fig. 17.2). In muscle, the concentrations of THg in Carn-M and Herb-M were more than 28 and 100 times lower than in SemCarn-M. In comparison to Carn-M, Herb-M had a 3.6 times lower level of muscle THg. In the muscles, similar to the liver, the concentrations could be arranged in a descending order (0.508 > 0.018 > 0.005 mg kg^{-1} ww), and all intergroup differences were statistically significant.

3.6.2 Mercury Concentrations in Avian Soft Tissues

In birds, the lowest levels of THg in the liver, kidneys, muscles and brain occurred in the TerrOmn-B group, and their medians ranged from 0.024 to 0.067 mg kg^{-1} ww. In some reports, especially in the case of muscles and the brain, the concentrations were very low, below the limit of detection, but increased levels ($\geq$0.10 mg kg^{-1} ww) were found in tissues of granivorous birds from Scandinavia in the 1970s, when large amounts of organic Hg fungicides were used in agriculture in that part of Europe (Holt et al. 1979).

Although in the liver and kidneys of waterfowl (W-B group) we found an order of magnitude higher THg concentration than in the TerrOmn-B group, the differences between these groups were not statistically significant. The largest number of differences were recorded between piscivorous birds (Pisc-B) and other analysed groups of birds. Pisc-B had the highest concentration of THg in the liver, kidneys, muscles and brain (3.21, 2.69, 0.78, 0.72 mg kg^{-1} ww, respectively) and significantly differed in this regard from TerrOmn-B and W-B. Pisc-B and TerrPred-B showed no statistically confirmed difference in muscle THg (0.78 vs. 0.44 mg kg^{-1} ww) and brain THg (0.72 vs. 0.35 mg kg^{-1} ww).

In contrast to mammals, the WVDL list (2015) does not include the normal THg level for or different systematic groups of birds. Normal concentration is proposed of avian liver in the range of 0.01–0.10 mg kg^{-1} ww and for the kidney at <0.02–0.30 mg kg^{-1} ww. Puls (1988) suggested that normal concentrations of THg in the liver, kidney, muscle and brain of poultry were 0.01–0.10, 0.05–0.30, 0.008–0.100 and 0.10 mg kg^{-1} ww, respectively. These levels coincide with those we calculated for TerrOmn–B, i.e. typical terrestrial birds, including galliformes. Other researchers, investigating various wild water birds, argue that hepatic and renal THg residues represent background concentrations when they are 0.3–3.0 mg kg^{-1} ww (Ohlendorf 1993; Badzinski et al. 2009). This range includes median hepatic THg concentrations calculated by us for two groups of bird: W-B and TerrPred-B (Fig. 17.2). In the group of piscivorous birds (Pisc–B), hepatic THg exceeds 3.0 mg kg^{-1} ww (3.21), but for the kidneys it is lower (2.69 mg kg^{-1} ww).

Mammals and birds are characterized by different sensitivity to Hg, and depending on the type of intaken food, they accumulate different amounts of this toxic element. Significantly, the lowest adverse effect level (LOAEL) has not been

established for most wild endothermic animals. In the common loon, in the case of the liver, kidney, breast muscle and brain, LOAEL values do not exceed 4.0, 2.3, 1.2 and 0.80 mg kg^{-1} ww, respectively (Zhang et al. 2013). The quoted values coincide with the THg levels proposed by us for piscivorous birds, with the exception of muscle THg, which we estimated to be ~0.80 mg kg^{-1} ww.

3.7 *Mercury Concentrations in Hair and Feathers of Inland Wildlife*

Hair (fur) and feathers are often used in ecotoxicological studies because they can be taken from living individuals. Here, the dominant form of Hg is MeHg, which reaches hair/fur/feathers in the period of their growth and reflects only that period. As in the case of soft tissues, the concentration of Hg in fur/feathers is closely related to the ecotrophic association of wildlife and Hg contamination of habitats. Sheffy and St Amant (1982) based on various furbearers from Wisconsin (USA) considered that Hg 1–5 mg kg^{-1} ww (ppm dw) in hair to be normal background levels. In herbivorous mammals (such as American beaver, muskrat, white-tailed deer and lagomorphs), the average concentration of hair Hg does not exceed 0.3 ppm dw, and in many individuals it is below the limit of detection (Cumbie and Jenkins 1975; Sheffy and St Amant 1982; Stevens et al. 1997; Lourenco et al. 2011). In omnivorous mammals, such as common opossum *Didelphis marsupialis*, average hair Hg, depending on the environmental Hg pollution, ranged from 1.3 to 44 ppm dw (Cumbie and Jenkins 1975). Until recently, piscivorous mammals were thought to have the highest hair Hg concentrations among terrestrial mammals. The average hair Hg concentrations in these mammals from North America in the twentieth and twenty-first centuries usually exceeded 5, and sometimes 15 ppm dw (Sheffy and St Amant 1982; Stevens et al. 1997; Wolfe & Norman 1998; Mierle et al. 2000; Yates et al. 2005; Strom 2008). The maximum values in river otter and mink from the United States (Maine) reached 234 and 68.5 ppm dw, respectively (Yates et al. 2005). However, several years ago even greater concentrations were detected in the hair of insectivorous bats from Virginia (the South River, USA): little brown bat *Myotis lucifugus* and big brown bat *Eptesicus fuscus*, at 274 and 65.4 mg kg^{-1} dw, respectively (Wada et al. 2010; Nam et al. 2012). Probably, the concentrations greater than 30 ppm dw in fur are associated with the clinical neurological effects, or they may be lethal (Wobeser and Swift 1976; Evers 2005; Basu et al. 2007), but there is little data on wild mammals in this respect.

In monitoring programs, feathers have low priority status for several reasons. Feather Hg concentration is characterized by high variability even in the same individual (depending, among others, on the type and location of feathers). Moreover, it relatively weakly correlates with the Hg concentration in soft tissues. Usually, the times of moulting and replacement of certain types of feathers are not known for most species, and it is even more complicated for migratory birds. In

addition, the period of feather growth is accompanied by the redistribution of Hg in internal organs and its increased transport to feathers, both in chickens and older individuals (Honda et al. 1986; Eagles-Smith et al. 2008; Ackerman et al. 2011, 2016; Odsjo et al. 2012). In general, bird feathers have average Hg concentrations in the range of 0.1–5 ppm dw (Lodenius and Solonen 2013), but in some European herbivores, such as wood pigeon *Columba palumbus* and red-legged partridge *Alectoris rufa*, it may be <0.1 ppm (Hahn et al. 1993; Lourenco et al. 2011). Natural background levels of Hg in feathers of non-piscivorous raptorial birds are in the range 1–5 ppm dw (Scheuhammer 1991). Among adult piscivorous birds, it is estimated that this level for bald eagle in North America is much higher and in some regions ~20 ppm dw (DeSorbo et al. 2008). Among piscivorous birds the maximum concentration of Hg in feathers sometimes exceeds 190 ppm, for example, in osprey from Canada (DesGranges et al. 1998) and white-tailed eagle from Germany (Niecke et al. 1998). Mercury levels in feathers that are associated with adverse effects in birds are 5 ppm fresh weight or 7.5 mg kg^{-1} dw. Concentrations of 15 ppm are required for adverse effects of mercury in some predatory birds (Burger and Gochfeld 2009). In raptorial birds concentrations >20 ppm may be connected with toxic effects, but in bald eagle it is probably >60 ppm (Scheuhammer 1991; DeSorbo et al. 2008).

Despite the large number of works with Hg concentration in mammalian fur and bird feathers, huge species and ecological diversity of wildlife make interpretation of results difficult, especially since the correlation between Hg concentration in these tissues and concentration in soft tissues in general are usually very weak or non-existent. Therefore, information on Hg obtained from fur and feather samples is not sufficient to clearly assess Hg intoxication of wildlife and their habitats.

4 Conclusions

Long-term studies of the abiotic environment, human toxicology and the ecotoxicology of Hg hold major gaps in knowledge on the behaviour of Hg in nature (including MeHg biomagnification) and subsequent long-term ignoring of the evidence of the negative effects of this metal on humans and other vertebrates. Maintaining the functioning of the various economic sectors based on Hg and coal-based energy has led to a dramatic increase in the environmental problems associated with Hg. Currently, the most important way to reduce anthropogenic Hg emissions and to reduce the health risks to humans and ecosystems globally is to act in international agreements. The first formal and very important preventive action was the signing of the Minamata Convention on Mercury in October 2013 (Kessler 2013; Larson 2014). However, its ratification, implementation and raising of awareness of entire societies and individuals will determine not only the health condition of this and future generations and the different environments and also the survival of many sensitive species, especially those directly or indirectly dependent on aquatic food chains. This requires, among other things, control of the presence of Hg in abiotic and biotic environments, including biomonitoring.

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Chapter 18
Silver, Ag

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Abstract The profile of silver (Ag) emission to the environment has changed significantly in recent decades. Although the photography industry has lost its importance, global Ag production continues, together with rising demand for nanosilver (nano-Ag), which is widely used in many products. Hence, increasing volumes of Ag waste are expected to be released into waters and on land. The results of experimental studies has demonstrated the hazardous impact of Ag/nano-Ag on mammalian organisms. However, the belief exists that Ag is extremely toxic for aquatic species only, so studies conducted on terrestrial wildlife are scarce. The data presented here indicate that Ag accumulates in high amounts in the soft tissues and bones of the investigated mammals and birds. It also appears to be present in higher concentrations in liver and brain, which could, hence, be pointed to as target organs. In addition, birds inhabiting aquatic areas and those connected with aquatic food chains seem to be suitable bioindicators of water-body contamination, whereas small birds, such as the great tit, may be useful indicators of urban pollution. Consideration should also be given to the value of current observations concerning the close relation between the presence of Ag in organisms and their environments. It should also be highlighted that detailed studies on avian and mammalian terrestrial wildlife merits high priority in order to evaluate the possible hazardous impact of increased environmental emission of Ag and nano-Ag.

1 Introduction

Metals have become increasingly important as a group of environmental pollutants and potentially dangerous toxins. Major advances have been made in recent decades in our understanding of the biological effects of silver (chemical symbol: Ag, from

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the Latin *argentum*) in experimental animals, but we still do not know enough about its environmental levels, bioavailability, bioaccumulation, and ecotoxicology. Silver is a nonessential element. It is known to bioaccumulate in and to be highly toxic to aquatic organisms (Luoma 2008). Since in terrestrial mammals this metal is not extensively metabolized and its absorption is low, the belief exists about its relatively low toxicity to this group of organisms. However, it should be remembered that metals, because of their persistent nature in the environment, may generally be more dangerous when accumulated over a long period of time. The industrial pattern of Ag use has changed significantly over the years. Parallel to the reduced importance of analog photography, the manufacture of Ag-containing electrical goods has increased (Eckelman and Graedel 2007). Moreover, the widespread use of Ag in its particulate form has been observed recently. The expanding development of nanotechnologies has led to increased production of engineered silver nanoparticles (AgNPs) utilized in many medical and consumer products (Rejeski 2011). Nano-Ag-based textiles, plastics, and cosmetics with antimicrobial effects are enjoying increasing popularity in Asia, North America, and Europe. Their growing production and use represent a significant source of Ag emissions and enhance the likelihood of environmental exposure to AgNPs (Eckelman and Graedel 2007). Thus, environmental concerns about Ag have currently switched from its ecotoxicological to its nanoecotoxicological impacts (Kahru and Dubourguier 2010). The increasing economic importance of nanomaterials has not been accompanied by appropriate safety regulations (Bondarenko et al. 2013). This creates an increasing need to assess the potential adverse health effects of AgNPs in animals and humans. Although recently progress has been made in research on experimental nano-Ag toxicity, there are still few data concerning its ecotoxicological effects. Much remains to learn about nano-Ag behavior in environmental media, its bioavailability in wildlife, and its interactions at the molecular level. Current data concerning nanotoxicity, including AgNPs toxicity, are incomplete and inconsistent owing to differences in experimental approaches and should be extended to those test species and biological endpoints that are usually used in environmental hazard assessment (Bondarenko et al. 2013). All these issues have become a challenge for nanoecotoxicological research, which is expected to contribute to new regulations being issued by European Commission and US authorities (Kahru and Dubourguier 2010).

2 General Properties of Silver

Silver is a chemical element with atomic number 47 that belongs to the group of transition metals. In the periodic table, Ag is situated in period 5, group 11, and d-bloc. It has an atomic mass of 107.868, a density of 10.49 g cm^{-3}, and melting and boiling points of 961.78°C and 2162°C, respectively (Wieser et al. 2013; http://periodictable.com/Properties/A/CrustAbundance.html). It possesses the lowest contact resistance and the highest electrical and thermal conductivity of metals. It is water-insoluble but dissolves in nitric acid. Elemental silver Ag(0) and monovalent

silver Ag(I) are the most common oxidation states (ATSDR 1990). Other oxidation states, Ag(II) and Ag(III), although rare, are also possible. Silver ions are dissociated from particulate Ag and from different salts. There are 2 natural stable isotopes of Ag, ^{107}Ag and ^{109}Ag, and 20 artificial radioisotopes, of which the radioisotope ^{110}Ag has the longest physical half-life (253 days). None of the radioisotopes occurs naturally (Eisler 1996; WHO 2002). Several compounds of Ag possess explosive properties: silver oxalate ($Ag_2C_2O_4$) explodes when heated; silver acetylide (Ag_2C_2) detonates on contact; and silver azide (AgN_3) detonates spontaneously under certain circumstances (WHO 2002).

Silver occurs relatively rarely in the Earth's crust, appearing in the 65th position in the natural elements (Yaroshevsky 2006). The mean concentration of Ag in the upper continental crust is estimated to be between 0.053 and 0.070 mg kg^{-1} (Rudnick and Gao 2003; Yaroshevsky 2006).

3 Silver in Nature: Geogenic Sources of Metal

Crustal Ag occurs naturally as native Ag, alone or with other metals, frequently with gold, although Ag deposits tend to be of a rather polymetallic nature. It is predominantly concentrated in basalt (0.10 mg kg^{-1}) and igneous rocks (0.07 mg kg^{-1}) in the form of minerals: acanthite (Ag_2S) and chlorargyrite (AgCl). Chlorargyrite, Ag chloride, is also known as horn Ag when weathered by air. Acanthite, the sole form of Ag sulfide stable in normal air temperature, transforms to argentite above 173°C. It is the main ore from which Ag is extracted. Important sources of the metal are also pyrargyrite (Ag_3SbS_3), known as dark red Ag, and the corresponding proustite (Ag_3AsS_3), or light red Ag (US EPA 2006). From these natural sources Ag is released into the environment through the weathering of rocks and erosion of soils. Some areas in the world are rich in Ag, including the Cordilleras region of the Americas, Abitibi and Cobalt areas on the Canadian Shield, certain mountain ranges of Europe (Cornwall, Central Massive, Harz, Internal Carpathians), the Caucasus, Altai Mountains, Chukotka, Japan, and Eastern Australia. Fine large and pure crystals are found in Saxony and Harz Mountains (Germany), in Joachimsthal (Czech Republic), in the Calstock, Cambourne, and St. Just districts of England, and in Cornwall. In the USA, Ag ores occur in large masses in the Lake Valley district, in the states of New Mexico, Arizona, and Nevada (Palache et al. 1951; Klein and Hurlbut 1985).

The average content of Ag in rocks has been determined to be 0.05 mg kg^{-1} in acidic and ultraalkaline rocks, and about 0.1 mg kg^{-1} in alkaline rocks. In abiotic elements of the environment, its concentrations are also naturally elevated in crude oil (as high as 100 mg kg^{-1}) (Eisler 1996; WHO 2002). Among other energy resources, Ag content of coal is about 0.011 mg kg^{-1} (Schweinfurt 2009).

The background Ag in soils is of lithogenic origin and range in concentration from 0.4 to 0.8 mg kg^{-1} dry weight (dw), as reported for both eastern and western regions of the USA (US EPA 2003). According to Kabata-Pendias (2011) average

background Ag content in continental soil is 0.13 mg kg^{-1}. Understanding background concentrations of metals in soil is important for interpreting the toxicity-derived so-called ecological soil screening levels (Eco-SSLs).

High Ag content is exhibited by some geothermal water reservoirs, for example, Salton Lake (California, USA) and Taupo Lake (New Zealand): 0.8–2.0 and 2–7 mg L^{-1}, respectively. Benthic salt muds of the Red Sea exhibit 18 mg Ag L^{-1}, whereas uncontaminated sea and ocean waters have scant levels of Ag and contain on average 0.15–0.29 ng L^{-1} or even less, 0.03–0.10 ng L^{-1} (WHO 2002; Luoma 2008). Average Ag concentrations in natural inland waters like rivers and lakes are in the range of 0.2–0.3 μg L^{-1} (US EPA 1980). The measurements of Ag in freshwater reservoirs show levels even below 0.01 μg L^{-1} in unpolluted areas and much lower concentration ranges are observed for Ag content in air (ng m^{-3}) (US EPA 2003).

Another form of the metal is nanoparticulate Ag (nano-Ag), which is generally a product of anthropogenic activity. However, it was reported that AgNPs may be formed via the reduction of Ag^{+} in the presence of humic acid, which is the element of water sediments and soils. This suggests that nano-Ag might be not only of anthropogenic origin but could be naturally formed under the proper environmental conditions as well (Akaighe et al. 2011).

4 Silver Production and Uses. Anthropogenic Sources of Silver

Silver was discovered around 4000 BC and has been used for millennia for currency and jewelry. Owing to the strong antibacterial properties of its ionized form, it was also used in food service and water disinfection in ancient times (Barillo and Marx 2014). Its medicinal application in wound care has been known for 200 years. Silver compounds have also been used in the treatment of mental illness, epilepsy, and infections like syphilis and gonorrhea (Marshall and Shneider 1977). In crafts and industry, it was used for many centuries in mirror production and photographic materials. Other traditional industrial applications of metallic Ag included coin and metal fabrication, electrical and electronic components, soldering, and plating. As an antibacterial agent it has been used in medical instruments and materials like central venous and bladder catheters, endotracheal tubes lowering the risk of ventilator-associated pneumonia, wound dressing, and gels.

The rediscovery of the biocidal properties of Ag for medicinal and many other uses occurred owing to the development of nanotechnologies (dos Santos et al. 2014). The twenty-first century has been a time of growing importance of nanoparticles (NPs) in general and AgNPs in particular. Engineered NPs are defined as materials having less than 100 nm in size at least in one dimension. Thanks to their large surface area per unit mass, NPs display enhanced properties compared with microsized materials, including a high reactivity both in chemical and biological systems (Nel et al. 2006). Furthermore, the unique physicochemical properties

of NPs may be modified by coating their surface with different substances and chemical groups (Mody et al. 2010). Interesting properties of the nanometer-sized form of Ag that make it different from the bulk form have allowed for its extensive use in medicine and medical devices, as well as in optics, sensing, and painting, and its further extension to many other consumer products. The market for commercially available nano-Ag-containing products continues to expand. Currently, about 30% of all NP-based products contain AgNPs (WWC 2013; Rejeski 2011). Because of their potent antimicrobial effect, exceeding that observed for ionic Ag, AgNPs have found application in various home appliances like refrigerators, dishwashers, washing machines, and water filters. The antibacterial properties of nano-Ag-coated textiles are also popular in the fields of sports and medicine. They are also utilized wherever hygienic conditions and sterile procedures are particularly important, for example, in hospitals, kitchens and food preparation, sanitary facilities, air conditioning and ventilation systems, and material packaging (Bondarenko et al. 2013; Fewtrell 2014; Gaillet and Rouanet 2015). Important fields of nano-Ag applications are sensors (25%), antimicrobial agents (19%), catalysis (13%), optics (8%), and sensing devices (7%) (Bondarenko et al. 2013).

In conventional medicine, the coating of various medical devices, such as catheters, stents, implants, or prostheses with nano-Ag, significantly minimizes the risk of infection during surgical procedures (Ge et al. 2014). Apart from that, AgNPs are also very important tools in next-generation medicine as vehicles for gene therapy and targeted drug delivery systems, as well as biomarkers and elements of imaging systems (Leite et al. 2015).

Because of the global development of nanoindustry, nanoproducts have found application in almost all areas of life. As a result, the growing importance of nano-Ag relative to its metallic or ionic forms is currently observed.

There is a long list of countries around the world where Ag is mined. In the twentieth century most of the world's Ag in the Northern Hemisphere (75%) was mined and produced in the Mexico, USA, Canada, Japan, and Russia; among these countries the USA produced about 50% of the world's Ag (Eisler 1996). Up to 1970 the USA produced less than 15% of the world's Ag and consumed more than 60%, exceeding extractions from ores (Eisler 1996). World production of Ag increased over the years from 7700 tons in 1964 to 12,700 tons in 1984. At the end of the last century, the estimated world mine production of Ag had increased to 14,200 tons (Table 18.1). The major producers of the metal were Mexico (17% of the total), the USA (14%), Peru (12%), the former Soviet Union (10%), and Canada (9%) (Eisler 1996; http://minerals.usgs.gov/minerals/pubs/commodity/myb/). A sharp increase in Ag mining has occurred in the current century. Global mine production of Ag during the period 2004–2014 increased from about 19,800 to 27,200 tons. In 2010, 13,800 tons of Ag were used in industrial applications, including 4734 and 2860 tons used for Ag jewelry and coins/medals, respectively (https://www.silverinstitute.org). In 2013 global Ag use increased by 13% compared with 2012, with a concomitant decreased use for electric, electronic, and photographic applications (http://minerals.usgs.gov/minerals/pubs/commodity/myb/).

Table 18.1 Global mine production of silver over last 50 years (1964–2014)

Year	Tons of silver
1964	7700
1974	9060
1984	12,700
1994	14,200
2004	19,800
2014	27,200

According to U.S. Geological Survey, http://minerals.usgs.gov/minerals/pubs/commodity/myb/

Table 18.2 Silver production in top ten countries, 2000–2013

Country	Silver production (tons) in selected years		
	2000[a]	2010[a]	2013[b]
Mexico	2620	4411	4892
Peru	2145	3640	3342
China	1600	3500	3339
Australia	2060	1864	1675
Russia	370	1545	1273
Boliwia	434	1259	1165
Chile	1242	1287	1109
Poland	1100	1181	1064
USA	1980	1280	990
Argentina	78	723	699

According to data supplied by [a]U.S. Geological Survey (http://minerals.usgs.gov/minerals/pubs/commodity/myb/) and [b]Silver Institute (https://www.silverinstitute.org)

In recent years Mexico has been the dominant player in Ag production, at nearly 4900 tons; Peru, China, Australia, and Russia are the world's other leading producers (Table 18.2).

China's Ag production, including mined, byproduct output, and recycled material, grew by almost 15% every year from 1990 to 2009. By 2010, China was producing over 3000 tons of Ag per year, making it the world's third largest producer of mined Ag and transforming it from a net exporter to a net importer of the metal (https://www.silverinstitute.org/site/supply-demand/silver-production/). Along with China and Mexico, Russia, with 1273 tons of Ag, was responsible for much of the global increase in the metal's supply in 2013. Poland is at the forefront of Ag-producing countries, posssessing the second-largest Ag reserves in the world, estimated at 85,000 tons.

Apart from being exploited from its natural deposits, Ag is frequently obtained as a byproduct in the process of copper, gold, nickel, and lead-zinc ore refining (Eisler 1996). Other important anthropogenic sources of Ag in the biosphere, except mines, are smelters, manufacture of photographic and electrical supplies, coal combustion, and cloud seeding with Ag iodide (Eisler 1996). Silver is emitted into the atmosphere mainly in the forms of Ag sulfide, Ag sulfate, Ag carbonate, Ag halides, and metallic

Ag (Smith and Carson 1977), of which about 50% is transported more than 100 km and is eventually deposited in precipitation (US PHS 1990). It may be found in wastewater from mines and various industries but is also emitted in fallout from coal-fired power plants, from where it can pass into surface waters or accumulate in the soil (Nordberg and Gerhardsson 1988). It has been reported that liquid effluents from the nuclear industry often contain significant quantities of radionuclide ^{110}Ag (Eisler 1996). In the late 1970s it was estimated that Ag released into the environment from industrial sources was approx. 2500 tons per year just in the USA. Nowadays, the amount of Ag waste entering terrestrial or aquatic ecosystems each year worldwide is 300 tons (Wijnhoven et al. 2009). Almost all (about 95%) of the Ag emitted from anthropogenic sources remains in the soil and wastewater compartments (Shafer et al. 1998). As much as 80,000 tons of Ag per year is used on agricultural lands and ends up in industrial sewage sludge; 150 tons of Ag enters aquatic environments every year from the photography industry, mine tailings, and electroplating. Measurements of Ag in rivers and lakes show levels of about 0.1 μg L^{-1} in urban and industrialized areas (WHO 2002). The atmosphere receives 300 tons of Ag each year from a variety of sources. Maximum concentrations of total Ag recorded during the 1970s and 1980s in selected areas were as follows: 36.5 ng m^{-3} in air near smelters; 2.0 μg m^{-3} in atmospheric dust; 6.0 μg L^{-1} in groundwater near hazardous waste sites; 260 μg L^{-1} near photographic manufacturing waste discharge; and as much as 150 mg kg^{-1} in river sediments (WHO 2002).

Regionally, Asia emits high amounts of Ag from landfills directly to the land. Asian countries, such as China, India, and Indonesia, emit significant amounts of the metal into water (Eckelman and Graedel 2007). A survey conducted in North Pacific waters in 2002 found significant (1.2 ng L^{-1}) Ag contamination, the most likely source of which were emissions from coal-burning and coastal waters, especially in Asia. Levels of silver were about 50 times over baseline levels found in uncontaminated waters of the Atlantic Ocean. Increased concentrations of the metal in the open ocean suggest Asia may be a so-called hotspot where Ag contamination is high (Stephens 2005; http://currents.ucsc.edu/04-05/03-14/silver.asp).

Engineered nano-Ag may be considered a significant anthropogenic source of Ag potentially affecting the environment. The issue of AgNPs released into the environment and a potential risk of contamination of natural water systems and aquatic organisms is currently under debate (Blaser et al. 2008; Fabrega et al. 2011). It was estimated that currently about 320 tons per year of nano-Ag are produced and used worldwide (Gottschalk et al. 2010). In Europe , up to 2010, approximately 110–230 tons of Ag was used in the form of nano-Ag-containing biocidal products, where Germany alone used about 8 tons, mainly for water purification purposes (Blaser et al. 2008). In China, the market demand for AgNPs used as antibacterial agents was estimated to have increased to 366 tons by 2014 compared to 45 tons in 2008 (Gao et al. 2013). Worldwide annual production of Ag-containing nanomaterials is reported to be in the range of 5.5–550 tons per year (Piccinno et al. 2012). According to Massarsky et al. (2014), who reviewed data on worldwide Ag production, the amount of nano-Ag increased from 0.4–46 tons per year in 2006 to 7.2–716 tons per year in 2014. Assuming that increase, environmental concentrations of nano-Ag

predicted for 2016 in surface water may even range between 163 and 1306 ng L^{-1}, reaching a maximum value of 57.1 mg kg^{-1} in sediments.

The first relevant processes leading to the mass flow of nano-Ag into terrestrial systems are the disposal of sewage sludge and solid waste management (EEA 2001). Hence, the concentration of nano-Ag in soil will likely continue to rise. The future emission scenario envisions increasing Ag use for the production of different categories of biocidal products and, therefore, increasing flow of Ag into the environment. Silver sulfide concentrations expected in the wastewaters of the European Union in 2015 were estimated to be at 15.7 μg L^{-1} (Blaser et al. 2008).

Silver bioavailability depends on water characteristics such as hardness, natural organic matter (NOM), the presence of chloride, sulfides, and sulfates, all of which lower Ag toxicity. Part of wastewater Ag enters natural freshwater reservoirs where it settles in sediment or is kept in solution in colloidal or complexed form. When associated with colloidal sediment fractions, Ag may naturally occur in the form of NP clusters (Luther and Rickard 2005). To form complexes, it tends to react with available inorganic anionic ligands, mostly with chloride (Cl^-), sulfide (S^{2-}), thiosulfate ($S_2O_2^{-3}$), or organic thiolate (e.g., glutathionate, cysteinate) (Hiriart-Baer et al. 2006). The formation of complexes increases together with enhanced salinity, so that in marine environments ionic Ag binding in complexes with chloride predominates (Ratte 1999). In freshwater and soils, the primary Ag compounds under oxidizing conditions are bromides, chlorides, and iodides; under reducing conditions the free metal and Ag sulfide predominate (US PHS 1990). The opinion also exists that under environmental conditions, neither AgCl (seawater) nor Ag-NOM (freshwater) dominates in Ag speciation, but Ag sulfides are expected to be the predominant forms of the metal (Kramer et al. 2002). Hence, in the current risk assessment, Ag sulfides are considered to be the environmentally relevant Ag compounds.

5 Biological Status of Silver

The global biogeochemical cycle of Ag in nature occurs by its release into the atmosphere, water, and land from natural and, mainly, anthropogenic sources, its long-range transport in the atmosphere, wet and dry deposition, and absorption in soils and sediments (US PHS 1990). Although anthropogenic emission of Ag is still increasing, the mechanisms of its environmental behavior are poorly understood, because no urgent environmental problems have been caused by Ag, in contrast to other metals like mercury, cadmium, or lead.

In soil, Ag is generally highly immobile, relative to other metals, due to precipitation into insoluble salts. Manganese and iron oxides have a strong affinity for binding to it. Silver present in ionic form or in the form of organic complexes in soil solutions is considered the most bioavailable fraction. The amount of soluble Ag (I) depends on dissolved organic carbon (DOC) concentrations, which strongly binds to Ag in soil water extracts. It is also related to the pH, redox conditions,

and strength of binding and complexation with dissolved organic matter (US EPA 2006; Settimio et al. 2015). Microorganisms are very important biocomponents of soils because they are involved in the cycling of chemical elements that are responsible for their mobilization and accumulation in soils (Kabata-Pendias 2011). Since Ag exhibits very high toxicity toward microorganisms, soils contaminated with Ag may be deficient in microbiota, which is of importance in the case of cultivated soils.

Eco-SSLs are concentrations of contaminants in soil that are protective of biota living in or on soil. These values are applied at the screening stage of an ecological risk assessment, which are assumed to provide adequate protection of terrestrial ecosystems. The silver Eco-SSL value calculated for plants is 560 mg kg^{-1} dw in soil, while values for avian and mammalian wildlife range from 4.2 to 14 mg kg^{-1} dw, respectively (US EPA 2006). These concentrations significantly exceed background concentrations in soil in the USA (US EPA 2003).

As a nonessential metal, Ag fulfills no biochemical or physiological roles in tissues.

Bioaccumulation of this metal may occur via the body surface and food in aquatic organisms (bioconcentration) or mainly via the alimentary tract in terrestrial invertebrates and vertebrates. In microorganisms, the bioconcentration of Ag takes place by adsorption on the surface. In terrestrial plants bioaccumulation through the leaves and roots predominates (Ratte 1999).

Microorganisms take up Ag by the adsorption process, that is, by binding on the surface by covalent, electrostatic bonds. In higher organisms uptake of Ag requires energy-dependent active transport with a macromolecular carrier (Ratte 1999). In marine invertebrates, Ag accumulates more intensively than other metals like cadmium, indicating a specific salinity-dependent process (Luoma et al. 1995).

Since Ag is highly toxic to microbes, mechanisms of bioconcentration can be investigated in species with high tolerance. Several bacteria from the genus *Pseudomonas* were found to exhibit extremely high tolerance followed by an accumulation rate over 300 g Ag kg^{-1} dw (Charley and Bull 1979). The strong bactericidal properties of Ag influence bacteria, which fix nitrogen and break down organic matter in soil ecosystems. It was demonstrated that Ag inhibits the growth of heterotrophic and chemolithotrophic bacteria in soil even in concentrations well below those characteristic of heavy metals (Throbäck et al. 2007). Soil organic matter binds Ag strongly, limiting its absorption.

Regarding plants, the absorption of Ag from soils by terrestrial plants is generally low, even if the soil is amended with Ag-containing sewage sludge (WHO 2002). It accumulates mainly in the root systems of plants occurring in the vicinity of mines or in areas contaminated with metal-containing wastewaters. This concerns both trees and other plants, including agricultural crops, grasses, or fungi. Suitable for the detection of soil contamination by Ag is the earthworm *Lumbricus terrestris*. Exposed to soil with increasing concentrations of Ag_2S, it exhibited low bioaccumulation of Ag but reduced growth due to the contact toxicity (for review see: Ratte 1999).

While the biological status of ionic Ag is well established, what happens with AgNPs in both environmental and biological media remains under investigation. It is important to understand the mechanisms of their biotransformation to assess their potential environmental impact. It has been found that NPs lose surface-coating agents such as citric acid, sodium dodecyl sulfate, and amino acids, for example, which are added to prevent the agglomeration of NPs and thereby protect their dispersed state. The result of this process is the unstable state of nano-Ag, leading to aggregation and agglomeration (Li et al. 2013; McShan et al. 2014). Another mechanism involved in biotransformation is the oxidation of NPs' surface to Ag oxide, resulting in the release of ions after interaction with redox-active compounds (Liu et al. 2010). This mechanism of AgNP transformation occurs in environmental and biological media, as it does inside cells. It has also been pointed out that the concentration of sulfur ions, dissolved oxygen, chlorine ions, and biological macromolecules (mainly proteins) is of importance for interactions with AgNPs (McShan et al. 2014). In the environment, AgNPs should be released and concentrated in water systems. In natural water systems, as well as in plants treated with Ag-containing wastewaters, sulfidation of AgNPs has been observed (Choi et al. 2009; Kim et al. 2010a). The lower solubility of nano-Ag sulfide results in a significantly reduced toxicity (Levard et al. 2012). NOM formed from degraded plants and animals is ubiquitous in natural water systems. It was reported that large polymeric NOM molecules, such as humic acid and fulvic acid, might adsorb NPs, increasing their stability (Sharma et al. 2014). The stable state facilitates dispersion, allowing NPs to remain longer in the water system (Tripathy 2008; Liu et al. 2010).

Nano-Ag affects denitrifying bacteria, disrupting denitrification processes at very low concentrations (0.14 mg L^{-1}). This is important because it can result in eutrophication of rivers, lakes, and marine ecosystems. Nitrifying species, which are used for wastewater treatment, are especially susceptible to nano-Ag inhibitory action (Punita 2012; Choi et al. 2009).

Information on Ag toxicity to organisms living in soil and sediments is limited. However, like ionic and metallic forms, AgNPs could have a toxic effect on bacteria that are essential for soil formation. It seems that Ag can disrupt soil microbial species, inhibiting the growth of bacteria well below concentrations of other toxic metals (Murata et al. 2007). As in waters, toxicity depends on physicochemical soil and sediments properties.

Heterotrophic ammonifying bacteria and chemolithotrophic bacteria that consume inorganic material and are essential in soil formation are especially vulnerable to nano-Ag. Nematodes, which are widely found in soils and play an important role in the production, decomposition, and cycling of nutrients, and are food components of many higher animals, serve in natural ecosystems as useful indicators of the presence of soil pollutants. It was found that both AgNPs and bulk Ag are toxic to nematodes (including *Caenorhabditis elegans*), impairing their growth and reproduction (Wang et al. 2009).

The environmental toxicity risks of nano-Ag are poorly understood. No studies have examined the mechanisms of biotransformation and transmission of Ag to plants and further into the food chain. Mammals overexposed to Ag exhibit a characteristic gray or blue-gray and irreversible skin discoloration known as argyria. Silver accumulation in the skin leads to argyria when the body burden is >1 g, which is an effect of the precipitation of insoluble Ag salts such as Ag chloride and Ag phosphate (Stokinger 1981; ATSDR 1990). Silver granules are mostly deposited in both pigmented and unpigmented skin together with sulfur and selenium in lysosomal fractions (Lansdown 2007). Skin discoloration may be caused by a photoreduction of Ag chloride to metallic Ag, which is further oxidized in the tissue to black Ag sulfide (Danscher 1981). Argyria was suggested to be a mechanism of Ag detoxification in tissues (Venugopal and Luckey 1978).

With respect to nano-Ag, recent studies have revealed that besides absorption from nanotechnology products, it might be formed in organisms following exposure to an ionic form of Ag (Liu et al. 2012). The chemical mechanisms of nano-Ag biotransformation are virtually unknown. Many of them have not yet been explored, like interactions with selenium and photoreaction of nano-Ag-biocomplexes in the skin (Cheng et al. 2011). Others, like mechanisms of dissolution in the gastrointestinal tract, are still unclear. Studies by Liu et al. (2012) on nano-Ag reactions in biological media mimicking the composition of fluids in different compartments of the human (mammalian) body suggest the existence of an argyrialike pathway of transformation. In addition, it seems that Ag particles deposited in the skin or other tissues have a similar composition and contain sulfur and selenium regardless of whether ionic or nanoparticulate Ag was administered (Hadrup and Lam 2014).

Investigations of the possible environmental fate of nano-Ag under experimental conditions mimicking estuarine mesocosms revealed a high rate of adsorption and bioaccumulation in different biota, such as biomagnification via trophic transfer from sand to clams (Cleveland et al. 2012). According to Dehn et al. (2006) trophic transfer of Ag may occur also in the benthic food chain. Since Ag has a high affinity to sulfur ligands in water and sediments, it may accumulate in the benthic food web (cephalopods, bivalves, crustaceans). In turn, the results of a study by Yoo-iam et al. (2014) revealed no evidence of biomagnification of either Ag^+ or AgNPs in the food chain, although aquatic organisms in lower trophic groups such as phytoplankton and zooplankton accumulated higher concentrations of Ag^+ and nano-Ag than animals in a higher trophic group (fish). Generally, a few existing studies on the bioaccumulation and biomagnification of Ag have been carried out mainly using aquatic ecosystems. The potential of Ag bioconcentration and biomagnification in terrestrial ecosystems remains unclear. Based on research conducted by Dauwe et al. (2004), one may suspect food chain exposure in certain bird species. Silver concentrations in food (vegetative plants and caterpillars) and excreta of great tit (*Parus major*) from polluted areas were positively correlated. On the other hand, magnification was insignificant for higher organisms analyzed as components of the Arctic food web (Dehn et al. 2006).

5.1 *Toxicity of Various Forms of Silver in Homeothermic Animals*

Silver has no known physiological function. It has been considered for a long time to be nontoxic to humans and terrestrial animals, although it is known to be, after mercury, the most toxic metal for aquatic organisms and is classified as a priority pollutant of surface waters (US EPA 1980; Luoma 2008). However, regarding the fact that in all major Ag-producing countries emissions in tailings and landfills have the greatest environmental impact, the question regarding Ag toxicity has arisen in connection with the contamination of terrestrial ecosystems (Eckelman and Graedel 2007).

Years of research on Ag toxicity have shown that it depends on the specific Ag compound rather than on total Ag concentration. The metallic form of Ag is less toxic than the ionic form, of which the most toxic is Ag nitrate solution. This compound has been reported to be highly irritating to the skin, mucous membranes, and eyes, causing ocular damage. Applied to the gingival mucosa may result in necrotizing, ulcerative gingivitis (Stokinger 1981).

Silver toxicity to wildlife is of importance mainly in aquatic environments, where the probability of ion formation is high. In surface waters it is classified as a pollutant that is extremely harmful to freshwater fish and invertebrates, with lethal concentrations for some sensitive species as low as 1–5 μg L^{-1} (US EPA 1980; CEC 1996; Wijnhoven et al. 2009). According to Eisler (1996) and the World Health Organization's (WHO) "Assessment of Environmental Aspects of Silver and Silver Compounds," no data are available on the effects of Ag on wild birds or mammals (WHO 2002). In general, there are very few reports concerning Ag concentration in wildlife-derived samples. In terrestrial animals, the toxicity of Ag ions and AgNPs has been investigated predominantly in laboratory conditions using rodents, most frequently rats and mice (Matuk et al. 1981; Rungby and Danscher 1984; Skalska et al. 2015; El Mahdy et al. 2015).

5.1.1 Acute and Chronic Toxicity

Acute toxicity through inhalation exposure to Ag(0) or Ag compounds causes both upper and lower respiratory tract irritation, where the action of Ag nitrate is the most intense likely due to the corrosive effect of the nitrate itself (Rosenman et al. 1979). The inhalation of an aerosol containing colloidal Ag was shown to lead to ultrastructural damage to the epithelial cells of the trachea in rabbits (ATSDR 1990). In humans, accidental ingestion of large doses of Ag nitrate has led to corrosive damage to the gastrointestinal tract, abdominal pain, diarrhea, vomiting, shock, convulsions, and death (US EPA 1985).

Chronic toxicity is connected to exposure to metallic Ag and Ag compounds in small doses over periods of months or years, commonly resulting in argyria, regardless of the route of exposure (Gulbranson et al. 2000). Argyria is recognized as the most common indicator of long-term exposure to Ag or Ag compounds in

humans. However, rats experimentally exposed to 222 mg Ag kg^{-1} b.w. day^{-1} for 37 weeks also exhibited granular Ag deposits in the eyes, apart from growth depression and shortened lifespan (Matuk et al. 1981). Long-term oral exposure of experimental animals resulted in a thickening of the basement membranes of the renal glomeruli and granular Ag-containing deposits in skin, eyes, and internal organs, as well as as cardiac enlargement and anemia (Matuk et al. 1981; Drake and Hazelwood 2005). Mild allergic responses have been reported in connection with prolonged dermal exposure to Ag (ATSDR 1990). Oral administration of repeated doses of nano-Ag to mice induced an inflammatory response and significant increase in liver enzymes, indicating hepatotoxicity. Additionally, histopathological changes in kidney have been reported (Park et al. 2010).

5.1.2 Genotoxicity

The genotoxicity of metallic/ionic Ag was not confirmed in experimental studies using in vivo models of exposure. However, the combined effects of Ag and other environmental factor, such as ultraviolet (UVB) radiation, were investigated in vitro using human keratinocyte cell line HaCaT. It was found that Ag(I) interacts with cellular DNA and spurs the formation of pyrimidine dimers in both cellular and isolated DNA in previously radiated cells (Zhao et al. 2014). Similarly, the genotoxic effect of nano-Ag was not confirmed in exposed animals (Kim et al. 2011), although in vitro studies in mammalian cells demonstrated DNA damage. The induction of DNA strand break formation, the inhibition of enzymes required for DNA repair, and the upregulation of DNA damage repair proteins have been reported (Ahamed et al. 2008; AshaRani et al. 2009), just as chromosomal aberrations and sister-chromatid exchanges were noted in Chinese hamster fibroblast cell lines (Ahlberg et al. 2014).

5.1.3 Carcinogenicity and Teratogenicity

There are no data indicating the carcinogenicity of Ag to humans or animals irrespective of route of exposure (Furst and Schlauder 1978). Silver is placed in the group of substances not classifiable as being carcinogenic to humans (US EPA 1997). There are also no studies indicating that Ag, in either ionic or nano form, can act as a teratogen (ATSDR 1990).

5.1.4 Endocrine System Toxicity

The issue of Ag-induced endocrine disruption has received limited attention. Available data mostly originate from in vitro studies. Scant in vivo results were obtained using aquatic species, wherein increasing levels of the stress hormone cortisol and

estrogenic effects were shown, signaling the endocrine-disrupting potential of nano-Ag (for a review see Iavicoli et al. 2013).

5.1.5 Reproductive Toxicity

Exposure of male Wistar rats to nano-Ag damaged DNA in germ cells and decreased epididymal sperm count (Gromadzka-Ostrowska et al. 2012). In addition, disturbances in the proliferation signaling cascade of spermatogonial stem cells were observed, indicating an inhibitory effect on reproductive processes (Braydich-Stolle et al. 2010).

Additionally, relevant rodent studies on nano-Ag indicate its harmful effect on fetal development. Developing embryos of mice treated with nano-Ag had a high concentration of the metal in the liver, spleen, and visceral yolk sac (Austin et al. 2012). Rat fetuses obtained from mothers exposed during pregnancy to different doses of nano-Ag (0.4–0.8 mg kg^{-1} b.w.) exhibited significantly reduced weights and lengths. Placental weight and volume were also lowered relative to control animals (Mahabady 2012).

5.1.6 Neurotoxicity

In long-term studies in orally exposed rodents, hypoactivity and granular Ag-containing deposits in the central nervous system (CNS) were observed, mainly in areas responsible for motor control (Rungby and Danscher 1984). The cellular distribution pattern indicated large motor neurons and protoplasmic astrocytes as a place of preference (Rungby 1986). However, it is unclear whether Ag possesses neurotoxic properties. Although some experimental data demonstrate that Ag ions penetrate the blood–brain barrier (BBB) and accumulate in glial cells and neurons in hippocampus and pons (Rungby and Danscher 1983), others are contradictory (Scott and Norman 1980). It is claimed that Ag does not meet the criteria for neurotoxin, and pathological or behavioral changes induced by this metal are somewhat rarely observed (Lansdown 2007). However, recent data obtained by the author's team indicate that prolonged exposure of rats to low doses (0.2 mg kg^{-1} b.w. day^{-1}) of ionic Ag leads to ultrastructural and biochemical changes in brain synapses (Skalska et al. 2015).

Things are different in the case of Ag nanoformulations. Although few investigations have been conducted into Ag's neurotoxic effects, interest in such studies is on the rise. The ability of nano-Ag to freely cross cell membranes is of great concern in neuroscience due to the development of new therapeutic nanotechnologies, wherein AgNPs are applied as drug carriers or elements of drug-carrier systems (Yang et al. 2010; Leite et al. 2015). Unlike the ionic form, nanoformulation of Ag not only penetrates the brain but has been shown to cause destruction of the BBB, astrocyte swelling, and neuronal degeneration (Tang et al. 2009; Yang et al. 2010). Orally administered, it affects neurotransmitters (5-HT and dopamine) concentration

in rat brain (Hadrup et al. 2012). Moreover, while accumulating in brain parenchyma, it aggravated existing brain pathologies. Administration of nano-Ag to rats prior to their being subjected to heat stress led to greater BBB disruption, edema formation, impairment of cognitive and motor functions, and brain damage (Sharma and Sharma 2007).

Experimental studies of prolonged oral exposure of rats to small (10 nm) commercial-grade AgNPs revealed their efficient absorption into the blood and induction of changes in nerve endings, even at very low concentrations (Skalska et al. 2015). This experimental design reflects a possible profile of toxic events in animals exposed to low doses of nano-Ag that is relevant to events occurring environmentally.

Exposure to even low concentrations of toxic substances may have a detrimental effect on fetal development. Hence, there is also concern about the toxic effect of nano-Ag on the developing CNS. Processes ongoing in the developing CNS during embryogenesis, such as cell division, differentiation, and migration, are extremely responsive to even weak stimuli derived from the intra- or extracellular environment. Since nano-Ag was reported to interfere in vitro with the growth of human embryonic neural precursor cells, further research is needed to assess its adverse effects on the CNS during embryonic development (Soderstjerna et al. 2013).

5.1.7 Cellular Mechanisms of Ionic Silver/Nanosilver Toxicity at Molecular and Biochemical Levels

Ionic Ag exhibits a high affinity for the thiol groups (–SH) of cellular compounds, binding mainly to the reduced glutathione (Baldi et al. 1988) and thus depleting its pool for other biochemical pathways. A strong binding to –SH groups in the collagen of connective tissues and basement membranes has also been observed (Lansdown 2007). It forms complexes with proteins and nucleic acids as well by binding to sulfhydryl, amino, carboxyl, and phosphate groups.

Moreover, exposure to Ag induces the expression of metallothioneins (MTs), which serve a protective function in cells (Bremner and Beattie 1990). These cystein-rich proteins bind Ag absorbed by tissue. In parallel, zinc ions may be liberated from zinc-MT complexes, leading to an excessive amount of this metal first in intracellular and then in extracellular compartments (Lansdown 2007). This mechanism may be of importance in the case of the neuronal form of MT, MT-III, due to the neurotoxic effects of excessive zinc (Koh et al. 1996).

Molecular mechanisms of nano-Ag toxicity are currently under intensive investigation. Unique physical properties of nano forms include a higher reactivity, which is inversely proportional to the particle size and directly proportional to the toxicity (Christian et al. 2008). Substantial evidence exists for and against the different toxic mechanisms of ionic and nano-Ag (for a review see Hadrup and Lam 2014). Nevertheless, the toxicity of AgNPs seems to be mediated by two combined mechanisms: Ag ions released from their surface and unique features of nano formulations (Pratsinis et al. 2013; Hadrup and Lam 2014; Ziemińska et al. 2014;

Skalska et al. 2015). Studies using a variety of experimental animal models have shown that they perturb the function of mitochondria, increasing free radical production and subsequently leading to oxidative stress (Rahman et al. 2009; Strużyński et al. 2014; Wu and Zhou 2013). The generation of excessive reactive oxygen species (ROSs) results in cell death through apoptosis (Piao et al. 2011; Yin et al. 2013). Recently, excitotoxicity via the activation of glutaminergic receptors, followed by calcium imbalance, destabilization of mitochondrial function, and ROS production, was suggested as a mechanism involved specifically in nano-Ag neurotoxicity toward cultured cerebellar granule cells (CGCs) (Ziemińska et al. 2014). Moreover, under nano-Ag exposure an imbalance between extracellular and intracellular zinc levels was also noticed. Zinc supplementation positively influenced nano-Ag-induced changes in CGCs, which was presumed to be due to an inhibitory effect on NMDA-sensitive calcium channels (Ziemińska and Strużyńska 2016).

5.2 Toxicokinetics of Silver and Its Effects in Homeothermic Animals

Due to overexposure, Ag may accumulate mainly in the skin, corneas, gingivae, mucose membranes of the body, liver, kidneys, and spleen. Since it is thought not to evoke serious toxic risks to terrestrial (but not aquatic) organisms, safe reference values are difficult to assess. Studies on the toxic effects of Ag in wild animals are very limited. However, it is evident that the concentration of Ag measured in tissues of exposed organisms is not strictly related to its toxicity. Vertebrates may be exposed to Ag via different routes: orally, by inhalation, or by dermal contact. The results of studies in humans and experimental animals indicate that Ag compounds are mainly absorbed orally, by inhalation, and, to a lesser extent, through the skin (ATSDR 1990).

Absorption, mainly investigated in experimental rodents, was found to be relatively low, much like in domestic birds fed Ag-containing food (for a review see Ratte 1999). It was estimated that about 10% of the initial dose of Ag is absorbed by an animal's body, and of this 4% is retained in tissues. The biological half-life of Ag in human liver ranges from several to 50 days (Nordberg and Gerhardsson 1988). The liver is also one of the main organs absorbing Ag and involved in its excretion with bile in the feces (US EPA 1980). Fecal excretion values reported by Furchner et al. (1968) were 99.6% for mice, 98% for rats, 90% for dogs, and 94% for monkeys; limited amounts were excreted in urine, regardless of the animal species examined. Following oral administration, Ag is absorbed in the digestive tract into portal venous circulation, passes through the liver, and is partially excreted in bile. The remaining portion is distributed to tissues by systemic circulation (ATSDR 1990). In addition to the high concentrations of Ag in rat liver, high concentrations were observed in spleen, bone marrow, lymph nodes, kidney, bladder, and all parts of the gastrointestinal tract (Olcott 1948; Rungby and Danscher 1983; Loeschner et al.

2011; Hadrup and Lam 2014). Some authors also mention muscles and brain as locations of Ag deposition (Rungby and Danscher 1983; Fung and Bowen 1996). After inhalation of metallic Ag by dogs, the largest part of the initial dose was found in the lungs (96.9%); the rest was deposited in the liver, gallbladder, intestines, and stomach (Phalen and Morrow 1973). Intravenous injection of radio-labeled Ag leads to its absorption mainly by the liver and of lesser amounts in testes, where it was found in all cell types of spermatogenesis and in the Sartoli cells (Ernst et al. 1991). In animals exposed experimentally via inhalation, 90–99% of absorbed Ag was excreted in the feces (Phalen and Morrow 1973; US EPA 1985).

The toxicokinetics of nano-Ag is generally similar to that observed in its ionic form. Following oral gavage, it was found at the highest concentrations in the liver, kidney, and small intestine, with the lowest observed in the lungs and brain of rats. Excretion in the feces was estimated to be 63% ± 23% of a daily dose (Loeschner et al. 2011). Rats exposed chronically (90 days) by inhalation showed enhanced Ag concentration in blood, liver, olfactory bulb, brain, and kidney (Sung et al. 2009), whereas in mice 4% of the total Ag dose retention was observed in the lungs (Stebounova et al. 2011). According to the most recent studies, comparison of the bioavailability of different forms of Ag after oral administration revealed a lower level for nanoparticulate than ionic Ag, based on higher fecal excretion (68% vs. 49%) and lower absolute levels in organs (Loeschner et al. 2011; van der Zande et al. 2012; Hadrup and Lam 2014). These data are inconsistent with earlier results indicating high fecal excretion of ionic Ag. However, measurement of Ag concentration in the blood of rats following 2-week oral exposure to ionic and nano-Ag (0.2 mg kg^{-1} b.w. day^{-1}) revealed equal absorption into the serum compartment regardless of the form of Ag (Skalska et al. 2015).

Studies on oral exposure using Ag nitrate, Ag oxide, or Ag chloride in various animal species have reported lethal doses in ranges that are considered indicative of slight to moderate toxicity. Lethal doses for Ag (LD_{50}) were estimated to be 280 mg kg^{-1} b.w. for rats and 800 mg kg^{-1} b.w. for rabbits (Tamimi et al. 1998). LD_{50} values for reported for mice oral colloidal Ag or Ag nitrate are 100 and 129 mg kg^{-1} b.w., respectively. The experimentally assessed no-observed-adverse-effect level (NOAEL) for $AgNO_3$ in test conditions of lethal effect was 181.2 mg kg^{-1} b.w. for orally exposed rats and 137.13 mg kg^{-1} b.w. in guinea pigs following dermal exposure. NOAEL assessed for neuronal effects in mice exposed chronically to $AgNO_3$ or AgCl was 18.1 mg kg^{-1} b.w. (Ratte 1999). In mice NOAEL for nano-Ag administered orally was 0.50 mg kg^{-1} b.w. day^{-1} based on the hepatotoxicity and histopathological changes visible in kidneys at the highest dose examined, or 30 mg kg^{-1} b.w. day^{-1} based on the increased Ag concentration in kidney with no adverse effect observed (Kim et al. 2009; Park et al. 2010). A similar NOAEL value (30 mg kg^{-1} b.w. day^{-1}) was established for rats in a 90-day repeated-dose oral study based on decreased kidney weight (Kim et al. 2009). The lowest-observed-adverse-effect level (LOAEL), the lowest concentration of nano-Ag that causes observed adverse changes in morphology, function, growth, or development of a target organism, was 125 mg kg^{-1} b.w. day^{-1} based on morphological changes in the liver, bile duct, and intestine (Kim et al. 2010b).

The lungs and liver were determined to be the main target organs of rats chronically exposed to nano-Ag (20 nm) by inhalation (Sung et al. 2009). The authors determined a NOAEC (no-observed-adverse-effect concentration) of 0.1 mg m^{-3} based on histopathological changes in the bile duct and features of inflammation in the lungs.

The highest available dose in the literature of nano-Ag tested was 5000 mg kg^{-1} b.w. day^{-1} and was not lethal to guinea pigs (Maneewattanapinyo et al. 2011).

5.3 *Bioaccumulation of Silver in Mammalian and Avian Species*

The uptake of this trace element in environmental conditions mainly depends on dietary levels, digestion, and absorption from the gastrointestinal tract. It might be suspected that it occurs to a marginal extent via damaged skin. Silver absorbed into the blood is initially deposited in soft tissues, where the levels mirror the recent exposure.

Of all the tissues, bones reflect long-term exposure to metals. From the research of Hamilton et al. (1972) it is apparent that in human Ag achieves the highest concentrations in bones, i.e., 1.1 mg kg^{-1} in ashed bones, which is 0.67 mg kg^{-1} dw assuming a ratio of ash to organic matter in human ribs of 61–29% (Table 18.3) (Call et al. 1965). In different regions of the world and different decades of the 20th and twenty-first centuries, the concentration of Ag in the bones of modern humans has changed within a considerable range (from <0.01 to >2.0 mg kg^{-1} dw), mainly depending on environmental conditions. In the period 1970–2000 it generally did not exceed 0.5 mg kg^{-1} dw of Ag in Europeans, whereas it was ten times higher in old inhabitants of industrialized Taiwan in Asia (Table 18.3). Samples collected recently from residents of the city of Obinsk (central Russia) showed that the concentration of Ag in intact bones is very small and does not exceed 0.003 mg kg^{-1} dw, which can be considered the value reflecting the geochemical background (Zaichick and Zaichick 2015).

Information concerning Ag values in human samples was included in the current meta-analysis since data derived from wild mammals are scant. Unpublished data of Kalisinska and coworkers concerning Ag content in mammal bones of predatory semiaquatic racoon *Procyon lotor* from Poland, which is an alien species in the European fauna originating from North America, revealed accumulation of the metal one to two orders of magnitude higher than the typical value (0.01 mg kg^{-1} dw) in mammalian bones reported by Gough et al. (1979). The fact that samples were collected from the "Warta-Mouth" National Park in Poland, located in the vicinity of the copper mining region of Lower Silesia, may explain the enhanced Ag levels.

Research conducted in the 1970s on birds, especially those connected to aquatic food chains and inhabiting water reservoirs contaminated with metals, including Ag,

Table 18.3 Silver concentration in mammalian and avian bones

Species	Location and time period	Concentration mg kg^{-1} dw	Remarks	References
Mammals				
Humans *Homo sapiens*	Taiwan, <2000	2.8 ± 3.5 2.32 ± 1.93 3.06 ± 3.61 2.23 ± 1.19 5.07 ± 8.54	$n = 70$, all groups <40 years 41–60 years 61–80 years >80 years	Kuo et al. (2000) Age differences among bone Ag levels NS
Homo sapiens	Verona, Italy, 14th century	0.01	$n = 1$; ad	Apostoli et al. (2009)
Homo sapiens North American Pecos Indian	North America, ~14th century	$n = 14$, ad + im 0.15 ± 0.15 0.039–0.560 ad: 0.066–0.560 im: 0.039–0.13	Inner part of bone, ad $n = 10$ im $n = 4$	Ericson et al. (1991)
Homo sapiens	Europe	0.01–0.44	Modern people	Ericson et al. (1991)
Homo sapiens	Russia, <2015	0.0027 ± 0.0015 0.00026–0.0047 0.0074 ± 0.0188 0.00064–0.0967	intact bone, $n = 27$ osteogenic bone, $n = 27$	Zaichick and Zaichick (2015)
Homo sapiens	United Kingdom, <1970	1.1 0.67	$n = 22$, rib, ash[a] $n = 22$, rib, dw	Hamilton et al. (1972)
Phocoenoides dalli Dall's porpoise	Japan, 2000	0.001	$n = 1$, ad male	Yang et al. (2006)
Raccoon *Procyon lotor*	Poland, polluted area, 2009–2012	0.325 ± 0.047 0.244–0.421	$n = 14$, ad	Kalisinska unpubl. Data
Birds				
Larus crassirostris Black-tailed gull	Japan, Rishiri Island, 1999–2001	0.006 ± 0.004	$n = 4$	Agusa et al. (2005)
Great cormorant *Phalacrocorax carbo*	Japan, 2003	<DL	$n = 4$, ad	Nam et al. (2005a)
Great tit *Parus major*	Belgium, 2000	0.018 <DL – 0.154	$n = 10$, ad <DL one tit	Dauwe et al. (2005)
Brown pelican *Pelecanus occidentalis*	USA, Florida, 1969	2.51 2.03–3.12	$n = 5$	Connors et al. (1972)
	USA, California, 1969–1971	2.32 1.95–2.75	$n = 5$	
White pelican *Pelecanus erythrorhynchos*	USA, California, 1969–1971	1.92	$n = 1$	Connors et al. (1972)

n number, *ad* adult, *im* immature, *DL* detection limit
[a]61% ash in rib, see Call et al. (1965)

identified >2 mg kg^{-1} dw of Ag in bones (Connors et al. 1972; Lande 1977; Ohlendorf et al. 1986). The values correspond to those noted in the inhabitants of industrialized Taiwan (Table 18.3).

The observed decrease of Ag concentrations in the bones of homeothermic vertebrates (including humans) within a few years could be associated, at least in part, with the development of digital photography and the subsequent reduction in metal emissions into the environment. However, it should be kept in mind that at the same time, the mining, production, and use of Ag in other industrial sectors is continuously increasing. Nevertheless, a growing awareness of the necessity to protect the environment reflects the activities undertaken for this purpose.

Experimental studies on Ag toxicokinetics indicate that Ag absorbed into the blood of orally exposed animals is initially deposited in soft tissues such as liver, kidneys, intestines, muscles, and brain (Sect. 5.2). Preferentially it accumulates in the liver, in nuclear, lysosomal, and mitochondrial fractions. Among soft tissues in human tissues, the highest Ag concentrations were reported in liver and brain, 0.020 and 0.018 mg kg^{-1} dw, respectively (Hamilton et al. 1972). The content of Ag in other human tissues such as kidney, lung, muscles, and gonads ranged between 0.010 and 0.007 mg kg^{-1} dw.

Fragmentary studies on wildlife species also demonstrated bioconcentration of Ag within liver tissue (Table 18.4). The concentration was usually in a range of 0.013–-4.3 mg kg^{-1} dw, but it varied by location of sample origin. The values were higher in the liver of Javan mongoose *Herpestes javanicus* from Japan than in the liver of Arctic fox *Alopex lagopus* from Alaska (0.043–4.300 vs. < detection limit – 0.100 mg kg^{-1} dw). In turn, samples derived from the same species were similar regardless of place of collection. In Canadian polar bear *Ursus maritimus* and in polar bear from Alaska, Ag concentrations reached on average 0.65 and 0.53 mg kg^{-1} dw, respectively (Dehn et al. 2006; Rush et al. 2008).

For different avian species concentrations of metal found in liver usually ranged between 0.010 and 1.000 mg kg^{-1} dw, with extreme values below (< detection limit) and above (44.000 mg kg^{-1} dw) the range. As was reported, the major part of Ag in the body of adult birds accumulates in the liver (~60%) (Nam et al. 2005a). Previously, apart from the liver, from which a sample was usually collected, kidneys, muscles, and brain were also frequently utilized for analysis. In the most recent studies, eggs and feathers are also used, owing to the fact that birds are frequently protected species. In the liver and kidney of the white-tailed eagle, *Haliaeetus albicilla*, from breeding sites on the Polish coast of the Baltic Sea, Ag was found to be present in rather low concentrations of 0.056 and 0.037 mg kg^{-1} dw, respectively, with maximum values of 0.23 and 0.13 mg kg^{-1} dw (Falandysz et al. 2000, 2001). Apparently resulting from background exposure, these concentrations are rather low and do not induce any acute toxic effects. Much higher concentrations of metal were reported for the bald eagle, *Haliaeetus leucocephalus*, from the US state of Maine (Mierzykowski et al. 2011), which is is heavy metal-burdened area (http://www.nrcm.org/projects-hot-issues/healthy-waters/open-pit-metal-mining-in-maine/). In the liver of this species, 0.67 mg kg^{-1} dw (range 0.21–3.40 mg kg^{-1} dw) of Ag was found, and this value was an order of magnitude greater than that presented by

Table 18.4 Silver concentration (mg kg^{-1} dw) in soft tissues of wild terrestrial and semiaquatic mammals and birds. Conversion of wet weight (ww) on a dry weight basis are given in parentheses (calculations assume that the liver, kidney, and brain of mammals and birds contain an average of 70%, 75%, 80% water, respectively)

Species	Place and years	Liver	Kidney	Muscle	Brain	Remarks	References
Mammals							
Hedgehog, T *Erinaceus europaeus*	Belgium, 2002–2003	0.12 ± 0.02 <DL–0.48	0.04 ± 0.02 <DL–0.62	<LD ± 0.002 <DL–0.057		Liver, $n = 43$ Kidney, $n = 44$ Muscle, $n = 44$	D'Havé et al. (2006)
Javan mongoose, T *Herpestes javanicus*	Japan, 2004–2005	0.143 ± 0.194 0.013–1.290 (0.477 ± 0.647) (0.043–4.300)	0.002 ± 0.002 <DL–0.008 (0.008 ± 0.008) (<DL–0.032)		0.011 ± 0.003 <DL–0.014 (0.055 ± 0.015) (<DL–0.070)	ww Liver, $n = 53$ Kidney, $n = 30$ Brain, $n = 4$	Horai et al. (2006)
Arctic fox, T *Alopex lagopus*	USA, Alaska 1999–2000	0.01 ± 0.01 <DL–0.03 (0.033 ± 0.033) (<DL–0.100)				ww, $n = 27$	Dehn et al. (2006)
Polar bear, S *Ursus maritimus*	USA, Alaska 1999–2000	0.16 ± 0.08 0.05–0.35 (0.53 ± 0.26) (0.17–1.17)				ww, $n = 23$	Dehn et al. (2006)
Polar bear, S *Ursus maritimus*	Canada, 2002						Rush et al. (2008)
	East Baffin Island	0.13 ± 0.11 (0.43 ± 0.34)				ww, $n = 13$	
	Northern Baffin Island	0.21 ± 0.11 (0.70 ± 0.34)				ww, $n = 13$	
	Lancaster Sound	0.28 ± 0.11 (0.93 ± 0.34)				ww, $n = 13$	
	Alaska, 1994–1999	0.16 ± 0.10 (0.53 ± 0.33)				ww, $n = 6$	

(continued)

Table 18.4 (continued)

Species	Place and years	Liver	Kidney	Muscle	Brain	Remarks	References
Birds							
Great tit, T *Parus major*	Belgium, 2000	0.023 0.004–0.150	0.008–0.008 <DL ($n = 3$)	0.003–0.012 <DL ($n = 2$)	0.013 0.007–0.026	Median; ad, F, $n = 10$	Dauwe et al. (2005)
White-winged dove, T *Zenaida asiatica*	USA, Texas, 2003	<DL <DL–22.2				<DL 69 out of 70	Fredricks et al. (2009)
Black-tailed gull, W *Larus crassirostris*	Japan, Rishiri Island, 1999–2001	0.019 ± 0.008	0.028 ± 0.027	0.006 ± 0.005 <DL $n = 1$	0.030 ± 0.010	ad, $n = 5$	Agusa et al. (2005)
Great cormorant, W *Phalacrocorax carbo*	Japan, Lakes Biwa and Mie, 1993 and 2003	0.084 ± 0.021	0.028 ± 0.019	0.001 ± 0.001	0.036 ± 0.002	Liver 1993 0.081 ± 0.043 0.021–0.160 Liver 2003 0.047 ± 0.024 0.022–0.092	Nam et al. (2005a)
Great cormorant, W *Phalacrocorax carbo*	Japan, Lakes Biwa and Mie, 2003	0.117 ± 0.179	0.011 ± 0.020	<0.001		$n = 17$; ad+juv	Nam et al. (2005b)
Mallard, W *Anas platyrhynchos*	Japan, Izumi, 2003	0.190 ± 0.241	0.014 ± 0.009	<0.001		$n = 13$	Nam et al. (2005b)

Cammon teal, W *Anas crecca*	Japan, Izumi, 2003	0.083	0.003	<0.001		$n = 2$, ad	Nam et al. (2005b)
Pintail, W *Anas acuta*	Japan, Izumi, 2003	0.010	0.010	<0.001		$n = 2$, ad	Nam et al. (2005b)
Bald eagle, W/T *Haliaeetus leucocephalus*	USA, Maine, 2001–2007	0.96 0.21–3.40				$n = 47$	Mierzykowski et al. (2011)
White-tailed eagle, W/T *Haliaeetus albicilla*	Poland, 1991–1995	0.056 0.002–0.230	0.037 0.003–0.130	0.010		$n = 10$–12	Falandysz et al. (2000)
Greater scaup, W *Aythya marila*	USA, San Francisco Bay, 1982	1.050 ± 0.146 0.390–3.100				$n = 18$, ad (16 M+2F); 94% with residue; contaminated area	Ohlendorf et al. (1986)
Surf scoter, W *Melanitta perspicillata*	USA, San Francisco Bay, 1982	0.900 ± 0.179 0.330–3.700				$n = 22$, M (21 ad+1 juv); 91% with residue; contaminated area	Ohlendorf et al. (1986)
Greater scaup, W *Aythya marila*	Canada, British Columbia, 1976						Vermeer and Peakall (1979)
	Iona Island	0.32 ± 0.08 (1.04 ± 0.27)				ww, $n = 10$	
	Roberts Bank	0.04 ± 0.004 (0.13 ± 0.013)				ww, $n = 10$	

(continued)

Table 18.4 (continued)

Species	Place and years	Liver	Kidney	Muscle	Brain	Remarks	References
Surf scoter, W *Melanitta perspicillata*	Canada, British Columbia, 1976						Vermeer and Peakall (1979)
	Iona Island	0.14 ± 0.03 (0.47 ± 0.10)				ww, $n = 10$	
	Roberts Bank	0.03 ± 0.004 (0.10 ± 0.013)				ww, $n = 10$	
Common eider, W *Somateria mollissima*	Norway, 1972–1973	44.00	7.00	2.00		ad, F, $n = 6$ polluted area	Lande (1977)
Lesser black-backed gull, W *Larus fuscus*	Norway, 1972–1973	2.00	1.00	3.00		ad, $n = 6$ polluted area	Lande (1977)

T terrestrial, *S* semiaquatic, *W* waterbird, *DL* detection limit, *F* female, *M* male, *ad* adult, *juv* juvenile

Falandysz et al. (2001) for white-tailed eagle, whose biology is very similar to that of the North American bald eagle.

In avian species inhabiting inland water bodies or coastal areas, Ag concentration in liver and other soft tissues varies to a large extent, depending on the degree of pollution and the metal content in the diet. It seems that exposure to elevated concentrations of Ag contained in seafood is a source of high body burden of metal in birds breeding in coastal locations. In the great cormorant, *Phalacrocorax carbo*, feeding in the large freshwater reservoir contaminated with heavy metals in Japan, high concentrations of Ag were noted in liver and brain (0.084 and 0.036 mg kg^{-1} dw, respectively), just like in kidney (0.028 mg kg^{-1} dw), whereas the concentration of Ag in feathers of this bird did not exceed 0.01 mg kg^{-1} dw (Nam et al. 2005a, b). However, the greatest Ag abundance was detected in certain duck species (common eider, *Somateria mollissma*) inhabiting Norwegian fjords highly polluted with heavy metals (Lande 1977). In the liver, kidney, and muscle, average concentrations of Ag was 44.0, 7.0, and 1.0 mg kg^{-1} dw, respectively. This seems to be the largest average value of the metal estimated in the avian liver. Simultaneously, it should be highlighted that environmental Ag contamination, mainly of anthropogenic origin, results in an increased accumulation of the metal in the bodies of homeothermic vertebrates, especially those associated with aqueous food chains, including aquatic birds. This is confirmed by both the earlier research conducted during the period of the environment burdening with uncontrolled discharge of pollutants and works carried out in the twenty-first century, while in Europe, the USA, and Canada strict regulations on environmental protection were introduced (Lande 1977; Ohlendorf et al. 1986; Mierzykowski et al. 2011).

Silver is incorporated to a lesser extent into avian eggs compared with internal organs. The levels of this element seem to be low in eggshell and egg content: $<$0.001–0.012 and 0.004–0.013 mg kg^{-1} dw, respectively (Agusa et al. 2005; Ikemoto et al. 2005). However, higher Ag levels were observed in eggs taken from birds originating from heavy-metal-polluted areas in Norway (common eider, *Somateria mollissima*, and lesser black-backed gull, *Larus fuscus*) (Lande 1977) and Belgium (great tit) (Dauwe et al. 1999, 2005).

It is also noteworthy that the distribution of Ag is very large in feathers. Studies by Nam et al. (2005a) showed that adult birds accumulated about 30% of absorbed Ag in their feathers. Among birds from various trophic and taxonomic groups, Ag content in feathers generally was in a narrow range of 0.010–0.094 mg kg^{-1} dw (Table 18.5) or even undetectable (Scanlon et al. 1980), although feathers sampled from great tit living near smelters exhibited much higher Ag concentrations (over 3.5 mg kg^{-1} dw in adult specimens) relative to that from unpolluted areas (0.13 mg kg^{-1} dw). In addition, tit nestlings from polluted areas had higher Ag concentrations in feathers compared with nestlings from referenced area: 0.020 vs. 0.001 mg kg^{-1} dw (Janssens et al. 2001).

Table 18.5 Silver concentration (mg kg^{-1} dw) in feathers of various bird species

Species	Location and time period	Concentration	Reference
Unpolluted area			
Ruffed grouse *Bonassa umbellus*	USA, Virginia, 1977–1979	< 0.010	Scanlon et al. (1980)
Black-tailed gull *Larus crassirostris*	Japan, Rishiri Island, 1999–2001	0.019 ± 0.003	Agusa et al. (2005)
Great cormorant *Phalacrocorax carbo*	Japan, Lake Biwa and Mie, 2003	0.010 ± 0.004	Nam et al. (2005a)
Great tit *Parus major*	Belgium, Brasschaat, 2000	0.130 ± 0.070	Janssens et al. (2001)
Sparrowhawk *Accipiter nisus*	Belgium, Flanders, 2001	0.023 ± 0.012 (0.013–0.040)	Dauwe et al. (2003)
Little owl *Athene noctua*	Belgium, Flanders, 2001	0.018 ± 0.009 (0.013–0.025)	Dauwe et al. (2003)
Barn owl *Tyto alba*	Belgium, Flanders, 2001	0.021 ± 0.005 (0.018–0.027)	Dauwe et al. (2003)
Tawny owl *Strix aluco*	Belgium, Flanders, 2001	0.061 ± 0.009 (0.029–0.094)	Dauwe et al. (2003)
Polluted area			
Great tit *Parus major*	Belgium, Antwerp, 1997–1998	3.590 ± 0.600	Janssens et al. (2001)

5.4 *Ecological Effects of Silver*

As discussed earlier, free Ag ions are extremely toxic to aquatic organisms and even lethal to certain sensitive species of invertebrates and fish at concentrations of 1.2–4.9 μg L^{-1}. Available data on Ag toxicity concern mainly its effects on small laboratory mammals and poultry. Toxic effects on avian or mammalian wildlife have not been extensively studied since it was believed to be an element of low toxicity. Many of the review papers on the presence and toxicity of Ag in wild species highlight the fact that there are no data concerning the ecological effects of this metal in terrestrial avian and especially mammalian species (Eisler 1996; WHO 2002).

For mammals, no data are available to predict the ecotoxicological effects of Ag. Some of the species studied include polar bear (semiaquatic species from an ecological point of view), Arctic fox, and Javan mongoose (Table 18.4). Reported Ag concentrations in liver fell within a relatively high range (from below the detection limit to 4.30 mg kg^{-1} dw). Despite this, liver may be considered a location of the highest Ag accumulation. The limited types of samples prevent identifying another target organ. However, samples derived from Javan mongoose (carnivore) indicate that Ag concentration in soft tissues reaches its highest levels in liver and then in the brain and kidney (Horai et al. 2006).

Birds, while affected environmentally, usually exhibit the highest bioconcentrations of metal in liver and brain, the lowest in muscles, and intermediate levels in the kidneys. Concentrations in avian tissues were frequently found to be elevated mainly in the vicinity of metal-contaminated areas in Europe and the USA and were higher in liver compared to other examined tissues like kidney or muscles (Lande 1977; Ohlendorf et al. 1986). Its presence was especially observed in birds in connection with aquatic systems. Maximum concentrations of total Ag, recorded in field collections of living organisms, were found in the liver of four species: lesser black-backed gull, surf scoter (*Melanitta perspicillata*), greater scaup (*Aythya marila*), and common eider. Whole tissue concentrations ranged in these species between 0.9 and 44.0 mg kg^{-1} dw (Lande 1977), whereas in conspecifics from areas remote from anthropogenic contamination, Ag concentrations were usually much lower, within a range of 0.010–0.190 mg kg^{-1} dw (Agusa et al. 2005; Nam et al. 2005a, b).

Aquatic and other birds may be exposed to Ag mainly via their diet or accidentally swallowed small Ag-containing things like gastroliths, although contamination by respiration cannot be excluded in industrial areas (Agusa et al. 2005; Dauwe et al. 2005; Fredricks et al. 2009). The latter publication reports extremely high concentrations of Ag found in the liver of one white-winged dove, *Zenaida asiatica*, from Texas (Fredricks et al. 2009).

Data collected in Table 18.4 indicate that Ag may be preferentially enriched in some avian tissues, mainly in liver and brain. The same may be concluded based on the results obtained from human and mammalian specimens. Thus, these organs should be considered targets for Ag. As has been suggested, lying eggs may constitute the specific mechanism for Ag excretion by female birds. However, a decrease in the Ag body burden by its transfer to eggs is limited (Dauwe et al. 2005). Although avian eggs have been widely used as indicators of heavy metal exposure, they seem not to be suitable in the case of exposure to Ag. However, the negative influence of accumulated metal on embryonic development cannot be excluded and may be relevant in the context of ecotoxicological effects (Dauwe et al. 2005).

Recent studies emphasize the need to develop safe methods of biomonitoring that will make it possible to assess the bioconcentration of various elements in living organisms. Bird feathers are good for this purpose because they are easy to collect noninvasively and repeatedly without affecting investigated individuals. Silver shows high affinity for the sulfhydryl groups (−SH) of keratin. Thus, it accumulates in feathers, which can be considered an important excretory pathway for this metal (Agusa et al. 2005). Moreover, birds eliminate heavy metals from tissues by sequestering them into plumage during the molting period. Since birds are in many cases protected, noninvasive techniques of sample collection are desirable. Feathers provide an alternative to internal organs and have proven to be suitable biomonitors for Ag pollution (Dauwe et al. 2003). Feathers of species that inhabit uncontaminated or relatively lightly contaminated environments and are nonmigratory, are presumably the best source of background concentrations because such concentrations are observable in the case of ruffed grouse, *Bonassa umbellus*, from forested areas in the vicinity of the US state of Virginia (Scanlon et al. 1980). Moreover, external contamination may have an important impact on the level of Ag

detected in feathers, resulting in higher concentrations of metal in feathers most exposed to external atmospheric conditions or preening (Dauwe et al. 2003).

The present collection of data provides some information on the abundance of Ag in various avian and mammalian species. First of all, ranges for Ag concentrations, regardless of the analyzed tissue, can be related to their local environment and to the pollution status of ecosystems. However, it is essential to realize that this collection may be of limited value. The dearth of research on Ag toxicity in the wild, together with the recognition that individuals may differ in their responses to Ag, may cause difficulties in predicting the exact ecotoxicological effects of Ag. However, these data in conjunction with knowledge of local pollution levels show that Ag present in the environment is capable of entering both avian and mammalian species (including humans). Additonal issues emerge from the data collected in Table 18.4. First, the research does not cover the last 10 years and, second, it comes mainly from the USA and Europe. There are almost no data relating to individuals inhabiting large territories of Asia (except Japan). This is a significant consideration in light of the fact that Asia emits substantial amounts of Ag to the land and into water bodies (Eckelman and Graedel 2007) and is regarded as a hotspot of Ag/nano-Ag pollution. We do not know exactly yet how nanotechnological advances may change human and animal environments. Drastically increasing both the production and abundance of nano-Ag in the environment may spur increases in toxicity for wildlife than has been estimated so far.

Based on current information on the fate of nano-Ag in the environment, it may have ecotoxicological effects, particularly after being discharged into water. Flowing into water bodies, nanometer-sized Ag has a variety of physiological effects on living organisms, including fish and invertebrates (Fabrega et al. 2011; Schirmer et al. 2013). Therefore, the ecotoxicological effects of nano-Ag (similarly to ionic Ag) could be expected to be closely linked with the aquatic environment and affect species inhabiting water ecosystems.

5.5 Bioindicators and Biomarkers for Silver in Ecotoxicological Studies

Since the problem of Ag pollution of the environment is predicted to increase, it is important to look for organisms that might be useful as bioindicators of Ag contamination. Species to be used as biological indicators of Ag contamination should reflect the level of environmental pollution. Birds are often used as bioindicators since they are particularly well-known organisms with well-established behavior and biology and have relatively long life spans, which makes it possible to assess the long-term effects of exposure (Furness 1993). The food items and metal concentrations in the diet of birds may vary considerably in different areas. Analysis of the data collected in Table 18.4 indicates that birds feeding in differently contaminated zones reveal an interdependence between metal concentrations in tissues and the

higher level expected in their habitat. Bioaccumulation of Ag in sea ducks—surf scoter and greater scaup—feeding exclusively in the marine and estuarine habitat of Iona Island polluted by wastewater from Vancouver (Canada) was dependent on the level of contamination of their feeding areas as well as prey (Vermeer and Peakall 1979). Moreover, samples of aquatic birds from extensively polluted areas such as San Fransico Bay in California (Ohlendorf et al. 1986) or Trondheimsfjorden, Norway (Lande 1977), reflected well the high concentrations of Ag, regardless of the investigated species of surf scoter/greater scoup and common eider/lesser black-backed gull, respectively. Aquatic, especially coastal/marine, ecosystems are of concern in the case of Ag contamination since Ag is known to bioaccumulate and to be highly toxic to aquatic organisms. Current meta-analysis performed on the basis of limited studies suggested that aquatic birds may be treated as potential bioindicators of Ag pollution in costal/estuarine areas since high concentrations of metal have been encountered in tissues of many species. In analyzing other avian species, strong evidence can be found confirming relationships between Ag concentrations in tissues versus those in more typical habitats. Birds such as the great tit, which inhabit urban areas, exhibited higher Ag levels in tissues (Dauwe et al. 2005) relative to migratory species like the white-winged dove (Fredricks et al. 2009). This implies that food preferences may significantly contribute to the bioaccumulation of Ag in birds. The rate at which the diet passes through the gastrointestinal tract and dietary composition may affect metal absorption and increase its levels in avian tissues. Primary determinants of food retention are food characteristics and the digestive anatomy of the avian species (Nam et al. 2005a, b). Because birds may ingest toxicants through food or water, soil contamination may represent a significant hazard for birds. Airborne deposition of Ag on feathers may also be a significant source of exposure during bird self-grooming. In turn, female birds may eliminate pollutants by depositing them in eggs. During the breeding period, the great tit collects food in its territory, so the metal content in the eggs is derived to a large extent from local sources, making the eggs suitable bioindicators of local pollution (Dauwe et al. 2005). However, the egg load factor of Ag may have limited value. According to Dauwe et al. (1999), metal concentrations in egg contents and eggshells, although high, were poorly correlated with metal concentrations in internal tissues and feathers. Collected data indicate that Ag concentrations in the egg content of black-tailed gull and great tit are 0.008 mg kg^{-1} dw (Agusa et al. 2005) and 0.012 mg kg^{-1} dw (Dauwe et al. 2005), which is comparable to concentrations in the muscles of those species (Table 18.4).

Generally metals, including Ag, are incorporated into the keratin structure of a feather during the growth period, when the feathers receive a supply of blood. However, Ag may also be deposited onto the surface of feathers by airborne dust. Thus, feathers may reflect both endogenous contaminations originating from bird diet and exogenous adsorption. It is stressed that analyzing the level of different metals present in feathers is a method of monitoring the ecological consequences of environmental metal pollution. Consequently, feathers can be used as bioindicators (Markowski et al. 2013), including of Ag contamination. In feathers of ruffed grouse from forested areas of the US state of Virginia, Ag was not detected at sensitivity

levels (Scanlon et al. 1980). In contrast, in feathers of the great tit from polluted areas of Antwerp, Belgium, Ag levels were very high (Janssens et al. 2001).

Silver concentrations in feathers of birds of prey are significantly lower than in the great tit (Table 18.5). One might think, then, that birds of prey would be useful for assessing environmental Ag contamination because of their high position at the top of the food chain. However, to date, there is no convincing evidence of Ag biomagnification in trophic chains, especially in the higher trophic groups. Currently available data do not confirm an increased concentration of Ag in comparisons of levels in tissues of predators and their prey. Moreover, the extended home range and feeding area of birds of prey make it difficult to determine the exact location of their exposure. For these reasons, resident passerine birds like the great tit seem to be better suited for the biomonitoring of Ag ecotoxicological effects within limited regions such as urban areas. As a resident species in a relatively small home range, the great tit feeds within a limited area, and the content of Ag present in organisms may reflect local contamination. Feathers of the great tit, both adult and nestlings, were shown previously to reflect well the profile of Ag pollution in urban areas (Janssens et al. 2001; Dauwe et al. 2004).

However, it should be kept in mind that the aforementioned conclusions are limited by insufficient studies focusing on terrestrial organisms, especially semi-aquatic mammals from inland ecosystems.

6 Conclusions

To understand the bioavailability and uptake of Ag within natural ecosystems, efforts have focused on wildlife. Concentrations of many pollutants may increase with trophic level. Thus, studies should begin with the transfer of Ag contaminating terrestrial environments in species within a food chain to assess the risks posed to upper-trophic-level organisms, especially mammals and birds. This is very important given the increasing usage of nano-Ag-containing products. Particular attention should be directed toward understanding natural nano-Ag cycling and predicting the risk of environmental hazards.

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Chapter 19
Tin, Sn

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Abstract The harmfulness of tin (Sn) on the environment depends on the chemical form in which it occurs. In general, organic Sn compounds are more toxic than metallic tin and inorganic tin compounds. Some studies suggest that tin is an essential trace element for animals and perhaps for humans, but no consensus exists in this regard. Concentrations of inorganic tin in the air, soil, and water are usually low, apart from those areas with naturally high Sn content and regions surrounding tin processing plants. The toxic activity of Sn, caused by environmental exposure to tin, has not been reported in plants, animals, or humans. From an ecotoxicological point of view, the most important compounds are the organotins, mostly due to their androgenic activity and contribution to the increasing number of imposex individuals between marine vertebrates and invertebrates. Literature data about the bioaccumulation of inorganic tin in land ecosystems is very limited, especially in relation to mammals. Also, most of the data concerning the aptitude of some species of animals and biological parameters to be used as bioindicators and biomarkers of environmental exposure to tin usually relate to marine habitats and organic forms of this element. It seems that the problem of land habitat pollution with tin is not well elucidated.

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1 Introduction

Metallic tin (Sn) is a natural compound of the earth's crust, in concentrations reaching about 2–3 mg kg^{-1} (Budavari 2001). Tin is released into the environment from both natural and anthropogenic sources, but for the organic forms of this element, the anthropogenic sources are dominant. Tin reaches the atmosphere with soil and road dust and agricultural activity. Fires and volcanic emissions are also sources of tin, but their significance is quite low. Industrial emissions of tin are mostly related to smelting and refining, the industrial use of tin, and combustion of waste and fossil fuels (WHO 2005).

Pesticides, landfilling with Sn-containing wastes, and the application of pretreated municipal sludge and urban refuse as soil amendments are sources of tin in soils (ATSDR 2005). The concentration of tin in European soils ranges from <2 to 106 mg kg^{-1}, while in unpolluted soils it usually does not exceed 5 mg kg^{-1} (De Vos et al. 2006). In natural water reservoirs (rivers, lakes, estuaries, and oceans), tin is present in trace amounts and usually does not exceed 5 ng L^{-1} (WHO 2004).

Tin is an essential trace element for plants and fungi. Some studies suggest that tin is an essential trace element for animals and perhaps for humans, but there is no consensus on this issue. The toxicity of tin to animals depends on the form in which this element is present. Inorganic tin, due to its low solubility, poor absorption, and small retention in tissues, is relatively harmless (Johnson and Greger 1982). Some organotin compounds show a high biological activity, as used in the production of biocides as pesticides with antifouling agents (WHO 2005).

Literature data on the bioaccumulation of inorganic tin in land ecosystems is very limited, especially in relations to mammals. No reports concerning the transfer of this element along land trophic chains are available. A little information in this regard was provided in the study by Hsu et al. (2006); however, the results were insufficient to completely understand this issue.

Bioindicators and biomarkers are important tools in ecotoxicological studies and in evaluation of the risk of exposure. In highly toxic compounds, scientific literature provides abundant information on the usefulness of different species and biological parameters used in evaluations. However, in the case of metallic tin or its inorganic compounds, almost no data is available. A slightly better situation exists in regard to organic forms of tin, due to their higher toxicity, but most of the reports concern aquatic ecosystems, particularly marine habitats.

In relations to land habitats, some interesting information was provided in two publications by Mizukawa et al. (2009) and Miedico et al. (2016). The first indicates the usefulness of bird feathers as a noninvasive research material to monitor the level of organotins, while the second indicates ruminants (particularly sheep) as good biomonitors of environmental pollution of metallic tin, mostly in the neighborhood of its emitters.

2 General Properties

Tin (Sn, atomic weight 118.7) is a metallic element located in the 14th group of the periodic table, showing oxyphilic and chalcophylic properties. It is a silvery white, soft, malleable metal with +2 and +4 degrees of oxidation. Tin is found in the two allotropic forms: β form, white tin (density 7.31 g cm^{-3}); and α form, gray tin (density 5.85 g cm^{-3}). The melting point of Sn is 231.9 °C, and boiling temperature ranges between 2260 °C and 2270 °C. Cassiterite (SnO_2) is the main mineral of tin and the only one with commercial significance. The other minerals are stannin (Cu_2FeSnS_4) and teallite (Cu_2SnS_4).

The average concentration of tin in the earth's crust is 2.5 mg kg^{-1}. The highest concentrations are found in loamy rocks at 6–10 mg kg^{-1}, magma rocks at 0.3–-3.6 mg kg^{-1}, and carbonaceous and arenaceous rocks at 0.5 mg kg^{-1} (Kabata-Pendias and Pendias 1999). Among the rock-formed minerals, the highest content of Sn is typically in biotite and muscovite. During the erosion process, Sn is released probably as Sn^{4+}, composing hydrolyzates (Migaszewski and Gałuszka 2007). Form Sn^{4+} is absorbed by loamy materials, iron and aluminum oxides, and organic matter, leading to a secondary accumulation of Sn in sediments and coal, in which the concentration may reach even 2.3 mg kg^{-1} (Llorens et al. 2000).

In Europe, soils contain from <2 to 106 mg kg^{-1} of tin (De Vos et al. 2006). The mean content of tin in uncontaminated soils ranges between <0.1 and 4.0 mg kg^{-1}, with the lowest amounts found in sandy soils and rendzina and the highest in heavy clay soils (Kabata-Pendias and Szteke 2012) (Table 19.1).

Geochemical background levels for Sn in the soils in Western European and Scandinavian countries are 1–2 mg kg^{-1} (De Vos et al. 2006), in Slovakia 5 mg kg^{-1} (Curlik and Šefeik 1999), and in Lithuania 2.1 mg kg^{-1} (Kadûnas et al. 1999). Acceptable Sn concentration in soils is 50 mg kg^{-1}, while in heavily polluted soils, even 800 mg Sn kg^{-1} is found (Kabata-Pendias and Pendias 1999).

Table 19.1 Content of tin in soil

Country	Layer of soil (cm)	Mean level (mg kg^{-1})	Range (mg kg^{-1})	References
Cyprus	0–25	0.8	<0.2–96.3	Cohen et al. (2012)
	50–75	0.6	<0.2–52.8	
Italy	0–20	5.0[a]	2.1–12.8	Adamo et al. (2014)
	30–40	5.0[a]	2.1–13.0	
Greece	0–10	5.5[b]	0.6–156	Argyraki and Kelepertzis (2014)
Norway	14	0.749	<0.15–10	Reimann et al. (2015)
	30 (10–80)	0.443	<0.1–4.28	
Spain		0.23[b]	–	Peña-Fernández et al. (2015)
		0.21[c]	–	
Poland	0–20	0.4	0.1–2.6	Pasieczna (2012)

[a]Polluted agricultural lands
[b]Urban soil
[c]Industrial soil

Table 19.2 Production and reserves of Sn in selected countries (in metric tons)

Country	Refined tin production[a]	Mine production[b]	Reserves[b]
Australia	nd	5900	240.000
Bolivia	12.106	18.000	400.000
Brazil	nd	11.900	700.000
China	114.200	100.000	1.500.000
Indonesia	27.431	40.000	800.000
Malaysia	30.260	3.700	250.000
Peru	20.224	26.100	91.000
Russia	nd	300	350.000
Thailand	10.502	300	170.000
World total	nd	230.000	4.700.000

nd no data
[a]ITRI 2016 (data for 2015)
[b]MSC 2014 (data for 2013)

3 Tin Uses and Production

Tin is used mostly in metallurgy and also in the paint and enamel industry and in the production of plastics and biocides. It is estimated that about 80% of tin production is used in the production of tinplate, bronze, and solder (Adriano 2001). In the USA, the major uses for tin are cans and containers 23%, construction 18%, transportation 17%, electrical 12%, and others 30% (MSC 2014). Butyltin compounds such as monobutyltin (MBT), dibutyltin (DBT), and tributyltin (TBT) are used mostly as biocides (antifouling and anti-mollusk agents, fungicides, insecticides, rodenticides, and acaricides), as well as stabilizers in many branches of industry. Organic compounds of tin are used to stabilize polyvinyl chloride (PVC) to protect it from thermal and photochemical degradation, as well as catalyzers in the synthesis of silicon rubbers and polyurethane foams and as coolers in transformers (Falandysz 2003). Other uses include production of lithium-ion batteries, combustibility reducing agents, glass packages, and TFS conversion (ITRI 2012).

Global reserves of tin are located mostly in western Africa, southeastern Asia, Australia, Bolivia, Brazil, China, Indonesia, and Russia. Mine production and reserves of tin are presented in Table 19.2.

4 Tin in Nature: Geogenic and Anthropogenic Sources

Tin is released into the environment from both natural and anthropogenic sources. Metallic tin is a natural compound of the earth's crust, where it is present at concentrations between 2 and 3 mg kg^{-1} (Budavari 2001). Cassiterite (SnO_2) is

the main ore of Sn; the other significant minerals of Sn are stannite (Cu_2SnFeS_4) and montesita ($PbSn_4S_5$) (Alloway 1990).

Inorganic tin may originate from natural and anthropogenic sources; organotin compounds are emitted mostly as the effect of human activity. Relatively low amounts of organic Sn forms arise in chemical and biochemical methylation reactions where inorganic Sn compounds are transformed into a methyltin form.

Tin is a compound present in dusts from soils, roads, agriculture, and industry. Small amounts of Sn are also released into the environment from fires or volcanic eruptions. Anthropogenic Sn sources play a main role in contaminating the environment. Emission takes place during the production, use, storage, and recycling of Sn, as well as during waste combustion, such as for municipal waste. The concentration of Sn in volatile dusts may reach 8.7 mg kg^{-1} (Llorens et al. 2000).

Organic Sn compounds may be released into the air by spraying of fertilizers and antifouling agents; evaporation; incineration of materials treated with organotins or stabilized with organotin compounds; and the processes of glass coating. It has been said that the evaporation of organotin compounds into the air is not a significant source due to their low vapor pressures and rapid photodegradation (Fent 1996).

Natural concentrations of tin in the atmospheric air range between 0.01 and 0.1 ng m^{-3} (Kabata-Pendias and Pendias 1999). Tin and its compounds in environmental conditions are considered nonvolatile and related mainly to atmospheric dust. Atmospheric transport of tin depends therefore mostly on the size and weight of dust particles and the meteorological conditions (Senesi et al. 1999). In the air, tin largely associates with small respirable particles from 1–3 μm diameter (WHO 1980). Huang and Klemm (2004) reported that organotins such as butyltins, methyltins, and octyltins are found in the gas phase (<100 pg m^{-3}) with a dominance of tri- and di- substituted organotins and octyltins.

In general, the concentration of tin in the atmospheric air is quite low, apart from the areas in which sources of tin emissions are located. In urbanized areas, the concentration of tin in the air is <6 ng m^{-3} (e.g., Barcelona 2.3, Athens 1.1, Oporto 5.9, Zurich 5 ng m^{-3}), while in rural regions it is <1 ng m^{-3} (Minguillóna et al. 2012; Martins et al. 2016).

The soil environment absorbs tin from organotin-containing pesticides, landfilling of Sn-containing wastes, or the application of pretreated municipal sludge and urban refuse as soil amendments (ATSDR 2005). Sewage sediments are particularly rich in tin at 40–700 mg Sn kg^{-1} dw. Much smaller amounts of Sn are found in manure and poultry wastes, 3.7–7.4 and 2.0–4.1 mg Sn kg^{-1} dw, respectively (Senesi et al. 1999; ATSDR 2005).

In natural water reservoirs, tin is present in trace amounts. The concentration of tin in rivers, estuaries, and oceans is generally <5 ng L^{-1} (WHO 2004). The main sources of inorganic forms of tin are ground surface flows from agricultural and industrial areas, whereas for organic forms of tin, mostly triorganotin compounds, their use in antifouling paints is considered to be the main source.

5 Biological Status of Tin

5.1 Toxicity of Tin

Although Sn is an essential trace element for plants and fungi, in the case of animal organisms, no unambiguous opinion about its necessity has been agreed. There are however some studies indicating that this element may be an essential ultratrace element for rats and maybe for animals generally. Yokoi et al. (1990) observed a weaker growth of Wistar rats fed with fodder containing 17 ng Sn g^{-1}, in comparison to rats fed with fodder supplemented with 1.99 mg kg^{-1}, as well as hair loss and lowered response to sound. Additionally, the authors observed significant differences in mineral concentrations in tissues between the two groups. They noted, for example, that the Sn-deficient group was characterized by a higher concentration of Ca and lower Mg in the lungs, a lower level of Cu and Zn in the heart muscle, and a higher content of Fe in the spleen and kidneys, in comparison with the group fed with the abundant Sn dose.

The toxicity of Sn to animals depends on the form in which the element exists. Inorganic Sn, due to its low solubility, poor absorption, and low retention in tissues, is not relatively harmful (Johnson and Greger 1982). On the other hand, organotins show a high biological activity. For plants, the most toxic are the alkyl Sn compounds which inhibit cellular proliferation in plants (Radecki et al. 1989).

The toxicity of inorganic Sn to animals is mostly related to its ability to interfere with the activity of some enzymes and the metabolism of some crucial elements like Zn, Cu, Ca, and Fe. Still, organotin compounds are much more toxic and—as lipophilic substances—mostly attack the central nervous system; myelopathy and spongiform encephalopathy are observed (Nath 2000).

Typical for abiotic habitats, the degradation processes of organotins involving the removal of subsequent alkyl (dealkylation) or aryl (dearylation) groups lead to inorganic Sn according to the following scheme: $R_4Sn \rightarrow R_3Sn^+ \rightarrow R_2Sn^{2+} \rightarrow RSn^{3+} \rightarrow$ Sn (IV) (Maguire et al. 1986). This process results in a decrease in toxicity of tin compound, which, from the ecotoxicological point of view, is very advantageous for the environment. Unfortunately, the process of biomethylation may run in parallel, leading to more toxic organotins (Ostrakhovitch 2013).

The toxicity of the various forms of tin, including the organic compounds in relation to marine vertebrates and invertebrates, has been widely described in literature (see reviews: Okoro 2011; Graceli et al. 2013; Schilithz et al. 2013). Still, no data concerning the harmful effects of Sn compounds in terrestrial wildlife are available. Studies on laboratory animal models have been a good source of knowledge in this area.

5.1.1 Inorganic Tin

Exposure to Sn causes hematological changes in animals (ATSDR 2005). Inorganic tin compounds, similarly to Pb, disturb the process of heme synthesis and contribute

to hemolytic anemia caused by an improper use of Fe (Chmielnicka et al. 1993; Chmielnicka 2006), replacing Zn in δ-aminolevulinic acid dehydratase (ALADH), thus decreasing the activity of the enzyme. The effect of Sn on heme biosynthesis was shown to depend on the concentration of Zn (Chmielnicka et al. 1992). It has been shown that exposure to Sn results in a disturbance in the metabolism of many elements. Reicks and Rader (1990) observed that the uptake and metabolism of Cu are negatively influenced by dietary Sn, resulting in a Cu deficiency in animals. Other studies have shown that Sn negatively affects the metabolism of Ca and P (and in consequence the bone mineralization process; Yamaguchi et al. 1981) and also inhibits the synthesis of collagen (Yamaguchi et al. 1982). In the bones of the golden retriever and Labrador retriever dogs suffering from osteoarthritis, a significantly higher content of Sn in the bones was found in comparison to the healthy dogs (Nganvongpanit et al. 2016).

Reicks and Rader (1990) demonstrated that exposure to Sn leads to a reduction in liver antioxidant protection, mostly due to a decrease in the activity of numerous antioxidative enzymes like liver glutathione peroxidase and superoxide dismutase.

5.1.2 Organic Tin Compounds (OTs)

Organotins are characterized by the presence of a single or multiple numbers of covalent bonds between the atoms of Sn and C and are depicted by the general formula R_nSnX_{4-n} (R, an alkyl or aryl group; X, an anionic species; $n = 1,\ldots,4$). The differing chemical structures of the compounds cause particular organotins to differ in the physicochemical properties translating into biological availability, tissue distribution, and the biological activity and toxicity of the organotins which depend mostly on the number and type of organic group bonds with the central atom of Sn, with activity decreasing accordingly: (tri) R_3SnX > (di) R_2SnX_2 > (mono) $RSnX_3$.

The relatively high biological activity of triorganotin most likely results from the ability to bind to some proteins; however the locations in which these binding arise are not well known. It has been observed that trimethyltin compounds express a high toxicity to fungi and insects and triethyltin to mammals. In turn, tripropyl- and tributyltin show a higher toxicity to fungi, mollusks, fish, bacteria, and plants (de Carvalho and Santelli 2010).

Organic Sn compounds inhibit oxidative phosphorylation in mitochondria, leading to discrepancies in mitochondrial oxidation and damage to the mitochondria themselves. It was shown that triethyltin may build complexes with hemoglobin. Some organotins have the ability to interfere with the transport of Ca, Mg, K, and Na ions through cellular membranes, which in turn may result in blocking ATP-ases in the brain (Chmielnicka 2006).

Organic compounds, especially TBT, show an androgenic activity and are a reason for an increased frequency of imposex occurrence among aquatic vertebrates and invertebrates (Shimasaki et al. 2003; Horiguchi et al. 2004). The additional

development of masculine sex organs in females results in masculinization of a population. No such data referring to terrestrial organisms has been noted.

5.2 *Bioaccumulation*

5.2.1 Inorganic Sn

Bioaccumulation happens when the rate of absorption of any substance clearly exceeds the potential to expel it from the organism. In the case of inorganic tin, it was found that the alimentary tract absorbed only a small percentage of ingested Sn (3–5%; Johnson and Greger 1982), with the absorption of divalent tin higher than tetravalent (Hiles 1974). In studies on rats, it was demonstrated that after oral administration of Sn compounds (in fruit juice), almost 99% of the ingested tin was passed from the organism in the feces over the next 24 h (Benoy et al. 1971). Therefore inorganic Sn is characterized by a low potential to accumulate.

It was also shown experimentally that the amount of absorbed tin depends on the size of the dose. Johnson and Greger (1982) stated that at a daily dietary intake of 49.7 mg Sn, retention in the organism was 1.3 ± 1.5 mg day^{-1} (about 3%), while at lower doses like 0.11 mg day^{-1}, the retention and absorption of Sn were 0.05 ± 0.03 mg day^{-1}, about 50%.

The small amounts of Sn, which remain in an organism, accumulate mostly in the bones, thymus, lungs, and muscles, wherein Sn (IV) shows a higher bone uptake and less soft tissue accumulation than Sn (II). Generally, the descending concentrations of Sn in particular organs are as follows: bones > lymphatic gland > lungs > muscles > liver > kidneys > brain (Chmielnicka 2006). With chronic exposure, bones are the main place of Sn deposition. It is estimated that its biological half-life in bone ranges from 34 to 100 days, depending on the species of animal, while in the liver and kidneys 10–20 days (Hiles 1974; Chmielnicka 2006).

Plants are a very important link in the trophic chains of terrestrial habitats that determine the intake of various elements by animals. Tin is an immobile element in arable soil, especially at neutral pH, which causes a low intake by plants. A decrease in soil pH results in a higher content of soluble forms of Sn and in consequence a higher Sn absorption by plants. Usually the concentration in plants ranges from <0.10 to 3.0 mg kg^{-1}. Plants are able to accumulate Sn in the roots, with only a small amount translocated to the foliage. Transfer coefficients for Sn in a soil-plant system are between 0.01 and 0.10 (Kloke et al. 1984). This means that plants may be a source of tin for animals, but only for those that consume whole plants or just the underground parts.

Literature data on the bioaccumulation of inorganic tin in terrestrial ecosystems is very limited, especially in reference to mammals. Only a few studies on the concentrations of Sn in avian and mammalian tissues are available, with those usually have a fragmentary character, originating from the 1980s to 1990s (Tables 19.3 and 19.4).

Table 19.3 Butyltin residues in avian liver and kidney of piscivores

Species	Country	Residues (μg kg^{-1} ww)		References
		Liver	Kidney	
Red-throated diver *Gavia stellata*	Poland	610	nd	Kannan and Falandysz (1997)
Razorbill *Alca torda*	Poland	330	nd	Kannan and Falandysz (1997)
Great crested grebe *Podiceps cristatus*	Poland	540	nd	Kannan and Falandysz (1997)
Great cormorant *Phalacrocorax carbo*	Poland	870	nd	Kannan and Falandysz (1997)
	Japan	270	290	Guruge et al. (1996)
	Japan	385	370	Mizukawa et al. (2009)
Long-tailed duck *Clangula hyemalis*	Poland	4600, female 280, male	nd	Kannan and Falandysz (1997)
White-tailed eagles *Haliaeetus albicilla*	Poland	35, female	nd	Kannan and Falandysz (1997)
Guillemot *Uria aalge*	Poland	500	nd	Kannan and Falandysz (1997)
Surf scoter *Melanitta perspicillata*	Canada	41	nd	Elliott et al. (2007)

nd no data

Table 19.4 Metallic Sn and organotin concentration in mammals

Species	Country	Residues	References
Japanese macaque *Macaca fuscata*	Japan	Liver, μg kg^{-1} ww MBT: <4.0 DBT: <3.0 TBT: <2.0–2.7	Takahashi et al. (1997)
Raccoon dog *Nyctereutes procyonoides*	Japan	Liver, μg kg^{-1} ww MBT: 9–120 DBT: 18–280 TBT: 3–10	Takahashi et al. (1997)
American mink *Neovison vison*	Canada	Liver, mg kg^{-1} dw Sn: 5.4 Kidney, mg kg^{-1} dw Sn: 5.9	Harding et al. (1998)
Otter *Lontra canadensis*	Canada	Liver, mg kg^{-1} dw Sn: 3.3	Harding et al. (1998)
Polar bear *Ursus maritimus*	USA, Alaska	Liver, mg kg^{-1} dw Sn: 0.071	Kannan et al. (2007)

MBT monobutyltin, *DBT* dibutyltin, *TBT* tributyltin

The most complete elaboration is likely the study by Hsu et al. (2006), showing the results of heavy metal bioaccumulation (including tin) in the ecosystem of Kenting National Park (Taiwan). The studies included animals such as insects (six specimens), earthworms, snails, crabs, amphibians, lizards, snakes, fish, and bats

(whole organism) as well as soil samples, plants and fungi. The highest mean concentrations of Sn were noted in snails and plants, reaching, respectively, 16.8 ± 21.6 and 11.91 ± 33.6 mg kg^{-1} dw, followed by insects, snakes, earthworms, bats, lizards, and amphibians, in which the mean concentrations of Sn ranged from 10.6 to 6.94 mg kg^{-1} dw. In the soil and in fungi, the Sn content was <1 mg kg^{-1} dw. Bioconcentration factors (BCF) calculated from the collected data were between 0.58 and 19.44 and were arranged in the following descending order: snail > plant > insect > snake > earthworm > bat > lizard > amphibian > crab > fungi > fish. An interesting fact arose where, although in the land organisms quite high values of BCF were found, the soil itself still did not contain an elevated level of Sn and the enrichment factor was low (Sn in soil/Sn in upper continental crust = 0.16).

Data about the content of Sn in the kidneys of American mink (*Neovison vison*) and livers of the mink and river otter (*Lontra canadensis*) from Canada by Harding et al. (1998) are presented (Table 19.4). The examined animals were collected from several regions: otters, from upper Fraser River, lower Fraser River, upper Columbia River, lower Columbia River, and Kootenay River; and minks, from upper and lower Fraser River (Canada). The concentrations of Sn in the livers and kidneys of the mink were comparable at an average 5.2–6.3 mg kg^{-1} dw, while in the livers of the otters, the concentration of Sn was lower, usually <4 mg kg^{-1} dw. The authors did not find any differences in Sn concentrations between the collection areas, sexes, or species.

One of the most recent works is Miedico's et al. (2016) in Italy. While studying the accumulation of Sn in animals (bovine and ovine species) raised in an area surrounding oil wells in Italy, the authors observed that the concentrations of Sn in the organs were arranged as follows: lungs > liver > kidneys (which indicates that the main pathway of exposure was the respiratory tract). The noted concentrations of Sn in these organs (for both species together) were 0.081 ± 0.145, 0.055 ± 0.128, and 0.022 ± 0.045 mg kg^{-1} ww, respectively.

There are many works confirming the ability of organic Sn compounds to bioconcentrate and bioaccumulate in aquatic ecosystems (especially marine) (Harino et al. 2000; Zhang et al. 2003; Strand et al. 2005), yet almost no works studying terrestrial habitats are available. Usually such studies are limited to animals which do not in fact live in an aquatic ecosystem but still are strongly associated with it, for example, with some trophic relationships. An example of such work is Lilley et al. (2013), in which the authors made an evaluation of the accumulation of TBT in Daubenton's bat (*Myotis daubentonii*), considered to be very vulnerable to numerous environmental pollutants due to their long life expectancy and high position in the trophic chains. These animals prefer to feed above the water surface on newly hatched adult chironomids, which are effective vectors for the transport of OTC from aquatic to terrestrial ecosystems (Laws et al. 2016). The authors noted only trace amounts of TBT in bat fur samples. A significant positive correlation between sampling site sediment TBT concentrations and bat fur DBT concentrations was found. The analysis of results with regard to selected biological factors showed a comparable concentration of TBT in male and female bats (8.2 vs. 7.77 mg kg^{-1})

and a higher level of TBT artifacts in adult individuals in comparison to juveniles (8.95 vs. 3.49 mg kg^{-1}), although in the last example the observed differences were not confirmed statistically.

In the case of wild migratory birds, the accumulation of butyltins (BTs) such as monobutyltin (MBT), dibutyltin (DBT), and tributyltin (TBT) was reported in soft tissues, muscle, and feathers (Guruge et al. 1996; Senthilkumar et al. 1998). In this study it was shown that of the BTs, MBT was the predominant compound retained in the birds, with concentrations recorded in the tail feathers at 73–360 μg kg^{-1} ww, while DBT and TBT concentrations were 29–56 and 37–67 μg kg^{-1}, respectively.

Guruge et al. (1996) while studying the remains of BTs in common cormorants (*Phalacrocorax carbo*) from Lake Biwa (Japan) found that the accumulation of BTs in cormorant bodies followed the orders MBT > DBT > TBT and muscle ≥ feathers > skin > liver > rest of the tissues and organs. The authors suggest that the higher levels of BT residues in the feathers occurred due to excretion of BT (about 25% of body burden) during a complete molting cycle and that it may be a natural mechanism of organism detoxication.

In birds, differently than in mammals, concentrations of BTs in the kidney and fat are usually comparable to those in the liver (Guruge et al. 1996; Mizukawa et al. 2009), where it suggests that this may result from the presence of a specific protein in birds which is able to bind BTs in the kidneys, a weak binding affinity of BTs to proteins in the liver and/or different metabolic and elimination pathways for BTs. In the case of fish and marine mammals, TBT accumulates mostly in fats and muscle and DBT in the liver and kidney (Guruge et al. 1996; Kannan et al. 1996). Unfortunately, no such information is available in reference to land mammals.

Kannan et al. (1998) have stated that habitat and feed preferences affect the levels of BT artifacts in the liver of birds. The aforementioned authors observed that concentrations of BTs in the liver of birds collected from areas surrounding a lake were ≤27 μg kg^{-1} ww, whereas those from marine coastal areas contained amounts more than three times higher, and saltwater mollusk-feeding ducks accumulated greater concentrations of BTs than predatory birds feeding on fish, other birds, or small mammals.

An attempt to evaluate biomagnification in piscivorous birds was undertaken by Guruge et al. (1996). The authors assessed the biomagnification factor for the birds-fish level at 1.1–4.1. Unfortunately, there is no such information available on the potential transfer of inorganic tin or organotin compounds from lower trophic levels to higher levels, especially in terrestrial habitats.

5.3 Bioindicators and Biomarkers of Tin in Ecotoxicological Studies

Bioindicators and biomarkers play an important role in monitoring and evaluation of the status of an environment. In relation to the toxic substances of particular interest

to ecotoxicologists, many publications provide considerations on the usefulness of various animal species in the monitoring of land habitat quality and the health status of particular ecosystems. In the case of metallic tin or its inorganic compounds, not many such works are available, mostly as a result of its low toxicity. Moreover, as the main target of studies itself, tin is examined rarely, usually in combination with other more harmful elements.

In evaluation of the status of environmental pollution by tin in which atmospheric deposition plays an important role in the neighborhood of tin emitters, herbivorous animals seem to be the best bioindicators as they consume only what is deposited on the surfaces of the plants from the atmosphere and what penetrates an organism via the respiratory tract. Tin has a low absorption rate from the soil by plants, as well as a low translocation from the roots to the foliage, leaving the main vector as direct atmospheric deposition. In these conditions, tin intake occurs more via the respiratory tract than the digestive tract. Although wild animals are usually used in ecotoxicological studies (e.g., cervids), Miedico et al. (2016) point out that farm animals may also turn out to be useful, especially ruminants in extensive farming systems without any additional in fodder. The authors have stated that for exposures to metal (including tin), sheep are more useful as bioindicators/biomonitors than cattle, which are often raised under controlled feeding conditions, which have overly complex interactions between the elements to be representative of a contaminated area.

In more complex studies regarding bioaccumulation and tin transfer via the trophic chain, animals from the top of a selected trophic chain may be useful. Unfortunately in relation to terrestrial ecosystems, no such studies have been performed. Little data about the transfer of pollutants (Sn) from water to land habitats have been presented. Such studies are usually performed using water birds and also bats and mustelids (mink, otter), which are treated as a species equivalent to avian predators (Harding et al. 1998; Lilley et al. 2013).

The most common biomarker of exposure is the presence of a selected xenobiotic, in this case Sn or its metabolite(s) or products of Sn interactions with some target molecules (e.g., adducts) in tissues, body fluids, or secretions/excrements of an exposed organism. Although experimental studies suggest that the bones are a potential location of Sn accumulation, many literature references study Sn levels in just the liver and kidneys. This applies to both the organic and inorganic forms of Sn.

In some avian species, the feathers may be a useful research material to monitor the organic forms of Sn. Mizukawa et al. (2009), in their studies on the distribution of organic Sn compounds (OTs) in the tissues of cormorants, noted a significant correlation between the concentrations of DBT, DBT + TBT, and TPT (triphenyltin) in the ventral feathers and the liver and have stated that there is a possibility of using ventral feather samples as a nondestructive indicator in OT monitoring. The authors have developed equations (presented below) that may be advantageous in evaluating the hepatic levels of OTs in cormorants based on the concentrations of OTs in the ventral feathers:

$$\mathrm{DBT_{LIVER}} = 1.0 \times \text{ventral feather concentration} + 110$$

$$\mathrm{DBT_{LIVER}} + \mathrm{TBT_{LIVER}} = 1.0 \times \text{ventral feather concentration} + 110$$

$$\mathrm{TPT_{LIVER}} = 0.80 \times \text{ventral feather concentration} + 50$$

According to literature data, feathers may not be useful in every avian species to evaluate hepatic concentration of OTs. For example, in the study by Elliot et al. (2007) aimed at assessing residual BTs in the tissues of surf scoter (*Melanitta perspicillata*) wintering on the south coast of British Columbia in Canada, no artifacts of BTs were noted in feather samples taken from the breast, despite the fact that these compounds were found in the liver at a mean level of 41 μg Sn kg^{-1}.

An attempt to use the fur of bats in biomonitoring studies was undertaken by Lilley et al. (2013). However, the authors noted some limitations in using such material due to the fact that bats molt annually, so the measured concentrations would reflect relatively close exposure to BTs, and moreover, regarding the storing of these compounds in the fur as a detoxication mechanism, the results may also vary between individuals. The authors stated that liver samples would in that case provide more detailed information than fur samples.

There are no specific biomarkers of the effects of inorganic tin compounds. Still, the following biomarkers used in the evaluation of marine organism exposure to TBT are mentioned: metallothionein induction, acetyl cholinesterase inhibition, imposex, lysosomal enlargement, lysosomal membrane destabilization, peroxisome proliferation, lysosomal activity, genetic or molecular biomarkers, TBT-sensitive immunological biomarkers, apoptosis induction, phagocytic index, and amoebocytic index (Okoro 2011). Perhaps some of those would be useful in ecotoxicological studies on terrestrial animals.

6 Conclusion

After an analysis of literature data, it can be concluded that the problem of terrestrial habitat pollution with different forms of tin (Sn) is not yet well understood. The data concerning bioaccumulation of inorganic tin is very limited in reference to mammals and also to other groups of animals. Also it lacks data from which it would be possible to indicate the species that would be useful as bioindicators/biomonitors in ecotoxicological studies and in the evaluation of environmental exposure to Sn compounds. Data in this area would certainly be very useful for further studies.

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