Emerging Contaminants and Associated Treatment Technologies

Toqeer Ahmed
Muhammad Zaffar Hashmi *Editors*

Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies

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ISSN 2524-6402 ISSN 2524-6410 (electronic)
Emerging Contaminants and Associated Treatment Technologies
ISBN 978-3-030-96522-8 ISBN 978-3-030-96523-5 (eBook)
https://doi.org/10.1007/978-3-030-96523-5

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Preface

Environmental micropollutants are a diverse group in the form of microbes, organic pollutants, and air/dust particles present in all media causing serious environmental and health issues. Microbes in the form of bacteria, viruses, protozoan, and fungi produce toxins in the environment and food, causing harm to the human beings. Similarly, other micropollutants in the form of dust particles, allergens/pollens, and spores, which are present in the environment, are threats to human health, affecting both indoor and outdoor air quality. Micropollutants present in different form and in different environments/media, such as soil, air, and water, may pose serious hazards to people working in them. Organic pollutants in the form of polyaromatic hydrocarbons, polychlorinated biphenyls, DDT, organochlorine pesticides, hormones, and pesticides present in the soil and inorganic in the heavy metals causing serious issues to human food chain. Mycotoxins produced by certain types of fungi and bacteria contaminate different types of human and animal food and pose serious threat to life.

Climate change is not only impacting livelihood but also changing life/disease cycle, reproduction, and incidence of disease from pollutants along with huge impact on precious resources, such as water and food, and the environment. Similarly, infectious diseases caused by micropollutants are impacted by climate change both in positive and negative ways. Different factors like socioeconomic, urbanization, population density, land use, sanitation, and hygiene highly contribute to spreading infectious diseases caused by micropollutants. So, it is important to address all aspects of environmental micropollutants causing hazards to human health.

In this book, basic concepts along with the advances in research related to environmental micropollutants and treatment technologies to cope with the issues/hazards have been discussed in detail. Different chapters of this book provide detail of hazardous environmental micropollutants in different media like air, water, and soil and methods to deal with the hazards caused. Policy- and economy-related issues have been discussed in part. Antibiotics are undoubtedly one of the most effective drugs being utilized for animal and human therapy. They are not only used for preventing and treating different infectious diseases in animals and humans but also used for agricultural and farming purposes. There is an increasing concern over the past years about the effects of disposal and irrational use of antibiotics on both environment and human health. Environmental media, which include air, soil, and water, act both as a transmission medium and reservoir for antibiotic resistant bacteria. This most important aspect has been covered in detail. Health hazards in the form of toxic gases caused by burning of plastic waste and possible cohesive approaches for the remediation of plastic waste are discussed. Mycotoxins and aerial fungal spores and their human health impacts have been discussed. Other topics in this book include allied treatment technologies for the remediation of environmental micropollutants, which are discussed in depth.

Mostly knowledge provided in this book is updated and advanced level and should be of interest to graduate level students, early career researchers and scientists working in different domains and dealing with micropollutants and their toxic impacts like, mycotoxins, organic and inorganic pollutants, infectious diseases etc. We hope this book can be recommended for the students of environmental sciences and as reference book for courses like environment and health, poverty and environment etc.

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Contents

Chapter 1
Environmental Micropollutants and Their Impact on Human Health with Special Focus on Agriculture

Bushra Gul, Muhammad Kamran Naseem, Waqar-un-Nisa Malik, Ali Raza Gurmani, Ayaz Mehmood, and Mazhar Rafique

Abstract Micropollutants (MPs) are key contaminants present in the soil, water, and environment. They vary based on natural properties and classified as organic (polychlorinated biphenyls, polyaromatic hydrocarbons, organochlorine pesticides, DDT, hormones, EDC, pesticides) to inorganic (heavy metals). They enter the soil-water-environment system through variable sources that include irrigation water to agricultural system, disposal of expired pharmaceuticals, bio-solids or animal excreta, sewerage wastewater, fertilizer application, industrialization, etc. They further enter into the food system via a number of entry points such as groundwater, agricultural soil, irrigated water, etc. and become part of the food chain. Micropollutants largely impact the human health by triggering thyroid disorders, neurodevelopmental dysfunctions in children, endocrine-associated malignancies, and metabolic and bone abnormalities. Soil acts as an ultimate host for all such pollutants where soil microbes degrade them biologically, addition of chemical inputs can accelerate degradation, while use of physical approaches in remediating MPs is costly. These MPs damage soil quality and soil microbial diversity, alter various soil biogeochemical processes, and induce genetic changes in the microbial ecology. Persistence of the MPs makes them more vulnerable for human health as they enter the food chain. Phytoremediation is considered a proven technology to remediate MPs in soil and multiple types of hyperaccumulator plants are used in remediation. Developing nations do not yet have access to discharge limitations for new MPs into the environment. This requires attention so that limitations may be set based on scientific evidence.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_1

1.1 Introduction

Micropollutants (MPs) are inorganic and organic substances that can adversely impact the environment at very minute concentrations, in the range of micro-, nano-, and pico-grams (µg/L (10^{-6} g/L); ng/L (10^{-9} g/L); pg/L (10^{-12} g/L)) (Chapman 1996). Micropollutants are ubiquitous and are often used to improve human life as they are involved in daily life in the form of pharmaceutical and hygiene kits, pesticides, plastics, endocrine-disrupting chemicals, etc. The general tendency toward urbanization is the increasing number of untreated and treated wastewater, and MPs stay in water. The extensiveness of MPs in aquatic systems is a major worry worldwide. These MPs need disposal with minimum deterioration to the environment and a new generation of MPs, usually called emerging MPs. Wastewater is the standard source of these compounds, and this has generated difficulties among researchers and decision-makers dispensing with water use for household and production of food. These comprise of (a) need to change thought of wastewater disposal, (b) when water tables are intentionally recharged in order to rise volume of water sources, (c) in soil-aquifer treatment systems, (d) reuse of water for consumption and the reuse of wastewater for irrigation, and (e) where water levels are recharged indirectly through this activity. Earlier advances in mass selective detection and chromatographic separation techniques have approved the occurrence of organic micropollutants (OMPs) in environmental matrices (surface water, water table, soil, deposits, biota, and air-born particles), which enable a variety of concentrations to be recognized for some of these contaminants (Hao et al. 2007). Micropollutants are largely categorized into two types based on the nature of MP:

1. Heavy metals (specific density > 4.5 kg/L), for example, cadmium (Cd), lead (Pb), and copper (Cu), or "metal traces," such as iron (Fe) and manganese (Mn), and metalloids like arsenic (As) and vanadium (V). Heavy metals in various soil organic amendments such as compost and vermicompost bound onto organic matter and in convertible or adsorbed form. İn addition, typical chemical forms are, in general, split between soluble and insoluble species in relation to the condition of the metal in the starting materials and nature and chemistry of composting process (Zucconi 1987).
2. Organic MPs (DDT, PCB, PAH, Hormones and EDC, PPCPs, and pesticides) are comprised of a broad spectrum of compounds belonging to different chemical classes and used for many applications. Persistent organic pollutants (POPs) are poisonous, consistent with nondegradability and strong hydrophobicity, can compile in flora and fauna, and have the potential to wide-range move across atmosphere (Cindoruk et al. 2020; Olatunji 2019). The presence and toxicologic impact on environmental and human health of organic MPs have been broadly examined in different environmental spheres (air, soil, and aquatic environment) and food chains (Babut et al. 2019; Montuori et al. 2016; Poté et al. 2008). Three main types of POPs are commonly stated in the environment for many years. They are especially anthropogenically derived compounds involving polychlorinated biphenyls (PCBs), polyaromatic hydrocarbons (PAHs), and organochlorines

pesticides (OCPs). Furthermore, according to the Stockholm Convention 2004 regulations, conservation of the environment and human health from POPs' risk is a high preference. For instance, through a variety of food matrices' (e.g., vegetables, eggs, fish, meat, oils, and milk) usage, these contaminants were stated to induce health impacts such as neurotoxicity, endocrine disruption, cancer, reproductive disorders, leukemia, asthma, and health risks to fetal development (Fernandes et al. 2019; Kim et al. 2017). The POPs are very determined in soil and can affect crop quality and yield. Therefore, many studies stated the organic MP degradation mechanism pathways (such as photocatalytic degradation) and the remediation effectiveness of multielement contaminated soil to minimize exposure, guarantee food safety, and protect human health (Weber et al. 2019; Ye et al. 2020).

1.2 Sources of Micropollutants

In natural and urbanized environments, water resources can be contaminated by organic MPs through an extensive range of pathways, involving agricultural irrigation using wastewater (Calderón-Preciado et al. 2011); inappropriate disposal of expired pharmaceuticals (Tong et al. 2011); use of biosolids or animal excreta to modify agricultural soils (Clarke and Smith 2011); exfiltration of wastewater in sewerage systems (Wolf et al. 2012); and in some cases Arial deposition (Loos et al. 2007); in this perspective, it has been stated that wastewater is the major pathway of organic MPs to enter into the environment (Kümmerer 2008) (Fig.1.1).

The rapid intensification of soil contaminants caused real concern for people living around. Micropollutants attained more consideration in the last couple of decades. They get released from multiple sources such as antibiotics, anti-inflammatories, disinfectants, heavy metals, rare earth elements, iodized contrast media, spillage, leaching from dumps or landfills, endocrinedisrupting chemicals (EDCs), personal care products, pharmaceuticals mainly through domestic sewerage systems, etc. (Hai et al. 2018; Verlicchi et al. 2010). They further enter into the system through urban groundwater.

The dyeing industry is a major water-consuming and dye-utilizing economic sector (Spagni et al. 2012). It is evaluated that more than 50 billion tons of dyes are utilized annually in the process of dyeing, of which ~20% is released directly into aqueous effluent during the coloration process (Yurtsever et al. 2015) (Fig. 1.2).

Landfills are considered a major source of emerging contaminants (ECs). The leachate from the landfills carries organic MPs of anthropogenic origin (Table 1.1). The leachate may carry filtrate comprised of pharmaceutical, cleaning products, disinfectants, flavorings, etc. These ECs are persistent and have been found to withstand the natural attenuation process. Samples from differently aged landfills have highly resistive ECs. Exhaust from vehicles pollutes soil with heavy metals. A sharp rise in heavy metals concentration has been observed in soils of areas adjoining the heavy traffic. The upper layers of soil profile are polluted with high concentrations

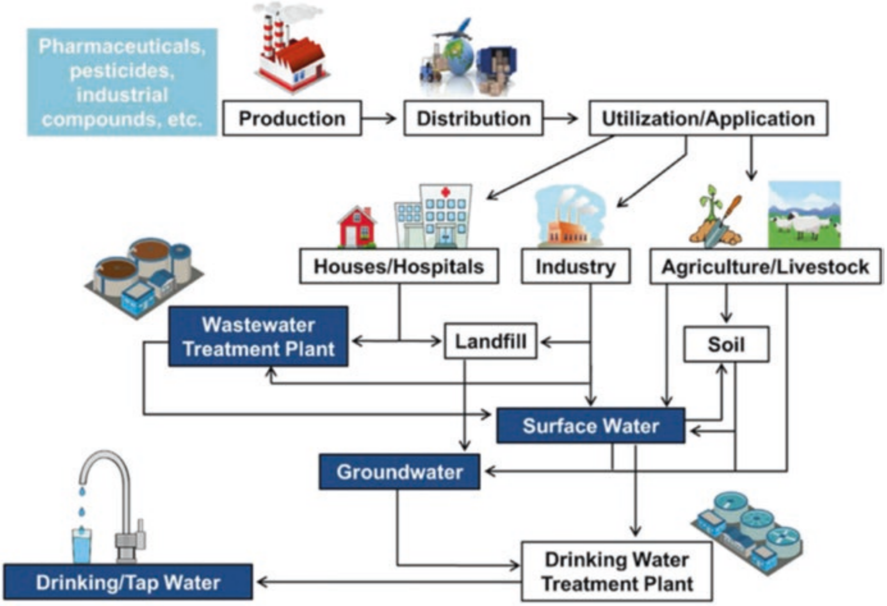

Fig. 1.1 Representative sources and routes of MPs in the environment. (Adapted from Barbosa et al. 2016)

of heavy metals intake mostly by aerogenic sources (Yudina 2017). Studies revealed that soil resists contamination of groundwater resources from contamination of As and Pb. Analysis of soils affected by the Chernobyl atomic reactor accident showed that Cs-137 could only penetrate for a few centimeters after 8 years. This shows that soil also protects the groundwater out of air too. The application of biosolids has been associated with the accumulation of MPs in soil. Application of biosolids from wastewater raised MP levels by 10 times in soil (Andrade et al. 2010). In water-scarce regions, wastewater is used for irrigation of agricultural fields. In developed countries, wastewater is treated and applied to the soil. However, studies revealed that even after treatment, recycled water carries many organic MPs. The level of these compounds gradually increased in the soil posing threat to environmental sustainability (Kinney et al. 2006).

1.3 Sources of MPs in Wastewater

The municipal wastewater comprises of numerous MPs due to anthropogenic activities. These MPs get added to municipal water through domestic and pharmaceutical wastes. The origin of every MP can be traced from sources associated with human activities directly or indirectly. The corrosion of metal surfaces leads to the addition of heavy metals into wastewater. Similarly, use of plastic retardants, etc. also adds

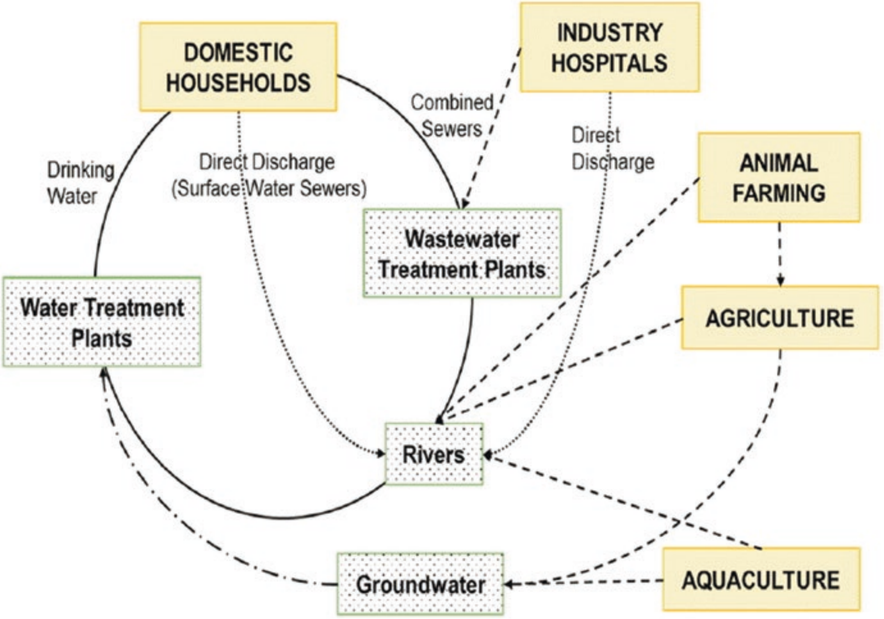

Fig. 1.2 Sources and pathways of MP (PPCPs) in the urban water cycle. (Adapted from Kim and Zoh 2016)

Table 1.1 Anthropogenic sources of inorganic MPs

	Cr	Hg	Sn	Fe	Cu	Mn	Zn	Ni	Cd	Pb
Paperboard, pulp, peppermills, board mills, paperboard, building paper, mills	×	×			×		×	×		×
Petrochemicals, organic chemicals	×	×	×	×			×		×	×
Inorganic chemicals, chlorine, alkalis	×	×	×	×			×		×	×
Fertilizers	×	×		×	×	×	×	×	×	×
Refineries of petroleum	×			×	×		×	×	×	×
Steel work foundries	×	×	×	×	×		×	×	×	×
Nonferrous metal work foundries	×	×			×		×		×	×
Plating and finishing of aircraft and motor vehicles	×	×			×			×	×	
Cement, flat glass, asbestos products	×									
Textile mill products	×									
Leather finishing and tanning	×									
Power plant of steam generation	×						×			

MPs to water. The urine and feces mostly contain MPs from pharmaceuticals, illicit drugs, and hormones. Artificial sweeteners are another important source of pollution in wastewater that enters through excretory products (Table 1.2). Some MPs are released into the wastewater directly. Surfactants, corrosion retardants, and personal care products are part of the MPs that are added directly into the municipal water.

Table 1.2 Origin of MPs, their class, and mode of entry into the environment

Organic micropollutants (OMPs)	Class	Mode of entry
Endocrine disruptive chemicals, personal care products, pharmaceuticals,	Veterinary drugs, cardiovascular drugs (-blockers), blood lipid regulators, psychiatric drugs, analgesics, and antibiotics	Farmland waste, accidental spills, hospital disposal, and discharge
Detergents, surfactants, and per-fluorinated compounds.	Insect repellents, fragrances, steroids, hormones antiseptics, UV filters, synthetic musks, per-fluorooctane sulfonate, Per-fluorooctanoic acid	Soil and groundwater, industrial waste, laundries, households, dispersants, dilutants, and pesticides
Agriculture Flame retardants	Herbicides, pesticides Organophosphorus compounds, organohalogen compounds	Household and agriculture waste, industries, baby products, electronics, furniture, etc.
Additives	Industrial, gasoline	Municipal waste, disposed engine oil
By-products of swimming pool disinfectants	Haloacetic acids, trihalomethanes	Chlorinated human material such as saliva, urine, skin, and hair

Besides these, synthetic chelating products and various industrial products are added into the water directly. The runoff water is contaminated by diffusion of plastic additives, flame retardants, and water-repellant compounds. The corrosion of metal surfaces also leads to the addition of heavy metals into the wastewater. The biocides and pesticides applied in the fields are leached into the runoff water during rain. Aside from this, rainfall is tainted by heavy metals and other persistent organic contaminants. In European countries, wastewater treatment plants (WWTPs) are installed to treat sewage waste of urban areas. Monitoring of the released water from WWTPs showed that it contains MPs. The treatment of water does not eliminate the MPs completely and is a threat to the environment if remains unnoticed for a longer period (Heeb et al. 2012).

1.4 Impacts of MPs

The influence of persistent organic pollutants (POPs) on human health may be highlighted in terms of exposure and the impacts of endocrine disruptors. Exposure to endocrine disruptor chemicals (EDCs) is now recognized to have a larger role in the causation of many more endocrine illnesses and disorders than previously assumed. Female reproductive dysfunction, impacts on male reproductive health, adrenal diseases, and the development of immune system difficulties are examples. Thyroid-related disorders, neurodevelopmental dysfunctions in children, endocrine-associated malignancies, and metabolic and bone abnormalities are further examples (Grob et al. 2015; Hughes et al. 1994; Humans 2010).

Soil is the ultimate host for all chemicals released as a result of anthropogenic activities. However, soil is enabled with a peculiar ability to maintain its natural composition and resist potential changes. In this regard, soil microorganisms have a pivotal role. They help to decompose contaminants and convert them into mobile and available forms for plants. The impact of microorganisms on soil and the environment can be ascertained through the relation of these compounds with soil and water microorganisms. As soil and water depend upon microorganisms for degradation of xenobiotics and ultimate restoration in the natural state, their study is very important. In this regard, soil microbial ecology helps to define the impacts of MPs on the environment and their possible degradation mechanism. The emerging MPs are a potential threat to the biogeochemical cycle, element cycles as well as energy flow of an ecosystem. Microorganisms, specially bacteria, have a variety of mechanisms to interact with xenobiotics. However, there are some species of bacteria that can be used for bioremediation of contaminated soils.

Microorganisms play similar roles in nutrient cycles in groundwater, and they help to attenuate a variety of chemical processes in subsurface ecosystems, such as MPs' breakdown and immobilization, redox cycling, and nutrient transport (Griebler and Lueders 2009). Several novel phylogenetic lineages have been discovered in groundwater environments, indicating that groundwater has a bacterial community capable of degrading xenobiotics and other MPs.

1.5 Xenobiotic Micropollutants

Xenobiotic: Both words are used interchangeably to refer to a man-made substance that is not recognized by the enzyme systems of living organisms and is frequently released into the environment at amounts that produce negative consequences. In recent years, a large number of xenobiotic chemicals have been released into the environment as a result of various industrial and/or agricultural activities. Pesticides, fuels, solvents, alkanes, polycyclic aromatic hydrocarbons (PAHs), nitrogen, and phosphorus compounds are examples of typical organic xenobiotics, whereas hazardous heavy metals are the most common inorganic MPs. Xenobiotic chemicals are substances that are present in living organisms or the environment but are not generated by the organism. Most bacterial strains in soil cope with xenobiotics through breakdown. Pesticide and pharmaceutical degradation characteristics are found in microbes on plasmids and transposons. Horizontal gene transfer (HGT) – also known as lateral gene transfer – or xenobiotic catabolic mobile genetic elements like plasmids allow them to acquire genetic information from comparable or phylogenetically distinct populations in the community. It is commonly assumed that MP-degrading enzymes are developed from isozymes in reaction to industrial production and xenobiotic environmental discharge. Individual cells that are most adapted to resisting or degrading the xenobiotic are selected, and their populations grow in number in comparison to the rest of the microbial community. When a xenobiotic, or organic substance in general, enters the soil, it might be exposed to two fundamental processes (Cheng 1990):

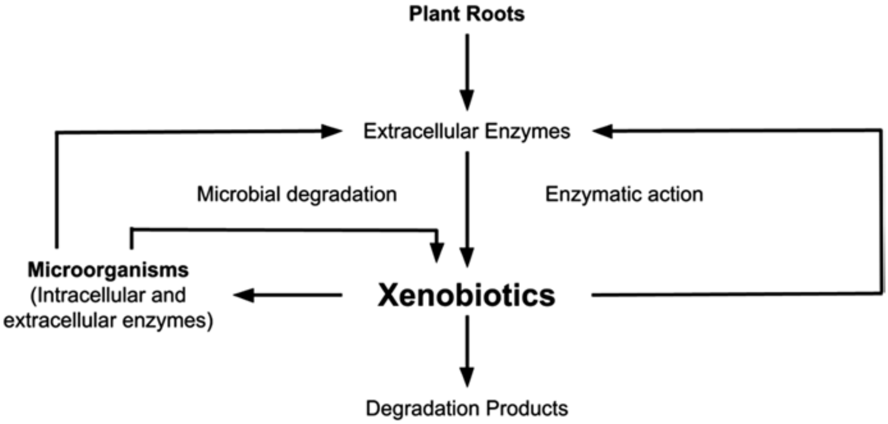

Fig. 1.3 Mutual interactions of xenobiotics with soil microorganisms and enzymes. (Adapted from Gianfreda and Rao 2008)

1. Transfer procedures that move a material without changing its structure. They include adsorption, crop retention, dissolved or sorbed runoff movements, diffusion and vapor-phase diffusion, and sorption and desorption on soil colloid surfaces. Among these processes, the interactions at interfaces between organic and inorganic soil colloids and xenobiotics through sorption/desorption mechanisms are the most important. Adsorption processes allow an organic molecule to be weakly or firmly linked with inorganic and organic colloids. Pure and polluted clays, humic compounds, and humic–clay associations are the abiotic soil components involved in the interaction with xenobiotics. Several of the processes just outlined will be heavily influenced by the existing interactions. They may impact xenobiotic mobility, availability for plant or microbial absorption, transformation by abiotic or biotic agents, and effect on soil activities.
2. Organic chemical degradation processes that change the chemical structure of the organic substances. They happen as a result of chemical, biological, and photochemical changes. Microorganisms, plants, and their enzymatic proteins, whether intracellular or extracellular, are the biotic components engaged in the biological breakdown of xenobiotics and, in general, in their interactions with them (Fig. 1.3).

1.6 Impact of Pharmaceutical MPs on Soil

The impact of pharmaceutical residues on soil flora and fauna is negatively related. It is reported that phenol has negative impact on soil microorganisms. It denatures the proteins formed by the bacteria (Zavarzin and Kolotilova 2001). Application of animal manures produces bacteria in soil that generate antibiotics resistant to these medicines. Later, these resistant genes get transferred to other bacterial strains found in plants and become a potential threat to humans that consume such plants. Genetic changes in bacteria appear on exposure to antibiotics. A study showed that antibiotic tetracycline impacts bacteria at pH 6–7 more actively as compared to pH 8. In soil, tetracycline deteriorates more as it forms complexes with metals and becomes more reactive towards bacteria. The biogeochemical cycles of many elements get disturbed by the action of pharmaceutical contamination of soil. Use of antibiotics for humans, poultry, animals and contamination of soil disturb the natural cycles of sulfate reduction, methanogenesis, and nitrogen (Ding and He 2010). Antibiotics such as glimepiride, glibenclamide, gliclazide, and metformin have been studied for their fate in soil. Drugs with high concentration of polar organic compounds had better sorption capacity. Hence, they were difficult to be biotransformed. They remain in the soil for a longer period and are potential threat to environmental safety. Studies have shown that due to better mobility, metformin is readily decomposed in the soiland has reduced half life. A comparison of sulfonylurea herbicides and their derivative pharmaceutical drugs showed that herbicides have less sorption ability and easier to degrade compared to sulfonylurea drugs (Mrozik and Stefańska 2014). Penicillin is a widely used antibiotic and its effect on cultured microorganisms has been studied. It has adverse impact on bacterial cell wall synthesis. Tetracycline and streptomycin also have an adverse impact on bacteria. They disturb the ribosomal protein synthesis of bacteria (Zavarzin and Kolotilova 2001) (Table 1.3).

1.7 Impact of MP Pesticides on Soil and Soil Organisms

Unjustified use of pesticides on crops and consequent deposition in soil poses threat to soil fertility. These contaminants can adsorb onto soil particles and contaminate soil for a longer period by deposition at the surface. In addition, crop pesticides can also influence soil microbes and disturb their physiological and metabolic processes. In this way, indiscriminate use of these chemicals degrades soil and disturbs the natural biogeochemical and elemental cycle in the environment (Savonen 1997).

1.7.1 Herbicides

- Triclopyr is a common herbicide used in landscape plants. It inhibits bacteria that helps in the transformation of ammonia into nitrate (Pell et al. 1998)
- Glycine/Glyphosate is the world's most frequently used herbicide (Dill et al. 2010). It functions by binding to enzymes and inhibits from the synthesis of aromatic compounds that are essential for bacteria and fungi. It is polar and has high sorption affinity in soil that makes it immobile. However, it is not persistent and can be transformed to aminomethylphosporic acid. Glyphosate adversely

Table 1.3 Micropollutants' application and their peculiar characteristics

Micropollutants	Applications	Characteristics
Carbamazepine	Anticonvulsant	Potential ecotoxicity, water-persistent in environment, degradation in sewage treatment plant, low removal efficiency on wastewater treatment plants (WWTPs).
N,N-Diethyl-m toluamide (DEET)	Insect repellent	Persistent in environment, little data about detection in aquatic environment, toxic for freshwater invertebrates, birds, and fish
2-Methylthio-benzothiazole (MTBT)	Stabilizers or fungicide in production of rubber	Sources include industrial plants, tire debris
Triphenyl phosphate (TPP)	Hydraulic fluid and flame retardant	Possibly neurotoxic, bioaccumulation, toxic effect to aquatic organisms
Tris(2-chlorethyl) phosphate (TCEP)	Plasticizers and flame retardants	Classified in the European Union as potential human carcinogen, nonbiodegradable, hazardous, toxic to aquatic organisms
Tris-(chlorpropyl)-phosphate (TCPP)	Flame retardants	Bioaccumulation potential, hazardous, readily biodegradable
Fluoranthene	Pyrene and fluoranthene like other PAHs form during combustion	Among the PAHs, persistent organic MPs, slow environmental degradation, bioaccumulation potential, toxicity, priority substances
Lidocaine	Local anesthetic, antiarrhythmic drug	Low potential for bioaccumulation
Caffeine	Psychomotor stimulant	High solubility in water, high stability under varied environmental conditions
Tonalide, Fixolide, (AHTN)	Polycyclic musk, chemosensitizers	Bioaccumulation potential
Galaxolide 50, Abbalide (HHCB)	Polycyclic musk, chemosensitizers	Bioaccumulation potential
Triclosan	Antibacterial and antifungal agent	Bioaccumulation, aquatic toxicity
Pyrene	Found in many combustion products	Among the PAHs, persistent organic MPs, toxicity, bioaccumulation

affects microbial population of soil. However, most microorganisms can tolerate its impacts using many functions such as rapid detoxification.

- Chloroacetamide includes metolachlor and acetochlor, which have different methods of detection (Table 1.4). They are commonly used herbicides that function in soil through inhibition of elongase enzyme. These enzymes play various important functions in bacteria and fungi (Rose et al. 2016)
- Sulfonylurea and Imidazolinone are used in cereal crops at relatively low concentrations. They act for inhibition of acetolactase synthase enzyme that is present in microorganisms. Application and deposition of this herbicide are expected to negatively impact microbes (Boldt and Jacobsen 1998).

- Triazines, phenylureas, and amides kill plant through disrupting photosystem ll. However, they are only expected to kill photosynthesizing microbes and have no such direct link with non-photosynthetic bacteria and fungi. Nevertheless, the mobile nature of these herbicides is a potential threat for off-site damage of other soil organisms.
- Phenoxycarboxylic acids are like the shape of auxins. They mimic the auxins and disrupt important roles played by them. One of the most significant roles of auxins is the facilitation of plant microbial association. So, the application of such herbicides can potentially affect association and disturb soil ecology.

Table 1.4 Group of chemical substances and analytical methods available

Group of substances	Analytical methods available		
Old organochlorines	GC-MS	LM-MS	GC-ECD
Chlordane	×		
PCBs	×		×
Metoxychlor	×	×	
HCHs	×		
Hexachlorobenzene	×		
Heptachlor	×		
Endrin	×		
Endosulphan	×	×	
Dieldrin	×		
DDTs	×		
New pesticides			
Alachlor	×	×	
Trifluralin	×	×	
Simazine	×	×	
Isoproturon		×	
Diuron		×	
Dicofol	×	×	
Chlorpyrifos	×	×	
Atrazine	×	×	
Chlofenvinphos	×	×	
PAHs			
Priority set and/or individual PAHS	×	×	
Old organochlorines			
BRFs, PBDEs, HBCD, TBBP-A	×	×	
Pentachlorobenzene	×		
hexachlorobutadiene	×		
Endocrine disruptors			
NP/NPEOs and related substances		×	
Dibutyl and diethylhexyl phthalate	×		
Octylphenol		×	
PFOS		×	

- Dinitroanilines such as trifluralin and pendimethalin halt cell mitosis through prevention of tubulin elongation. They hinder plant growth. However, not only eukaryotes but prokaryotes also divide using tubulin proteins (Löwe and Amos 1998). Microbes depending on tubulin cannot divide after interaction with Dinitroanilines.

1.8 Interaction of MPs and Sustainable Agriculture

Worldwide MPs are of great concern and they are present in various forms such as heavy metals, gases, volatile organic compounds, loud sounds, over-dumped places, excessive use of chemical fertilizers, pesticides, automobiles, and many others forms.

These MPs are involved in acute environmental changes. Changes caused by environmental MPs involve a variety of factors, such as: land degradation, water scarcity, damage to plants, food famine, biodiversity, climatic changes, etc. Agriculture is playing a noteworthy role from many decades in the economy and survival of humans. It is considered the backbone for many countries. Agriculture is a source of livelihood, revenue, economic development, foreign exchange, food supply, fodder for animals, raw materials, etc. Micropollutants are emerging contaminants that contain anthropogenic as well as natural substances. These MPs are leaving their impact on the environment as well as on agriculture. Continuous emissions of gases such as chlorofluorocarbon, carbon dioxide, lead, carbon monoxide, etc. causes the continuous rise in climatic changes. Emissions of gases are depleting the ozone layer and increase the temperature of the atmosphere. Excessive rise in temperature damages growth and yield of crops. It is damaging the soil, specially the areas with low annual rainfall. Excessive rise of temperature is another reason for drought conditions. It affects soil conditions, causing land degradation, erosion, etc.

Emission of sulphur and nitrogenous gases is the reason for acid rain, which affects soil and damages crops. Industries such as pharmaceuticals, pesticides manufacturers, etc. are emitting gases on combustion and dump their waste in water. The MPs are the reason for water scarcity for useful purposes. It is impossible to use the contaminated water for production of crops because it affects the yield of crops. This contaminated water also affects the soil nutrients' availability and microbial activities. Excessive concentration of nitrate that results because of nitrogen and oxygen is the reason of eutrophication. Its damages aquatic life and contaminates water. Excessive nitrate concentration makes the water unavailable for agricultural and household purposes.

MPs are an important issue to solve worldwide. It is affecting the land and atmosphere leaving its impact on agriculture. It is affecting our efforts of sustainable agriculture. These MPs are the reason for food scarcity in many areas, leading future generations to hunger, poverty, poor health, and economic losses. These problems can be solved by minimizing the use of sprays, organic fertilizers, pesticides, etc.; there is a need for awareness to avoid this problem.

1.9 Interaction of MPs and Microbial Activities in Soil

Microorganisms account for <0.5% of soil mass. These organisms are a major footprint for most soil properties and processes. About 60–80% of soil process and metabolism activities occur due to microflora. Microbial activities play a noteworthy part in the transformation of MPs. Microorganisms have the ability to control MPs and release useful chemical compounds. Microorganisms play a key role in the cycling of nutrients and their formation. Microbial activities are involved in a variety of processes, such as: nitrification, nitrogen fixation, carbon mineralization, nutrient availability, etc. Microorganisms commonly present in soil are bacteria, fungi, actinomycetes, protozoa, algae, etc. These organisms in soil help to control quality, depth, moisture, structure, and properties of soil. Most of the external factors, such as climate, topography, pollution, bedrock, etc., affect microbial activities. The interaction among multiple factors is responsible for variation in microbial activities and soil. Microorganisms decompose MPs present in soil and transform it to nutrients or organic compounds.

Pollutants are emerging contaminants involved in environmental changes. These MPs are leaving their impact on the microbial activities. Micropollutants allow the conversion of a large amount of nitrogen through the process of denitrification, ammonification, etc. Conversion of nitrogen will lead to the emission of sulfur dioxide and sulfur compounds that will result in acid rain. Acid rain reduces nutrient availability and soil processes. It results in soil erosion and ecological imbalance. It affects the microbial activities because of erosion and changes in soil process. Acidification impacts soil fertility and causes death of microorganisms responsible for the microbial activities in soil. Increase of salinity in soil is linked with the MPs present in soil. Deposition of nitrate and phosphorus because of irrigation and agricultural process results in increased salt concentration in soil. Rise in salt concentration affects microorganisms' growth and their activities which will result in growth of crops and reduce groundwater quality. Soil MPs result in water pollution. When chemicals such as heavy metals leach down the groundwater, it affects microbial growth and their activities. For proper functioning of microorganisms, it is important to provide favorable conditions. For proper microbial activities, it is important to reduce MPs' concentration from the soil.

1.10 Interaction of MPs and Human Health

Micropollutants are emerging contaminants that contain anthropogenic as well as natural substances. These MPs are leaving their impact on the environment as well as on human health. Humans always interact with environment on daily basis. This interaction between humans and the environment results in pollution, global warming, deforestation, etc. These problems have a major impact on the human health.

Pollutants present in the atmosphere are causing human health problems such as:

- Increase the chance of respiratory diseases.
- Risk of developing asthma problems.
- Increase the respiratory inflammation.
- Reduce lungs' functioning.
- Damage reproductive system and endocrine system.
- Commonly show wheezing and coughing.
- Increase risk of heart failure.
- Increase the risk of developing cancer.

Pollutants present in water are causing human health problems such as:

- Cancer development
- Hormone's disruption
- Rashes
- Hepatitis
- Damage reproductive system
- Damage immune system
- Damage respiratory system
- Cause heart problems
- Cause kidney failure
- Cause typhoid
- Cause polio and cholera

Pollutants present in soil are causing human health problems such as:

- Headache, vomiting
- Breakdown of central nervous system
- Cough, pain in chest
- High chances of developing of cancer
- Irritation of skin and eyes
- Damage to kidney
- Damage liver
- Muscular blockage

These all problems are caused by MPs present in the environment. These all problems are reducing the lifespan of humans. It is important to resolve these problems to reduce the risk of human health.

1.11 Strategies for Management of MPs

Micropollutants are of great concern worldwide. Changes caused by environmental MPs involve variety of factors, such as: land degradation, water scarcity, damage to plants, food famine, biodiversity, climatic changes, etc. Micropollutants also cause a major impact on human health. Management practices are required to reduce the risk of MP. There are different practices that are performed to reduce the risk of micro-pollution such as forest buffer (trees, shrubs, grasses) should be planted across the streams and banks of rivers. It will help to reduce pollution in water. It will reduce the risk of temperature increase.

Hydrochars produced through hydrothermal carbonization (pistachio shells) are a sustainable and efficient replacement to activated carbons for the removal of MPs from wastewaters that are difficult to treat using traditional methods. For the investigation of caffeine/hydrochars aqueous systems, a combined experimental and molecular simulation method is used. This case study is used to fine-tune a generic framework for rationally customizing surface functional groups on hydrochars for the selective adsorption of MPs from wastewaters (Román et al. 2018).

1.11.1 Air Pollutants

Air pollutants' control strategies involve two categories:

- Control of emission
- Control of gaseous emission

There are many methods and instruments used to control the emission from air, such as:

- Cyclone collector
- Wet scrubber
- Settling chamber
- Filtration devices
- Electrostatic precipitation

1.11.2 Water Pollutants

Water pollution may be controlled using a variety of methods and equipment, including:

- Physical method
- Chemical method
- Biological method

Many methods and equipment are used to reduce water contamination through physical processes, such as:

- Infiltration
- Screening
- Sedimentation
- Flotation

Many methods and equipment are used to reduce water contamination through chemical processes, such as:

- Chemical precipitation
- Adsorption
- Disinfection reaction

1.11.3 Solid Pollutants

There are many methods and techniques to control solid MPs such as:

- Landfilling
- Incineration
- Composting

These all are modern and most used methods for the reduction of MPs. These problems can be solved by minimizing the use of sprays, organic fertilizers, pesticides, etc.; there is a need of awareness to avoid this problem.

1.12 Conclusion

Micropollutants are of great concern worldwide as they are sublethal to the environment and living organisms on the planet. A wide range of toxic effects of MPs affect the organisms at cellular level. Changes caused by MPs involve a variety of factors, such as land degradation, water scarcity, damage to plants, food security, biodiversity, etc. Micropollutants also cause a major impact on human health. It is important to reduce problem for the better survival of mankind. Reduction of pollution is beneficial in many ways such as prevention of MPs will minimize the greenhouse gas emissions. Traditional bioremediation approaches such as phytoremediation, biostimulation, and bioaugmentation might all play a significant role. It leads to sustainable environment for ages by remediating the agricultural soils and limiting the MPs. In some situations, a mix of biological and chemical treatments may be advantageous to achieve optimum remediation efficiency. It reduces the finical cost (waste management and cleanup cost) and environmental cost (health problems and environmental damage). Reduction of environmental MPs is important for future generations, for their health and better life. Developing nations do not yet have access to discharge limitations for new MPs into the environment. This requires attention so that limitations may be set based on scientific evidence. To estimate the related pathophysiological risk to humans and other creatures, it is critical to determine the toxic effects of MPs in organisms using specialized and suitable assays at each level of biological organization. A comprehensive and cost-effective method for detecting and analyzing MPs and their metabolites in environmental samples is desperately needed. As a result, there is a need for a revised risk assessment methodology that incorporates consolidated toxicity data generated from systematic research in determining acceptable limits to safeguard human and ecological health.

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Chapter 2
Infectious Diseases, Challenges, and Their Impacts on Human Health Under Changing Climate

Toqeer Ahmed, Faridullah, and Rashida Kanwal

Abstract Climate variability like temperature changes, rainfall pattern changes, heatwaves, drought etc. effects the infectious diseases in human beings has been discovered in late nineteen century. Infectious diseases (IDs) like malaria, dengue fever, chikungunya, yellow fever, seasonal influenza, cholera, Asthma, TB, and other respiratory diseases are caused by bacteria, viruses, protozoans, and other parasites, but their mode of transmission, type, size, and impacts vary greatly. Some of the IDs are epidemic, while others are pandemic and have long-lasting effects on human beings and the economy of the world. These may be water- or food-related, waterborne, vectorborne, or others. Lots of challenges are ahead for the scientists in the twentieth and twenty-first century to cope with the impacts of ID on health and economy. In this chapter, linkages of ID with climate changes, challenges, impacts on human health and economy, control and remediations of ID, role of modelling, and future perspectives have been discussed in detail.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_2

2.1 Introduction

Climate change (CC) impacts include sea-level rise, melting ice, heat waves, droughts, floods, change in rainfall pattern and ecosystems, shift in seasons, etc., resulting in vulnerability of food and water along with the origin of infectious disease (IDs). IDs are impacted by change in climatic conditions, like change in rainfall pattern, temperature, humidity, heatwaves, etc. Shift in seasons impacts increase or decrease in growth, host specificity, and mode of transmission of microbes. Climate is changing due to rise in temperature as predicted by Intergovernmental Panel on Climate Change (IPCC) that temperature will rise in the twenty-first century (IPCC 2014), and accordingly, it will not only impact the natural resources but also affect human health-related infectious diseases like malaria, dengue fever, chikungunya, yellow fever, Zika virus, West Nile, seasonal influenza, cholera, Asthma, TB, and other respiratory diseases caused by bacteria, viruses, and fungi. A suitable environment is provided by the climatic conditions for their entry into the host, growth, and completion of life cycle of the microbes. Accordingly, host selection for specific environment, survival, reproduction, intensity, and geographical distribution varies due to climatic conditions, and by adopting preventive measures, health impact can be controlled (Xiaoxu Wu 2016). *Salmonellosis,* cholera, and *Giardiasis* outbreaks are common in monsoon and flooding, especially in warm and humid conditions (Chretien 2014). Similarly, VBDs malaria, dengue fever, yellow fever, etc. are increased during monsoon conditions and after rainfall especially under humid conditions. Suitable temperature (25–35 °C) and humidity 65–80% are the optimum conditions for the breeding of mosquitoes and larval growth (Toqeer Ahmed 2019). Socio-economic factors play important role in the spread of human infections and vulnerability due to climate change. There is long-term direct relationship among socio-economic factors, climate change, and prevalence of disease (Anwar 2019). The most common and emerging disease that appeared in 2019 in Wuhan city in China is COVID-19, which spread throughout the world and killed thousands, and millions are affected by this pandemic, and it has been reported that COVID 19 is dependent on meteorological parameters as low temperature and humidity favour the transmission of disease (Jiangtao Liu 2020). This pandemic disease impacts the ways of living, social contacts, and change in habits and environment (Stefano Capolongo 2020). This highlighted the need to transform the cities into healthy environment. The IDs spread throughout the world and are impacted by climate change (CC) without any restriction of boundaries, so there is a need to mitigate these and governance and policies to control IDs and CC. The World Health Organization reported that the changes in the pattern of infectious diseases are due to climate change and need to learn the complex phenomenon through modelling for the prediction of future impacts (WHO 2020) rather than observational studies. This chapter describes how human infectious diseases are impacted by climate change, challenges, and impact on human health, how to control IDs relate to climate change, and role of modelling on future impacts and perspectives. Predicted impacts of climate change on IDs and their control are shown in Fig. 2.1.

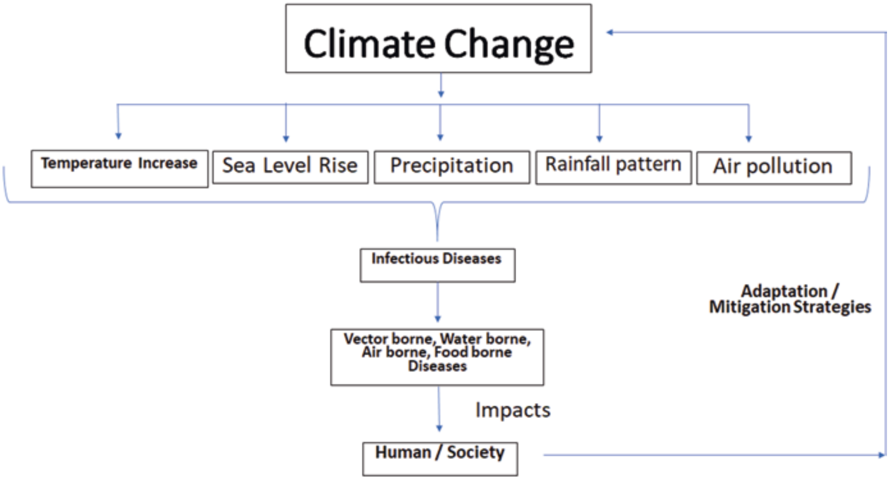

Fig. 2.1 Predicted impact of CC on IDs and control

2.2 Infectious Diseases (IDs) and Climate Changes (CC)

South Asian countries like India, Pakistan, Nepal, Bangladesh, Afghanistan, Sri Lanka, etc. are most vulnerable to a significant proportion of IDs due to CC and other factors like socio-economic factors, urbanization, sanitation and hygiene, land use, and population density (Bhandari, Climate change and infectious disease research in Nepal: are the available prerequisites supportive enough to researchers?, 2020b). Climate change is impacting and increasing the severity of some diseases in one part of the world and decreasing the impact in other parts like decrease in malaria cases in the last decades and increase in viral diseases (Flahault 2016). Another study reported that regression model showed that monthly diarrhoea cases increased by 8.1% by the increase of 1 °C average maximum temperature and 0.9% by the increase in 10 mm in rainfall (Bhandari 2020a). Similarly, *Salmonella* is foodborne pathogens influenced by temperature about 35% in European countries (Kovats 2004). Epidemiological triangle (host, agent, and environment) has been given to understand the behaviour of IDs and reported that without these aspects, a disease cannot occur (Smith 2019). To address the actual facts on disease-specific needs, more focused research is required to address the challenges under rapidly changing climatic world (Redshaw 2013). There are a number of diseases which are impacted by climatic parameters. Like Malaria, Yellow fever, Zika, COVID-19, and Dengue fever are caused by viruses. Second, COVID 19 is affected by CC and vice versa. Third, Cholera, TB, Asthma, and other respiratory disorders are caused by bacteria. Fourth, Zoonotic diseases, which transfer from animals to human beings, are caused by bacteria, viruses, and fungi, and *Anthroponosis*, which spreads from human to human and animals. There are many other diseases like Japanese encephalitis, Rift Valley Fever, Chikungunya, leishmaniasis, and human African trypanosomiasis caused by viruses and are impacted by CC (Florence Fouque 2019; Mordecai 2020). Fifth, waterborne diseases are impacted by climate change. High temperature and precipitation are predicted to have more impact on IDs, especially in the Arctic (Waits 2018). These diseases are posing serious threats and high risks to human beings. CC further exaggerates the situation in some cases. The above categories have been discussed in detail, that is how these are impacted by climate change.

2.2.1 Malaria, Yellow Fever, Dengue Fever, and Vector-Borne Diseases (VBDs)

A complex relationship has been found between CC and diseases caused by vectors. As reported, CC contributes to the spread of VBDs like Dengue, Zika, and Chikungunya, especially in developing countries (Filho 2008; Asad 2018). A warm and moist environment favours the growth of vectors and their breeding (Naish 2014), but in other way high temperature and drought conditions stop the growth of larvae and breeding of vectors or sometimes suppress the growth of vectors (Florence Fouque 2019). A detailed review on impact of CC on dengue and malaria through a systematic and modelling approach confirms the impact of CC on dengue and malaria spread (Naish 2014; Christine Giesen 2020; Ngarakana-Gwasira 2016; Martens (1997), p. 1997). These climatic parameters impact the diseases indirectly. CC will impact VBDs like malaria, yellow fever, and dengue fever, but how these will depends on the factors like population, the immune system of the population, deforestation, drainage, drug or insecticide resistance, demography, etc. as these factors can impact the ecology of the vectors (Fernando 2020). Change in vector and distribution in one region to another due to CC has been observed (Florence Fouque 2019). CC can impact and increase the disease burden caused by vectors especially in South and Sub-Saharan Africa (Mordecai 2020). Further, the impact of CC on these diseases can affect social and economic losses. *Chikungunya*, West Nile Virus, Zika, and Dengue are a diverse group of Arboviruses (Young 2018). A strong and positive relation has been found in spread of *Chikungunya* and rainfall (Shil 2018).

2.2.2 COVID 19 and Climate Change

There are two possibilities, either climate change is affecting the COVID and spreading the pandemic disease or Covid is impacting the climate change. In the first case, it is not clear that climate change directly impacts the spread of COVID 19 disease, but it can affect indirectly like people living in poor air quality can be more vulnerable to the worst symptoms of COVID and more people can die.

Similarly, some studies reported that there is no direct evidence that increase in temperature can stop the spread of COVID (Bernstein 2020; Bashir 2020; Iqbal 2020), but some others reported that temperature, wind speed, and humidity are negatively correlated with the daily new cases and temperature (>20 °C) positively correlated with daily new cases (Yuan 2021).

In the second case, human mobility and transport are reduced due to the spread of COVID pandemic throughout the world. As a result, the GHG emissions reduced by 25% and quality of air improved and decreased particulate matter had been observed (Sipra 2020; Jauregui 2020). Another study reported that the average temperature, minimum temperature, and air quality can be helpful in suppressing the disease (Bashir 2020). However, it is suggested that green environmental policies can be helpful in reducing this pandemic disease (Bashir 2020). Among the lessons learnt, acceptance of disease, preparedness like physical distancing, hygienic measures, mobility restrictions of ill persons, use of face masks, socio-economic restrictions, communication, and support, including early detection and warning, are the key factors that helped in controlling the spread of disease (Yuri Bruinen de Bruin 2020).

2.2.3 TB, Asthma, and Other Respiratory Disorder

Pollens and both indoor and outdoor allergens can cause respiratory issues. CC has immediate and long-term impacts on the human respiratory system (Gerardi 2014). Climate can increase pollens and allergens which are produced by moulds and plants (Gennaro D'Amato 2014), but the degree of effect is not clear (Ayres 2009). People who are sensitive to pollens and allergens are more vulnerable, like cardiopulmonary and asthma patients. Warming and increased unpredictability of weather cause negative impacts on humans with respiratory disorders (Manish 2020). More details on mould and aeroallergen have been given in separate chapters.

2.2.4 Zoonotic and Anthroponosis Diseases

Zoonotic diseases are the diseases which are transferred from animals to human, like bird flu, *brucellosis*, Ebola, *Giardiasis,* etc. or biting insects like *Leishmaniasis; malaria and dengue* are caused by biting insects and climate change can cause shift in animals and insects from one region to another (Cardenas 2008). Anthroponosis is the disease which transfers from human to human, and Anthropozonosis is the disease which transfers from animals to human under natural conditions like Anthrax, Rabies, etc. A study reported the decrease in abundance of tsetse fly in Zambezi valley due to change in climate, especially increase in temperature (Longbottom 2020). Recently reported *Dracunculus medinensis* is Zoonotic disease in Chad spread in dry weather through waterborne route when ponds and rivers are infected (Galán-Puchades 2020). Water and temperature are the major factors along with geographical distribution that can influence the Zoonotic heminths (Mas-Coma 2008). *Brucellosis* is caused by *Brucella spp*. transferred from animals to human through infected meat and unpasteurized milk and other sources and is highly affected by temperature. As reported, dry weather with increased temperature of 30 °C can decrease the incidence of disease (Dadar 2020). Similarly, West Nile Virus infections increased with an increase in temperature, while drought contributes 26% in prevalence (Smith 2020).

2.2.5 Waterborne Diseases

Aquatic pathogens of animal and human faecal origin may include bacteria, viruses, and parasites. Also, some naturally occurring microbes can become pathogenic, e.g. species of *Vibrio* (septicemia, diahorraea, and gastroenteritis), amoebae (encephalitis) *Pseudomonas aeruginosa* (infections of Ear and skin), and *Legionella pneumophila* (Legionnaire's disease) (WHO, Guidelines for drinking-water quality: incorporating, 2008). Waterborne diseases include cholera, *shigellosis, typhoid,* etc. Cholera is a bacterial disease and caused by *Vibrio cholera*. There is strong evidence that cholera is affected by meteorological parameters (Fig. 2.2) like high temperature and low precipitation can elevate the replication process of bacteria (Asadgol 2019).

Cholera disease can also be caused during occupational (fishing) and recreational activities (Redshaw 2013). A systematic analysis on *Vibrio* spp. and *Leptospira* spp., followed by *E. coli*, identified these microbes as commonly found pathogens in the outbreaks of waterborne diseases after flooding, mostly in Asia (Alderman 2012; Ahern 2005). Flooding and heavy rainfall contribute to gastrointestinal illnesses and contaminated water quality. There was a significant rise in diarrhoeal diseases among young children and the elderly after the 2007 Flooding in China (Ding 2013). About 21,401 cases of diarrhoea were treated in the hospitals of Bangladesh in August 2007, due to severe flooding (Nahar 2010). In 2010, diarrhoea was a principal reason of illness in Pakistan due to flooding accounting for more than 17% of medical sessions in the worst affected area (WHO, Floods in Pakistan-Health Cluster Bulletin No 12–16 August 2010 2010). Similarly, some examples of rainfall impacts on waterborne diseases by poor water quality include a case of waterborne outbreak of *Campylobacter jejuni* and *Escherichia coli O157:H7* in the Canadian town of Walkerton, which caused more than 2300 cases of gastrointestinal illness, 65 hospitalizations, and 7 deaths. In this case, the drinking water became polluted by livestock dung, following an intense rainfall (O'Connor 2002); a substantial association between outbreaks of waterborne disease and excess rainfall. This study analysed 548 already reported outbreaks in the United States from 1948 to 1994. The results showed that almost 51% of outbreaks were preceded by heavy rainfall (Curriero 2001).

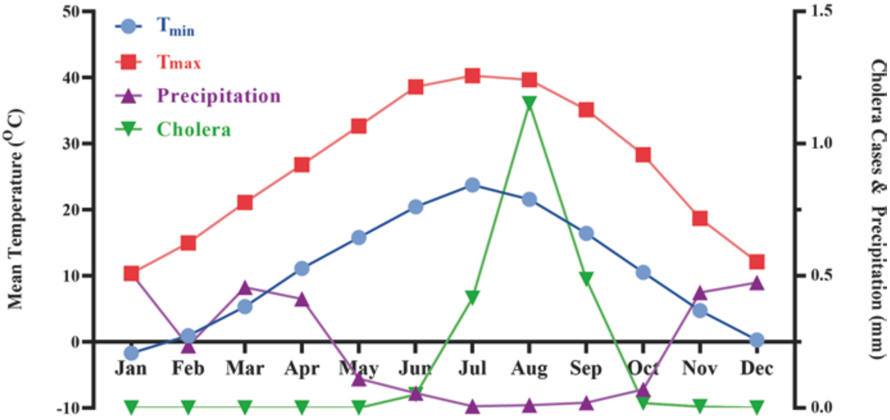

Fig. 2.2 Monthly variation in the number of cholera cases and climate variables, 1998–2016 (Adapted from Asadgol 2019)

More details on the infectious diseases related to climate change events are summarized in Table 2.1.

2.3 Remediation and Control of ID Related to CC

It is important to understand which ID is positively or negatively affected by CC. Geographical distribution is important in understanding the impacts of CC on IDs. In some regions, the incidence of IDs is lower by increasing meteorological parameters, but in other regions, the prevalence and incidence of diseases are increased by changing climate. Multidisciplinary and integrated approaches are required to understand the mechanism, relationship with vector, host, and pathogenicity, and deal with infections under changing climate (Mills 2010). Eco-epidemiological methods can help in decreasing zoonotic diseases like *Brucellosis* (Dadar 2020). Efficiency in monitoring and generation of risk maps can be helpful in controlling the VBDs (Fischer 2011). Preparation of a list of IDs which are climate-sensitive, adaptation and mitigation strategies, emergency preparedness, training of manpower, capacity building, developing testing kits, vaccines, developing models for projections, developing policies, and implementation of law and enforcement are important in controlling the IDs (Semenza 2009; Filho 2008). Improvements in sanitation, hygiene, and infrastructure are required to control IDs along with awareness on how the IDs spread under changing climate (Filho 2008). Use of remote sensing techniques for the detection of algal blooms for the improvement of water quality is suggested. Similarly, for ID, molecular techniques to trail contaminants are recommended (Rose 2001). Both operational research and humanitarian aids are important including turning research into policies and their

Table 2.1 Climate change events and their impacts on infectious disease

Climate change event	Type of disease	Infectious disease	Impacts	References
Temperature	Vector-borne disease	Malaria	Studies showed that pathogens of malaria, i.e. *Plasmodium vivax* and *Plasmodium falciparum,* develop below 15 °C in mosquitoes.	Snow (2003)
		Dengue fever	Increase in temperature and humidity during rainy season is associated with increase in dengue virus propagation in mosquitos, contributing to the outbreaks of dengue haemorrhagic fever.	Zhang (2008)
		Zika virus	Transmission of zika virus increases at higher temperature.	Winokur (2020)
		Leishmaniasis	The distribution of *Phlebotomus papatasi* in Southwestern Asia is dependent on temperature and relative humidity	Karimi (2014)
		Lyme borreliosis – LB	It is a tick-borne disease and studies showed that distribution of ticks in Northern was associated with very low temperature, below −12 °C.	Lindgren (2006)
	Waterborne disease	Cholera	Vibrio spp. showed an increased growth rate during the hot summers.	Colwell (1996)
		Skin infections, e.g. cellulitis	Rainfall after long drought increases the spread of waterborne diseases.	Czachor (1992)
	Foodborne diseases	Salmonellosis	Rise in temperature in the range between 7 °C and 37 °C increases the reproduction rate of salmonella bacteria.	D'Souza (2004)
		Campylobacteriosis	It was observed that warmer temperature supports the growth of Campylobacter spp. which enhances the disease.	Kovats (2005)
	Airborne	Allergy and asthma	Allergy increases during cold weather and pollen season.	Damialis (2019)

(continued)

Table 2.1 (continued)

Climate change event	Type of disease	Infectious disease	Impacts	References
		Chickenpox	Chickenpox increases at tempterature 5–20 °C.	Chen (2017)
		Coronavirus	Previous studies showed that SARS-CoV-1 is unstable at higher temperature (above 38 °C) and higher humidity (>95%).	Briz-Redón (2020)
		Tuberculosis	Studies showed that spread of tuberculosis increases at low temperature, low humidity, and low rainfall.	La Rosa G (2013)
	Zoonotic or Anthroponosis	Ebola	Studies showed that at temperature above 27 °C transmission of Ebola virus increases.	Kassie Daouda (2015)
		Avian influenza	Cold temperature and low relative humidity are favourable to the spread of influenza virus.	Gilbert (2008)
		Giardiasis	Studies showed that higher temperature resulted in increased death rate due to Giardia.	Balderrama-Carmona (2017)
Flood	Vector-borne disease	Malaria	Floods in Mozambique led to spread of malaria, typhoid, and cholera.	Epstein (1999)
		lymphatic filariasis	There have been reported increases in lymphatic filariasis in different areas.	Nielsen (2002)
		Leptospirosis diseases	Leptospirosis diseases may also increase during flooding in different areas.	Leal-Castellanos (2003)
	Waterborne disease	Cryptosporidium infection.	Flood favours waterborne disease transmission such as Cryptosporidium infection.	MacKenzie (1994)
Drought	Vector-borne disease	hantavirus pulmonary syndrome (HPS)	Drought has been found to be associated with hantavirus pulmonary syndrome (HPS).	Khasnis (2005)
		West Nile virus	Increased West Nile virus risks follow the drought.	Wang (2010)

(continued)

Table 2.1 (continued)

Climate change event	Type of disease	Infectious disease	Impacts	References
		St. Louis Encephalitis virus	The risk for transmission of St. Louis Encephalitis virus would increase, during the droughts.	Shaman (2002)
		Chikungunya fever	The Chikungunya fever epidemic may be associated with droughts.	Chretien (2007)
	Waterborne disease	Diarrhoea	Diarrhoeal diseases are frequent during drought especially in refugee camps.	Epstein (2001)

implantation are important (Small 2001). Global warming may have impacts on water quality including WBDs/IDs, so more efficient tools or strategies are required in the future, especially trained or skilled manpower (Levin 2002). Policies for decarbonization should be devised to reduce global warming and CC impacts on IDs and water quality. Inclusion of environmental perspectives into health assessment and integrated approaches for surveillance are being suggested. Lack of quality data and its authenticity are important for processing of scientific models to control IDs. Funding is the main requirement for all the data collection, modelling, management, capacity building, and training purposes (Hess 2020). Establishment of local early warning system for the prediction of health impacts by climate change have been proposed (Wu 2016). Another study suggested the integrated surveillance system, trans-border collaboration, and interdisciplinary research which can control the disease burden caused by the IDs (Bhandari, Climate change and infectious disease research in Nepal: are the available prerequisites supportive enough to researchers?, 2020b). Due to less equipped and under-resourced laboratories in the developing countries, they are more vulnerable to IDs. Hence, there is need to provide/generate funding for the high-performance equipment and qualified and trained manpower to run the labs working for the diagnosis of the climate-sensitive diseases. Similarly, international collaboration can boost the training of the manpower and their deputation in the diagnostic laboratories is suggested. Similarly, another study suggested the micro-stratification for malaria and other disease controlling measures like use of mosquito nets, insect repellents, and fever checking not only at borders, but also in the different districts and cities to control infectious diseases including COVID-19, malaria, and other asymptomatic cases (Dhimal 2014). Maintenance of health surveillance system and continuous efforts can provide support in achieving the goals.

2.4 Future Prospective and Role of Modelling on ID

Modelling is important to understand the risk of infectious diseases in the future under different climate scenarios. These models can be statistical, mathematical, or climate change to understand the water quality and infectious diseases' risks (Patz 2003). Empirical studies indicated that the global CC impacts on WBDs and VBDs and is reported likely to increase with the increase in population and social inequalities in developing countries and where the conditions are favourable (Fig. 2.3). Different models are used to predict cases of dengue fever like ARIMA model reported to be a good prediction model for a longer period as compared to other models (Siriwan Wongkoon 2012; Luz 2008). Similarly, Artificial Neural Networks (ANNs) have been found effective to simulate the CC impacts on cholera to find the future trend of cholera outbreaks (Asadgol 2019). A study conducted to use the spatial regression model to assess the distribution of IDs found that malaria, diarrhoea, and HAV infections are significantly related to floods after controlling other meteorological parameters (Gao 2016). Entomological models are used for the assessment of mosquito abundance, growth status, and development, and the same can be used for locusts.

Different models like MARA/ARMA model, container-inhabiting mosquito simulation model (CIMSiM), CLIMEX model, Malaria-Potential-Occurrence-Zone model, mathematical-biological model (simulation of malarial forecasts on the basis of seasonal weather forecasts), classification and regression tree (CART), and principal component analysis (PCA) for variability of cholera cases and dengue simulation model are used for the control of malaria and dengue fever-related infectious diseases (Patz 2003; Hoshen 2004; Islam 2009). A statistical model was used and found effective to assess the impact of temperature and drought in the spread of West Nile Virus disease. Similarly, scenario models are used to assess the scenario under changing drought and temperature and suggested to apply for other diseases (Smith 2020). The predicted population at risk by VBDs is shown in Fig. 2.3.

2.5 Conclusion and Recommendations

Climate change brings both positive and negative impacts on the spread of IDs in which geographic distribution and climate-specific conditions are important to impact vector host relationship, life cycle, and specific disease. Hygienic conditions, sanitation, and control of spread factors can help in controlling and decreasing the impact and disease burden. It is important to study in detail the specific disease in a specific geographic area and impacts of CC on the specific ID. It is not necessary that disease in one area impacted by CC behaves in a similar way in other areas and under different climates. Modelling studies can help in predicting the future trends and impacts of IDs under similar conditions. Scenario and other models can help in assessing the different scenarios under changing CC for the different IDs.

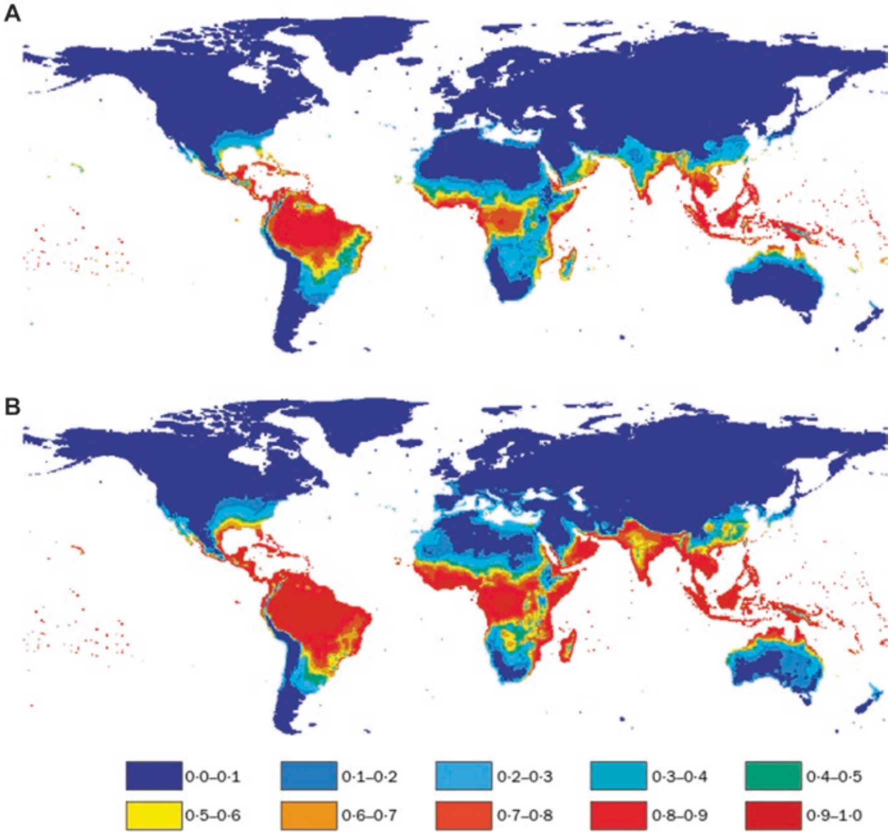

Fig. 2.3 Population at risk of VBDs in 1990 (**a**) and 2085 (**b**) by Regression Model. (Simon Hales 2002)

Capacity building and training in the lacking areas can help in improving the conditions. The most important is the implementation of policies by using the peanut and stick method, which can help in improving the existing conditions, especially in the developing countries.

The following are the important recommendations:

1. Integrated approaches are important to address the IDs.
2. Preparedness in emergency is highly vital to tackle the IDs during disasters.
3. Mitigation strategies are necessary to cope with the IDs.
4. Eco-epidemiological approach to address spatiotemporal dynamics and infectious diseases.

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Chapter 3
Marble Dust as an Environmental and Occupational Hazard

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Abstract With the increase in urbanization over the last century, mankind is enjoying sophisticated modern architecture. The use of different types of naturally occurring and synthetic materials is becoming very popular at industrial and domestic levels. Marble being a natural metamorphic rock is commonly used by our society because of its beautiful colors, easy maintenance, and lifelong durability. The other side of the picture of marble use is very ugly because of the environmental and health hazards that are caused by the marble industry.

Marble dust is produced by marble factories during the refinement and processing of raw marble into glass polished tiles, slabs, and tabletops. The dust produced during this process is added as a pollutant to the environment or is inhaled in high concentrations by the workers via the respiratory tract, thus making them more prone to chronic pulmonary diseases. These particles being highly irritant and allergic cause respiratory disease affecting both upper and lower respiratory tracts ultimately leading to decreased respiratory functions. Different literature showed that workers and residents living in areas adjacent to marble/granite factories are prone to lung disease, e. g., silicosis.

Also, dry cough and shortness of breath are the commonest complains with which these workers present. In spite of the latest advancements in medical field, only supportive treatment (antihistamine, Montelukast, and bronchodilators) can be given to these patients if preventive measures are not taken on time.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_3

International Agency for Research on Cancer (IARC) classified marble dust, heavy metals, and crystalline silica as carcinogens in 1997. International Labor organization (1919) protects workers' right and thus demands effective prevention techniques, safe working places, and awareness programs regarding commonly addressed health issue for the workers working in industries. If effective treatment is not given to workers who have developed the above-mentioned health issues on the right time, they might develop an end-stage lung disease (chronic lung disease/ lung cancer). Different epidemiological studies show that workers exposed to marble dust have an increased risk of developing chronic asthma, chronic bronchitis, and impaired lung functions and even lung cancer.

Marble dust, other than having serious health issues, can have a considerable economic impact as well; like decrease in working productivity, increase in health expenditure per person, and increase in mortality and morbidity. Health being the basic right of man, strict preventive measures should be taken for and by these workers as they constitute a substantial number of chronically affected patients of respiratory tract.

3.1 Introduction

With the increase in urbanization over the last century, mankind is enjoying sophisticated modern architecture. The use of different types of naturally occurring and synthetic materials is becoming very popular at industrial and domestic levels. Marble being a natural metamorphic rock is commonly used by our society because of its beautiful colors, easy maintenance, and lifelong durability. Today, half of the world's marble extraction is mostly from six countries; Italy, China, India, Spain, Egypt, and Turkey. However, marble is produced by many other countries too (Ciccu et al. 2005).

The other side of the picture of marble use is very ugly because of the environmental and health hazards that are caused by the marble industry (Corinaldesi et al. 2010). Mechanical breakdown and other procedures of marble dealing have not only considerable effects on the environment but also on workers' health and safety and the communities residing in nearby villages. Cumulative impacts include lack of environmental protection, rehabilitation measures, community engagement, and inappropriate and unsafe operational procedures (Bui et al. 2017; Gorman and Dzombak 2018; Nuong et al. 2011). Well, in fact, the recognized truth is that the marble industry provides much-needed opportunities for employment to the poorest families of the nearby communities (Paracha 2009).

This particular industry in its present state is confronting different challenges along with the devastating conditions of the worker like fatal injury including rock fall, fires, explosions, mobile equipment accidents, falls from height, gas explosion, suffocation, and entrapment. Less common but recognized causes of fatal injury include flooding of underground workings, wet-fill release from collapsed bulkheads, and air blast from block caving failure (Donoghue 2004). In addition to this, workers are also exposed to toxic chemicals and dust that take a toll on their health (Ashraf and Cawood 2017). There is no mechanism to provide compensation to ailing or injured mine workers, to the families of those killed on the job, or to rural communities affected by mining operations (Azad et al. 2013). Linked to these issues, the International Labor Organization (ILO) estimated that about 2.3 million people die due to occupational accidents and occupational diseases, 317 million suffer from serious nonfatal occupational injuries, and 160 million suffer from occupational illnesses and most of them belong to rural areas in less developed countries (Takala et al. 2014).

Mechanical breakdown like grinding, cutting, drilling, crushing, explosion, or strong friction results in emission of dust. All over the world, the marble industry is considered a high waste-producing industry. It is estimated that round about 70% of the precious marble is wasted as marble dust during the procedures of mining and polishing. This wasted marble is dumped in roads, rivers, and agricultural fields and causes environmental pollution and generation of marble dust (El-Gammal et al. 2011; Gazi et al. 2012). This polluted environment directly or indirectly affects health by polluting the air quality (Nakao et al. 2018). The dust that penetrates inside the lungs is particulate matter (PM), and usually 15–20% of cases of common chronic obstructive pulmonary disease (COPD) are linked with prolonged occupational exposure to dust, vapors, gases, and fumes over a long period of time (Azizah 2019; Borup et al. 2017; Faisal and Susanto 2017; Sudrajad and Azizah 2016) (Fig. 3.1).

The particulate matter ($PM_{2,5}$) enters the alveoli and causes inflammation and reduces lung function. The maximum harmful exposure to particulate matter is measured (10 mg/m_3) for 8 h. The dust particulates are divided into two categories, namely PM_{10} and $PM_{2.5}$ (Khoiroh 2020) (Table 3.1). Dust clouds in a working place

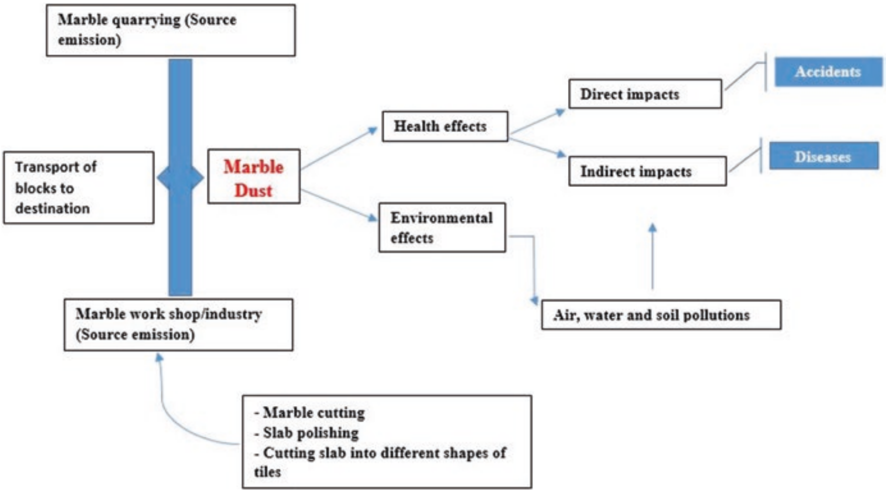

Fig. 3.1 Exposure of workers to marble dust as occupational hazard

Table 3.1 Exposure to dust concentration and rate of intake in different media

Variable	Exposure concentration in different parameters	Rate of intake
Concentration in media	Mg/l (Water)	l/hour, l/day
	mg/m^3 (Air)	Mg/inhaled per minute or per hour
	Mg/100cm^2 (Contaminated surface)	Mg/kg body weight ingested per day or per meal
Quantity available for absorption (Potential dose)	Mg inhaled, total	
	Mg inhaled/kg body weight	
	Mg ingested total	
	Mg ingested per kg body weight	
	Mg-on skin total	
	Mg/cm$_2$ skin area	

reduce visibility and deposited dust may cause slipperiness, increase the risk of accidents, and lead to degradation of materials and environmental pollution due to its deposition on various structures, machinery, and equipment (Park 2005).

In addition, fine dust covers the ground and prevents rainwater from percolating into the soil. Marble dust also destroys plants by covering their leaves and reducing exposure to sunlight which indirectly affect the health (Noreen et al. 2019).

To avoid the occupational factors and conditions hazardous to the health and safety of workers, such as occupational diseases and workplace accidents, the protection and promotion of the health of workers are necessary. Nowadays, it is considered an occupational health multidisciplinary and comprehensive approach that includes general health, the worker's physical, mental, and social well-being, and personal development (Humans and Cancer 2006).

3.1.1 Potential Hazards from Marble Quarrying to Waste

Marble dust is produced from marble quarrying by cutting of rocks to marble factories during refinement and processing of raw marble into glass polished tiles, slabs, and tabletops. The dust produced during this process is added as a pollutant to the environment or is inhaled in high concentrations by the workers via the respiratory tract, thus making them more prone to chronic pulmonary diseases (Rajgor and Pitroda 2013). These particles being highly irritant and allergic cause respiratory disease affecting both upper and lower respiratory tracts ultimately leading to decreased respiratory functions (Chen et al. 2012). Different literature showed that workers and residents living in areas adjacent to marble/granite factories are prone to lung disease, e.g., silicosis (Nij et al. 2003). People with silicosis have a higher risk of developing tuberculosis (Álvarez et al. 2015). Similarly, various epidemiological studies indicate that workers exposed to marble dust have an increased risk of occupational asthma, impairment of lung function, chronic bronchitis, renal impairment, and nasal inflammation (Angotzi et al. 2005; Armaeni and Widajati 2016; Leikin et al. 2009; Morton and Dunnette 1994; Pulungan 2018). Workers are exposed to marble dust, heavy metals, and crystalline silica, which are classified as known carcinogens by the International Agency for Research on Cancer (IARC) in 1997 (Golbabaei et al. 2004; Scarselli et al. 2008; Yaghi and Abdul-Wahab 2003; Yassin et al. 2005). Marble dust is abrasive in nature and causes allergies to the skin (Scleroderma) and eye irritation. Workers with these diseases can go undiagnosed and untreated, and worst of all, effective preventive measures are not taken because of a lack of awareness of the problem. Also, dry cough and shortness of breath are the commonest complains these workers present. In spite of the latest advancements in medical field, only supportive treatment (antihistamine, Montelukast and bronchodilators) can be given to these patients if preventive measures are not taken on time.

3.1.2 Exposure to Marble Dust Concentration

Different processes involved in marble quarrying to marble workshop produce marble dust cloud into the atmosphere. Occupationally, these workers are exposed to high content of dust in their workplace during their routine working hours (Bickis 1998), which is known as "primary airborne dust" (WHO 1999). This dust comprises of particle sizes in the range of 1–400 μm, and particles larger than 100 μm easily settle down near the source. All these dust particles are divided into three size ranges, i.e., larger than 20 μm are termed large particles and 20–1 μm and less than 1 μm as fine and ultrafine particles, respectively (Leonard 1979). The particle size of a dust cloud may be different from that of the powder originated from its source. The determinants include the amount (mass), distribution of particle size, falling height from parental rock, material flow and moisture content and air movement in the workplace, etc. (Bickis 1998). Exposure of an individual to the workplace and their integration with the exposed media, dust concentration, and in relation to time can be calculated by the following equation.

3.1.3 Calculation of Exposure

$$Ej = \int_{t1}^{t2} Cj.(t)\,\mathrm{dt}$$

Where

Ej = exposure of the individual
$\int$ = integrated with exposure media

C = concentration of marble dust
d = exposure dose (mg/kg/day)
t = for a time period (Detels et al. 2011)

The main crystalline composition of minerals present in marble dust includes magnesium calcium bis (carbonate) (MgCa $(CO_3)_2$) and calcium magnesium aluminum catena- alumosilicate (Demirel 2010).

3.1.4 Inhalable and Respirable Marble Dust

The US Environmental Protection Agency (EPA) defined respirable dust as particulate matter less than 10 µm in diameter. Respirable dust enters into the lungs and causes pneumoconiosis in workers on prolonged exposure. In the working place, the quality of air must be maintained by keeping the concentration of respirable dust 2 mg/m^3 (Speight 2020) (Table 3.1). Marble dust other than having serious health issues can have a considerable economic impact as well, like decrease in working productivity, increase in health expenditure per person, and increase in mortality and morbidity. Health being the basic right of man, strict preventive measures should be taken for and by these workers as they constitute a substantial number of chronically affected patients of the respiratory tract.

3.2 Health Hazards at Workplace and in the Surrounding

Exposure to dust has always remained a known cause of occupational lung diseases. Different regulatory authorities have always tried to produce and maintain occupational guidelines and standards to minimize the exposure of workers to such inhalable particles that can ultimately result in end-stage lung conditions.

There are different routes through which workers are exposed to these occupational hazards. These routes are percutaneous routes, respiratory routes, and oral routes (Davidson and Davidson 1984; Gray and Harrison 2004; WHO 1999).

The most common health hazards at workplace and in the surroundings are as follows:

3.2.1 Silicosis

Overexposure to free crystalline silica's dust leads to a fibrotic lung disease that is called silicosis. This is a serious lung condition, and if not treated on time, it can prove to be fatal. It is a slow but irreversible, progressive, and fatal condition of the lungs. The severity of the disease depends upon the exposure time and the amount of free crystalline silica that is inhaled and eventually gets deposited in the alveolar region (exchange of pure oxygen takes place).

Depending upon the duration of exposure, silicosis is divided into two major types, acute silicosis and chronic silicosis.

3.2.1.1 Acute Silicosis

Acute silicosis occurs after a few months to a maximum two years of exposure to silica's high concentration. The patient experiences difficulties in breathing (dyspnea), which later on may become very severe. This respiratory insufficiency is the result of fibrosis and emphysema which ultimately causes cor pulmonale and leads to death.

3.2.1.2 Chronic Silicosis

In chronic silicosis, symptoms show up after a decade after the person is exposed to low or moderate amounts of silica. The symptoms might be mild at first, and then with the passage of time, they will slowly worsen (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.2.2 Chronic Obstructive Pulmonary Disease (COPD)

Chronic obstructive pulmonary disease is characterized by poor airflow and longstanding breathing disorder. COPD mostly presents with dyspnea, shortness of breath, and productive cough. COPD is a progressive disorder and it worsens with the passage of time slowly affecting the quality of life. A person who suffers from COPD ultimately becomes so crippled that he/she cannot carry out his/her daily routine work easily because of difficulty in breathing. Emphysema and chronic bronchitis are now collectively named under the heading "COPD"

In developing countries, COPD is also the result of occupational health hazards. Prolonged exposure causes an inflammatory response in the lungs that leads to the narrowing of air passages and ultimately affecting the normal architecture of lung parenchymal tissue. This leads to poor exchange of gases inside the lung tissue, thus affecting the breathing of a person. Workplace exposure is believed to be the cause in 10–20% of the cases. Some industries producing high levels of dust like coal mines, cotton textile, silica, and fiberglass can lead to COPD (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.2.3 Pneumoconiosis

Pneumoconiosis is defined as “the accumulation of dust in the lungs and the tissue’s reaction to its presence”. It is basically caused by the dust inhaled in the workplace; that is why it is called occupational lung disease. The severity of Pneumoconiosis depends on the amount of dust particles inhaled. The most common type of it is called “miner lung”. Other forms of pneumoconiosis depend on inhalation of excessive amounts of iron oxide resulting in siderosis, inhalation of tiny particles causing stannosis, inhalation of beryllium causing berylliosis, talc, graphite, and mica (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.2.4 Lung Carcinoma

Many dust particles such as silica, asbestos, wood dust, and radioactive particles are known as carcinogens, leading to lung cancer, mesothelioma, nasal cancers, and blood carcinomas. Some particles, like those of silica, asbestos, and radioactive particles, get deposited in the lungs, causing cancer of the lung tissue. Carcinomas due to asbestos (mesothelioma) have been linked to occupations such as that of building maintenance, ships maintenance, etc.

The establishment of carcinoma depends upon the exposure time of workers to certain chemicals. The minimum the time between exposures, the minimum is the chance of development of Ca if proper preventive measures are taken (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.2.5 Skin Disorders

Skin being the largest organ of the body helps us to protect the inside of our body from the harsh environmental factors. Occupational skin disorders are caused when there is direct contact of a worker with one or more hazardous substances. Workers can come in contact with such substances via handling tools, dipping/immersion of objects or substances in chemicals, etc. These procedures lead to disruption of the normal barrier function of the skin.

The commonest occupational skin disorders include contact dermatitis, folliculitis, skin infections, and skin cancers.

The most common side effects are seen in hands and arms as they are most frequently in contact with chemicals in working areas. The commonest of all the above-mentioned conditions is contact dermatitis, which clinically appears as inflammation of skin, redness, dryness, blistering, scalding-like appearance, and starts to bleeds.

Infection of hair follicles means folliculitis. This condition is common in those workers who are exposed to minerals and soluble oils. Skin cancers are common in workers who deal in UV radiation industries, nuclear power plants, and industries dealing with tar products (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.2.6 Ophthalmic Disorders

Occupational ophthalmic diseases have a long latent period. Most of them cannot be treated, but all of them are preventable. Occupational eye illness can be divided into: chemical injuries; radiation injuries; electrical injuries; heat injuries; etc.

In industries, workers deal with different kinds of chemicals, especially liquids and gases. These are of major concern causing injuries to eyes, for example, if liquid chemicals splash into a worker's eyes giving him acidic/basic burns, it ultimately leads to the scarring of cornea if not treated on time. Same way, fumes, gases, and vapors can also damage the eyes.

Different forms of radiations, for example, UV radiations, infrared radiations, and high source visible light, can also damage the sensitive area of the eye that is called Retina. In industries like glassblowing and steel making, workers are exposed to high intensity of light which can cause irreparable damage.

Electrical cataracts have been reported to be a cause of electrical injuries.

Corneal tissue scaring and corneal damage are common in workers who deal with heat as a source of energy in industries (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.2.7 Occupational Renal Disorders

There are certain industries that have direct impact on renal functions of the workers working in them, for example, industries of mercury, cadmium, lead, and silica. These industries produce nephro toxins (those chemicals that affect renal functions via direct toxic action).

The most common occupational renal disorders are acute renal dysfunction and chronic renal insufficiency.

Acute renal dysfunction is of sudden onset and develops hours to days after the exposure to a specific toxin. It causes the necrosis of tubules and is also called acute tubular necrosis ATN. It is characterized by decreased output of urine (less than 500 ml/day). On microscopic examination of urine, there are renal tubular cells, cellular casts, and little or no proteins.

Chronic renal insufficiency develops slowly over time. Symptoms develop slowly and include nausea, vomiting, loss of appetite, stomatitis, nocturia, and seizures. However, final diagnosis is based on renal biopsy (Davidson and Davidson 1984; Gray and Harrison 2004; Richards 2003; WHO 1999).

3.3 Health Hazards Due to Inappropriate Management

The poor working conditions, not only at mines but also at workshops, increase the work-related issues and also make a big chunk of the population vulnerable to occupational diseases and disorders and also increase government budget on health-related issues (Jiskani et al. 2020).

Worldwide, the prevailing key issues in the marble sector are:

- Use of old techniques/machinery
- Financial constraints
- Institution mismanagement
- Lack of experts and technical knowledge
- Lack of workers' safety measures, etc.

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The prevailing issues call for a great attention of the government as well as the stakeholders towards health protection of the workers, provision of better working environment, (Jiskani et al. 2019) workers training, and implementation of strict guidelines.

3.4 Hazard Prevention and Control

Hazard prevention and safety measures should be taken into account in the workplace either in the quarry or in the marble workshops with increased emphasis on risk management. The risk management not only benefits in a healthier and happier workforce and increased productivity but also protects the health of the workers and promotes the economic well-being of the country. It requires the involvement and cooperation of management and administrative support, workforce with technical knowledge and experience, occupational health professionals, allocation of suitable financial resources, and political will. A multidisciplinary approach should design, implement, and maintain dust emission and control strategies to prevent health hazards and occupational disease at a workplace. The impact of these concerns over the whole field of occupational health and safety has been considered in an ILO publication (Brune 1997). Several measures for the prevention of health hazards and occupational diseases are grouped under three main headings: medical, engineering, and legislative.

3.4.1 Medical Measures

It is the basic requirement of occupational health. The implementation of medical measures includes periodical examination and clinical evaluation should be carried out at least once a year. In addition to workers' health history and physical examination, specific laboratory tests must be carried out every one or two years, such as spirometry and chest radiography in quarrymen exposed to dust as well as those exposed to noise in marble processing. In preplacement examination, the fresh candidate may totally be rejected or may be given a job on the basis of a thorough physical, biological, and radiological examinations. Special test for endemic disease and medical history of worker having anemia, hyper tension, kidney disease, family history like asthma, skin bladder disorders, occupational history, and social history (exposure if any other) must be considered before induction. First aid services must be provided at work in case of accident or any causality. There should be provision of medical as well as immunization services and health insurance schemes for workers and their families. Periodic inspection of working environment should be carried out for checking temperature, lighting, ventilation, humidity, noise, air pollution, and sanitation. Occupational physician should be familiar with the raw material processes and products manufactured and dust produced at workplace and adverse health consequences. Also, it is important to maintain the workers' health and disability record too. Arrange health education and counselling programs for workers to reinforce them to use PPE (masks, gloves, and goggles) in workplace to protect their respiratory airways and lungs (Angotzi et al. 2005; Park 2005).

3.4.2 Engineering Measures

The other most significant measures for reducing health hazards in the marble industry are appropriate engineering procedures, because worldwide, this industry is known as the most labor-intensive industry. There should be adequate building design for industry, good housekeeping to boost the morale of the worker, and general ventilation and for dust, which settle down on the machinery, floor, racks, and beams should be promptly removed by vacuum cleaner or by wetting agent. The wet method should be tried to combat dust with regular water spray as moisture in processes of grinding, sieving, and mixing. Hood should be used for suction of dust, fumes, and gases into the collecting units. Mask, apron, gloves, respirator, and other protective equipment should be regularly used and general hygiene should be maintained. The workers should be educated about the type of respirator to use and when and how to use. For protection against noise pollution and other workplace factors, air plugs, ear muffs, helmets, safety shoes, gumboots, barrier creams, screen, and goggles should be reinforced and the worker should be trained for the appropriate use of the protective devices. The good machined plant will play a positive role in reducing the hazards of the contact with the harmful substances to the fullest possible extent. Dermatitis can be prevented if hand mixing is replaced by good mechanical devices. Grinding machine can be completely enclosed and combined with exhaust ventilation. Further research and periodical environmental surveys should be carried to determine whether the dust and other gases escaping in the atmosphere are within the permissible limits or not (Park 2005).

3.4.3 Legislation

Many countries around the world have comprehensive occupational health legislations, like the "Occupational Safety and Health Act (1970) legislation in the United States. In 1974, a regulation was enacted in the United Kingdom, "Health and Safety at Work Act," and further, the European Union adopted a policy in 1989 on the "Fundamental Social Rights of the Workers". The main goal of occupational health legislation is to ensure a safe and healthy working environment along with strong emphasis on primary prevention of health hazards. Proper implementation of legislation develops and promotes a positive social culture and enhances smooth operations and increases the productivity of the working environment. Different countries have different occupational safety and health practices such as legislation, guideline, enforcement, and incentives. Some nations adopted a pooling system and some have health and safety insurance system for their workers. For instance, some member states in the European Union promote Occupational Safety and Health (OSH) programs by providing grants and subsidies and tax system incentives for compliance (Elsler 2007; Esler et al. 2010). But significant variations were observed in compliance of occupational safety and health between countries, economic factors, and sizes of enterprise because the number of fatalities is more in the developing countries as compared to developed countries (World Bank 1995).

3.5 Conclusion

International Agency for Research on Cancer (IARC) classified marble dust, heavy metals, and crystalline silica as carcinogens in 1997. International Labor organization (1919) protects workers' right and thus demands effective prevention techniques, safe working places, and awareness programs regarding commonly addressed health issues for the workers working in industries. If effective treatment is not given to workers who have developed the above-mentioned health issues at the right time, they might develop an end-stage lung disease (chronic lung disease/ lung cancer). Different epidemiological studies show that workers exposed to marble dust have an increased risk of developing chronic asthma, chronic bronchitis, and impaired lung functions and even lung cancer. Marble dust other than having serious health issues can have a considerable economic impact as well; like decrease in working productivity, increase in health expenditure per person, and increase in mortality and morbidity. Health being the basic right of man, strict preventive measures should be taken for and by these workers as they constitute a substantial number of chronically affected patients of the respiratory tract.

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Chapter 4
Environmental Degradation and Micro-pollutants in Light of Environmental Laws

Furqan Mahmud Butt, Umair Bin Nisar, and Toqeer Ahmed

Abstract Environment is everything surrounding human beings. Biotic and abiotic contributors of environment affect natural, build, and social aspects of human beings. For healthy livelihood, human beings are dependent on environment. The increase in population, urbanization, and industrialization is having severe effect on world environment. Climate change further aggravates the situation. Despite several laws drafted for the awareness and reduction of environmental degradation, no profound results have been obtained. Environmental issues induce several negative externalities and contribute to market failure, thus affecting economic growth; this becomes a serious problem in developing and underdeveloped countries where there are no strong rules for reducing these negative externalities. Pakistan is ranked fifth among the most affected countries in terms of climate change despite the contribution of less than 01% in emissions. The air quality index of Pakistan is getting poor with every passing day; Lahore and Faisalabad were ranked as most polluted cities all over the world in terms of air quality index. The government of Pakistan has taken some time to realize environmental degradation and has initiated projects like billion tree tsunami and air quality laws to address climate change and environmental degradation.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_4

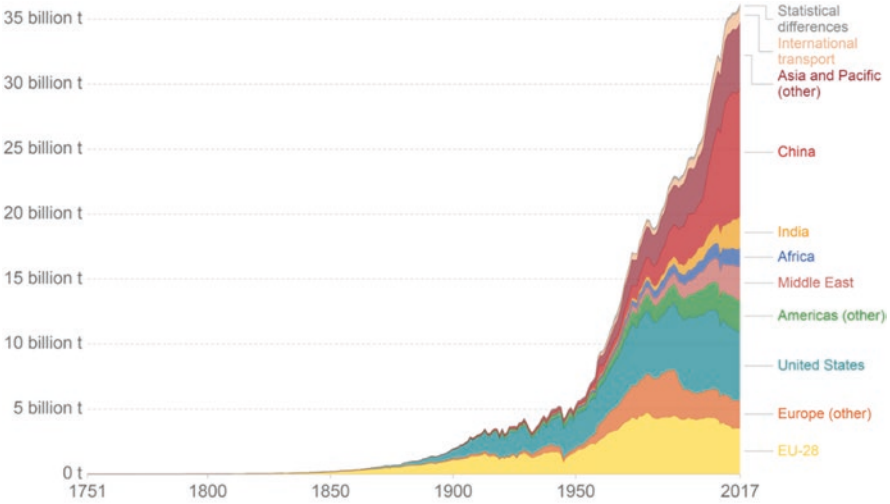
4.1 Pollution and Environment

Pollution is addition of harmful chemicals/contaminants into the atmosphere which can cause severe damage to health and the environment (Nathanson 2015), whereas the environment is everything that surrounds us and comprises both biotic and abiotic components. These components represent both living and nonliving things in ecosystems. These components represent a relationship between producers, consumers, and decomposers that relay on fluctuations of temperature air and sunlight. With increase in population, urbanization, and industrial developments, the environment is severely affected (Nisar et al. 2018); most of the pollution induced in the environment is the result of automobiles, industrial sector, and solid wastes (Ekins 2010). World population has drastically increased over the years and if it continuously exceeds at the same pace, it will cause severe loss to environment (Hamrick 2004), as population increase demands utilization of more resources thus resulting in overburden on natural resources and increase in environmental degradation (Behrens et al. 2007). World Health Organization (WHO) has estimated that about 4.2 million children die due to ground-level air pollution, causing heart disease, lung cancer, stroke, and acute respiratory infections (WHO 2018). Pollution is unequally induced by some prominent countries in the world, but price is paid by every living organism on earth. Despite the steps taken after Paris accord (2016), the CO2 emissions are continuously increasing, which are causing an increase in temperatures. With China being the largest CO2 emitter, it accounts for more than one-quarter of emissions, followed by the USA with 15% emissions, the European Union (EU-28) with 10%, followed by India and Russia with 7% and 5%, respectively (Lelieveld et al. 2019). A regular passenger car emits around 4.6 metric tons of pollutants each year (Masiol et al. 2014). The average gasoline vehicle on the road has a fuel efficiency of about 22 miles per gallon, with an average annual travel distance of about 11,500 miles (this statement does not apply to developing nations, where average vehicle fuel usage is between 10 and 15 miles per km). At this proportion, every gallon of fuel burned produces about 8,887 grammes of CO_2 (Pachauri et al. 2014). Annual total CO_2 emissions by world region are shown in Fig. 4.1.

Increase in population has severe effect on waste generation which plays a vital role in waste generation. The world annually generates 2.01 billion tons of municipal solid waste, out of which 33% is not managed in environmentally friendly manner. Waste generation by single individual worldwide is about 0.74 kg per day ranging from 0.11 to 4.54 kg. The future projection portrays the generation of wastes could go up to 3.40 billion tons annually, which shows a drastic increase from 2.01 billion tons today (Kaza et al. 2018). Share of global population and municipal solid waste for G20 countries has been shown in Fig. 4.2.

The situation gets worse in developing countries, especially in the SAARC countries where population is increasing rapidly and resources are overutilized, and as a result, pollution is severely affecting the environment (Hasnat et al. 2018).

The global cost of air pollution caused by fossil fuels in South Asia is $8 billion a day (Liu et al. 2015), or roughly 3.3% of the entire world's economic output



Source: Carbon Dioxide Information Analysis Center (CDIAC); Global Carbon Project (GCP)
Note: The difference between the global estimate and the sum of national totals is labeled "Statistical differences".
OurWorldInData.org/co2-and-other-greenhouse-gas-emissions • CC BY

Fig. 4.1 Annual total CO_2 emissions by world region. (Ritchie and Roser 2017)

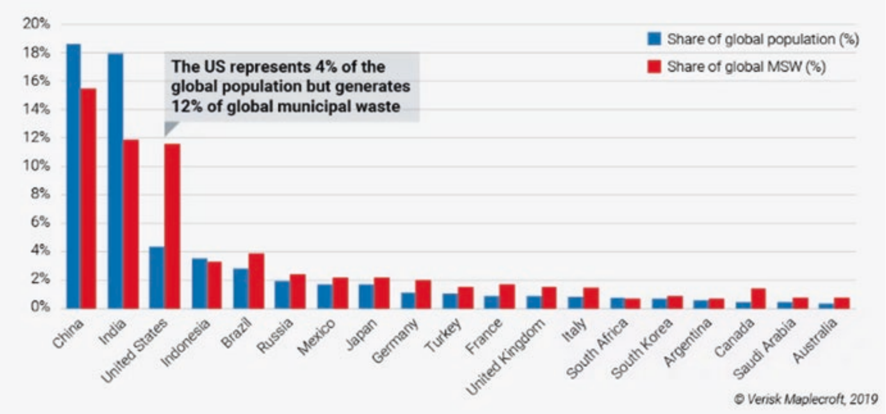


Fig. 4.2 Showing share of global population and municipal solid waste for G20 countries. (Ritchie and Roser 2017)

(CREA and Greenpeace Southeast Asia report). Pakistan is one of the leading countries in Southeast Asia; despite the environmental laws, the implementation faces a big problem.

Presently, several environment-related laws such as pesticide control, motor vehicles emission's regulation, and control of industrial pollution through Pakistan Environment Protection Ordinance 1983 exist. However, these laws are not being implemented fully and effectively.

4.2 Micro-pollutants and Environment

The phrase “micro-pollutants” refers to various chemicals found in trace concentrations in the water-soil-air matrix, ranging from micrograms to picograms per liter, and emphasizes the substances’ small concentrations range. Micro-pollutants include pharmaceuticals, cosmetics, synthetic musk, industrial chemical substances, pests, and disinfectants. Agricultural and nonagricultural sources release these pollutants into the water supply (Antakyali et al. 2015). Micro-pollutants are anthropogenic contaminants that appear in the marine ecosystem well above a (potential) normal background level because of human activities, but at trace levels -(Stamm et al. 2016). As a result, micro contaminants are characterized by their anthropogenic origin and low concentration presence, and thousands of chemicals fall into this group (Schwarzenbach et al. 2006). Ice covers more than 70% of the earth’s surface, with 97.2% contained in oceans, 2.15% in ice sheets and glaciers, with just 0.65% fresh water available for use. Water is used in agriculture, industries, households, and in every aspect of life (Lutgens et al. 2006).

Around onefifth of the planet’s population lack access to clean drinking water, and two-fifths suffer from unsanitary living conditions (WWAP 2003). Waterborne pathogens kill over 2 million people per year, the majority of whom are children under the age of five. The growing chemical contamination of surface and groundwaters, which has relatively unknown long-term consequences on marine life and human health, could easily contribute to a similar or even larger crisis. More than a third of the world’s clean freshwater is used for farming, commercial, and domestic uses, and most of these operations pollute the water with a variety of synthetic and geogenic compounds. As a result, it should come as no surprise that chemical contamination of aquatic environments has become a significant public issue in almost every nation (Schwarzenbach et al. 2006).

The municipal drainage scheme and dispersed sources such as irrigation provide input to the aquatic ecosystem. Persistent substances can move through the wastewater treatment plant (WWTP) without being broken down. In addition, input of easily degradable pollutants happens by out-of-date WWTPs and flood water or mixed sewage overflows on a regular basis. Micro-pollutants may accumulate along the strip or in lakes if many WWTPs drain into the same water body. Micro-pollutants from urban runoff can contaminate groundwater used for drinking water through infiltration of polluted surface water (Gälli et al. 2009). Industry and communities use approximately 10% of the commonly available water, resulting in a current of wastewater that drains or makes its way into rivers, wetlands, reservoirs, or coastal seas (WWAP 2003).

Various chemical compounds of different proportions can be found in these wastewaters. Around 300 million tons of artificial chemicals used in commercial and consumer goods end up in natural waters every year (Schwarzenbach et al. 2006). Agricultural sector, which consumes 140 million tons of fertilizer as well as several million tons of chemicals per year, contributes to additional problems related to water pollution (FAO 2006). For example, in the European Union, there are over

100,000 identified chemical compounds, among which 30,000–70,000 are used on a regular basis (EINECS, European Inventory of Existing Chemical Substances). Another significant cause of water pollution is the consumption of 0.4 million tons of oil and diesel components because of accidental spills. The infiltration of salty water into reservoirs due to aquifer overexploitation; the human-driven mobilization of naturally occurring geogenic hazardous chemicals, such as heavy metals and metalloids; and the biological development of pesticides and malodorous compounds are all notable causes of pollution (Schwarzenbach et al. 2006).

To date, there is a scarcity of a successful and long-term global plan to combat this pervasive and still unnoticed contamination of marine ecosystems. In highly developed nations, source controls and technological infrastructure, such as wastewater treatment plants, serve as partial hurdles, but significant obstacles remain (Schwarzenbach et al. 2006). The source, action, and management of the limited number of macro-pollutants found at μg/liter to mg/liter concentrations, such as acids, salts, nutrients, and natural organic matter, are relatively well-understood: Increased primary productivity, oxygen loss, and harmful algal blooms will all result from high nutrient loads. Predicting environmental responses, optimizing treatment technologies, and developing coordinated policies at the size of river basins are all problems in such situations (Mengis et al. 1997; Jackson et al. 2001).

Several investigations in Europe and North America have recently confirmed the detection of these "micro-pollutants" in wastewater, surface water, ground water, and drinking water (Ternes 1998; Daughton and Ternes 1999; Daughton and Jones-Lepp 2001; Heberer 2002; Kolpin et al. 2002; Calamari et al. 2003; Frick and Zaugg 2003; Boxall et al. 2004; Metcalfe et al. 2004; Ternes et al. 2004; Glassmeyer et al. 2005; Sedlak et al. 2005; Loraine and Pettigrove 2006). The quantities of these substances in surface waters were as low as a few micrograms per liter. Pollutants were found in ground water and drinking water at levels as low as one microgram per liter. Eventually, there are fears that other pharmaceuticals intended for specific biological causes could be harmful for the environment as well (Ternes et al 2004). For the contraceptive 17α-ethinylestradiol (EE2) and the antiphlogistic diclofenac, respectively, estrogenic effects and renal alterations at environmental concentration levels have already been published (Routledge et al. 1998; Triebskorn et al. 2004). It has been highlighted and confirmed that residues from these micro-pollutants are likely to cause renal failure in vultures, resulting in a drastic reduction of the vulture population in Pakistan (by more than 95%) (Oaks et al. 2004).

Water, as we all know, is necessary for human socioeconomic activities. However, owing to overexploitation of water resources and deforestation, stresses on the water system have increased, posing a threat to human health and long-term socioeconomic stability (Vörösmarty et al. 2010; Shevah 2014). This dire situation necessitates elucidating the relationships between the water ecosystem and socioeconomic processes, as well as using appropriate water environment management instruments to deter water environmental destruction and promote socioeconomic growth that is consistent with the water environment's viability. As a result, complete awareness of the social, economic, and environmental settings is needed for both water quality management and the supply and demand balancing of water supplies (Yang et al.

2015). Evaluating the influence of micro-pollutants in water bodies is a daunting challenge that necessitates enhanced analytical and modelling techniques to investigate the distribution, bioavailability, and biological effects of single compounds and chemical mixtures. Current and emerging methods for classifying chemicals based on their ability to affect humans and the atmosphere must also be refined. Micro-pollutant mitigation methods, as well as techniques to mitigate their penetration into the water systems, need to be further developed. The development of "green" chemistry, which involves the creation of more environmentally sustainable manufacturing processes and materials, is a complementary solution (Schwarzenbach et al. 2006).

4.3 Landscape of Environmental Laws for Pollution Remediation and Micro-pollutants

Environmental law is a generalized term that encompasses various laws that support the environment (Sands and Peel 2006). It can be defined as a collection of different common laws and pacts that govern how humans will interact with Mother Nature (Hempel 1996). The purpose of making such laws is to protect the environment and devise some rules for utilizing the natural resources (Palmer 1992) Most of these laws restrict pollution, stress on the sensible use of natural resources, and protect forestation and animal population (Wiggins et al. 2004). The vast field of environmental laws includes topics in legal settings; for example, regulation of standards of emission in Germany, green great wall initiative in China, and the bottle return law in the United States are among the several other laws that focus on environmental protection. Environmental laws are relatively new and lawmakers started documenting these laws in the twentieth century (Palmer 2002). History reveals the implementation of laws to safeguard environmental issues regarding human health as a societal part; in 80 AD, a legislation was passed by the senate of Rome to protect water supply for drinking and bathing. In the fourteenth century, the British banned burning of coal and dumping waste into waterways (Evans 1997). Benjamin Franklin organized many trips to correct disposal of trash when William Penn, the Quaker leader of the English colony of Pennsylvania, issued an order to conserve one acre of woodland for every 5 acres of land acquired for habitation. The British government established rules to limit the harmful consequences of coal burning and chemical manufacturing on humans and the environment in the mid-nineteenth century, when environmental pollution was at its worst (owing to the industrial revolution) (Fenger 2009). Twelve European nations signed an agreement for the preservation of agriculturally valuable birds around twenty-first century (Ferrero-García 2013). The United States, Japan, Russia, and the United Kingdom signed a treaty in 1911 to preserve and conserve fur seals. This treaty, which was ratified by the United States and the United Kingdom (on behalf of Canada) in 1916, cleared the way for the protection of migrating birds. It was later extended to Mexico in

1936 (Dorsey 2009). The conference for the conservation of flora and fauna in Africa in the form of nature reserves was adopted by Belgium, Egypt, Italy, Portugal, South Africa, Sudan, and the United Kingdom in 1930, signaling a shift in the framework towards flora and fauna sustainability in their original environment. Spain and France, while signing the agreement, never ratified it (Adams 2013).

The environmental movement began to gain traction in the West in 1960, both politically and philosophically. Or, to put it another way, many events/incidents led to the understanding of the necessity for environmental preservation. The stage was set by Rachel Carson's publication of Silent Spring (Carson 1962), which studied chlorinated hydrocarbon insecticides and the damage they produced (Gavrilescu et al. 2015). This work led to the realization of actual environmental hazards on broader scale. After this realization, majority of environmental developments took place at that time. Lawmakers began to pass environmental laws in the twentieth century. United States government passed several environmental laws that challenged the status quo dominated by industrialists, including solid waste disposal, air and water pollution, and endangered species protection. The final step was the establishment of an environmental protection agency to oversee the implementation of these laws (Kolln and Prakash 2002). This environmental legislation expanded the national government's role, as these issues had previously been deemed to be the responsibility of local governments.

There has been rapid industrialization in Japan, especially after world war-II (Tsurumi 2015). As a result of this industrialization, industrial wastes were released indiscriminately into the human food cycle. The tragedy in Minamata, where a significant number of people were poisoned by mercury after eating a fish tainted with industrial toxins, sparked the movement (Harada 1995). This resulted in consideration by the Japanese government in the early 1960s to formulate a comprehensive pollution control policy; the efforts materialized in 1967 when Japan created the first law for Environmental Pollution Control (Sumikura 1998).

After realization by leading countries in the world, several other countries started joining in the issue by devising or joining pacts for several environmentally friendly laws. The Ramsar Convention, which focuses on Wetlands of International Importance, particularly as Waterfowl Habitat, was signed by thirty-four countries in 1971. This agreement went into effect in 1975, and it presently has over 100 signatories (Gardner and Davidson 2011). The accord required participating countries to establish one protected wetland area so that the importance of wetlands in preserving natural balance could be recognized. As countries became more aware of environmental issues, they began to work together to address them. The United Nations conference in 1972 led to the formation of the United Nations Environment Program (UNEP) (Ivanova 2007). Despite its little influence in implying the sanctions on different countries, it serves as a baseline for many consortiums to follow. Two commissions directly raised under the influence of UNEP were established in 1972 (marine life) and 1973 (endangered species of flora and fauna), respectively (Coggins 1974).

European countries were slow responders in managing environmental legislations until the Stockholm conference. In 1972, European countries started realizing that industrial growth should be balanced with environmental issues (Coggins 1974). In the same year, the European Commission published its first environmental implementation strategy, and European governments began to make environmental policy a priority (Wallace et al. 2020). Quoting the example of Germany, the public perception about environmental legislations changed drastically in the 1980s, which became evident when they elected the Green Party in Germany as a representative in the national parliament in 1983 due to its strict environmental campaign; at the end of the twentieth century, this party got its share in government and developed Germany extensive policies (Otto and Steinhardt 2014). Later on, with integration with Netherlands and Denmark (green troika), it took environmental laws to the next level (Liefferink and Andersen 1998). The Chernobyl incident marked the development in transboundary effects of environmental degradation as the countries that were facing the downwind effects of the incident had to devise some laws and reduce the consumption of daily intakes of food (Howland 1987). This incident generated two international agreements. The first convention was on sharing of information on priority basis of an incident. The second convention focused on assistance to prevent the loss of life and environment due to nuclear incidents. These two conventions were drastically drafted and implemented in 1986 (IAEA 2016). Another convention on nuclear prevention was applied in 1994 that compelled the signatories to develop basic procedures to safely manage the nuclear assets.

The interesting thing regarding the unreliability of datasets associated with impacts of human activities is often a problem. It has always been a challenge to write laws that handle human involvements; these rules were frequently adaptable enough to meet scientific and technical advances.

Convention in Vienna on the Depletion of the Ozone Layer was another step toward solving worldwide environmental problems (Bodansky 2001). In 1995, the breakthrough in global environmental development was the UN conference on environmental development, known as “Earth Summit,” in which 178 countries adopted this law (Grub et al. 2019). The environmental laws after 1995 were seen in global perspective. Another important development during this year (1995) was the development of Intergovernmental Panel on Climate Change (IPCC) jointly by the UNEP and the world meteorological organization (WMO) (Metz et al. 2001). IPCC was a global initiative to study the human influence on global temperature changes. The work of IPCC was criticized by communities for using insufficient datasets as reports ring the bell about severe climate changes due to emissions. Kyoto protocol came as an answer to the IPCC report critics and assigned the signatories emission targets for sustainable development (Meyer 1999). This protocol introduced a brilliant concept of emissions trading that was intended for controlled emissions throughout the world. This protocol allowed the developed countries to sell their emission reduction units, which they have earned by controlling the emission well below the authorized limits. In addition, those developed countries can also earn these reduction units by supporting the developing countries in terms of supplying the technology for the reduction of emissions. It is a wonderful rectification protocol, but since its adoption, it faced strong opposition, especially from developed countries such as the United States (Hovi et al. 2012).

With development in analytical methods involving detection of concentrations from micro to nanograms in water samples, new pollution directories for the world have been opened (Allan et al. 2006). Unfortunately, now new legislations/laws are being devised to tackle the micro-pollutants that are causing a serious threat to the human populations. The main reason for increase in micro-pollutants is the growing population and industrialization. Several research projects in European countries (Riskwa2, Strategie, COHOBAI etc.) are identified and addressed reduction measure for substance pollution in water (Amann et al. 2011). The major contribution was by German Environment Agency (also known as Umweltbundesamt), which in collaboration with other international partners (Rhine protection commission) has devised several strategies and decisions on this matter. The developments have occurred in the form of competence centers and equipping 19 treatment plants with fourth treatment stage (NA 2000)

Switzerland has introduced several additional measures in wastewater treatment since 2016 in addition to the introduction of several laws (Czekalski et al. 2014). European water frame directive (WFD) also stressed and provided directives on the reduction and prevention of micro-pollutants. These legislations focus on ecosystems biodiversity and availability of drinking water by using natural treatment methods. Micro-pollutants have become a growing world problem and are often linked with climate change (Delpla et al. 2009). Ever-growing climatological changes throughout the world have triggered higher concentrations of micro-pollutants in rivers, oceans, and subsurface aquifer system. It is the need of time to address these issues considering growing climate changes. The laws associated with micro-pollutants are at early stage. Most commendable work is done by European Union (EU) with legislations focusing on the treatment at source of micro-pollutants. The micro-pollutants from pharmaceutical industry and plastic industry are stressed to be treated at the source before dumping them in water. German water protection policy has set up benchmarks in addressing the issues associated with micro-pollutants that have small concentrations and can end up in water bodies, which later become part of the food chain, thus having adverse effects on health (Metz 2011).

Actors participating in development policy and development in the rest of the world have discussed how to deal with the problem. To decrease the use of dangerous pollutants at the source, proposed legislative measures might target consumers, farmers, or industry (Press 2020). An alternative policy approach addresses the end of pipe agreement that focuses on the treatment of sewage before introducing it to the water body (Triebskorn et al. 2019). The three principles (source control, polluter pays, and end of pipe treatment) legislated in the EU, if implemented in true sense, can set an example for rectification of micro-pollutants, but despite strong environmental laws' implementation, EU has lot more to do in devising laws for addressing micro-pollutants. The same stands for the rest of the world, where majority of countries don't have details regarding micro-pollutants' effects on their environment; thus, a strong legislation about awareness and eradication is desired all over the world.

4.4 Micro-pollutants: A Threat to Growing Economy of Pakistan

Pakistan, like other developing countries around the world, is experiencing severe water scarcity and pollution. The country's available water supplies are almost depleted. The rising toxicity of Pakistan's drinking water supplies, as well as the implications on human health and the environment, is a major cause of concern (Azizullah et al. 2011).

Since ground aquifers provide water to most of Pakistan's population (roughly 70%), surface water is also a significant source of water for irrigation, drinking, and domestic uses (Aziz 2005). The most basic source of supply in most Pakistani cities is groundwater, which includes a variety of pathogens, including many infectious, bacterial, and protozoan agents, resulting in 2.5 million deaths per year from endemic diarrheal disease (Daud et al. 2017). Every year, an estimated 250,000 children die because of waterborne diseases. Diseases such as diarrhea, typhoid, intestinal worms, and hepatitis are caused by insufficient quantities or consistency of water, as well as a shortage of sanitation facilities. The annual risk of drinking contaminated water is projected to be Rs 114 billion. Similarly, patients with waterborne diseases occupy 20–40% of all hospital beds in Pakistan (Khalid and Khaver 2019). The consequences of the lack of clean drinking water and sanitation facilities are observed not only on public health, but also on the economy. Pakistan spends Rs 365 billion a year on environmental depletion. A third of this amount is spent on health-related costs because of insufficient water supplies and sanitation (Mughal 2016).

Contaminated water is the most common cause of water contamination, which has a negative impact on Pakistan's economy and has a negative impact on Pakistani people's living standards (Ahmad et al. 2019). According to an estimate of the gross economic burden of inadequate sanitation, it was calculated to be 343.7 billion PKR (US$5.7 billion). This is the equivalent of 3.94% of Pakistan's GDP. The direct financial burden, which is equal to 0.8% of GDP, is 69.52 billion Pakistani rupees (US$1.15 billion). Most overall economic costs were attributed to health-related issues. They accounted for 87.16% of all quantified economic expenses, or 3.43% of gross domestic product. The gross economic burden on health is projected to be 299.55 billion PKR (US$4.93 billion), with financial losses accounting for 48.76 billion PKR (US$801.53 million). The economic burden of inadequate sanitation due to water is projected to be 15.98 billion PKR (US$262.68 million), or 0.18% of GDP. This accounts for 4.65% of the overall damage, with financial losses of 15.51 billion PKR (US$254.85 million) accounting for 15.51 billion PKR (US$254.85 million). Other welfare losses, such as consumer needs (which include comfort and acceptability, privacy and ease, stability, avoidance of conflict, status and popularity, and time loss), are estimated to be 22.77 billion PKR (US$374.4 million), or 6.63% of overall impacts and 0.26% of GDP. Most of the expense comes from lost time due to household access to free defecation sites (16.5 billion PKR [US$271.6 million]), which accounts for 73% of all welfare costs or 5% of all costs (Nishat 2013).

According to a preliminary estimate, Pakistan is losing 25% of its possible crop production (Abedullah 2006). The contribution of environmental problems to Pakistan's economy is estimated to be about 1.8 billion dollars. This expenditure was attributed to the costs that citizens and the country expend on welfare, as well as the lack of productivity that happens as a result of labor and individual absenteeism from factories, workplaces, and schools due to poor health (Brandon and Ramankutty 1994). In January of 2000, the Ministry of Environment released a report stating that Pakistan spends about 17 million dollars per year on pollution-related issues, especially expenses related to clean-up activities, but that 84 million US dollars are needed to fully resolve Pakistan's environmental problems (Ahmad et al. 2019). This reduction in pollution would also contribute to the long-term survival of Pakistan's natural resources. The additional benefits that will most likely be provided by preserving existing capital have not yet been factored into the above calculations (Abedullah 2006).

4.5 Environmental Policy and Economic Relation in Pakistan

Every action done by the government, corporation, or other public or private entity to identify the impact of human activities on the environment, including actions aimed at preventing or reducing negative consequences on environments, is referred to as environmental policy (Bueren 2019). Air and water contamination, landfill control, habitat conservation, biodiversity preservation, nature conservation, habitats, and endangered animals are some of the topics that are addressed by environmental policies (Eccleston and March 2011). For example, environmental policies may be tackled by the introduction of a global eco-energy policy to resolve global warming and climate change concerns (Banovac et al. 2017). The policies include economic planning as well as the control of harmful substances such as pesticides and various types of industrial waste. This approach should be used to intentionally manipulate human behavior to minimize harmful repercussions for the biophysical climate and natural resources, as well as to guarantee that environmental changes do not have unfavorable consequences for humans (Jordan 2005).

Pakistan's Environmental Policy is focused on a collaborative approach to achieving long-term sustainability goals through constitutionally, administratively, and professionally strong organizations. On December 6, 1997, the Pakistan Environmental Protection Act was enacted to provide for environmental protection, restoration, recovery, and enhancement, as well as pollution prevention and control and the promotion of sustainable development (Ministry of Environment Government of Pakistan 2005).

The National Environment Policy establishes an overarching mechanism for tackling Pakistan's environmental challenges, including degradation of freshwater sources and coastal waterways, air pollution, inadequate waste management, erosion, habitat depletion, desertification, natural disasters, and climate change. It also offers recommendations on how to resolve cross-sectoral issues, as well as the root causes of environmental pollution and international commitments (Ministry of Environment 2005). Economic policies that ensure optimal resource use are a prerequisite, but not adequate, for establishing effective environmental incentives. Environmental strategies are often required to resolve industry failures that result in environmental concerns. Command and control policies and opportunity or market-based policies are two types of policies that can be used to fix environmental concerns. Government-imposed environmental quality requirements on emissions, technology type, or input usage are examples of command-and-control policies. Prices are used in incentive- or market-based programs to attempt to affect waste and resource utilization. Despite the benefits of market-based interventions, Pakistan, like many other countries, has largely relied on regulation policies. However, these initiatives have frequently struggled to produce outcomes because regulating agencies lack the financial and technological tools to successfully enforce them (Faruqee and Kemal 1996). In April of 1997, Pakistan has adopted market-oriented policy reform, which would support both economic development and the climate if it is enforced and extended rapidly. Non-distortionary economic policies that encourage economic development by optimizing resource distribution often generate adequate conditions for environmental conservation, according to experience in other countries. Of necessity, sound economic policies are insufficient. Environmental policies that fix industry failures are also expected. Economic policy failures also lead to environmental issues, such as forest, rangeland, and rainfed and irrigated agriculture. Subsidies for irrigation water, for example, allow farmers to overuse water, worsening the irrigated agriculture's waterlogging and salinity issues. Deforestation and depletion of Pakistan's forestland have been compounded by a loss of property rights in communal forests and a failure to provide local people with resources to engage in forest-management decisions (Faruqee 1997).

4.6 Steps Taken by Government to Tackle Micro-pollution

Plastic pollution is caused by the deposition of plastic trash in the ecosystem. The Greek term "plastikos" indicates "ability to be changed or molded into numerous forms/shapes." (Mukheed and Khan 2020). Plastic waste with a diameter of less than 5 mm is referred to as microplastics (Betts 2008), which are either immediately released into the atmosphere or created when larger plastic debris degrades. Microplastics are graded as primary or secondary microplastics based on how they are produced. Microplastics, such as microbeads in cosmetics, are manufactured on a microscale. The breakdown of macroplastic produces secondary microplastics (Horton et al. 2017).

The sources of microplastics in aquatic and coastal environments have already been addressed. (Duis and Coors 2016). Sewage leakage, microfibers from textiles, contaminants emitted from paints, and tires are all significant causes of micro-pollution (Browne et al. 2011; Klein et al. 2015; Coppock et al. 2017). Microplastics have been discovered in a variety of aquatic ecosystems, such as wastewater treatment wastes, industrial runoff, and wastewater discharge following heavy rain occurrences (Anderson et al. 2016).

Microplastics have become a regular part of the global ecosystem, posing a significant danger to marine and coastal environments (Cai et al. 2017; Bordós et al. 2019; Koongolla et al. 2018). The presence, distribution, and impact of microplastics have been extensively researched in aquatic environments, but less focus has been paid to freshwater systems, and as a result, research on microplastic pollution of rivers and lakes is scarce when compared to oceans (Zhang et al. 2016; Sruthy and Ramasamy 2017). Because of their smaller size range, microplastics are eaten by invertebrates, fish, and marine animals because they are identical to food sources (Thushari et al. 2017).

Many nations have banned the commercial usage of microplastics like microbeads owing to their harmful consequences. The Microbead-Free Water Act, for instance, was passed in the United States in 2015, prohibiting the use of microbeads (NOAA 2018). Canada approved legislation limiting the use of microbeads in 2017 (Lam et al. 2018). In 2016, the Australian Microbead Working Group was formed with the goal of negotiating voluntary agreements with the cosmetics sector to eradicate microbeads from rinse-off cosmetics (EPAN 2016; Lam et al. 2018). Since these laws were just newly enacted, the result is still unknown. Taiwan's Waste Disposal Act, which is administered by the Environmental Protection Agency, bans the use of microbeads (Central News Agency 2018). In Pakistan, there is no clear legislation on microplastic contamination. In Islamabad and the capitals of other provinces of Pakistan, regulations governing the use of plastic items such as polyethylene bags are made, in which the use of plastic bags is banned (Pakistan Environmental Protection Agency 2019). These rules prohibiting the use of plastics would act as a starting point for the creation of further legislation to combat plastic waste. Implementing a ban on the use of plastic materials would further mitigate microplastic waste by preventing unsafe disposal (Irfan et al. 2020).

In South Asia, Pakistan has the highest proportion of mismanaged plastic. Bangladesh, France, and Rwanda are among the countries that have outlawed the use of plastic bags. Plastic bags are prohibited in Pakistan's Capital Territory, Islamabad, as well as several other towns such as Lahore and Hunza, according to a Statutory Regulatory Order (SRO). Currently, there is no federal or regional regulatory system in place to address the issues of single-use plastics and plastic trash treatment in general (Mukheed and Khan 2020). Plastics are less expensive, more dependable, and more widely available in the country; in a struggling economy, a blanket prohibition will lead to the loss of many employments or a drop in consumer footfall if no other bag is available. Though PET bottles and other high-value plastics are scavenged, most of the single-use nonbiodegradable plastic ends up in uncovered waste sinks, landfills, or public sewers, clogging sewage treatment systems (Mukheed and Khan 2020). The root of the issue has been identified as the current municipal waste management scheme, which prioritizes picking waste from collection point and properly disposing of it in city outskirts without filtering, resource conservation, or recycling, as well as failing to require communities to take responsibility (Mukheed and Khan 2020). We all know that waste management firms cannot address this complicated challenge on their own; they need comprehensive policy, technology, and funding from both public and private stakeholders. Every year, 30 million tons of solid waste are generated in Pakistan, with plastics accounting for 9% of that total. A total of 55 billion plastic bags are manufactured here each year. These single-use nonbiodegradable bags typically end up in open waste dumps, landfills, or urban sewers, clogging waste collection systems and the service costs. Existing municipal waste management strategies exacerbate the problem by focusing solely on collecting garbage from community bins and dumping it on the outskirts of cities without segregation, resource reuse, or recycling, as well as failure to encourage people to act properly (Qari and Shaffat 2015; Rajak et al. 2019; Dawei and Stigter 2010).

In 2017, Pakistan introduced oxo-biodegradable technologies as a tool to combat plastic waste. After their useful life, oxy-biodegradable plastics completely biodegrade in the environment, leaving no adverse effects on the environment. As a result, all the problems related to plastic pollution will be addressed. After close analysis of both alternative solutions and empirical facts, the legislation was formulated (Daily Times Pakistan 2020). In 2019, the Islamabad Capital Territory adopted a new model, prohibiting the use of plastic bags and encouraging the use of biodegradable bags. The Ministry of Climate Change took the initiative (MoCC). The MoCC is trying to ensure that the prohibition is fully implemented by enforcing harsh penalties and hefty fines on anyone who break it. Polypropylene bags are nonbiodegradable; as major commercial polymers, polyethylene and polypropylene are extremely resistant to biodegradation, i.e., degradation by microorganisms (Mukheed and Khan 2020). Authorities have overlooked an important fact: polyethylene is not the only pollutant in the world. Plastic contamination is also caused by polypropylene and other single-use plastics. Nonwoven PP, BOPP, CPP, Metalized films, WPP, and shrink wraps are often found in single-use materials that are discarded in the field. The negative consequences of plastic waste accumulation are rapidly growing. As a result, removing them from the ecosystem is important (Daily Times Pakistan 2020). Plastic waste accumulation has a growing number of negative consequences. Therefore, it is important that they be excluded from the community. Fabric-like nonwoven polypropylene bags are made entirely of polypropylene, a plastic. These polypropylene bags in the industry are mistakenly labelled as biodegradable because they disintegrate into pieces, resulting in microplastics. Microplastics enter the food chain, posing a threat to the lives of thousands of land and sea mammals. Microplastics can’t be collected or seen by the naked eye because of their small size. As a result, rather than fixing the plastic waste issue, these bags will exacerbate it (Mukheed and Khan 2020).

4.7 Conclusion

Many organic materials, such as medicines, pathogens, chemical contaminants, etc., are found in wastewater as these contaminants are seldom eliminated during wastewater treatment; they are released into aquatic ecosystems, which are sometimes utilized to produce water for drinking.

Up till now, the effectiveness of biological and oxidative sewerage and water purification processes has been based mostly on the dispersion of target chemicals, even though it is well-known that the conversion of organic pollutants can result in products with equivalent or even higher toxicities. To comprehend and analyze the reactive and biological treatment methods, it is critical to unravel the degradation/oxidation routes and determine the products formed.

Many of Pakistan's environmental issues may be traced back to economic policies that have had unforeseen and indirect environmental consequences. The Environmental Protection Act of 1997 is a significant piece of environmental legislation in Pakistan's legal history. This policy was created with the goals of environmental preservation, protection, rehabilitation, and betterment, pollution prevention and control, and the implementation of sustainable development. The National Environmental Action Plan (NEAP), which was approved in February 2001 to follow the NCS program, intends to achieve four goals: clean air, clean drinking water, wastewater treatment, and sustainable development. Another important policy in Pakistan's history is the Pakistan's National Environmental Policy (2005–2015), which aims to improve the quality of life of Pakistan's citizens via environmental protection, preservation, and development, as well as effective cooperation among government entities, civil society, the private sector, and other partners.

Environmental authorities have not done a good job of monitoring and regulating natural resource usage and pollution.

To summarize, the government should not rely solely on regulation in the future, but rather progressively adopt market-based measures, which can be more successful.

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Chapter 5
Impacts of Micro Pollutants on Human Health and Enumerating the Environmental Refinement

Muhammad Nawaz and Sheikh Saeed Ahmad

Abstract Micro pollutants are chemical substances which are generated through natural as well as human activities. The anthropogenic sources of micro pollutants are so far greater than natural processes. These micro pollutants are present in diverse forms, e.g., pharmaceuticals, heavy metals, personal care products, and endocrine disrupting chemicals. The nature of their toxicity also ranges from mild to very chronic for the human health as well environmental dysfunctions. This chapter also deals mainly with the amount of the micro pollutants released, their main sources, toxicity ranges, and the way these pollutants produce ill impacts on the human health. It has been observed that all micro pollutants having any source can produce their adverse impacts on the health of humans, and these impacts include DNA mutation to organ modification, with the outbreak of certain diseases of which liver, lung, and kidney diseases are prominent. The possible pathway of these pollutants has been observed in the form of drinking or wastewater which enter in to human body through irrigating the fruits or foods and by drinking the water having such pollutants. The objective of this study is also to employ all possible options by which these pollutants could be eliminated completely from the environment. There are certain options which can be used for their reduction very simple to last techniques. This study also stresses to minimize all possible sources of these micro pollutants rather than to use possible option for their elimination once they enter in to the environment.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_5

5.1 Introduction

Micro pollutants are chemical substances which are always found in very low concentration, ranging from mgL^{-1} to ngL^{-1} in the environment and cause serious threat to the ecosystem. Micro pollutants occur in all aspects of the environment, atmosphere, soil, and water, but mostly they work effectively in the aquatic environment and pose direct impacts on the health of the environment. Wastewater from industries and domestic contains plenty of micro pollutants which are released into the aquatic ecosystem, causing disturbance in the ecosystem functioning. These micro pollutants are generated both by human activities and anthropogenically in the environment and disrupt the smooth working of the ecosystem (Wanda et al. 2017; Bunke et al. 2019). Due to micro pollutants, water pollution has become a great issue since 1990 due to uncontrolled discharge of these substances into the main water channels which serve for drinking as well as for agriculture purposes. Since the last two decades, global issues related to water and atmospheric pollution have emerged quickly because of ecosystem-unfriendly human activities,resulting in adverse effects on the environment. Multiple anthropogenic activities of mankind in the form of urbanization, transport, unwanted use of agriculture fertilizers, and industrial generation have enhanced the pollution of water as well as air, like fast production of greenhouse gases, carbon dioxide, particulate matter, nitrogen oxide species, chemicals, leachates, oil spills and nutrients in the soil, water, and atmosphere (Pablos et al. 2015; Grandclement et al. 2017; Rizzo et al. 2019). It has been estimated that from 1930 to 2000, the amount of chemicals produced by human activities has increased by one million to four hundred million tons per year; similarly during 2002–2011, among all produced chemicals, 50% are very harmful compounds which cause serious health impacts (Gavrilescu et al. 2015). According to a study by Barbosa et al. (2016) and Talib and Randhir (2017), 70% of the produced chemicals by human activities have prominent impacts on the water quality. It has been also observed that in Europe about 0.1 million chemicals have been registered, among them approximately 70, 000 are being used daily which mostly end up in the aquatic ecosystem after their use. It has also been estimated that about 300 million tons of micro pollutants are discharged into the water in the form of consumer products and industrial effluents annually, in which 970 have been identified as emerging micro pollutants. Due to having serious consequences, the EU commission has put some micro pollutants in the watchlist, which include 17-alphaethinylestradiol, 17-betaestradiol, estrone, diclofenac, 2,6-di-tert-butyl-4-methylphenol2-ethylhexyl-4-methoxycinnamate, macrolide antibiotics, methiocarb, neonicotinoids, oxadiazon, and triallate (Bunke et al. 2019). This chapter also focuses on the generation, transportation, and impacts of such micro pollutants which need to be eliminated from the environment by using some strategies.

5.1.1 Classes of Micro Pollutants

Micro pollutants are a certain group of chemicals which are generated naturally or by anthropogenic activities such as mining, ill agricultural practices, industrial discharge, and pharmaceutical synthesis. There are several types of micro pollutants depending upon the nature of sources and consumer ends. According to Jia-Qian et al. (2013), the major groups of micro pollutants are as follows:

(a) Pesticides
(b) Pharmaceuticals
(c) Endocrine-disrupting chemicals
(d) Personal care products (PCPs)
(e) Biocides
(f) Heavy metals

5.1.1.1 Pesticides

All kinds of animals in the form of plants, animals, or microorganisms which can destroy the food, luxuries, or health status of living things are termed as pests, while chemicals which can prevent, repel, or destroy the action of these pests are termed as pesticides (Dunn 2012). This group of pesticides consists of several compounds which are in the form of insecticides, rodenticides, fungicides, herbicides, acaricides, molluscicides, and nematocides. Sometimes these pesticides work in the form of microorganisms like fungi or bacteria, also may be in the form of components of living organisms like endotoxin or whole organism for killing the pest, for example, wasps (*Trichogramma evanescens*), which are used as predatory organisms for controlling the pest in agriculture (Parastar et al. 2018). The use of pesticides has been increased tremendously worldwide since the last few decades, which has changed the farming practices resulting in environmental problems. It has been observed that during 2008–2012, about 45% of expenses on herbicides have been used among all pesticides including 14% on insecticides, 10% on fungicides, and 23% fumigants. These pesticides enter the soil through runoff, leaching, careless disposal, and container washing which have caused ecosystem dysfunction (Luo et al. 2016).

5.1.1.2 Pharmaceuticals

Several authors have defined the term pharmaceuticals as the group of chemicals which can be administered for the purpose of curing diseases of all animals and humankind, which includes veterinary medicines and some growth enhancer in plants as well. Frequently used pharmaceuticals include analgesics/anti-inflammatories, antibiotic, cardiovascular pharmaceuticals (b-blockers/diuretics), psychostimulants, estrogens and hormonal compounds, and antiepileptic drug (Bueno et al. 2012; Nicholas-Bateman 2012; Li et al. 2013). These drugs are being synthesized in greater amounts all over the world due to high consumption per capita, and it has been estimated that Asian countries, especially India and Pakistan, are consuming huge quantities of these chemicals annually. In this regard, India is among the top five countries that are generating pharmaceuticals, with expenses of about 45 USD billion annually, which are expected to rise 60 USD million by 2022 and the export of these drugs will rise from 30% to 60%. (KPMG International 2006; Kallummal and Bugalya 2012; Ebele et al. 2017). It can be said that every third tablet being used at global level is synthesized in India, but interestingly it is. In other words, every third pill taken in the world is manufactured in India, but it has been observed that 80% of the drugs are being consumed inside India. Despite the high rate of consumption of these drugs, the waste handling is not so much up to the mark (Subedi et al. 2015).

5.1.1.3 Endocrine-Disrupting Chemicals

Endocrine-disrupting chemicals have been defined by many agencies during late 1990s which have the opinion that these are some sort of exogenous drugs that after their release and transportation can disrupt the regulation, maintenance, homeostasis, and developmental process, which is being performed by some natural hormones present in the body. These endocrine-disrupting chemicals can eliminate functioning hormones in the body by binding with them or change the metabolism which creates the malfunctioning of these hormones. (Mocarelli et al. 2008; Damjan et al. 2011). According to the definition of Yilmaz et al. (2020), endocrine-disrupting chemicals are an exogenous group of compounds; probably more than 1000 which disrupt the biological functions of hormones in the body. These are sometimes grouped in the forms of heavy metals, pesticides, fungicides, pharmaceuticals, and industrial effluents and cause a worldwide problem for the environment and human health. Like other chemicals, the quantity of endocrine-disrupting hormones is also increasing day by day, and due to contamination, the physiology of living organisms has been disturbed. These chemicals are produced naturally as well as synthetically and many micro pollutants being produced in the environment act as endocrine-disrupting hormones which include pesticides, dioxins, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, phthalates, bisphenol A alkylphenols, and heavy metals like arsenic, cadmium, lead, and mercury which have shown negative impacts on the regularity and balance of endocrine (Gago-Ferrero et al. 2012). According to observations of Yoon et al. (2010) and Jeong et al. (2017), endocrine-disrupting hormones work as blockers of estrogen and thyroid gland which produce abnormality in the endocrine systems. About one thousand compounds have been identified which act as endocrine-disrupting chemicals and can be found in samples of urine, milk, serum, and placenta by biomonitoring studies.

5.1.1.4 Personal Care Products

Personal care products are those chemical substances which are used in our day-to-day life and range from medicines to shampoo, conditioner, lotion, and tooth pastes. These products, along with pharmaceuticals, have got much attention due to producing toxic impacts on human health as they contain various groups of compounds and one more interesting phenomenon concerned with them is that they are only confined to aquatic habitat by their ending up as consumer product (Radjenovic et al. 2009; Kasprzyk-Hordern et al. 2009). These products are used for improving hygiene and health, but even their low concentration can produce toxicity in the ecosystem. These products are also considered as endocrine-disrupting hormones (Tolls et al. 2009; Paulsen 2015). The problem of production of such products has been increased since last decades, and according to Tanwar et al. (2014), the Global Beauty Market has been categorized into five portions on the basis of synthesis of these products which are hair care, skin care, fragrance, colors, and toiletries items. The rate of discharge or decomposition is much faster than other pharmaceuticals as these are applied externally while drugs are used internally, so due to this property, these are a heavy burden on the water bodies. European countries like Italy, Germany, and Spain are the main producers of such products and represent about 70% of the total world cosmetic production.

According to Ebele et al. (2017) and Montes-Grajales et al. (2017), from 1998 to 2010, the sale of beauty items increased from 166.1 billion to 382.3 billion USD, which included a higher amount of skin growth substances. The review study of Montes-Grajales et al. (2017) reported that about 72 products have been identified which act as micro pollutants whose concentration varies from 0.09 ng/L to 7.82 ng/L.

5.1.1.5 Biocides

According to Parsons et al. (2019), biocides are chemical substances which are used for the preservation of addible goods durably, insects' control, and disinfection of surfaces. Nowadays, many antimicrobial applications are being used at house and commercial level, for example, detergents, seats of toilets, etc. About more than 200 active biocides are being used commercially for daily life. Exposure to products containing biocides is increasing at a high rate due to widespread use of daily life products, and after exposure, these biocides cause numerous problems when they come in contact with human skin, sometimes by way of inhalation inhalation. Many environmental impacts have been observed by using these biocides, but their effect increases many folds when more than one biocides are the component of a single daily life product. The general concerns noted by Pinto (2010) are the follows: first, these biocides make association with the target sites very similar to antibiotics which then cause mutation and resistant finally; second, due to difference in the activity of these biocides, antimicrobial efficiency is suppressed which causes the failure of antibodies of living organisms.

5.1.1.6 Heavy Metals

Heavy metals are those substances or elements that have their specific density more than 5 g/cm^3 and atomic weight above 40. These above 35 metals occur naturally in the environment and 22 metals among them are considered as heavy metals. These substances normally consist of higher electrical conductivity which loses their electron very easily to form cation (Li et al. 2017). These metals are found in each component of the ecosystem, including earth, aquatic parts, and mostly body parts of plants and animals. Metals like copper, iron, gold, nickel, silver, zinc, etc. are considered as heavy metals because of having high atomic number as well as adverse effects on living organisms. Some metals are very essential for the physiological function of living organisms and their deficiency leads towards diseases. These essential elements include zinc, copper, cobalt, magnesium, and iron selenium and are produced naturally as well as anthropogenically in the environment (Zambelli et al. 2016; Rahimzadeh et al. (2017), but when crossing their threshold limit, many biochemical disorders have been observed in the body of living organisms (Zhao et al. 2017). Contaminant metals in the form of lead, mercury, arsenic, and cadmium affect the food chain in the ecosystem because after entry in the ecosystem, they increase their concentration by the process of bioaccumulation and biomagnification (Alam et al. 2019). Industrial revolution and some environmental events like cyclones and volcanic eruptions are causing the release of such toxic metals in the ecosystem, and it has been observed that about two million tons of industrial and agricultural waste are being released into the aquatic environment every year. About 1.5 billion people are getting contaminated water worldwide because toxic metals after their release accumulate in the water as persistent organic pollutants for a longer period of time and consequently produce toxic impacts on the human health through food chain (Abdi et al. 2018; Adam et al. 2019).

5.1.2 Major Sources and Pathways

According to the opinion of Pal et al. (2010), Bo et al. (2016), and Magi and Di Carro (2016), micro pollutants present in any form (pesticides, pharmaceuticals, personal cleaner product, or endocrine-disrupting products) always end up in the aquatic environment and produce real threats to the ecosystem. Figure 5.1 shows the back and forth movement of micro pollutants in three layers of water, e.g., surface water, ground water, and then in the form of drinking water, which reaches the human body (Barbosa et al. 2016). It has always been found that these micro pollutants are present in surface water, ground water, and drinking water as well. Figure 5.2 shows the transportation of some micro pollutants with some other nanoparticles in the soil and ultimately ending up in the water. Water consists of many residues of these pollutants, which reach the human body through the food chain. Choi et al. (2008) investigated the concentration of different micro pollutants including acetaminophen, carbamazepine, cimetidine, diltiazem, and sulfamethoxazole in the

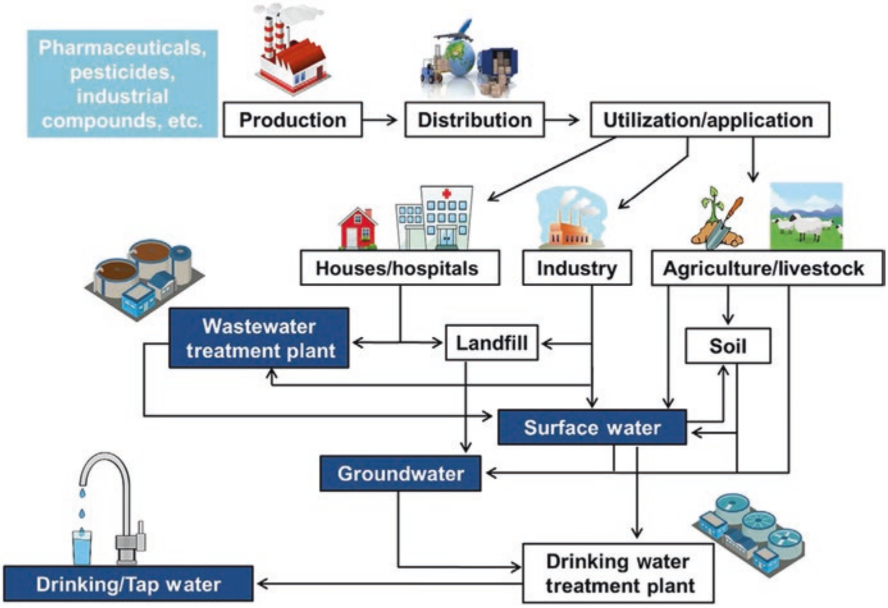

Fig. 5.1 Representative sources and routes of micro pollutants in the aquatic environments. (Barbosa et al. 2016)

wastewater of Korea and Wales, which was found about 10 ug/L which is the highest concentration ever found in the water. Kasprzyk-Hordern et al. (2009) found similar concentrations of gabapentin, tramadol, and acetaminophen in the wastewater produced from hospitals of the UK. These chemicals are ingested orally, and after utilization, these are secreted from the human body in the form of urine or feces. It has been observed by Vulliet and Cren-Olivé (2011) that ground water is less polluted as compared to that of surface water because it may be due to surface flow of water can disseminate the micro pollutants and far less reach of contaminants occur in the ground water. This ground water is only polluted when there is infiltration of pollutants from agriculture, sewer tanks, or through seepage of septic tanks (Lapworth et al. 2012). Soil can also play a significant role in groundwater pollution because it acts as a pathway for transportation of micro pollutants through the water which flows through it (Stepien et al. 2013). During the interaction of soil and water, the biochemical properties of soil and micro pollutants enhance the transfer of pollutants to ground water.

Some recent investigations (Loos et al. 2013) showed that micro pollutants primarily reach the aquatic ecosystem after their generation and it depends upon the mode of action of pollutants as well as binding sites of soil and water. Figure 5.2 shows the transportation of these micro pollutants clearly, and major pathways seem to be in the form of agricultural, urban runoff, municipal, industrial wastewater discharge, sludge disposal, and accidental spills (Dale et al. 2015). The micro pollutants along with nanoparticles remain in movement from the source (where

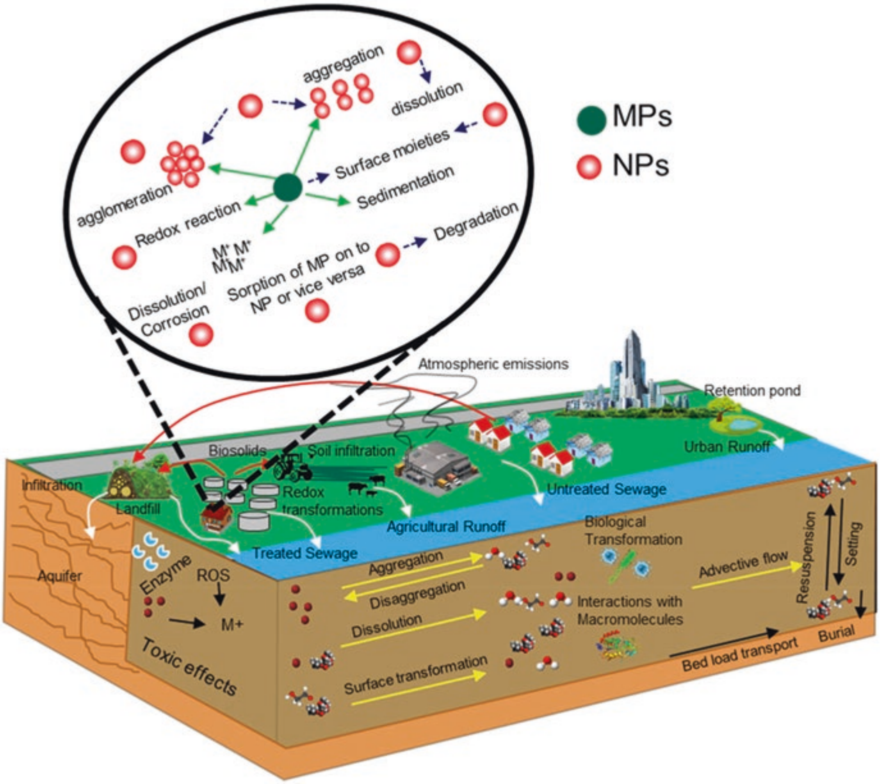

Fig. 5.2 Movement of micro pollutants along with other nanoparticles in the soil and aquatic ecosystem. (Dale et al. 2015)

generated) to their sink (degraded and accumulated). Micro pollutants in the form of heavy metals which are produced naturally are present in the environment. Garcia-Esquinas et al. (2013) reported that heavy metals being the major portion of micro pollutants are present in the biotic as well as abiotic portion of the environment. According to Krishna and Mohan (2016), heavy metals are always present in the ecosystem, but their exposure to humans mainly depends upon the many anthropogenic activities of man. The heavy metals present in the earth ores are recovered through mining, and toxic metals like zinc, arsenic, nickel, and lead are present in oxides or sulfides form. During the mining of such sulfides or oxides, toxic metals are released and spread throughout the environment by air, water, or soil. Sauve (2014) observed similar transportation of heavy metals which are released from industries and move through the environment as effluents or may move to soil as runoff, erosion, or acid rain. Furthermore, it has been also noted that heavy metals are also released as part of industrial products like paint, pesticides, cosmetics, and herbicides which cause deterioration of the ecosystem. The possible entry of heavy metals in human body may also occur through contaminated food items, sea foods, drinking water, or through breathing, and most probably exposure through mining (Kim et al. 2015; Ali and Khan 2018). These heavy metals always move in cyclic form in the environment, as if synthesized in industry, from the atmosphere to the soil, and then directly or indirectly into the human body. For this, heavy metals can move through several routes; for example, heavy metals like cadmium, lead, magnesium, and arsenic enter into the human body through the mouth along with food, fruits, vegetables, or water. Some chemicals also move into the human body through inhalation from the atmosphere, while some are absorbed through contacting the skin (Guo et al. 2019). After entry, these heavy metals are distributed in the body through the blood to the tissues and finally affect the target sites, like the liver, kidney, or lungs (Jawed et al. 2020).

Micro pollutants in the form of pharmaceuticals, personal care products, and endocrine-disrupting chemicals move to human body through aquatic water. These chemicals can be of two types by their sources which are point source as well as nonpoint source (Lapworth et al. 2012). According to the studies of Li (2014), the point sources are identified as industrial, hospitals, and sewage water, while the nonpoint source is not visible and very much difficult to locate, e.g., runoff, etc. Figure 5.3 shows the pattern of movement of pharmaceuticals and other related chemicals through different sources and pathways and it clearly shows that end up of these chemicals is always in the aquatic environment. It has been observed that about 70% of drugs are transported by households, while 20% come from livestock, 5% from hospitals waste, and 5% are not known by their source. The reports of Besse et al. (2012) and Qin et al. (2012), confirm the presence of trances of partially metabolized medicine in different water sources like in surface water, ground water, drinking water as well as wastewater. Similarly, Falconer et al. (2006) and Huang

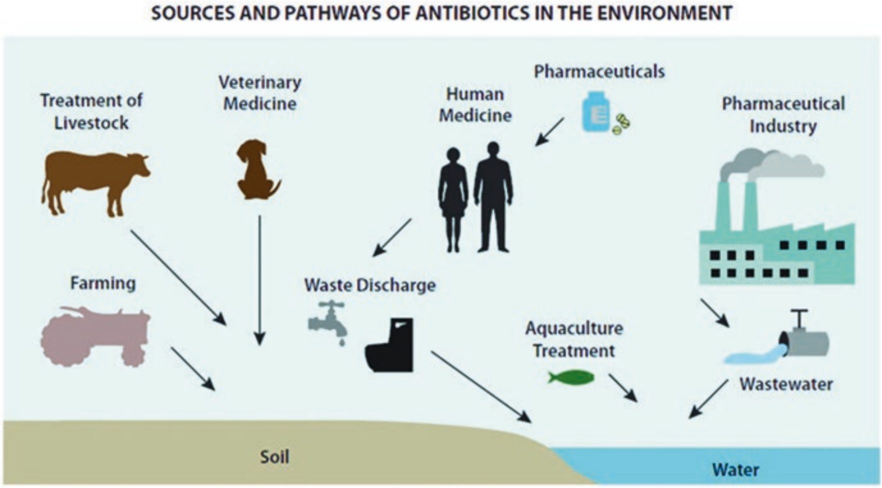

Fig. 5.3 Sources and pathways of pharmaceuticals and personal care products in the environment. (Kurwadkar et al. 2015)

et al. (2012) also confirmed the spills of chemicals like endocrine-disrupting and personal cleaner in the aquatic ecosystem. The entire pharmaceutically active compound can be found in the humans and animals, including the mixture of whole as well as half metabolized chemicals, which look more polar and hydrophilic. These chemicals can enter or move into the body of organisms by food, vitamins, or desired drugs, while can exit in the form of urine, feces, or bleeding. These pharmaceuticals when enter into the ecosystem cause adverse effects on the biochemical activities of other living organisms. According to Debnath and Khan (2017), the pathway of pesticides into the human body is also through inhalation, oral, or by skin, and after exposure, pesticides cause injuries or poison which need immediate treatment.

5.2 Impacts of Micro Pollutants on Human Health

Several authors have documented the impacts of different micro pollutants on human health as shown in Table. 5.1. The particulate matter and organic and inorganic pollutants which are released from different sources have chronic effect on human health as they have a high rate of transfer in the blood after their exposure. Luong et al. (2017) and Huy et al. (2017) noted the close interaction between the emissions of certain pollutants from industries and agriculture sector with the number of patients having chronic respiratory disorders in the hospitals of Vietnam. Similarly, Nhung et al. (2018) studied the status of ambient air of Vietnam with other Asian countries comparatively and found higher concentrations of polychlorinated biphenyls in the ambient air of Vietnam. In the case of some personal care products (PCPs), the oral entry of heavy metals is also one of the best examples of generation of toxicity after their application in the form of cosmetics when applied around the mouth or contact of hands to mouth having negative effects. This phenomenon is likely to be more frequent than the inhalation of these cosmetics. Heavy metals having higher concentrations in cosmetic products have been shown to have greater impacts on the human body. Lead has been found responsible for causing neurotoxins associated with the problems of learning, speaking, and behavioral aspects. Similarly, it has also been associated with certain problems of men and women. According to Lau et al. (2018), lead can affect fertility in human beings and bring changes in the hormones, irregularities in the menstrual cycle, and late onset of puberty in girls. Similarly, pregnant women are prone to more complications because lead can enter through the placenta and causes brain problem in infants. Cadmium can also enter the body through the application of cosmetics in the form of hair creams and absorbed in the body through contact with skin. It has been found stored in the kidney and liver, ultimately causing the cancer of these organs. Ingestion of high concentration of cadmium causes stomach problems in the form of vomiting and diarrhea, while lower but long-term exposure of lead can deform the bones and damage the liver and kidney. Chromium and mercury found in the daily used products have also adverse impacts in the form of skin allergy, ulceration,

Table 5.1 Multiple impacts of micro pollutants on human health

Micro pollutant	Impacts	Pathway	Author
Endocrine disruptors	Reduce fertility in male	Move through plasma	Li et al. (2012)
Personal cleaner products	Stop the growth of infants	Transported in the human milk	Yin et al. (2012)
Persistent and mobile organic compounds	Food toxicity	Absorbed and transported by water	Reemtsma et al. (2016)
Persistent organic pollutants (POPs)	Respiratory problems, asthma, and bronchitis like	As air particulate matters,	Phung et al. (2016) and Nhung et al. (2018)
Arsenic, 1,4-dioxane, and vinyl chloride	Carcinogens, cause cancer	found in wastewater	Nogueira et al. (2015)
Pesticides sprayers	Antioxidant status, and altered activities of cellular enzymes such as catalase, ligase	Runoff, lost via spray drift, off target deposition, Transported towards soil and water	Wafa et al. (2013)
Pesticides like atrazine organophosphorus, carbamates, organochlorines	Disturbance in the hormonal system	Through water and skin contact	Bergman et al. (2014)
PCPs (metallic elements)	Abnormal hormonal control causing reproductive impairments, decreased fecundity, increased incidence of breast and testosterone cancers, and persistent antibiotic resistance.	Present in water, transferred to the body by contact with skin or inhalation, and also can move to body via food.	
Endocrine-disrupting chemicals (Biphenyl A, Polychlorinated biphenyles, Dioxin)	Effects on infant's growth, decrease in the semen quantity, testosterone level decline	Through livestock feces, agricultural waste and through contaminated fruits and vegetables	Travison et al. (2007)
All micro pollutants	Cause of cancer, brain damage, liver problems, and reproductive problems.	Transportation through water, food, contacts, and inhalation	Ha et al. (2007), Diamanti-Kandarakis et al. (2009), and Swaminathan et al. (2013)
Micro pollutants (Plastic goods for packing, containing epoxy resin, Polychlorinated biphenyl, etc.)	Breast cancer, decrease in the androgen, feminizing like side effects in men	Transported via water and food due to contamination	Rogers et al. (2013)

(continued)

Table 5.1 (continued)

Micro pollutant	Impacts	Pathway	Author
Pharmaceuticals and PCPs (Carbamazepine Diclofenac Naproxen Gemfibrozil Bisphenol-A)	Male & female reproductive problems, kidney disorders, Immune syndrome, thyroid disorders, Cancer, bone problems, and metabolic syndrome.	Oral administration and drinking water	Alma et al. (2019) and IARC (2019)
Arsenic, Zinc, Selenium, Mercury, Copper (from plating, miming, and agriculture)	Cancer in the human body, DNA mutation, Syndrome, stomach ulcer.	Entry through food and water	Bessbousse et al. (2008)
Chromium from leather and plating industries	Cancer, bronchitis, Skin inflammation	Through drinking and irrigated water	Bilal and Iqbal (2019)
Mercury and zinc from mining.	Leukemia, Anemia, kidney, and skin problems	Fish is also one of the sources of Hg to human body	Engwa et al. (2019) and Bolisetty et al. (2019)
Trace elements of Pb and Cd	High concentrations of Pb and Cd cause blood cancer, liver necrosis, skin, and reproductive problem	Water and contaminated food	Guo et al. (2019)
Biocides (Tetrachlorsalicylanilide and Fentichlor)	DNA degeneration, Inhibition of cell growth. Respiratory syndrome.	Through vegetables, water, and food.	
Diphenylalkanes, polycarbonate plastic	Tissues damage, Decline biological activities, Endocrine disruption.	Inhalation, water and food	Meeker and Ferguson (2011)
Herbicides (Nonylphenol and Octylphenol)	Postnatal disorder, NP, and OP have been detected in human	Transported through human breast milk, seafood, and eggs.	Ademollo et al. (2008) and Calafat et al. (2008)
Pesticides like DDT and Phenols	Disorder of male reproductive system and hormonal imbalance	By absorption through irrigated water and vegetable consumption	Mnif et al. (2011)
Endocrine disruptive chemicals(Di-2 ethylhexylphthalate (DEHP)	Preterm births. Pregnancy failure	Food and water	Chang et al. (2017)
Pesticides (organochlorines, metabolites)	Risk of type 2 diabetes and its comorbidities	Through fruits and vegetables	Azandjeme et al. (2013)
Occupational herbicides like imazethapyr, a heterocyclic aromatic amine herbicide	Cause of bladder cancer and colon cancer	Through drinking water and contaminated foods	Koutros et al. (2009)

(continued)

Table 5.1 (continued)

Micro pollutant	Impacts	Pathway	Author
Pesticides, e.g., parquet, rotenone, and maneb), insecticides, e.g., organophosphate, fungicides (e.g., fenhexamid, and cyprodinil).	Parkinson disease, younger age death, cancer, and neurotic disorders	Food stuffs of vegetables, absorption by water	Chorfa et al. (2016)

nervous toxicity, immune syndrome, and reproductive issues in men and women. The studies of Murphy et al., McKelvey et al., and Lingamdinne et al. show that antimony, cadmium, mercury, and chromium are also present in the makeup powder, hair cream, shampoo, conditioner, and lipstick which cause the certain human disorders when their concentration reaches to threshold limits. Some of the metals like arsenic have synergetic effect when combined with the other metals or oxides. Singh et al. found that arsenic has its ecological and individual health impacts when it is in the form of salts, oxides, or sulfides of copper and iron because it is extensively carcinogenic in nature. Arsenic is also frequently detected in drinking water, which it can enter through pesticides containing arsenical salts, and lethally impact human and environmental health. Mazumder also observed its common use as suicidal substance by many people by causing the poison due to acute toxicity. Similar effects have been also noted in the case of lead, which can form chelates or complexes with other metallic substances, and its absorption is very easy compared to the rest of the heavy metals. Pesticides have also chronic effects on human health especially in people working in the agriculture fields, living nearby pesticides industries, and have close contact with pesticides, as shown in the Fig. 5.4. These pesticides affect human behavior and fertility and cause depression, anxiety, and nervous disorders. These pesticides are also available widely and sometimes available to everyone which looks supportive in attempting suicides as many cases have been observed in many Asian countries and Central America. Mostly, drugs when found in lower concentrations pose no impacts on human beings, but as their concentration reaches the threshold level, many neurological disorders have been found on them Zoeller et al. (2012). According to the reports of SEER (2003) and Fisher (2004), tumors mostly occur in the age of 20–35 which primarily originate from the germ cells; also the rate of testicular cancer has increased since the last decade, which has been found due to exposure to the environmental pollutants, which are in the form of endocrine-disrupting chemicals. These chemicals have also been found in increasing obesity in the people of Europe and Asia. Chemicals like vinyl chloride, benzidine, benzene, and polycyclic aromatic hydrocarbons have been found in increasing prostate cancer and diabetes in the human body (Azandjeme et al. 2013). PCBs have been associated with nervous disorders, lower IQ, problems in thinking, and writing in humans. These PCBs with other persistent organic compounds like polybrominated biphenyl ethers have also been found in impairing towards the neurotransmitter activity and synaptic disorders. Brominated flame retardants,

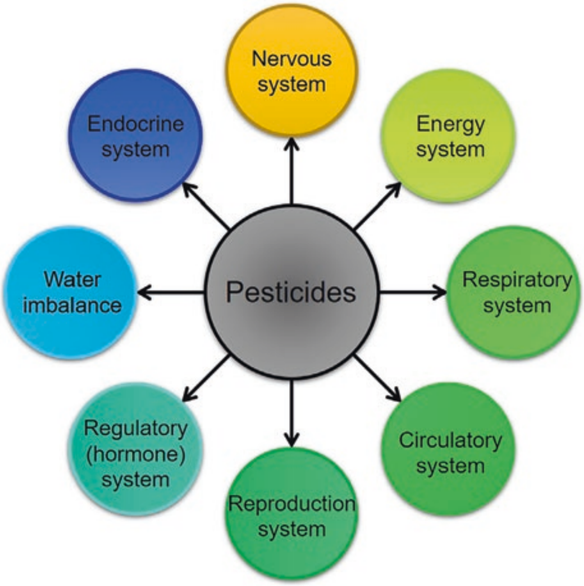

Fig. 5.4 Human health–related adverse effects of pesticides on different living being systems. (Bilal et al. 2019)

Tributyltin (TBT), and triphenyltin (TPT) are also the main causes of problems in thyroid hormones levels, puberty, and metabolisms disorders. Having strong association with some other endocrine-disrupting chemicals, it has been found that reproductive disorders like 50% decrease in the sperm count, lower fertility, early puberty, and genital malformations have been increased due to chemical abundance and exposures. Such estrogenic chemicals have also been observed to cause uterine fibroids, ovarian dysfunction, and subfertility in humans (Patisaul et al. 2013; Biro et al. 2013; Buck Louis et al. 2014).

5.3 Possible Options for Environmental Refinement

There is a serious problem concerned with the toxicity of micro pollutants in the environment generated due to human activity by different ways. These pollutants have created a threat for the ecosystem functioning and human health, so there is urgent need to eliminate such toxic elements from the environment. The possible ways being utilized for minimizing the effects of these pollutants have been list below.

5.3.1 Elimination by Physicochemical Application

It has been found that for the removal of personal care products (PCPs), there is a need for some comprehensive treatment methods for their removal, and simple coagulation or flocculation is not sufficient (Ternes and Joss 2006). In this regard, carbon in both forms, granular or powdered, is the best option for the removal of contaminants like nonpolar compounds or endocrine-disrupting compounds by the process of adsorption (Snyder et al. 2006; Bolong et al. 2009). Activated carbon through the process of adsorption can remove the micro pollutants up to 90% as Snyder et al. (2006) performed the process of adsorption for 66 PCPs and found that only nine had efficiency less than 50%, while all others were removed successfully at the five contacts hours by using 5 mg/L PAC. For this process, it is also necessary to dispose off PAC (powered activated carbon) and GAC (granular activated carbon) very carefully through landfilling or like other solid management systems because these spent PAC and GAC need a high amount of energy for degeneration and pose a risk to environmental health, because if these are left untreated, then it can be more dangerous than micro pollutants.

5.3.2 Use of Biological Treatments

Clara et al. (2005), Kimura et al. (2007), and Radjenovic et al. (2009) studied the process of removal of contaminants from the environment by using two types of technologies in the forms of conventional activated sludge process (CAS) and membrane biological reactor (MBR) with the help of nitrifying bacteria for degradation and sludge retention time for efficient removal. They observed that longer retention rate for about fifteen days provided the nitrifying bacteria with more diverse physiological, metabolic, and in return, increased the process of mineralization. Oppenheimer et al. (2007) also investigated that for some compounds (ibuprofen, methyl paraben, galaxolide, triclosan, caffeine), there is no difference for removal degree by conventional activated sludge and membrane biological reactor efficiencies. It has been also observed that for the removal of some other compounds from wastewater like mefenamic acid, indomethacin, diclofenac, and gemfibrozil, the MBR method works well than CAS which has been recorded 30–50%, but some compounds like carbamazepine persist and cannot be removed by using both methods (Radjenovic et al. 2009). Batt et al. (2006) and Miège et al. (2008) also observed the efficiency of nitrifying bacteria and found that these bacteria have a very important role in the process of decomposition of some highly toxic pharmaceuticals in wastewater treatment plants which use higher retention rate time. They also found that by using nitrogen with these biological systems, the removal efficiency of PCPs is more enhanced than other treatments, like the bio filter method.

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5.3.3 Removal by Reverse Osmosis (RO)

Many authors have described the authenticity of working of Reverse Osmosis for the removal of very toxic compounds, including personal care products (PCPs) and endocrine-disrupting compounds from wastewater (Snyder et al. 2003; Oppenheimer et al. 2007). It has been also confirmed by the studies of Braghetta and Brownawell (2002) that removal efficiency of RO is greater than 90%, while lower efficiency has been also noted for the diclofenac which is 55.2–60% and ketoprofen 64.3%. Similarly, WERF (2005) found the removal rates more than 90% or even better in case of naturally occurring and some synthetic compounds. It was also noted by Oppenheimer et al. (2007) that RO can remove all such compounds occurring naturally or synthetically, which are not possible to be removed by SRTs even for 30 days.

5.3.4 Application of Nano Filtration

This nano filtration method is very cheap, common, and almost in the access of every worker. This method consists of three steps which are followed by the next step one an other. These steps are in the combination of adsorption, sieving, and electrostatic repulsion and are mostly used for pharmaceuticals. The removals' efficiency also differs from compound to compounds depending on the structure and reactivity. Mostly, the efficiency of compounds is different depending on the solubility, polarity, and membrane structure. This method of filtration is also very good and 90% removal efficiency has been achieved by this from wastewater (Yoon et al. 2006; Watkinson et al. (2007); Bolong et al. 2009).

5.3.5 Implication of Ozonation Oxidation Processes

These processes are mostly used for the removal of pharmaceuticals present in the water. Many researchers including Huber et al. (2005), Andreozzi et al. (2005), Ternes and Joss (2006), and Zimmermann et al. (2008) have found that medicines such as antibiotics, carbamazepine, and some other pharmaceuticals have the tendency to be reactive with molecular ozone, while some pharmaceuticals like inflammatory compounds, diclofenac and indomethacin, are very stable and cannot be degraded easily through the process of ozonation. This ozonation process is influenced by many factors in the process of degradation of such pharmaceuticals, such as quantity of oxidants, quality of wastewater, and mode of operation. Solubility of compounds present in the water also matters in case of their degradation because particulate matters present in high concentration show high removal trend after reaction with ozone. Huber et al. (2005), Pauwels and Verstraete (2006), and Bouju et al. (2008) showed that soluble compounds always react with ozone readily and can oxidize hundred times more faster than insoluble ones because of having restriction of diffusion rate, but removal rate is decreased with the consumption of more oxidants due to high contents of particulates. So this technique can work best with the low concentrations of compounds present in wastewater.

5.3.6 Mechanism of Disinfection

The process of removal of toxic compounds through the process of ozonation sometimes performs partial decomposition in the case of some personal care products (PCPs) due to high concentration of waste material. Huber et al. (2005) observed that in the case of removal of PCPs, the oxidation process does partial disinfection because compounds present in the wastewater are normally shielded with ozone or hydroxyl ions. It has been also estimated that a concentration of 5–10 mg O_3/L with a contact time of 15–20 min is enough for the degradation of long chain of 2–3 unit long compounds of PCPs. Ternes and Joss (2006) found that chlorine with its compounds for the contact time of 30 min by adding 10 mg/L of ClO_2 removed most of bacteria and virus, while it is also very important to use the disinfecting compounds in adequate quantity because Emmanuel et al. (2004) found that when NaClO is used as a disinfecting agent with a dose of 1–8 mg/L, it can reduce the amount of bacteria very fast, but it has very serious consequences in terms of causing toxicity for aquatic organisms by polluting their habitats.

5.3.7 Construction of Wetlands for Natural Polishing

Constructed wetlands can be very effective in the removal of pharmaceuticals by the process of photolysis, phytoremediation, bioremediation, and soil uptake (White et al. 2006; Matamoros et al. 2008). This involves the process through the vertical and horizontal surfaces having benefits of consisting aerobic, anaerobic, and anoxic conditions with proximity to plant rhizosphere for the degradation of pharmaceuticals compounds. Some pharmaceutical compounds like ibuprofen can be best reduced by the aerobic process, while clofibric acid and diclofenac can be best removed by the anaerobic; similarly, halogenated compounds can be removed effectively in the toxic environment (Lin and Reinhard 2005). Matamoros et al. (2008), Bartels and von Tumpling (2008), and Zhou et al. (2009) found through experimental work that aerobic conditions are much efficient in removing the contaminants than anaerobic conditions, while surface flow system can eliminate some POPs and PCPs very actively from aquatic habitats. Similarly, high retention time rate enhances more degradation of toxic elements in the water.

5.3.8 Use of Membrane Bioreactor (MBR) Technique

This technology emerged recently emerged for water recycling, transforming waste water into high-quality effluents for various usages at a large-scale. The Membrane Bioreactors (MBRs) techniques have been available since the last two decades at commercial use and have been well-recognized for handling various contaminants such as pathogens, suspended solids, and nutrients. This can also work better than conventional activated sludge process (CAS) technology (Melin et al. 2006; Atkinson 2006). But this has some barriers in the case of treating trace elements like endocrine-disrupting chemicals (EDCs), pesticides, and pharmaceutically active compounds (De Wever et al. 2007). Tadkaew et al. (2010) studied the mechanisms of removal of these trace elements and observed that some trace elements like ibuprofen and bezafibrate can be removed completely, while compounds like carbamazepine and diclofenac cannot be removed at all. So this membrane bioreactor BMR can work best for selective removal of toxic compounds.

5.3.9 Elimination Through Ozone and Biofiltration Method

Ozone (O_3) is the most frequently used technique for the process of disinfection and as oxidants. This involves the transformation of organic compounds through reaction with ozone by reacting with O_3 and hydroxyl ions, which result in the destruction of compounds by decay of ozone in the waste water. The reaction of O_3 and hydroxyl radicals with organic compounds is very selective, while second order rate of reaction also plays a significant role in the degradation of compounds because the order of reaction changes after every 10 orders of reaction. In the case of OH, it is also a very less selective oxidant because its reactions with most of the compounds need the diffusion-controlled mechanism (von Gunten 2003). The advanced oxidation processes (AOPs) also depend upon the enhancement of the formation of OH radicles. In this case, the combination of O_3/H_2O_2 increases the conversion of O_3 to OH and reduces the reaction time needed for the micro pollutants. The combined use of ozone/hydrogen peroxide (O3/) accelerates the conversion of O3. Legrini et al. and Lee and von Gunten found that a combination of ultraviolet radiations (UV) and H_2O_2 results in the production of OH which can act as an AOP as well. It can also work for the transformation of micro pollutants by the direct process of photolysis and by reacting with OH. In the case of this technology, it has been also observed that OH acts as a powerful oxidant which scavenges dissolved organic matter, carbonates, and bicarbonates. The OH can also react actively with nitrates, but in this case, this behaves very poorly.

5.3.10 Removal Through Nitrifying Activated Sludge (NAS)

There is a serious effect of releasing of emerging pollutants like pharmaceutical and personal care products (PPCPs) from sewage treatment plants, which can affect the environment significantly, because these plants have been not upgraded with new technologies (Vieno et al. 2007; Smook et al. 2008; Radjenovic et al. 2009). For this reason, it is very essential to use the recent techniques for handling such emerging pollutants (Wick et al. 2009; Xu et al. 2010). In this regard, activated sludge process has played a significant role in the removal of such micro pollutants from the waste water with special emphasis on the biological degradation (Barret et al. 2010), but sufficient results have not been obtained by this treatment process due to certain factors. Nitrifying activated sludge (NAS) has been identified as one important technique for the decomposition of such compounds. Zhou and Oleszkiewicz (2010) and Hernández-Leal et al. (2011) found that 17a-ethinylestradiol can be degraded well by using this process. This has been also tested by other researchers (Suarez et al. 2010) by using nitrifying bacteria. This technique involves the elevated elimination of micro pollutants with NAS and has been attributed to the process of biodegradation with sorption mechanism (Tran et al. 2009).

5.3.11 Use of Bioaugment $KMnO_4$ and Oxidation

The frequent increase of micro pollutants and cyanobacteria into the drinking water has created a problem worldwide as it directly threatens human health as the pollutants cannot be removed completely by using any technique. In this regard, some latest techniques by using KMnO4 pre-oxidation have demonstrated very good results for the removal of such toxicants in the drinking water, but still are not useful in removing the toxicants completely because traces of cyanobacteria still remain in the water which can be toxic for its use. For this purpose, KMnO4 pre-oxidation in collaboration with bioaugmentation in the form of sand filtration method has been found good in removing cyanobacteria along with other micro pollutants from the drinking water. KMnO4 with bioaugmentation, being a very traditional chemical for oxidation, has been found very useful in removing the pollutants such as mutagens, microbial pollutants, and precursors of chloroform in drinking water. This is also very effective in the process of coagulation and removal of algal blooms in the water (Chen et al. 2009). Some authors (Ou et al. 2012) have reported that there is 10–30% increase with the use of 0–40 mg/L of aluminum salt as coagulants and pre-oxidation with 1.7 mg/L of KMnO4, but this is a drawback because this oxidation process can leave toxic traces, which can make the water unhealthy. For this purpose, $KMnO_4$ pre-oxidation combined with bioaugmentation process has been used with 2-hydroxy-4- methoxybenzophenone-5-sulfonic acid, which is a very chronic pollutant with one species of cyanobacteria (*Microcystis aeruginosa*) and has been found to be a model for removal of micro pollutant. In this case, biogenic manganese oxide (BMO) can also further purify the quality of drinking water by removing the cyanobacteria toxics (Zhang et al. 2017).

5.3.12 Through Enzymatic Bioremediation

Use of enzymes have been as widely accepted by producing the frequent results since many years and also with the development of immobilized oxidative enzymes have their multiple applications. Currently, these immobilized oxidative enzymes have produced a pathway towards green environment production by using their certain amounts for removal of very toxic micro pollutants which can be a challenge for human health. Gonzalez-Gil et al. (2018) have found that among these enzymes, laccases and horseradish peroxidase have been frequently used since the last five years, producing good results as these have enough capacity to withstand the reaction mixture and easy to separate. However, still there is need to develop new bioremediated techniques with the help of these enzymes as there is great diversity of micro pollutants.

5.3.13 By Advanced Anaerobic Digestion Systems

Current research work on the micro pollutants' removal by many techniques has found the useful aspects of manure toxicants' removal with the production biogas through advanced anaerobic digestion systems. This system can also work better for more treatments, including pasteurization, which can enhance the process of removal of pathogens along with micro pollutants. These micro pollutants in the form of antimicrobial compounds, manure contaminants, and other pharmaceuticals can be removed better through the use of activated carbon by the process of adsorption. The activated carbon can increase the production of methane gas with the removal of various antibiotic compounds such as lincomycin, ciprofloxacin, and erythromycin in the anaerobic digestion with the addition of chicken manure and food waste particles (Zhang and Cai 2019). The use of biochar precursors in this case also has been found to be good for the degradation of contaminants along with activated carbon. Duan et al. have also found that biochar has enough ability to produce the surface area for making the microbial colonies which can degrade the contaminants produced in the soil. Similarly, Basso et al. (2013) and Tang et al. (2013) reported the effect of using activated carbon in the form of biochar which contained removal ability for polychlorinated compounds. The studies of Zhang and Cai (2019) have also reported the importance of advanced anaerobic systems by using activated carbon with the combination of biochar for the removal of very toxic heavy metals present in the soil. It has been also found that there was an increase of 87–95% with the addition of activated carbon in the form of biochar. This system has been also found very cheap, accessible, and very easy to handle and precursors have no further harmful impacts on the environment.

5.3.14 Use of Microbial Genes for Degradation

In addition to some physical and chemical techniques being used for the removal of micro pollutants in the wastewater which can produce better results, microbial degradation for organic and inorganic micro pollutants is also one of the best options for their removal (Carey and Migliaccio 2009). According to another study (Gonzalez-Gil et al. 2018), microorganisms can enhance the removal of certain kinds of harmful nutrients such as extra organic carbon, nitrogen, and phosphorus from the waste streams. Among the removal of organic micro pollutants, only some of them can be removed, while others are partially removed through the possible pathways including biosorption and bioaccumulation, but most successful is the biodegradation which is done by the use of some microorganisms or their parts. This process involves three steps as follows:

1. Microorganisms use these micro pollutants as a source of carbon and energy, e.g., toluene (Woods et al. 2011) and some pesticides, by converting them to CO_2 or sometimes convert these into solid biomass. In the case of heavy metals which contain no carbon, these microorganisms can also convert them by using electron receptors through precipitation (Fischer and Majewsky 2014).
2. Microorganisms can also decrease the toxicity of these micro pollutants by transforming their molecular structure such as antibiotics by the process of hydrolysis. It is worth notable that all resistant antibiotic genes do not encode the protein that degrades the antibiotics, but many efflux pumps can provide resistance against the contaminants without changing their structure (Yelin and Kishony 2018).
3. Microorganisms can also change the micro pollutants by the process of cometabolism such as pesticides, bisphenol, and pharmaceuticals (Fischer and Majewsky 2014)). This process occurs when micro pollutants pass through small structural changes like acetylation, methylation, and hydroxylation by using other growth substrates. This process occurs by the consumption of these substrates by the enzymes which work on them. These enzymes cannot be regulated in the presence of micro pollutants but can work better in the presence of these substrates. It has been also observed that ammonia oxidizing archae can transform pharmaceuticals by oxidizing these compounds (Men et al. 2016).

Some authors (Gonzalez-Gil et al. 2017; Guo et al. 2017; Jiao et al. 2017) have reported that many enzymes can encode the microbial gene sequence, which are then useful in removing the micro pollutants such as antibiotics and b-lactamase.

5.3.15 Coagulation/Sedimentation

Coagulation or sedimentation is a very simple and older technique for the removal of colloidal particles; although it can remove the micro pollutant completely, results have been found sufficient for removing the different pollutants. Stackelberg et al. (2007) reported 15% of the micro pollutants in the form of pharmaceuticals through the process of coagulation. Similar findings have also been found by Vieno et al. (2007) that micro pollutants like organic materials, heavy metals, and some pharmaceuticals can be significantly removed by the process of coagulation. The reports of Ternes et al. (2002) and Adams et al. (2002) also indicated the removal of pharmaceuticals by about 30%, and during this process, Fe+3 were removed. In this process, coagulation with adsorption in the form of clay particles through electrostatic interaction between micro pollutants and coagulants was found successful under sunlight (Nikolaou et al. 2007). It has also been found by Huerta-Fontela et al. (2011) that the removal efficiencies of coagulation vary from 9% to 100% depending upon the conditions and nature of pollutants. It was found that removal tendency of pharmaceuticals was 70%, while 40–60% was found in case of PCPs.

5.4 Conclusion and Recommendations

Through this study, it is concluded that micro pollutants are present in different forms including organic to inorganic and have different sources in which human activities are playing a pivotal role in their generation and reaching to target sites. Among the sources, human activities are contributing largely than natural processes in the form of industries, pharmaceuticals industries, and irregular fertilizers use. These micro pollutants are found in the form of heavy metals, pharmaceuticals, and endocrine-disrupting chemicals. These micro pollutants after their release mainly travel through the water cycle and then reach the human body directly or indirectly and produce adverse impacts. Many researchers have observed their harmful impacts on the human body when exposed directly or indirectly to such micro pollutants. These impacts are mild to chronic and irreversible depending upon the nature of pollutants. Although these pollutants are being released from different sources, these mostly end up in the water, thus converting to waste water. Water having such toxicants reaches to human body directly or indirectly through the food chain and causes different problems. These can also produce changes from chromosomal to modification in different organs through different diseases which are sometimes irreversible depending upon the nature of pollutants. There is a dire need for the removal of such contaminants from the environment produced by any source through using different techniques. This chapter has focused on the availing of some possible tools based on old to very recent methods for their removal from the environment for the sake of saving human health. There are numerous technologies which can be used based on physical, chemical, and biological aspects. Through this study, it can be recommended that it is very necessary to reduce the possible sources mainly based on human activities and also to stop unnecessary use of chemicals fertilizers to the crops without any recommendation by the experts. It is also very important to minimize all possible sources rather than to remove them from the environment once these enter the environment.

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Chapter 6
Emerging Organic Contaminants, Pharmaceuticals and Personal Care Products (PPCPs): A Threat to Water Quality

Bashir Ahmad and Muhammad Imran

Abstract Underground water contamination is a big challenge of this century. Emerging organic contaminants (EOC), personal care products (PCPs), industrial products, pesticides, pharmaceuticals, engineered nanomaterials, veterinary products, and food additives may pose threat to human health, and ecosystem. The ground water contamination which is the main source of drinking water, is an area of greater concern for the present and future of human civics. This chapter encompasses the possible emission sources in groundwater, contaminated surface water, and the fate of EOC, PCPs, and pharmaceuticals. The advancements in analytical techniques and precise equipment, quantitative detection of these contaminants is now possible and more compounds can be speckled now. Probably it is not possible to remove these pollutants from underground water reservoirs; however; detection of contaminants, their control at source, awareness campaigns and regulatory framework are possible approaches to compete this alarming challenge.

6.1 Organic Contaminants

A distinct array of synthetic organic composites is widely utilized for industrial practices, human and animal healthcare, food making, and preservation worldwide. The interest in contaminants' occurrence in the aquatic ecosystem, their impact on the environment, and possible toxicity even at low concentrations are noted in recent

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_6

few last decades (Halling-Sørensen et al. 1998; Stan et al. 1994; Kümmerer 2009; Daughton and Ternes 1999; Schwarzenbach et al. 2006; Stan and Linkerhagner 1992).

Underground water contamination is an increasing concern, relatively poorly identified when compared with freshwater sources (Pal et al. 2010). Organic contaminants were beforehand not measured or recognized critical in groundwater as far as circulation or fixation was concerned, but now they are widely detected and known as emerging contaminants (EC) which are unfriendly biologically and for public health. Manufactured new chemicals or thier modifications or exiting chemical disposal could create new ECs. The ECs' significance and presence in the environment are only revealed now (Daughton 2004).

The organic micro-contaminants in an aqueous atmosphere detection was impossible but recently, analytical procedures improvement resolve this issue (Petrovic and Barcelo 2006; Lindsey et al. 2001). Richardson and Ternes analyzed recent emerging micro-contaminants (Richardson and Ternes 2011).

The term degradates is widely used for different compounds (as well as their metabolites and transformation commodities) such as product of personal care products (PCPs); pharmaceuticals, pesticides, engineered nanomaterials, industrial products, food additives, and veterinary products (Huschek et al. 2004; Hilton et al. 2003; Fent et al. 2006; Besse and Garric 2008; Crane et al. 2006; Celiz et al. 2009).

The ECs in atmosphere wastewater and surface water are easily characterized and have greater diversity as compared to groundwater. The burden ofcontaminants in waste and surface water is high. The surface water sources are used for public water supply, in which EC could be analyze (Pal et al. 2010; Houtman 2010), the incidence and fate of ECs founded trace contaminants (Murray et al. 2010). The Lapworth et al.'s (2012) systematic analysis raised the issue of worldwide ECs in the groundwater and thier widespread in groundwater sources, (Lapwort et al. 2012).

Environmentally significant concentration of ECs is 10^2–10^4 ng/L; several endocrine-disrupting ingredients have been identified in groundwaters. Many ECs have the maximum priority materials for treatment and management in terms of human health effects and potential environmental effects. Many ECs are unregulated which has current analytical institutional challenges (Kavanaugh 2003).

A wide-ranging diversity of PPCPs are detected in the aqueous atmosphere worldwide, stimulants, analgesics, cosmetics, disinfectants, antimicrobials, antipyretics, fragrances, antibiotics, steroids, and antidepressants, commonly used on daily basis for several purposes (Daughton and Ternes 1999).

The PPCPs can arrive in the aqueous atmosphere directly or indirectly via fertilizing, livestock breeding, landfill leachate, and sewage discharge, resulting in undesirable impacts on creatures and ecosystems (Grice and Goldsmith 2000; Corbel et al. 2009; Ricart et al. 2010).

The regulated pollutant number will produce slowly in the coming decades. The anthropogenetic microorganic contaminants observed in the river are needed under the framework of various state rules and regulations (EC. Groundwater Directive 2006; EPA 2006).

The overall aim is to improve and protect the water source quality. From the European perspective, groundwater condition is presently legalized in compliance with Water Framework Directive (WFD) and Groundwater Directive (GD). The drinking water is controlled by the Drinking Water Directive, while pesticides are controlled by Plant Protection and Biocides Directives. GD and WFD were established to protect groundwater and water-dependent ecosystems. These required standard protocols for ECs that achieved its unawareness on many micro-contaminant chemicals' poisonous behavior, impact, and limited surveillance data and limited values are not possible to yet establish.

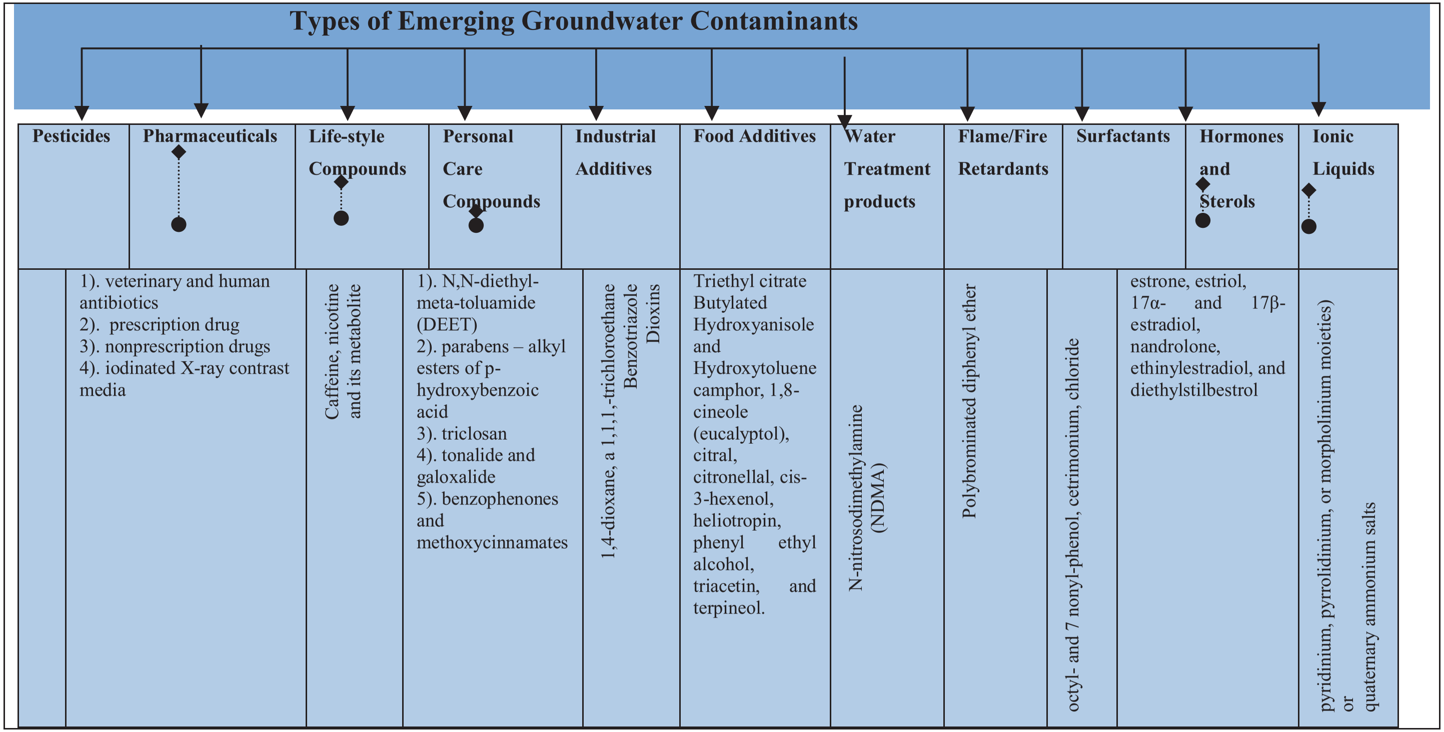
The European Drinking Water Directive (EDWD) sets some parameters for the organic micropollutants which consist of chlorinated solvents, aromatic hydrocarbons, and disinfection products. The significance of ingredients recognized in the WFD daughter directive included Di(2-Ethylhexyl) phthalate, octyl, and nonylphenols, benzene, specified polyaromatic hydrocarbons (PAH), and various chlorinated hydrocarbons (Water Framework Directive 2000, 2006).

The European Commission's objective is to set boundaries for 16 new substances underneath WFD containing synthetic contraceptives, anti-inflammatory medicine, and perfluoro octane sulfonate (PFOS) (EC. EQSD 2008; EC. Review of priority substances 2011).

A similar condition arises worldwide. Regulatory structures are required to control prospective micropollutant resources and to monitor the organic pollutants in the aquatic atmosphere. A large number of organic substances were not subjected to the current level of a rule. The US Environment Protection Agency sets legal standards for 125 micropollutants in drinking water; 31 might be considered as micro-organic contaminants excluding pesticides; no pharmaceuticals or PCPs contaminants were included. The US EPA announced the latest pollutant candidate list (CCL-3) 2009 that contained three pharmaceuticals, eight hormones, PFOS, and perfluorooctanoic acid (PFOA) (USEPA 2009; Petrovic and Barceló 2006).

6.1.1 Emerging Groundwater Contaminants (EGC) Types

It is much more identified about the groundwater pesticides when related with other substances like pharmaceuticals (poorly characterized). The risks for human health for several compounds are also recorded, their capacity to travel in the aqueous atmosphere is not fully investigated, and ecological persistence is unfamiliar. Considering their behavior, resources, mobility, physical and chemical characteristics throughout the aqueous atmosphere, and related risks, the following types of micro-contaminants are considered emerging in groundwater (Fig. 6.1).



Types of Emerging Groundwater Contaminants

Pesticides	Pharmaceuticals	Life-style Compounds	Personal Care Compounds	Industrial Additives	Food Additives	Water Treatment products	Flame/Fire Retardants	Surfactants	Hormones and Sterols	Ionic Liquids
	1). veterinary and human antibiotics 2). prescription drug 3). nonprescription drugs 4). iodinated X-ray contrast media	Caffeine, nicotine and its metabolite	1). N,N-diethyl-meta-toluamide (DEET) 2). parabens – alkyl esters of p-hydroxybenzoic acid 3). triclosan 4). tonalide and galoxalide 5). benzophenones and methoxycinnamates	1,4-dioxane, a 1,1,1,-trichloroethane Benzotriazole Dioxins	Triethyl citrate Butylated Hydroxyanisole and Hydroxytoluene camphor, 1,8-cineole (eucalyptol), citral, citronellal, cis-3-hexenol, heliotropin, phenyl ethyl alcohol, triacetin, and terpineol.	N-nitrosodimethylamine (NDMA)	Polybrominated diphenyl ether	octyl- and 7 nonyl-phenol, cetrimonium, chloride	estrone, estriol, 17α- and 17β-estradiol, nandrolone, ethinylestradiol, and diethylstilbestrol	pyridinium, pyrrolidinium, or morpholinium moieties) or quaternary ammonium salts

Fig. 6.1 Different types of emerging groundwater contaminants (EGC)

6.1.2 Pesticides

Pesticides are found in trace concentrations in groundwater and are known as highly recognized contaminants. In the 1990s, simazine, atrazine, and a variety of other herbicides were discovered in the groundwater across the world (Bauld 1996; Close 1996; Kolpin et al. 1998; Tappe et al. 2002; Zanella et al. 2011; Spliid and Køppen 1998; Water 2011). New parent compounds were dectected after improved analytical techniques e.g., metaldehyde (UK) (Source: http://www.water.org.uk/home/policy/positions/metaldehyde-briefing), and known as merging contaminant. If we study 20 year ago was obvious that pesticide degradates need to be taken into consideration (Galassi et al. 1996; Kolpin et al. 2000).

Several studies demonstrated that pesticide metabolites could be found in groundwater in higher concentrations, while the parent compounds of agronomic and amenity detection limits are low (Kolpin et al. 2004; Lapworth and Gooddy 2006). Naturally, the degradates are biologically active compounds that could be toxic. The pesticide registration procedure is common, but the monitoring process is not adequately observed.

6.2 Pharmaceuticals

Pharmaceutical substances in the aquatic ecosystem have been recognized and also have concerns (Richardson and Bowron 1985). The primary routes of these compounds into the environment are: (a) unused products disposal; (b) agriculture practices; and (c) humans excretion (Barnes et al. 2008). A wide spectrum of pharmaceutical goods have been found in groundwater-surface and discarded in wastewater (Nikolaou, Meric and Fatta 2007; Pérez and Barcelo 2007; Vulliet and Cren-Olive 2011; Miller and Meek 2006). These include the following:

1. Human and veterinary antimicrobials: Lincomycin, tetracycline, sulfamethoxazole, clofibric acid, and ciprofloxacin.
2. Doctor-prescribed medications: Salbutamol, codeine, diclofenac, and carbamazepine.
3. Nonprescription medications: Salicylic acid, ibuprofen, and acetaminophen or paracetamol.
4. Iodinated X-beam contrast media: Iopromide and iopamidol.

The prospective risks for surface water are noted from Tamiflu and chemotherapy drugs (cyclophosphamide or 5-fluorouracil, ifosfamide) and illicit medications (amphetamines and cocaine) (Singer et al. 2007; Moldovan 2006; Zuccato et al. 2000; Johnson et al. 2008; Buerge et al. 2006; Kasprzyk et al. 2008) (Table 6.1).

Table 6.1 Summary and statistics' analysis to maximum concentrations (ng/L) of ECs discovered in 4 studies (Kavanaugh 2003)

Class	Compound	Use ±	N	Lowest	Average	Highest
Pharmaceutical	Ibuprofen+	Anti-inflammatory**	14	0.6	1491	12,000
	Sulfamethoxazole	Antibiotic	15	5.7	252	1110
	Paracetamol+	Analgesic	8	15	15,142	120,000
	Diclofenac	Anti-inflammatory	11	2.5	121	590
	Clofibric acid+*	Lipid regulator	8	4	1113	7300
	Lincomycin	Antibiotic	5	100	188	320
	Ketoprofen	Anti-inflammatory	6	3	611	2886
	Triclosan	Antibiotic	6	7	509	2110
	Iopamidol	X-ray contrast media	5	130	760	2400
	DEET	Insect repellent	4	454	2251	6500
	Propyphenazone	Analgesic	5	15	553	1250
	Sulfamethazine	Veterinary medicine	5	120	298	616
	Salicylic acid+*	Analgesic	4	43	418	1225
	Phenazone	Analgesic	4	25	1503	3950
	Carbamazepine	Antiepileptic	23	1.64	5312	99,194
	Primidone	Barbiturate	4	110	3380	12,000

N = number of studies, $^{\pm}$primary use, *degrade, **also an analgesic, $^{+}$known or potential EDS

6.3 Lifestyle Compound

The groundwater is affected by sewage waste like caffeine, nicotine, and its metabolite cotinine (Godfrey et al. 2007; Teijon et al. 2010; Seiler et al. 1999). Saccharine, acesulfame, sucralose, and cyclamate are found in high concentrations in groundwater, which is affected through sewage infiltration ponds. Buerge et al. (2009) demonstrated acesulfame is a commonly detectable containment in the aquatic atmosphere due to its common use, persistence, and mobility.

1. N, N-diethyl-meta-toluamide DEET
2. Parabens-alkyl esters of p-hydroxybenzoic destructive
3. Bactericide and antifungal agents, such as triclosan
4. Polycyclic musks, such as tonalide and galoxalide
5. UV filters/sunscreen, such as benzophenones and methoxycinnamates.

Triclosan and methyl triclosan were detected in the surface water in Switzerland, which reflected persistent metabolite (Van Stempvoort et al. 2011; Buerge et al. 2009; Lindström et al. 2002). Tonalide (AHTN), HHCB-lactone, and galoxalide (HHCB) were found in wastewater (Horii et al. 2007) and compounds used as a marker for wastewater surface (Fromme et al. 2001; Buerge et al. 2003a).

The synthetic musk compounds were discovered in aquatic sediment, surface water, digestion in fish, biota samples in bioaccumulation, and environmental, sewage, and sewage sludge; human hazard assessment (Table 6.3) was debated (Heberer

2002). Most of these compounds are being used as sunscreen lipophilic conjugated aromatic compounds found in an aqueous atmosphere (Jeon et al. 2006).

6.4 Industrial Condiments and Their By-products

Industrial compounds are released in the atmosphere in wide range, which are problematic and alarming for the world. These compounds are polyaromatic hydrocarbons and fuel oxygenate methyl tertiary-butyl ether, plasticizers or resins bisphenols, adipates, chlorinated solvents, and phthalates (Jeon et al. 2006; Garrett et al. 1986; Verliefde et al. 2007; Moran et al. 2005, 2007). Mostly industrial compounds are not emerging contaminants and have limits in drinking water. But some degradation products are known as emerging contaminants (ECs).

Industrial emerging contaminants (ECs) are:

1. Benzotriazole derivatives
2. 1,4-dioxane, a 1,1,1, -trichloroethane
3. Dioxins, e.g., antimicrobial additive (triclosan) (Abe 1999; Giger et al. 2006; Voutsa et al. 2006; Stuart and Lapworth 2013; Mezcua et al. 2004).

6.5 Food Additives

Some nutritional supplements are known as oxidizing agents or endocrine disrupters (Jobling et al. 1995). Triethyl citrate is a food additive which stabilizes foams, pharmaceutical coatings, and plasticizer. Both Hydroxytoluene and Butylated hydroxyanisole are food-fat preservatives. Other food additives are citronellal, camphor, triacetin, cis-3-hexenol, phenyl ethyl alcohol, 1,8-cineole (eucalyptol), terpineol, citral, and heliotropin.

6.6 Water Treatment By-products

The haloacetic acids and trihalomethanes are used for the water disinfection process (Boorman 1999). N-nitrosodimethylamine (NDMA) is referred to as a drinking water pollutant resulting reactions occurred in the chlorination process or industrial contamination, due to high concentrations of carcinogen agents in wastewater during the chlorination process is used intentional or unintentional in municipal wastewater (Mitch et al. 2003). The disinfection by ozone instead of chloramines can increase the potential risk of toxic products (Richardson and Bowron 1985). Other products of water purification are epichlorohydrin and polyacrylamide (Mezcua et al. 2004).

Table 6.3 US Geological Survey's (USGS) National Water-Quality Assessment (NAWQA), Compounds with Detections Meeting Applicable Criteria (Bexfield et al. 2019)

Analyte	Conc used for detections (ng/L)[a]	Number of detections meeting criteria	Detection frequency (%)	Detection frequency for PAS sites alone (%)	Detection frequency for MAS sites alone (%)	Median of detected concentrations (ng/L)
7-Dimethylxanthine'	21	9	0.8	0.7	1.2	160
Bupropion	3.6	3	0.3	00	1.2	9.3
Cimetidine	21	1	0.1	0.1	0.0	23.6
Pseudoephedrine	5.5	4	0.4	0.0	1.6	8.1
Acyclovir	4.4	1	0.1	0.1	00	5.7
Atenolol	4.8	1	0.1	0.1	00	8.7
Carisoprodol	25	1	0.1	0.1	0.0	58.2
Caffeine	65.6	3	0.3	00	1.2	212
Carbamazepine	2.2	18	1.6	1.2	3.2	8.5
Acetaminophen	3.6	4	0.4	0.1	1.2	8.8
Hydrocortisone	29	1	0.1	0.1	0.0	69.3
Fluconazole	35	1	0.1	0.1	0.0	50.8
Lamivudine	3.2	1	0.1	0.1	0.0	11.4
Dextromethorphan	1.6	2	0.2	0.2	0.0	3.5
Fenofibrate	71	1	0.1	00	0.4	32.9
Metformin	6.6	2	0.2	0.2	0.0	35.6
Fluoxetine	5.4	1	0.1	0.1	0.0	17.1
Methotrexate	26	3	0.3	0.4	0.0	39.1
Citalopram	3.3	2	0.2	0.1	0.4	5.5
Pentoxifylline	4.7	1	0.1	0.1	0.0	8.1
Meprobamate	17	8	0.7	0.7	0.8	21.1
Metaxalone	7.8	1	0.1	0.1	0.0	22.2
Lidocaine	19	2	0.2	0.1	0.4	33.6
Methadone	3.8	1	0.1	0.1	0.0	43.0
Nordiazepam	10	1	0.1	0.1	0.0	17.1
Hormone						
Testosterone	1.6	1	0.1	0.1	00	3.0
Bisphenol A!	160	7	0.6	0.4	1.6	193
4,4′-Bisphenol F	10	1	0.2	0.3	00	70.8
Cholesterol	400	3	0.3	0.2	0.4	480

Groundwater Samples, and Summary of detections and detected Concentrations for Hormone and Pharmaceutical

Maxi- mum of detected concentrations (ng/L)	Human-health benchmark (ng/L)b	Human-health benchmark type/ sources	Lowest therapeutic dose (mg/ day)’	Maximum concentration as % of HHB	Number of detections > HHB	Number of detections > 10% of HHB	Maximum lifetime cumulative mass as % of LTD
416	–	–	NA	NA	NA	NA	
22.7	NA	–	300	_			0.48
23.6	30,000	MDH.WSV	0	0.079	0	0	
15.2	NA						0.40
5.7	NA	–	600	NA	NA	NA	0.06
8.7	2,000	MDH.WSV		0.44	0	0	
58.2	30,000	MDH.WSV	0	0.19	0	0	
667	–	–	NA	NA	NA	NA	
162	40,000	MDH.HRL	0	0.41	0	0	
17.0	200,000	MDH.HRL		0.009	0	0	
69.3	20	MDH.WSV		347	1	1	
50.8	400	MDH.WSV		12.7	0	1	
11.4	NA	–	100	NA	NA	NA	0.73
5.2	NA	–	60	NA	NA	NA	0.55
32.9	600	MDH.WSV		5.48	0	0	
38.7	4,000	MDH.WSV	0	0.97	0	0	
17.1	200	MDH.WSV		8.54	0	0	
86.0	NA		0.7				780
7.4	NA	–	20	NA	NA	NA	2.35
8.1	90,000	MDH.WSV	240				
164	10,000	MDH.WSV	1.64	0	0		
22.2	NA	–	2400				0.06
39.6	NA	NA	NA	NA	NA	NA	NA
43.0	NA		5				55
17.1	NA		NA				
3.0	7,000	AUS		0.43			
430	20,000	MDH. HRL		2.15			
70.8	NA						
570							

6.7 Flame or Fire Retardants

The polybrominated diphenyl ether flame retardants utilized in industries and household entered the environment through waste disposal by landfills or incineration processes. Phosphate-based retardants (tris-(2-chloroethyl) phosphate) formed nonflammable barriers, utilized in consumer products and industries (Rahman et al. 2001; Weil et al. 1996).

6.8 Surfactants

The cationic, amphoteric, anti-foaming anionic, and nonionic surfactants agents are found in wastewater (Gonzalez et al. 2007). The priority pollutants, octyl and nonylphenol (OP and NP), are used for the manufacturing of alkylphenol ethoxylates (APEs) that produced by nonionic surfactants (Table 6.2). The parent ethoxylates and their metabolites, alkylphenols and carboxylic degradation products are persistent in the aquatic atmosphere (Soares et al. 2008; Montgomery and Reinhard 2003). Nonionic polyethylene glycol-based composites and Siloxanes (anti-foaming agents) were used in several PPCPs, having concern about the possibility of intoxication and transportation in the aquatic atmosphere (Richardson 2007).

The cationic surfactants contain quaternary ammonium salts, like emulsifiers, cetrimonium chloride (antiseptics), and homologs, recognized as ECs in marine sediments (Ahrens et al. 2009). Amphoteric surfactants are coconut-based products (Cocamidopropyl betaine). The anionic surfactants are perfluorinated compounds (PFOS and PFOA), being utilized in the surfactants, firefighting foams cosmetics, paints, food packaging, and cookware coatings. They are observed in wastewater and surface water, persistent in the environment (Lara-Martin et al. 2010; Poynton and Vulpe 2009). PFOS was found in the surface water and waste effluents of Japan (Harada et al. 2003; Saito et al. 2003).

6.9 Hormones and Sterols

Sex hormones, including androstenedione, testosterone, progesterone, estrone, estriol, 17α-, and 17β-estradiol, as well as their synthetic hormones, such as nandrolone, and synthetic estrogens (xenoestrogens) such as diethylstilbestrol and 17α-ethinylestradiol, are commonly used as contraceptives agents (Table 6.2). Several compounds were present in wastewater and treated as effluent (Vulliet and Cren-Olive 2011; Johnson et al. 2000; Standley et al. 2008); the cholesterol and its metabolite (5β-coprostanol), plant sterols (stigmasterol, β-sitosterol, and stigmastanol), and related molecules. The sterol (phytoestrogens) is used in the plants which

Table 6.2 Different intensities of PPCPs were found in groundwater in 2012–2014

PPCPs	Research area	Samples #	Detection frequency (%)	Conc (ng/L)	References
Antibiotic					
Sulfamethoxazole	Switzerland	16	12–19	BDL-17	Morasch (2013)
	Baix Llobregat, Barcelona, Spain	121	29	9–46	Cabeza et al. (2012)
	Barcelona, Spain	32	80–100	BDL-65	López et al. (2013)
	Jianghan Plain, China	27	4–42	BDL-0.8	Tong et al. (2014)
	Vicinity of municipal landfills in Guangzhou, China	28	24	28.7–124.5	Peng et al. (2014)
	Barnstable County, Massachusetts, USA	20	60	0.1–113	Schaider et al. (2014)
Sulfamethazine	Baix Llobregat, Barcelona, Spain	121	46	BDL-83.9	Cabeza et al. (2012)
	Barcelona, Spain	32	23–100	BDL-29.2	Cabeza et al. (2012)
	Jianghan Plain, China	27	8–63	BDL-1.2	López et al. (2013)
Ofloxacin	Barcelona, Spain	32	100	10.2–367	Tong et al. (2014)
	Jianghan Plain, China	27	10–68	BDL-7.6	López et al. (2013)
	Vicinity of municipal landfills in Guangzhou, China	28	9	BDL-44.2	Tong et al. (2014)
Norfloxacin	A karst system near Yverdon-les-Bains, Switzerland	16	6–19	BDL-2	Peng et al. (2014)
	Barcelona, Spain	32	69–100	BDL-462	Morasch (2013)
	Jianghan Plain, China	27	64–79	BDL-47.1	López et al. (2013)
Azithromycin	Danube River, Serbia	44	5	BDL-68	Tong et al. (2014)
	A karst system near Yverdon-les-Bains, Switzerland	16	12	BDL-10	Radovic et al. (2014)
	Barcelona, Spain	32	80–100	BDL-1620	Morasch (2013)
	Jianghan Plain, China	27	100	0.2–0.7	Morasch (2013)

(continued)

Table 6.2 (continued)

PPCPs	Research area	Samples #	Detection frequency (%)	Conc (ng/L)	References
Trimethoprim	A karst system near Yverdon-les-Bains, Switzerland	16	6	BDL-0.4	López et al. (2013)
	Baix Llobregat, Barcelona, Spain	121	19	BDL-3	Tong et al. (2014)
	Barcelona, Spain	32	20–100	BDL-9.41	Morasch (2013)
	Jianghan Plain, China	27	4–68	BDL-5.2	Cabeza et al. (2012)
	Vicinity of municipal landfills in Guangzhou, China	28	4	BDL-10.5	López et al. (2013)
	Barnstable County, Massachusetts, USA	20	5	BDL-0.7	Tong et al. (2014)
Anti-inflammatories					
Ibuprofen	Serbia	6	17	92	Schaider et al. (2014)
	Barcelona, Spain	32	46–92	BDL-988	Petrovic et al. (2014)
	Rastatt, Germany	51	2	BDL-104	Petrovic et al. (2014)
	Vicinity of municipal landfills in Guangzhou, China	28	11	BDL-57.9	López et al. (2013)
	An experimental agricultural field in Ottawa, Canada	NA	NA	10	Wolf et al. (2012)
	An urban-influenced karst aquifer in the Wadi Shueib, Jordan	32	14	BDL-65	Peng et al. (2014)
Naproxen	Serbia	6	17	27.6	Wolf et al. (2012)
	A karst system near Yverdon-les-Bains, Switzerland	16	6–12	BDL-12	Gottschall et al. (2012)
	Baix Llobregat, Barcelona, Spain	121	NA	145	Petrovic et al. (2014)
	Barcelona, Spain	32	8–40	BDL-5.59	Morasch (2013)
	Vicinity of municipal landfills in Guangzhou, China	28	3	BDL-86.9	Cabeza et al. (2012)

(continued)

Table 6.2 (continued)

PPCPs	Research area	Samples #	Detection frequency (%)	Conc (ng/L)	References
Diclofenac	A karst system near Yverdon-les-Bains, Switzerland	16	6–12	BDL-3	López et al. (2013)
	Baix Llobregat, Barcelona, Spain	121	NA	15–55	Tong et al. (2014)
	Barcelona, Spain	32	40–100	BDL-380	Morasch (2013)
	Rastatt, Germany	51	2	BDL-129	Cabeza et al. (2012)
	Urban catchment area in Singapore	138	4	BDL-17	López et al. (2013)
Salicylic acid	Serbia	6	83	BDL-2.5	Wolf et al. (2012)
	Baix Llobregat, Barcelona, Spain	121	41	BDL-9.3	Zemann et al. (2015)
	Barcelona, Spain	32	100	26.6–620	Petrovic et al. (2014)
	Vicinity of municipal landfills in Guangzhou, China	28	98	BDL-2015	Cabeza et al. (2012)
	Urban catchment area in Singapore	138	58	BDL-1994	López et al. (2013)
Lipid regulators					
Bezafibrate	Baix Llobregat, Barcelona, Spain	121	45	BDL-4.22	Zemann et al. (2015)
	Barcelona, Spain	32	54–100[a]	BDL-25.8	Peng et al. (2014)
	Rastatt, Germany	51	8	BDL-19	Cabeza et al. (2012)
Gemfibrozil	Baix Llobregat, Barcelona, Spain	121	NA	15.5	López et al. (2013)
	Barcelona, Spain	32	62–100	BDL-751	Wolf et al. (2012)
	Rastatt, Germany	51	2	BDL-23	Cabeza et al. (2012)
	Barnstable County, Massachusetts, USA	20	5	BDL-1.2	López et al. (2013)
	Urban catchment area in Singapore	138	4	BDL-17	Wolf et al. (2012)

(continued)

Table 6.2 (continued)

PPCPs	Research area	Samples #	Detection frequency (%)	Conc (ng/L)	References
Clofibric acid	Barcelona, Spain	32	31	BDL-7.57	Schaider et al. (2014)
	Rastatt, Germany	51	4	BDL-1350	Zemann et al. (2015)
	Vicinity of municipal landfills in Guangzhou, China	28	3	BDL-73.9	López et al. (2013)
	Urban catchment area in Singapore	138	9	BDL-18	Wolf et al. (2012
Psychiatric drugs					
Carbamazepine	Serbia	6	17	3.4	Zemann et al. (2015)
	Danube River, Serbia	44	23	BDL-41	Peng et al. (2014)
	Baix Llobregat, Barcelona, Spain	121	48	BDL-62.4	Petrovic et al. (2014)
	Barcelona, Spain	32	92–100[a]	136[b]	Radovic et al. (2014)
	Rastatt, Germany	51	33	BDL-35	Cabeza et al. (2012)
	Barnstable County, Massachusetts, USA	20	25	BDL-72	López et al. (2013)
	Urban catchment area in Singapore	138	67	BDL-9.3	Wolf et al. (2012)
	An urban-influenced karst aquifer in the Wadi Shueib, Jordan	32	13	BDL-100	Schaider et al. (2014)
Diazepam	Baix Llobregat, Barcelona, Spain	121	36	BDL-8.28	Zemann et al. (2015)
	Barcelona, Spain	32	23–100[a]	35.1[b]	Gottschall et al. (2012)
Primidone	A karst system near Yverdon-les-Bains, Switzerland	16	6–19[a]	BDL-11	Cabeza et al. (2012)
	Baix Llobregat, Barcelona, Spain	121	41	BDL-27.62	López et al. (2013)
	Berlin, Germany	36	NA	BDL-140	Morasch (2013)
Stimulants					
Caffeine	Baix Llobregat, Barcelona, Spain	121	40	BDL-55.5	Tran et al. (2014)
	Urban catchment area in Singapore	148	80–83[a]	BDL-16249	Cabeza et al. (2012)

(continued)

Table 6.2 (continued)

PPCPs	Research area	Samples #	Detection frequency (%)	Conc (ng/L)	References
Insect Repellants					
DEET	Barnstable County, Massachusetts, USA	20	5	BDL-6	Zemann et al. (2015)
	Urban catchment area in Singapore	148	100	1.9–3481	Cabeza et al. (2012)
X-ray contrast media					
Iopamidol	Switzerland	8	100	36–94	Zemann et al. (2015)
	Rastatt, Germany	115	4	BDL-79	Schaider et al. (2014)
	An urban-influenced karst aquifer in the Wadi Shueib, Jordan	39	51	BDL-1900	Hass et al. (2012)
Diatrizoic acid	Switzerland	8	100	24–32	Wolf et al. (2012)
	Rastatt, Germany	165	27	BDL-4240	Gottschall et al. (2012)
	An urban-influenced karst aquifer in the Wadi Shueib, Jordan	39	79	BDL-220	Hass et al. 2012)
Beta-blockers					
Propranolol	Serbia	6	67	BDL-4.5	Gottschall et al. (2012)
	Barcelona, Spain	32	23	BDL-9.38	Wolf et al. (2012)
Metoprolol	A karst system near Yverdon-les-Bains, Switzerland	16	6–12	BDL-9	Petrovic et al. (2014)
	Barcelona, Spain	32	100	95.3–355	López et al. (2013)
Musks					
Galaxolide	Baix Llobregat, Barcelona, Spain	121	100	42.9	López et al. (2013)
Tonalide	Baix Llobregat, Barcelona, Spain	121	100	7.5	Morasch (2013)
Sunscreen agents					Cabeza et al. (2012)
Octocrylene	Baix Llobregat, Barcelona, Spain	121	96	8.42	Cabeza et al. (2012)
Ethylhexyl methoxycinnamate	Baix Llobregat, Barcelona, Spain	121	100	35.31	Morasch (2013)

excreted in the wastewater that is considered the main source of these compounds for the ecosystem (Liu et al. 2010).

6.10 Ionic Liquids

Ionic liquids exist in salts having low melting point, regarded as ‘green’ replacements in industrial volatile composites (Table 6.2). These mixtures have heterocyclic rings of pyrrolidinium or morpholinium moieties and pyridinium or quaternary ammonium salts. Ionic liquids are not generally utilized, but their formulations are important for water solubility, toxicity, and poor degradation (Petrovic and Barcelo 2006; Pham et al. 2010).

6.10.1 Antibiotics

Antibiotics’ existence are broadly utilized for human and animals diseases treatment; metabolized and unmetabolized antibiotics excreted via feces and urine, which are originated in wastewater purification plants and surface water which partially decomposed in the environment which accumulated in the water. The presence of antibiotics at low concentrations might increase the risk of antibiotic-resistant bacterial species in river base flow (streamflow that is discharged from groundwater and seeps streams) and some extent should increase drug resistance microorganisms (Martínez 2008; Watkinson et al. 2009; McArthur and Tuckfield 2000).

The existence of antibiotics in the groundwater is more considered worldwide in recent times. A national exploration was conducted in the USA; pharmaceuticals and more organic pollutants in water sources indicated antibiotics in 47 groundwater samples with >30% detection frequency (Barnes et al. 2008). The drinking, surface, and groundwater report show the contamination with pharmaceuticals products such as antibiotics (including enoxacin, trimethoprim ciprofloxacin, and ofloxacin) in pharmaceutical industrial area-collected water samples (Fick et al. 2009).

The groundwater was also reported contaminated with veterinary antibiotics near farmland or breeding facilities. For example, the occurrence of veterinary drugs such as sulfonamides (sulfamethazine, sulfamerazine, sulfathiazole, and sulfamethoxazole), lincomycin, tiamulin, monensin, and erythromycin was detected (29 ng/L–2000 ng/L) in groundwater samples collected from pools and adjacent groundwater operational for beef and swine livestock facilities. The existence of various veterinary antibiotics was detected in organic vegetable farms groundwater of northern China.

The sulfamethazine, sulfamonomethoxine, and sulfadiazine drugs with 1.5, 130, and 19 ng/L,1.5 concentrations, respectively, were found in Guangxi Province groundwater samples collected from a pig farm. The antibiotics that were detected in groundwater collected from many countries having variable concentrations and species suggested distinct consumption habits (Bartelt et al. 2011; Hu et al. 2010; Zhou et al. 2012).

6.10.2 Anti-inflammatories and Analgesics

The most frequently detectable analgesics and anti-inflammatories in groundwater are diclofenac ibuprofen and paracetamol since they are used in daily life. Several pharmaceuticals and their metabolites such as diclofenac, ibuprofen, and ketoprofen were found at different concentrations in the drinking groundwater of Berlin and Germany (Heberer 2002b).

The exfiltration process for wastewater to groundwater found a high concentration of analgesics and anti-inflammatories. The concentration of diclofenac (120 ng/L) and ibuprofen (250 ng/L) was detected at depth of 0.5 m below the main drain sewer pipe in North East London; high concentrations indicate pollution in wastewater exfiltration in the groundwater (Ellis et al. 2003).

Repercussions of recycling in the ground and surface water of a medium-sized Mediterranean catchment showed diclofenac and paracetamol (211 ng/L) in the drinking supply which probably contaminated the water (Rabiet et al. 2006). A monitoring survey was done to investigate the ECs in Barcelona (Spain); ibuprofen was found in higher concentration in aquifers rather than wastewater treatment plant influent or effluent, which indicates natural groundwater recharge consisting of river water, crude wastewater, or other discharge sources of ibuprofen (Teijon et al. 2010).

6.11 Lipid Regulators

The lipid regulators' detection frequencies and their metabolites such as clofibric acid, bezafibrate, and gemfibrozil in groundwater were low as comparedsome anti-inflammatories, anti-inflammatories, carbamazepine, and caffeine. The groundwater of two municipal water resources (Guangzhou and China) landfills gemfibrozil and bezafibrate were not detected; clofibric acid was detected at 3%; salicylic and sulfamethoxazole were found 98% and 24%, respectively (Peng et al. 2014).

The clofibric acid and gemfibrozil were found <10 % in the groundwater samples collected from Singapore sewerage drainage, while caffeine and carbamazepine were detected up to 90% and 72%, respectively (Tran et al. 2014); bezafibrate (54–100%) and gemfibrozil (62–100%) were detected from Barcelona (Spain) groundwater. Average levels of pharmaceuticals were higher which indicated severe groundwater contamination and it might be possible for more frequent lipid regulators detection (López et al. 2013).

6.11.1 *Caffeine*

Caffeine contaminates the wastewater through a household plumbing system or human urine; the average amount of caffeine is 360 mg/L which is present in soft drinks, tea, and coffee; early data presented the caffeine existence in landfill leachates, septic tanks, sewage effluent, and surface water pollution through wastewater (Seiler et al. 1999; Gilbert et al. 1976). The groundwater may be contaminated with caffeine by natural recycling. The caffeine concentration up to>16,000 ng/L with detection frequency of 83% was recorded in the groundwater samples taken from Singapore.

The North Shore of Kauai and Hawaii ground and surface water founded 100% detection frequency of caffeine in August, which was 33% in February; maximum concentration (88 ng/L) was noted in groundwater in the summer season. A larger-scale survey was done; total 1231 samples were collected from California, the caffeine was 290 ng/L in untreated groundwater that used for public water supply (Tran et al. 2014; Knee et al. 2010; Fram and Belitz 2011).

Incidence of caffeine in ground and surface water was higher as compared with PPCPs, could be removed through wastewater treatment or rapid degradation process, and less constant to the subsurface environment (Bradley et al. 2007; Jim et al. 2006).

In surface waters, caffeine was consider the most frequently utilized indicator for human-derived waste of surface water; for groundwater, it could be an indicator of discharge in certain conditions wherever the biodegradation process is limited, which rapidly degrades groundwater rich in bacteria (Buerge et al. 2003; Glassmeyer et al. 2005; Knee et al. 2010).

6.11.2 *Carbamazepine*

The carbamazepine is included in the list of specified ingredients for the monitoring account by the EU Water Framework Directive (Stuart et al. 2012). The detectable concentration in groundwater was high. The carbamazepine was detected 42% in 64 samples collected from 23 European countries; the highest concentration was 390 ng/L. In two German cities (Leipzig and Halle), carbamazepine concentrations was 2–75 and 2–51 ng/L in the groundwater, respectively. In Montana (USA), 12 out of 38 well water samples were tested, and carbamazepine was detected upto 400 ng/L (Musolff et al. 2009; Loos et al. 2010; Miller and Meek 2006; Osenbrück et al. 2007).

The groundwater studies showed that the carbamazepine would survive intact after 8–10 years in the subsurface, neither degraded nor adsorbed, which might be ubiquity in the groundwater (Drewes et al. 2000; Clara et al. 2004).

6.11.3 DEET

The DEET is an active substance used in commercial as insect repellents globally and enters the marine environment through septic system and sewage treatment. The PPCPs were detected in groundwater underneath and adjacent wastewater treatment systems of the coastal plain (North Carolina). Average concentrations of DEET was 540–1010 ng/L in groundwater-dependent on location. However, its presence on the ground and surface water showed that pathways and sources of DEET in groundwater required further research. The DEET was universally detected in sewage-impacted groundwater samples and also detected in groundwater samples collected from catchment areas without identified wastewater sources with comparatively higher concentration levels up to 298 ng/L (Del et al. 2014; Tran et al. 2014).

6.11.4 Others PPCPs

Other PPCPs investigation consist of beta-blockers, X-ray contrast media, musks, and sunscreen agents. A 5-year study was performed in urban areas of Wadi Shueib (Jordan); diatrizoic acid was a standard compound in X-ray diagnostics broadly used in 2008 with the continuous occurrence of up to 79% but moderately lower concentrations (BDL-220 ng/L) in the groundwater. The iopamidol was gradually detected with maximum concentration up to 1900 ng/L (Zemann et al. 2015).

The sunscreen agents (Ethylhexyl methoxycinnamate and octocrylene), the musk (galaxolide and tonalide), were found in the groundwater samples taken from Barcelona and Spain. The galaxolide and Ethylhexyl methoxycinnamate had been detected at higher levels than 100 ng/L at least in the sample. The intensities of beta-blockers in the urban groundwater were underlying; beta-blockers, propranolol and metoprolol, were detected in Barcelona, Spain. Previously, it exhibited a quite low detecting frequency (23%) and concentrations (BDL-9.38 ng/L); maximum concentration was up to 355 ng/L in all groundwater samples (Cabeza et al. 2012; López et al. 2013).

6.11.5 Sources of PPCPs in Groundwater

The PPCPs in groundwater were directly associated with human activities, mostly compounds used in products' synthetic processes. Only several PPCPs such as caffeine can yield over 60 plant varieties (Knee et al. 2010). Common sources and pathways used for PPCPs-contaminated groundwater are presented in Fig. 6.2.

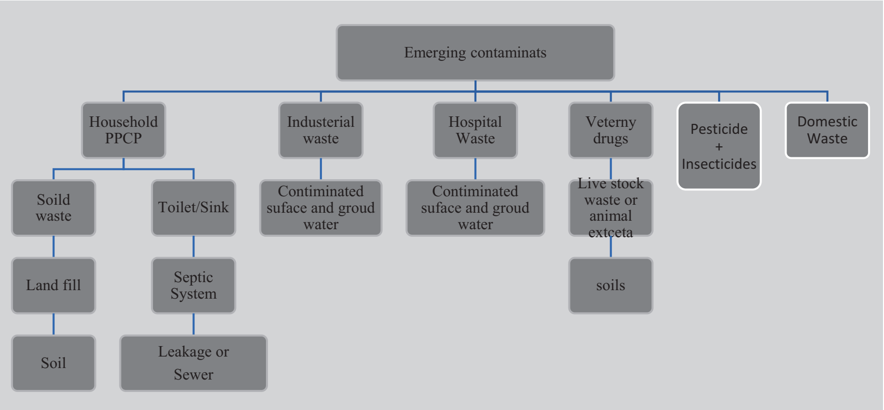


Fig. 6.2 Common sources and pathways used for PPCPs-contaminated groundwater

6.11.6 Wastewater and Contamination of Surface Water

Wastewater is known as the most significant source of PPCPs in the aquatic atmosphere. The household PPCPs excreted from a human after washing off through tap water, sinks, and toilets and entered in the sewerage system; limited removal was found during the primary treatment of sewage treatment plants (STPs) because sludge absorbtion was limited (Behera et al. 2011).

The biological purification variable elimination efficiencies could be achieved; the PPCPs in final effluent were noted at various levels. The diclofenac showed low degradation (< 25%); ibuprofen and ketoprofen were degraded (>75%), and both were categorized in the same therapeutic group (Salgado et al. 2012).

The PPCPs containing effluents discharged contaminated surface water and remained at the surface water body which undergoes low natural attenuation (Gurr and Reinhard 2006). The PPCPs transferred from groundwater via the hyporheic zone. The carbamazepine is used as an indicator for the surface trace wastewater and underground water exchange procedures (Lewandowski et al. 2011; Gasser et al. 2010).

The Managed aquifer recharge (MAR) term used for surface water; recycled water to artificially recharge groundwater structure and represented a significant probable source of PPCPs in groundwater, particularly when residence time is short and wastewater treatment regulated inadequately. The Riverbank filtration and well injection are widely adopted at MAR processes. The potential transportation processes of various effluent-derived pharmaceutical contaminants from the surface to shallow groundwater during riverbank filtration detected that infiltration of effluent contaminated surface water could lead to the existence of PPCPs. The carbamazepine and sulfamethoxazole were found to be >20 ng/L in groundwater of stream bank (Missimer et al. 2011; Bradley et al. 2014).

The selected PPCPs in groundwater recharge showed that diclofenac, naproxen, caffeine, ketoprofen, gemfibrozil, and ibuprofen were proficiently removed after <

6 months where secondary or tertiary wastewater was treated. The primidone and carbamazepine were endured in recharged groundwater with retention of 8 years (Drewes et al. 2003).

The warnings must be taken in recharging of the aquifer with sewage effluents, used to undergo advanced treatment methods that can efficiently take out the residue PPCPs or enhanced biodegradation of refractory PPCPs. Biodegradable metabolites of PPCPs were removed during residence times of riverbank filtration (Jurado et al. 2014; Heberer et al. 2004).

6.11.7 Landfills

The most frequent way used for municipal solid disposal waste is landfilled. The advantage of this method is operational simplicity with low cost, but contamination in the surrounding atmosphere cannot be unnoticed. Landfills are a decisive depositories technique for different solid and semisolid wastes containing PPCPs; resources of PPCPs are soft drinks and unwanted medications. After being discarded in landfills, the PPCPs can be either metabolized by the microorganism or absorbed into the waste solids, but mostly dissolved in the land leachate. Numerous PPCPs with significantly high concentrations were found in landfill leachates, For example, naproxen (520 µg/L), ibuprofen (167 µg/L), and carbamazepine and phenazone (1000 µg/L) were found (Eggen et al. 2010; Musson and Townsend 2009; Daughton and Ternes 1999; Kosjek et al. 2009; Slack et al. 2005). The anaerobic state in landfills and groundwater can slow the biodegradation process of organic compounds and resulted PPCPs' abundance and persistence in groundwater (Erses et al. 2008). The naproxen (67–87 ng/L), sulfamethoxazole (29–125 ng/L), and salicylic acid (2000 ng/L) were detected in the groundwater of municipal landfills in China (Peng et al. 2014). The landfill leachate-affected ground water ibuprofen (3100 ng/L) which was detected in Elkhart, Indiana (Buszka et al. 2009).

6.11.8 Septic Systems

Septic systems or on-site wastewater treatment systems are the sources of PPCPs that contaminated the ground and surface water. The septic system is a small-scale sewage dealing system, typically used in towns or rural areas where's no main sewage pipes supplied were available by local governments or private corporations. The water utilized domestically or recycled to complement the local groundwater supplies could provide opportunities to PPCPs enduring incomplete treatment into septic systems that entered into underground water. In certain regions of the northeastern United States, around 85% of wastewater disposal is carried out by septic systems (Godfrey et al. 2007).

With its widespread uses, it is tough to monitor effectively and regulate contamination from septic systems. Concentrations of caffeine, paraxanthine, and other micropollutants, in the residential septic system and downgradient ground water were found. Ambient concentrations of caffeine (17,000–23,000 ng/) and paraxanthine (55,000–65,000 ng/L) were high in the septic tank which was very high concentrations of compounds in the nearest well (>1700 ng/L) which fail to distance and depth.

Recent research has shown that pharmaceuticals and more micropollutants in groundwater networks that influenced by septic systems, for the levels of various PPCPs such as carisoprodol and lidocaine, were >0.1 μg/L in groundwater beneath and downgradient of the leaching bed (Swartz et al. 2006; Phillips et al. 2015).

6.11.9 Livestock Breeding

Veterinary medicine is used to treat disease and supported in livestock breeding growing concerned, but it contaminated the environment. The veterinary used antibiotics not entirely absorbed or metabolized in vivo. Almost 50–100% of antibiotics secreted via urine and feces (Kim et al. 2011), stored on waste ponds and released into the environment having a threat for groundwater contamination. The tetracycline and sulfonamides with a maximum level of up to 250 μg/L in water and 170 μg/kg in the soil were detected near swine manure (Awad et al. 2014). The application of veterinarian drugs contaminated manure for fertilizer and polluted the groundwater (Hu et al. 2010).

The probable resource of veterinary drugs in soil and groundwater is farm burial of livestock. The maximum concentration of monensin was found up to 12 μg/L in leachate dead cattle burials (Bartelt-Hunt, 2013; Yuan et al. 2013).

6.11.10 Sewer Leakage

Leaky sewers are the potential sources of pollutants in urban aquifers. Damaged sewage systems pipelines linked in long time overuse unrepaired due to use of poor material or negligence during construction. The PPCPs entered in soil zone by exfiltrating sewage through great probability to impact groundwater; concentration was usually 1 to 2 orders of magnitude lower than sewage influents of 50 urban groundwater underlying Tokyo, where unintended ground contamination takes place due to the sewer networks breakage; the concentration of the sample was quite comparable. It was proposed that some PPCPs could act as preventive indicators of groundwater contamination through sewage leakage. Specific tracers including X-ray contrast agents, primidone, diclofenac, carbamazepine, ibuprofen, caffeine, and artificial sweeteners were tested (Wolf et al. 2012; Kuroda et al. 2012; Ellis et al. 2003; Buerge et al. 2003).

However, no markers are generally applicable for groundwater systems because both the input and background concentrations vary spatially and temporally (Cronin et al. 2006).

6.11.11 The Fate of PPCPs in the Underground Environment

PPCPs are measurable in groundwater, soils, and sediments. The major processes are adsorption, degradation, and migration. Chemicals in the soil surface can transfer down to the lower layer and saturated and unsaturated zones. The natural attenuation was reduced in soil; pharmaceuticals could reach in groundwater (Laws et al. 2011). The fate of PPCPs changed in the ground environment affected by environmental factors and physical and chemical properties.

6.11.12 Adsorption and Migration

Adsorption can affect the fate of PPCPs in underground environments having an impact on their bioavailability, movement, and plant uptake (Lin and Gan 2011). Chemicals that have strong absorption are typically less mobile in the soil with limited leaching potential; however, ones with weak sorption probably move down-gradient and permeate in groundwater.

The adsorption of residue PPCPs in the soil is related to physicochemical parameters like molecular structure, hydrophobicity, and water solubility. The carbamazepine and gemfibrozil were inadequately adsorbed in soils, while triclosan showed good adsorption and was instantly retained in the soils (Yu et al. 2013).

Such differences are probably due to its different chemical characteristics. The strong propensity for triclosan will be sorbed on both silt loam soils and sandy loam. The caffeine is proven strongly sorbed in sandy loam soil and hence had more potential reasons for groundwater pollution (Karnjanapiboonwong et al. 2010).

Characteristics of soils, in particular the content of dissolved organic matter in soils, effect on PPCPs adsorbing. A study of sulfadimethoxine, sulfamethazine, and sulfaquinoxaline in four Brazilian soils showed sorption capacities; sulfonamides were higher in clay soils than sandy soil. This concluded that sulfonamides lipophilicity and organic matter content of the soil are related to sorption (Doretto et al. 2014).

The naproxen has a low sorption affinity with sandy aquifer material from low organic matter which indicates a highly mobile compound in the aquifer media and is ubiquitously detected in the groundwater (Teijón et al. 2013).

The environmental conditions also had an impact on PPCPs' adsorption behavior in the underground environment. The impacts of solution chemistry such as ionic strength and pH on the conservation and transport of sulfamethoxazole and ciprofloxacin in saturated porous media were noted. Solution for the ionic strength and pH played a major role to control ciprofloxacin transportation, but showed little impact on sulfamethoxazole transport under the experimental conditions (Chen et al. 2011).

The positive effect on the sorption of sulfonamides was noted at low pH because cations existed at low pH. The attraction is toward negatively charged minerals surfaces by electrostatic interactions; even though the electrostatic repulsion among negatively charged minerals and anionic sulfonamides at high pH would negatively affect sorption affinity (Zhang et al. 2014).

These conclusions could have significant consequences for the destiny of ionic PPCPs during underground environment altering. The PPCPs undertake almost no adsorption in soils; their migration in subsurface environments is principally impacted by geological locations, aquifers hydraulic environments, and soil characteristics. The high hydraulic conductivities and groundwater velocities in the saturated and unsaturated zone of the karstic area probably did groundwater region pollutants (Katz et al. 2009).

The groundwater below deposits may be exposed with PPCPs' residues pollutants emitted from wastewater effluents via artificial aquifer recharge, primarily due to the high transmissivity of shallow alluvium. The dynamic soil column leaching test demonstrated the mobility of sulfadiazine that acted stronger in sandy soils as compared to loamy soils and clays. The soil texture is considered the most important factor affecting sulfadiazine's downward movement (Heberer 2002; Bruchet et al. 2005; Chefetz et al. 2008).

6.11.13 Degradation

It is broadly acknowledged that the multiple composites degraded quicker and easier in aerobic environments as compared to aerobic related with different microbial activities (Johnson et al. 1998). In groundwater, microbes are rarer and more distinct in comparison to soils, and redox condition is poor (Lapworth et al. 2012).

The PPCPs in groundwater can endure imperfect degradation, possibly changed into lethal metabolites, or will remain intact in groundwater for long. Redox controls were commonly noted for groundwater PPCPs. The redox-dependent elimination of 27 wastewater-derived trace compounds with tank aeration tests, compounds including propyphenazone, doxycycline, and phenazone, was proficiently taken away beneath oxic circumstances and exit in anoxic situations. Three antibiotics, clarithromycin, clindamycin, and roxithromycin, have been removed under anoxic circumstances (Burke et al. 2014a).

The fate of various PPCPs at the hyporheic zone was affected in the winter and summer environment. The findings proved that temperature changed the result; iopromide, diclofenac, and metoprolol were more effective in summer (Burke et al. 2014b).

Various physicochemical properties of various PPCPs biodegrade are different. Caffeine and paracetamol were commonly used, endured more degradation in wastewater treatment, and were transported in the subsurface; generally detected less commonly as compared with other resistant degradant PPCPs such as sulfamethoxazole and carbamazepine (Benotti and Brownawell 2009; Grossberger et al. 2014).

The degradation analysis of sulfonamides in sandy soils leads to the differences in degradation (Zhang and Wang 2007). The environments difference influences on PPCPs degradation with various properties. The degradation rates of tetracycline, chlortetracycline, and tetracycline were much different at changed pH and temperatures. The sulfathiazole, sulfachlorpyridazine, and sulfadimethoxine were less susceptible to pH and temperature change; pH-associated reactions such as hydrolysis were probably not the removal mechanisms in groundwater (Loftin et al. 2008) (Table 6.3).

6.11.14 Sources to the Environment

The contaminate transported in the aqueous environment is described via the source-pathway-receptor model, shown in Fig. 6.3. Some of the contaminant pathway receptor sources are unclear since there are limited data about such pollutants. The direct pathways for pharmaceuticals and industrial contaminants are discharged by landfill leachate, effluent leaking sewers, leaking storage tanks and in-ground bypassing the soil zone, like septic tanks. The humans and groundwater pathway, human, animal, and pharmaceuticals were proposed (Daughton and Ternes 1999; Stuart et al. 2012; Jones et al. 2002). Compounds which have threaten for world are impossible to analyze at low levels and those that have physical and chemical properties enable them to persist in the water treatment procedure.

The soil surface contaminants could migrate across the soil to groundwater. This practice is applied for biosolids to soil and is crucial part of world waste management methods. The fertilizer application and biosolids from sewage sludge treatment have an advantage for enriching soil nutrition, but residual concentrations in the solids were found in incomplete ECs' removal during wastewater treatment. The high concentrations in sludge and high solubility, the Halogenated hydrocarbons of polychlorinated, and perfluorochemicals alkanes are essential for groundwater contaminants with relatively higher concentrations and solubility. Veterinary antibiotics and saccharin were reported in soil excrement (Sarmah et al. 2006; Hu et al. 2010; Buerge et al. 2011; Focazio et al. 2008).

However, fertilizer and biosolid-derived ECs reached groundwater in elevated levels through indirect routes, like excess and surface water-groundwater (SW-GW) exchanging, rather than downward migration due to attenuation in soil and unsaturated zone (Lapworth et al. 2012).

SW-GW interaction has a significant pathway. The surface waters comprise higher levels with large range ECs than groundwaters, indicating direct entry from wastewater sources, short residence times, and limited dilution capability of surface water compared with groundwater (Lapworth et al. 2009; Barnes et al. 2004).

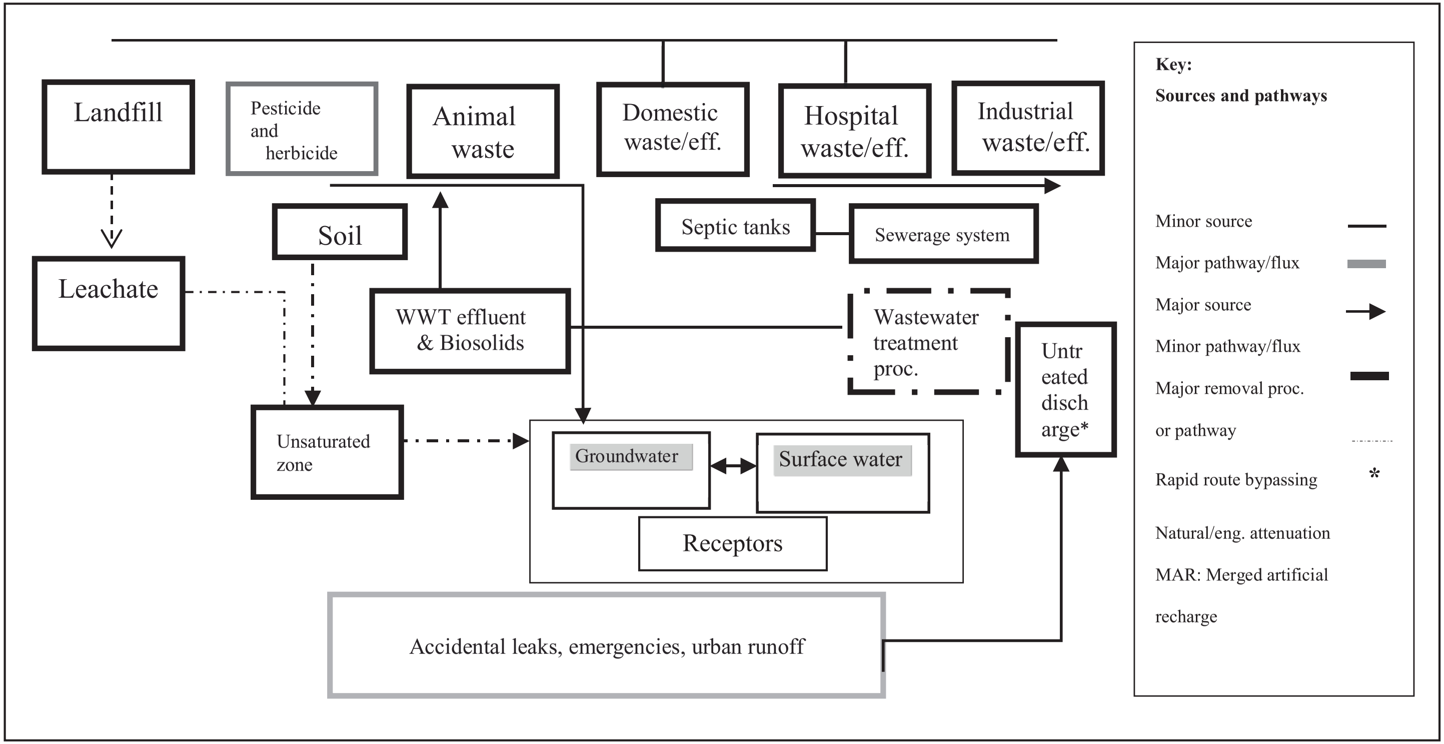


Fig. 6.3 The pathway receptor source approach for emerging contaminants ECs. (Adapted from Lapworth et al. 2012)

SW-GW exchange is significant in aquifers below and adjacent to watercourses, e.g., in shallow alluvial aquifers, essential sources of drinking water on the globe. MAR refers to surface water use and treated wastewater to recharge aquifer artificially. This is suitable in semiarid areas where water resources are scarce or replenish aquifers or used as natural treatment and temporary storage systems (Buerge et al. 2009; Drewes 2009; Mueller et al. 2011; Gasser et al. 2010)

However, artificial recharge has short circuit natural attenuation mechanisms in soil and subsurface and leads to potential long-term groundwater sources' contamination; diffuse leakage from poor maintenance and reticulated sewerage systems can pose the risk of EC pollution in groundwater. Nonvolatile compounds can be mobilized in atmospheric transmission route and aerial sources including industry, agriculture, and transport dust; diffuse with low loading in land surface and not known significant for groundwater pollution (Hamscher and Hartung 2008; Ellis 2006).

6.12 Conclusion and Future Prospects

Over the past few years, emerging organic contaminants, personal care products, and pharmaceuticals have been detected in the groundwater. More compounds may be spotted with the help of advanced analytical methods and techniques. It is almost impossible to remove these contaminants from the groundwater; hence, this is the only robust approach to detect the source and control them at the source of release to the water cycle. Momentarily, this is an immediate measure to regulate these contaminants by awareness campaigns about toxicity, risks, distribution, and occurrence of these contaminants present in the underground drinking water.

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Chapter 7
Environmental and Health Effects of Heavy Metals and Their Treatment Methods

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Abstract Heavy metals (HMs) are natural constituent that exist in ecosystem and are used for various industrial and economics purposes. Mercury is the naturally occurring heavy metal, mostly use in industries. It is commonly present in the form of elemental mercury, methyl-mercury, and inorganic mercury. The main sources of mercury and cadmium are earth crust, volcanoes, and vaporization from natural water bodies. Mostly mercury is used in producing dental amalgams, thermometer, and some batteries. It can be found in some chemicals, electrical equipment, metal processing, and building industries. Mercury is released into the ecosystem by different ways such as agriculture sources in the form of seed preservation, pharmaceuticals, speeding organic reactions, and in chlorine and caustic soda production. It has also many negative impacts on environment as well as human health.

Mercury and cadmium are the deleterious substances which have indirect role in human chemical and physiochemical processes and do not naturally occur in living bodies. Mercury and cadmium contamination occur in human beings through anthropogenic activities such as municipal and industrial wastewater discharge and through agricultural runoff. Mercury and cadmium produced during metal processing and building industries can cause many health hazards such as blindness, deafness, and digestive problems. Fetal exposure to mercury will causes miscarriages, inborn diseases, and mental retardation.

Mercury is present in an unreactive form in the air. Workers and residents living near the mercury extraction sites have greater chances of exposure. According to the U.S. Environmental Protection Agency, HMs are possible carcinogens. Methyl-

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_7

mercury is made primarily by minute organisms present in water and soil. The current standard of mercury by EPA and WHO for drinking water is 0.002 mg/L, and for industrial effluent, it is 0.001 mg/L.

Removal of HMs from wastewater can be carried out by precipitation, coagulation, ionic exchange, electrochemical operation, and biological treatment, while removal of mercury from drinking water can be done by using coagulation, granulated activated carbon, lime softening, and reserve osmosis. HMs pose serious health issues and also have economic impacts such as decrease in working productivity, increase in health expenditure per person, and increase in mortality and morbidity. Health is the basic right of every human, so strict protective measure should be taken by workers which are mostly exposed to mercury. Hence, major research is needed to further explicate the public health impact associated with human exposure to such toxic metal.

7.1 Introduction

Increasing industrialization results in the generation of heavy metals, which causes environmental pollution as a global issue (Usman et al. 2019). Heavy metals are actually elements having atomic number and density greater than 20 and 5 g/cm^3, respectively (Ali and Khan 2018). Arsenic (As), lead (Pb), copper (Cu), cadmium (Cd), nickel (Ni), chromium (Cr), and mercury (Hg) are a few examples of heavy metals and are toxic, bioaccumulative, and persistent in nature. They are released into various components of the environment, i.e., water, air, and soil, from various natural and anthropogenic sources like volcanic eruptions, weathering of rocks, mining, industries, domestic, and various agricultural activities (Ali et al. 2019; Usman et al. 2019).

Some heavy metals are known as essential metals as they play a vital role in various biological functions of living organisms and are harmful beyond a certain dose and exposure time. However, nonessential heavy metals are toxic even at a very low concentration. Heavy metals are mutagenic, teratogenic, and carcinogenic, which have serious effects on public health as well as on the environment (Mohamed et al. 2017). They result in the generation of ROS (reactive oxygenic species) and cause oxidative stress. Oxidative stress in living organisms results in the development of various abnormalities and diseases like renal, brain, and neurological disorders (Ali et al. 2019).

Chronic or long-term exposure to heavy metals is a real hazard for the environment and living organisms (Wieczorek-Dąbrowska et al. 2013). The most common routes of chronic exposure of heavy metals to human beings and animals are through inhalation of pollutants, utilization of contaminated food and water, or exposure to contaminated soil and industries (Mohammadi et al. 2019a; Shen et al. 2019). Contamination of various sources of food like vegetables, fruits, fishes, and grains can also occur by the accumulation of heavy metals in them from polluted water and soil sources (Sall et al. 2020). Heavy metals' exposure can result in various diseases in humans like cancers, respiratory, neurological, and kidney problems. For instance, carcinogenic chromium can aggravate skin abrasions, cancer, and respiratory problems (Mohammadi et al. 2019a).

Heavy metals' concentration above the threshold limit not only reduces fertility of soil, but also affects its microbiological balance (Barbieri 2016). Bioaccumulation of heavy metals in biota of various ecosystems has different adverse effects on living organisms (Malik and Maurya 2014).

Many elements are classified into the category of heavy metals, for instance Cr, Ni, Zn, Cu, Pb, As, and Hg, but some are relevant in the environmental context (Barakat 2011). Chromium and copper are among various environmentally toxic heavy metals (Ali et al. 2019), and in the current chapter, our focus is on these two heavy metals.

7.1.1 Chromium and Its Oxidation States

French chemist Louis Vauquelin, in 1797, discovered chromium in the mineral crocoite (lead chromate) and named it chromium as its compounds have different colors. Chromium is derived from the Greek word (χρωα) chroma, meaning color. Chromium has the atomic and mass number of 24 and 51.99, respectively. It is present in the IV period and group VI B of the periodic table. The gemstones emerald and ruby contain chromium (chromic oxide) in their structure, so they have green and red colors, respectively. Chromium is the abundant element, i.e., on number 21 on the earth's crust, and is also the sixth most plentiful transition metal (Mohan and Pittman Jr 2006).

Chromium occurs in nature in different oxidation states from −2 to +6 (Tumolo et al. 2020). However, chromium usually exists in water in two main stable oxidation states, i.e., trivalent Cr (III) chromium and hexavalent Cr(VI) chromium, whereas other oxidation states of chromium are unstable in aqueous solution (Honnannavar and Hosamani 2014). Cr (III) has less solubility and mobility and is adsorbed by the soil particles which prevents it to enter into underground water and ultimately stops its uptake by the plants (Haroon et al. 2020).

Cr as Cr (III) is a significant element which helps in the metabolism of lipid and protein (Briki et al. 2017). However, Cr (VI) has high solubility, mobility, and oxidizing power; that's why it is 100 folds more toxic compared to the trivalent chromium and it remains available within the human body for 39 h. Cr (VI) is 1000 times more toxic, cytotoxic, mutagenic, teratogen, and cancer-causing chromium than Cr (III) in living systems (Bansal et al. 2019; Haroon et al. 2016). The United States Environment Protection Agency and International Agency for Research on Cancer classified Cr (VI) as a Group A and Group I carcinogen, respectively, for humans because of its highest toxicity level (Xia et al. 2019). Cr (VI) is included in the list of eigh most toxic chemicals for human beings and has been found commonly as a third hazardous pollutant on the waste dumping sites (Jin et al. 2016). The main focus of Erin Brockovitch, the Hollywood blockbuster movie, is on the toxicity of hexavalent chromium (Saha and Orvig 2010). Cr (VI) toxicity was linked with its oxidizing power; it strongly oxidizes various biomolecules, for instance, protein and DNA (Parlayıcı and Pehlivan 2019). High mutagenic properties of Cr (VI) can trigger the reproductive system and the DNA and can cause several birth defects (Parlayıcı and Pehlivan 2019).

According to EPA guidelines, many countries have the standard limits of Cr (VI), i.e., 0.05 mg L^{1}, 0.1 mg L^{-1}, and 0.25 mg L^{-1} for drinking water, inland surface water, and industrial effluent, respectively. Cr (VI) is usually present in the form of hydrogen chromate ($HCrO_4$) and dichromate ($Cr_2O_7^{2-}$) anions in acidic conditions and as chromate (CrO_4^{2-}) anions in basic media (Jobby et al. 2018). These all Cr (VI) ions are highly soluble and have strong oxidizing property which make them very active in various environmental portions like water and soil (Antoniadis et al. 2018).

Because of the elevated level of Cr (VI) solubility as well as mobility in aqueous solution, it can easily move into various living biota and causes numerous physiological disorders, for example, anemia, diarrhea, nausea, epigastric discomfort, circulatory shutdown, internal hemorrhaging, stomach damage, skin irritation, ulcers, vomiting, lung cancer, and kidney cancer (Jobby et al. 2018).

7.1.2 Copper and Its Oxidation States

Copper (Cu) is the transition element which is placed in the fourth period and group IB of the periodic table (Wuana and Okieimen 2011). It has the atomic and mass number of 29 and 63.546, respectively. Globally, it is the third most used element and is twenty-fifth most abundant constituent of the earth (Karlin and Tyeklár 2012).

There are three main oxidation states of copper, metallic or solid copper having zero oxidation state, i.e., Cu (0), whereas cuprous Cu(I) and cupric Cu (II) ions are other two forms. The most important oxidation state of copper is Cu (II), which is coordinated with six water molecules and is usually encountered in water. Compounds of cupric are of green or blue color and commonly water-soluble. After entering into the environment, Cu (II) binds itself with the various organic and inorganic materials which are present in the water, soil, and sediments depending on the presence of various competing ions, pH, and oxidation-reduction potential of the environment.

7.2 Sources of Chromium and Copper

Chromium and copper enter into the environment from both natural and anthropogenic processes (Fig. 7.1). However, its concentration is low, when occurs naturally, and becomes high when released into the environment from industries.

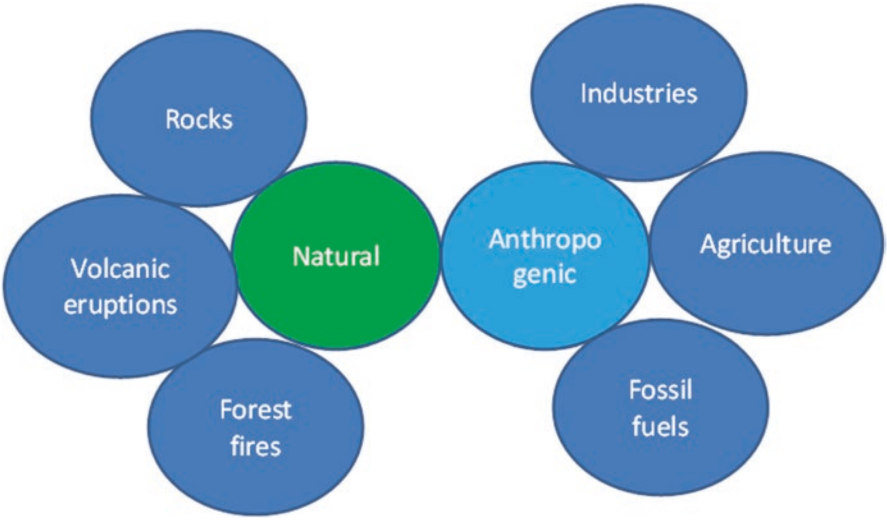

Fig. 7.1 Different sources of chromium and copper

7.2.1 *Natural Sources*

Chromium occurs naturally in different types of rocks, minerals, and ores and is released into the environment by its natural degradation, interaction, and reactions. It is the twenty-first largely available element in the rocks, having an average concentration of 100 mg/kg rock. Some examples of natural rocks having chromium are igneous rocks, sedimentary rocks, ultramafic rocks, and felsic rocks (granites). Chromite and a range of spinel-type minerals are a natural source of chromium (Kabata-Pendias and Mukherjee 2007).

Likewise, copper is a reddish-brown element which exists naturally in rocks, sediments, soil, air, and water. Out of total copper, which is present on earth, almost two-third is present in igneous (volcanic) while one-fourth in sedimentary rocks. It is also released through volcanic eruptions, windblown dust, forest fires, decaying of organic material, and sea spray.

7.2.2 *Anthropogenic Sources*

Man-made activities are the major source of environmental contamination with chromium. Some major sources of chromium are brass, paper and pulp, automobile, fertilizer, steel, textile, metal finishing, chromite ore processing industry, magnetic tapes, wood protection, leather tanning, petroleum distillation, electrical equipment, etc. (Kabata-Pendias and Mukherjee 2007; Mohan and Pittman Jr 2006). These all sources produce a huge quantity of chromium-containing effluents which pollute both surface and groundwater resources. Although chromium can be derived from natural sources, a high amount of it is entering into the environment as a result of industrial activities, like electroplating and leather tanning (Blowes 2002). During chrome tanning process of hides, almost 40% of unused salts of chromium are released in the effluents (Chowdhury et al. 2016). Other important anthropogenic chromium sources are municipal wastes and resultant sludge of municipal waste. Industrial and residential sewage treatment plants also discharge a significant amount of chromium into water bodies. More or less, all chemical laboratories such as research, academic, and industrial releases significant chromium (both trivalent and hexavalent) amount into the environment (Testa et al. 2004).

Vehicles are another contributor of Cr emission into the environment (Ferretti et al. 1995). Incineration, coal, and wood combustion also release 50,000 tons per year of Cr worldwide (Merian 1984). A significant amount of Cr is present in fertilizers (Krüger et al. 2017). According to the International Agency for Research on Cancer (IARC), normally the cigarettes made in the US have 0.24–6.3 mg of Cr per kg. Higher levels of Cr have been found in areas near landfills and hazardous waste disposal sites. House dust and soil also contain Cr (VI) (Shankar and Venkateswarlu 2011).

Copper is also released through various anthropogenic sources, for instance, mining, fossil fuel combustion, solid waste, traffic emissions, and wastewater of various industries like chemicals, paints, fertilizer, fungicides, etc. (Ameh and Sayes 2019). Bulk of copper is mined each year because of its application in different processes, so copper mining itself is a cause of pollution as it involves different steps from mining to milling of copper and is therefore deteriorating the environment.

Another main source of copper release into the environment is through various agricultural practices. Copper in the form of copper sulfate has been known to be used as the first chemical against various plant diseases, whereas other hydroxides and oxychlorides of copper are also used as pesticides, herbicides, fungicide, nematicides, etc. (El-Hak and Mobarak 2019; Iwinski et al. 2017). Phosphate-based fertilizers also contain a large quantity of copper and are a key source of copper in soil. Copper is also used for wood preservation. In North America, greater than 79,000 tons of copper are used annually, which showed a 50% share of the wood preservation in the global market (Anjum et al. 2015). Because of the antimicrobial properties of copper, it also has wide applications in the field of medicines (Anjum et al. 2015).

7.3 Environmental Effects of Chromium and Copper

Environmental pollution due to Cr (VI) is attaining more attention as it is present globally with elevated levels in water and soil due to both natural and anthropogenic sources (Ashraf et al. 2017; Brasili et al. 2020). These comprise mining, dyeing, incineration, fertilizers, wood, and paper processing which results in elevation of Cr (VI) in water and soil (Jones et al. 2019; Yang et al. 2020).

Chromium has been reported globally above the permissible limit in water and soil of different countries like Pakistan, China, and India (Bhattacharya et al. 2019; Raza et al. 2017). A number of tanneries (both registered and unregistered) in Pakistan are releasing chromium in their effluent, which ultimately contaminates the environment. Drinking water pollution with a high chromium concentration of 5.50 mg L^{-1} has also been noticed in Sahiwal, Pakistan (Zahir et al. 2015). Increase in chromium concentration in the soil results in the appearance of genetic modification in the plants. Acidification of soil can also affect the utilization of chromium by plants (Hayat et al. 2012). Plant physiology is also affected by Cr (VI), along with reduction in plant growth, chorosis, and necrosis (Haroon et al. 2020). Literature showed that numerous medicinal plants which are grown near industries have accumulated various heavy metals like chromium and copper (Bolan et al. 2017; Kohzadi et al. 2019). Even though Cr (III) is a vital nutrient for humans' metabolism, if its concentration increases from 150 mg L^{-1}, it is harmful for the plant physiology (Haroon et al. 2016).

In Mexico (Sonora), almost 43% of drinking water from different sources (storage tanks and wells) showed higher amount of Cd, Cu, As, and Pb (Organization 2018). Elevated levels of Cu, Cd, and Pb have been reported in the drinking water of 10 different cities of Saudi Arabia which is ascribed with Kuwaiti and the Gulf War oil fires (Chowdhury et al. 2016). Another report of ten years in rural regions of India indicated the high values (above WHO values) for As, Cr, Mn, Pb, Zn, and Ni in groundwater, which was associated with the pharmaceutical, pesticide, paint, and fertilizer industries (Bajwa et al. 2017; Chowdhury et al. 2016). Wastewater from industries pollutes the nearby water bodies. Coal combustion in industries is the key source of air pollution, as coal contains trace amounts of chromium, while dumping of resultant chromium-containing solid waste will result in elevated concentration of chromium in air and soil, respectively. In contrast, globally, the release of chromium in soil, water, and air is 896, 142, and 30 thousand metric tons per year, respectively (Mohan and Pittman Jr 2006).

Copper is a vital micronutrient for different biotic components of the environment (Zitoun 2019), but a high level of copper can also result in environmental pollution. It is known as a priority pollutant as reported by US-EPA and is normally present in various water bodies (Sruthi et al. 2018). Copper speciation in the water bodies is actually responsible for the toxicity of copper (Tait et al. 2018). Cu has attained great consideration because of its dual effect towards plants, i.e., at optimum amount, it is essential, whereas it becomes toxic at higher concentrations (Ameh and Sayes 2019). Copper is among the eight important micronutrients which are needed for the growth of plants (Nazir et al. 2019) and is also linked with several physiological as well as biochemical processes (Garcia et al. 2014). Copper is a part of the structures of various regulatory proteins (enzymes) and helps in protein synthesis, respiration of mitochondria, metabolism of cell wall, photosynthetic electron transport, oxidative stress response, and hormone signaling (Nazir et al. 2019; Zhang et al. 2019). Plastocyanin (an electron carrier proteins) also contains a large amount (50%) of the copper inside the plastids (Zhang et al. 2019). Copper has the ability to easily gain and lose electrons; therefore, it acts as a cofactor in various enzymes like laccase, polyphenol oxidase, and amino oxidase and plays an important role of antioxidants under conditions of stress (Nazir et al. 2019; Zhang et al. 2019).

On the other hand, exposure to excess copper by the plants will affect various bio-physiochemical processes (Ameh and Sayes 2019; Jaime-Pérez et al. 2019) and will result in oxidative stress along with alterations in RNA and DNA (Ameh and Sayes 2019; Jaime-Pérez et al. 2019). 20–30 mg kg^{-1} is the toxic range of copper for plants (Marschner 2011). Excess uptake of Cu can affect photosynthesis, enzymatic activity, respiration, and growth of plant (Lillo et al. 2019; Zhang et al. 2019). Various visual symptoms of excess copper content in plants are chlorosis, nutrient deficiency, necrosis, reduced growth of shoots and roots, and even death in severe toxic conditions (Zhang et al. 2019).

In the soil of the USA, the threshold limit of copper for crops plantation is 100 mg kg^{-1} (Kabata-Pendias 2010). As copper has high density, so its mobility in soil is less and it mostly accumulates in topsoil (Araújo et al. 2019; Ju et al. 2019). About 80% of copper is present in soil as sulfides and oxides, which are not soluble and have low phytoavailability (Mihaljevič et al. 2019). However, some Cu (20%) is present as carbonates and hydroxyl compounds in soil and is mostly available to the plants in this form. Copper in Cu^{2+} form is generally absorbed by plants because of its strong binding ability with organic materials than other species of copper (Ogunkunle et al. 2019). The presence of a higher amount of copper in soil reduces crop production and ultimately threatens the health of humans (Rizwan et al. 2016). Another source of environmental pollution is the release of inorganic Cu into the atmosphere in the form of particulate matter, mist, and dust particles (Fang et al. 2011). High concentration of copper has been found in the river (Nyam-wamba) near the copper mine of Kilembe, Western Uganda. Another study showed a high copper level of 15.01 mg/L in both ground and surface water at 33 places, which are located near mines of copper at Malanjhkhand in India. Cu's highest concentration, i.e., 2.8 mg/L, was reported in well water of Pothi Bala (AJ&K) (Javaid et al. 2008). The permissible Cu concentration in the case of soil on which application of sewage sludge is carried out is 50–140 mg/kg as per European Standards (Radojevic and Bashkin 2006). Different regions of Pakistan revealed the copper range of <6–412 mg/kg in both dust and soil, whereas the highest content of copper was reported in contaminated soil of the Kohistan region (Muhammad et al. 2011). The industrial area of Islamabad (Pakistan) also showed elevated copper concentration level, from 8.88 to 357.40 mg/kg (Malik et al. 2010). A high concentration of copper was found in the sediments of Malir River (Karachi, Pakistan), i.e., 272 mg/kg, and River Ravi (Punjab, Pakistan), i.e., 159.79 mg/kg (Abdul et al. 2009; Siddique et al. 2009). Elevated range of copper (09–75 mg/kg) was reported in different vegetables grown in Gillgit (Northern Pakistan) (Khan et al. 2010). The mentioned values here are alarming as the allowable intake value for copper is 10 mg per day. The maximum amount of Cu reported in Chile, Hong Kong, India, Nigeria, and the USA was 1.2 mg/L, 4.6 mg/L, 1.9 mg/L (Xu et al. 2006), 0.01 mg/L (Olalekan et al. 2018), and 4.8 mg/L, respectively (Zahoorullah and Zai 2003).

7.4 Health Effects of Chromium and Copper

On the basis of time of exposure, toxicity can be defined as acute and chronic. Acute toxicity is displayed within a short time due to the short-term single exposure of a few minutes or several days with the toxic substance like heavy metals and is used to indicate a hazardous event or toxic properties of a substance. However, chronic or toxic effects (toxicity) are defined as sub-lethal effects due to the prolonged exposure generally to a small quantity of toxic substances.

Public health concerns in the case of chromium are mainly related to the Cr (VI), due to its toxic properties on animals, microorganisms, plants, and humans (Alemayehu et al. 2011). The human health risks depend on dosage, exposure level, and time duration of Cr (VI). Chromium enters into the body of living organisms through either food or water, whereas acute and chronic effects include neurological, cardiovascular, renal, hematological, gastrointestinal, hepatic, and even death. A long-term and continuative exposure, i.e., occupational exposure, to even low amount of chromium, can affect the blood, skin, immune, and respiratory system (Zhang et al. 2014). Nonoccupational exposure includes cigarette smoke, contaminated water, air, and food (Shankar and Venkateswarlu 2011). Workers in a German chrome ore industry developed lung cancer. Numerous studies also confirmed elevated level of cancers (lung and nose) in people exposed to different Cr processing industries (Shankar and Venkateswarlu 2011).

The genotoxicity effect of chromium at cell level results in the damage of DNA, oxidative stress, and development of the tumor (Wise et al. 2019). According to USEPA (United States Environmental Protection Agency), Cr(VI) is listed among seventeen hazardous metalloids and metals that are risky to the health of humans. Moreover, exposure to Cr (VI) by other living things like animals and plants also results in severe health issues in them (Jobby et al. 2018).

In order to protect environmental health, the recommended maximum permissible limit of Cr is 64 mg per kg (Shahid et al. 2017). Literature revealed the elevated levels of various heavy metals including Cr in the blood of welders who are occupationally exposed to the fumes of welding and also displayed more oxidative stress than control group (Mahmood et al. 2015). Similarly, welders working in the stainless steel industry are exposed to the Cr (VI) and have high risk of pharynx and larynx cancer (Gustavsson et al. 1998). Another study in Lahore, Pakistan, reported higher amount of Cr, Pb, and Cd in cancer and diabetic patients (Shafique et al. 2011).

Cr analysis in groundwater catchment of Luan River (China) indicated 2.074 hazard value for people living in the surroundings of the study area, which is greater than the permissible value (1) and 3.99×10^{-5} was the average carcinogenic risk value for studied metal of Cr (Liu and Ma 2020). Literature revealed the highest cancer risks (6.54×10^{-3}) probability in public of Khorramabad, Iran, through drinking water contaminated with chromium (Mohammadi et al. 2019b). Cr (VI) was also reported in the ground (1.35 mg L^{-1}) and surface water (0.027–2.48 mg L^{-1}) of India in Odisha state of the Sukinda area. The cancer risk due to Cr contaminated water in children and adults was 1.05×10^{-3} and 1.21×10^{-3}, respectively, while the oral hazard index was 1.64 and 1.90 times higher in children and adults, respectively (Naz et al. 2016). Generally, chromium does not accumulate in the body of fish, but when a large amount of chromium enters into surface water it can affect fish gills. In the case of animals, chromium can weaken the immune system and cause respiratory difficulties, genetic disorders, infertility, and development of tumors. Chronic exposure of chromium in humans can result in skin lesions and causes various respiratory diseases even cancer of broncho pulmonary (Ahmad et al. 2012).

Copper is an important element for living organisms, but in excess amount it has many negative effects on plants, animals, and humans (Zhou et al. 2018). Daily intake of copper occurs through diet, i.e., 75% and 25% through food and drinking water, respectively (Brewer 2015). Copper is mainly present as organic cuprous (Cu^+) form in solid food (Ceko et al. 2014) and as inorganic cupric (Cu^{2+}) form in drinking water. The Cu^{2+} is toxic and carcinogenic when used in excess amount through ingestion. The excessive consumption of Cu^{2+} will result in its liver deposition following vomiting, abdominal pain, headache, liver failure, etc. (Akar et al. 2009).

The average intake of Cu from drinking water is in the range of 0.1–1 mg per day. The permissible limit of Cu^{2+} for industrial effluent is 1.3 mg/L by US, EPA (Shawabkeh et al. 2004), whereas for drinking water the allowable limit of Cu^{2+} is 1.5 mg/L as recommended by WHO (Organization 2018). The acute effects of copper intake in humans include various gastrointestinal symptoms, for example, abdominal pain and nausea (Taylor et al. 2020). The RfD (oral) value of 0.04 mg Cu/kg/day is protective for children and adults of any acute or chronic toxicity (Taylor et al. 2020). It is reported that excess amount of copper in drinking water has caused pink disease (toxic syndrome) in infants (Thornton 1983). However, another disease (chronic) due to the excess use of copper is hepatolenticular degeneration, also known as Wilson's disease, which damages various body organs of a person and will result in death (santé et al. 2004).

Another occupational hazard of copper intake through aerosol is the vineyard sprayer's lung disease (Todd et al. 1934). Exposure to a large amount of copper for a long time will result in a high percentage of copper in tissues and serum, which affects the immune system and leads to oxidative stress (Turnlund et al. 2004). If excess of copper is present in freshwater bodies, then it will impair the osmoregulatory mechanism of aquatic organisms (Lee et al. 2010).

Copper piping network is mostly used in homes and public supply of drinking water which is the main source of copper exposure to people (Uauy et al. 2008). Cases of liver cirrhosis were reported in various regions of India in some young children, when they used milk which was stored in the copper containers (Nayak and Chitale 2013; Uauy et al. 2008).

7.5 Treatment Methods for Hexavalent Chromium and Copper Removal

7.5.1 Physicochemical Methods

7.5.1.1 Adsorption of Chromium and Copper

Adsorption is considered an effective method for the removal of heavy metals. It is an economical method capable of removing heavy metals at very low concentration (Ali 2012). During adsorption, soluble gases and liquids attach onto the surface of adsorbents. The adsorbents used for the removal of heavy metals include activated carbon (Sounthararajah et al. 2015), fly ash (Weng and Huang 2004), modified chitosan (Justi et al. 2005), landfill clay (Ghorbel-Abid and Trabelsi-Ayadi 2015), peat (Ho and McKay 1999), and manganese oxides (Kim et al. 2013).

Adsorption can be divided into two main types, i.e., physisorption and chemisorption. In physisorption, van der Waals force is responsible for the attachment of pollutant and adsorbent. On the other hand, chemisorption occurs as a result of chemical bonding between adsorbent and adsorbate. Adsorption capacity of the adsorbents depends upon the characteristic of adsorbent surface. For example, surface charge, surface area, and functional groups on the adsorbent can have different removal efficiencies for different pollutants.

Several studies have been focusing on the removal of hexavalent chromium using natural (Enniya et al. 2018), synthetic (Huang et al. 2015), waste (Valentín-Reyes et al. 2019), and composite materials (Geng et al. 2019; Vakili et al. 2018). A wide variety of adsorbents can be used for the treatment, such as activated carbon (Valentín-Reyes et al. 2019), carbon nanotubes (Huang et al. 2015), chitosan (Vakili et al. 2018), graphene oxide (Geng et al. 2019), apple peels, etc. (Enniya et al. 2018). Recent studies on chromium removal are shown in Table 7.1.

The Fourier Transform Infrared (FTIR) results before and after Cr (VI) adsorption suggest that band stretching of C = O, C-O-C, C = C, and C≡C groups was involved for the binding of Cr (VI) (Enniya et al. 2018). The nitrate, amine, and amide groups can also be involved in the binding process (Geng et al. 2019). Other mechanisms involved chelation, electrostatic interaction, and reduction (Geng et al. 2019; Vakili et al. 2018). Several studies focused on the reduction of Cr (VI) to Cr (III) besides adsorption, as 50% reduction was observed on modified activated carbon (Valentín-Reyes et al. 2019).

Several factors might affect the removal efficiency of the Cr (VI). Mostly, the highest adsorption occurs at acidic pH 2.0 (Enniya et al. 2018; Geng et al. 2019; Haroon et al. 2017; Vakili et al. 2018), with adsorption capacity ranging from 39 to 436.2 mg/g. It fits best with Freundlish isotherm, follows pseudo-second-order kinetics, and is spontaneous and endothermic reaction (Enniya et al. 2018; Huang et al. 2015). The Langmuir isotherm is also reported (Huang et al. 2015), while Geng et al. reported that Cr (VI) adsorption initially followed pseudo-second-order and at the end it became multistep influence (Geng et al. 2019). This suggests that Cr (VI) adsorption is highly dependent on the type of adsorbent used.

Table 7.1 Technologies used for chromium removal

S. no.	Method	Types	Mechanism	Removal effficiency (%)	Adsorption capacity (mg g^{-1})	Medium	References
01	Adsorption	Activated carbon, graphene oxide, apple peel,	Chelation, reduction, binding with acid components, etc.	99	39–436	Aqueous	Enniya et al. (2018), Geng et al. (2019), Huang et al. (2015), Vakili et al. (2018), and Valentín-Reyes et al. (2019)
02	Electrocoagulation	Use of iron, aluminum, copper as electrodes.	Charge neutralization, aggregate formation, and reduction to Cr (III)	88–100	–	Aqueous	Arroyo et al. (2009), Khan et al. (2019), Mahmad et al. (2016), Pan et al. (2017), and Pikna et al. (2020)
03	Membrane filtration	Microfiltration	Cr (VI) aggregation by micelle, coagulation, etc. and size-based separation.	99.6	–	Aqueous	Doke and Yadav (2014), Liu et al. (2020), Vasanth et al. (2012), and Visvanathan et al. (1989)
		Ultrafiltration	Cr (VI) size enhancement and size-based separation.	90–100	–	Aqueous	Aliane et al. (2001), Aroua et al. (2007), Ghosh and Bhattacharya (2006), and Muthumareeswaran et al. (2017)
		Nanofiltration	Selective removal of divalent and larger ions and particles.	80–99.8	–	Aqueous	Mnif et al. (2017), Wei et al. (2019), and Zolfaghari and Kargar (2019)
		Reverse Osmosis	Selective rejection of monovalent and larger ions.	99	–	Aqueous	Gaikwad and Balomajumder (2017) and Piedra et al. (2015)
04	Ion exchange	Anion exchange	Adsorption or binding with functional groups on ion exchange resins.	97–100	236–277	Aqueous	El-Mehalmey et al. (2018), Meshram et al. (2018), Rapti et al. (2016), and Xie et al. (2019)
05	Bioremediation	Fungi	Reduction of Cr (VI) to Cr (III) and bioaccumulation.	89–99.4	2.12–4.9	Aqueous	bibi et al. (2018) and Kumar and Dwivedi (2019a, b)
		Bacteria	Reduction using chromate reductase enzyme.	92–100	–	Aqueous	Baldiris et al. (2018), Hossan et al. (2020), Tariq et al. (2019), and Tharannum (2020)

Different studies on copper removal are shown in Table 7.2. In a study, chitosan was modified with ethylenediaminetetra-acetic acid (CS-EDTA) and was used for copper removal from aqueous solution. The adsorption capacity of CS-EDTA was also compared with chitin and chitosan. The adsorption capacity of CS-EDTA for copper was maximum, i.e., 58. 67 and 110 mg g^{-1}. The adsorption kinetics was best fit to pseudo-second-order (Labidi et al. 2016). In another study, sulfur microparticles were synthesized by using facile method. These microparticles were used for the removal of copper from aqueous solution of ethanol. Sigmoidal kinetic mode best explained the adsorption process. Sulfur microparticles caused physical adsorption (Xie et al. 2017). Batool et al. (2017) removed copper from water using low-cost farmyard and poultry manure-derived biochars. Both types of biochars efficiently removed copper from water. The adsorption capacity of farmyard-based biochar was maximum (44.50 mg/g). Chemisorption was observed during that study (Batool et al. 2017). Anbinder et al. 2019, studied the structural mechanism involved in the adsorption of copper. The interaction between copper and chitosan matices was through NH_2 groups in a pendant fashion. In the case of chromium, the adsorption was due to azanide and OH functional groups (Anbinder et al. 2019). Dong et al. (2019) recently removed copper ions from aqueous solution by using modified wheat straw. The wheat straw was modified with polyethylenimine (PEI) by using epichlorohydrin (ECH) as grafting agent. The mechanism behind this adsorption was coordination. The adsorption capacity of modified wheat straw was 48.6 mg/g. The copper adsorbed wheat straw was also regenerated by using 0.1 molar HCl solution (Dong et al. 2019).

7.5.1.2 Electrocoagulation-Based Chromium and Copper Removal

Electrocoagulation (EC) is the electrochemical process which generates metal ions. These metal ions destabilize the pollutants by neutralizing the electric charge on them. The charged metal ions with the oppositely charged pollutants form flocs. EC process is very effective for the removal of pollutants. This process produces little amount of sludge, there is no chemical requirements, and its operation is simple (Rajeshwar and Ibanez 1997).

Electrochemical process mechanism in an aqueous solution is very complex (Lin et al. 1998). There are three most commonly involved mechanisms during the electrochemical process, i.e., electrocoagulation (EC), electrooxidation (EO), and electroflotation (EF). EC process results in the destabilization of pollutants by the production of electric current. During the EC process, metals and metal hydroxide cations are used. EO process breaks down organic pollutants into carbon dioxide, water, and other oxides by oxidation. EF, on the other hand, produces hydrogen and oxygen gas bubbles which carry the pollutants to the surface. Other possible mechanisms during electrocoagulation are sorption and coagulation (Malkin 2003).

The electrocoagulation is a simple electrochemical process relying on the flow of current through electrodes (usually Iron or Aluminum) which dissociates in the solution to neutralize the Cr(VI). Compared to aluminum anodes, the iron anodes

Table 7.2 Technologies used for copper removal

Method	Types	Mechanism	Removal efficiency (%)	Adsorption capacity (mg g^{-1})	Medium	References
Adsorption	Chitosan- ethylenediaminetetra-acetic acid (CS-EDTA)	Pseudo-second-order	–	58. 67 and 110	Aqueous	Labidi et al. (2016)
	Sulfur microparticles	Mass transfer, coordination and physical adsorption	–	–	Ethanol-aqueous solution	Xie et al. (2017)
	Farmyard and poultry manure-based biochars	Multilayer sorption, chemical interaction	–	44.50	Water	Batool et al. (2017)
	Chitosan matrix	Amino groups in a pendant fashion	–	–	Aqueous	Anbinder et al. (2019)
	Wheat straw (WS) was modified by polyethylenimine (PEI)	Coordination	–	48.6	Aqueous	Dong et al. (2019)
Electrocoagulation	Mucilage of Opuntia ficus indica (OFI)	Electrochemical production of metal ions and buoyant gas bubbles	100	–	Water	Adjeroud et al. (2018)
	New cell design	Electrochemical production of metal ions	98	–	Copper plating plant Effluents	Kilany et al. (2020)
	Electro-Fenton and electrocoagulation	Oxidation, electrochemical production of metal ions	–	–	Wastewater	Guan et al. (2018)
	Photovoltaic Electrocoagulation	Electrochemical production of metal ions	99.01	–	Aqueous solution	Thanh et al. (2019)

Method	Types	Mechanism	Removal efficiency (%)	Adsorption capacity (mg g^{-1})	Medium	References
Ion exchange	Polymeric submicron ion exchange resins	Solid phase ions shared with equal ion numbers from contaminated water	46	–	River water	Murray and Örmeci (2019)
	Amberlite IRC-86	Solid phase ions shared with equal ion numbers from contaminated water	78.9	–	Bioleached wastewater	Choi et al. (2020)
	Chelating resins	Solid phase ions shared with equal ion numbers from contaminated water	–	167	Synthetic effluents	Edebali and Pehlivan (2016)
	Phosphorylated fullerene/sulfonated polyvinyl alcohol (PFSP) cation exchange membrane	Solid phase ions shared with equal ion numbers from contaminated water	73.2	1.67	Wastewater	Rikame et al. (2017)
	Hydrophilic nanoporous ion exchange barrier membrane,	Stripping	100	–	Aqueous solution	Song et al. (2018)

(continued)

Table 7.2 (continued)

Method	Types	Mechanism	Removal efficiency (%)	Adsorption capacity (mg g^{-1})	Medium	References
Membrane filtration	PEI-based nanofiltration membranes	The membrane structure acts as a selective barrier that allows movement of molecules to pass through with the help of a driving force producing large residual volumes	86	–	Wastewater	Bandehali et al. (2019)
	Reusable novel membranes	Bacterial cellulose (BC) nanofibril network as a template and chitosan (Ch) as the active phase	50	–	Wastewaters	Urbina et al. (2018)
	Modified cellulose acetate ultrafiltration membranes	Increases the available sites in the modified membranes	99.1	–	Synthetic wastewater	Kanagaraj et al. (2020)
	Novel membranes based on polyethersulfone (PES)	Increases the available sites in the nanocomposite membranes	90	–	Water	Rafieian et al. (2019)
	Electrospun nanofiber membrane	Pseudo-second-order, Langmuir-type adsorption	–	120.77	Industrial wastewater	Chen et al. (2018)

Method	Types	Mechanism	Removal efficiency (%)	Adsorption capacity (mg g^{-1})	Medium	References
Bioremediation	*Myriophyllum aquaticum*	Metabolism by the plants and biodegradation by rhizosphere microorganisms	–	–	Wastewater	Guo et al. (2020)
	Aquatic plant species	Metabolism by the plants	–	63.1 mg/kg	Synthetic wastewater	Lu et al. (2018)
	Pistia stratiotes	First-order elimination kinetics	96.38	–	Surface and distilled water	Tang et al. (2020)
	Limnocharis flava	1st order, Rate Law model	39.9	–	Distilled, mineral, and surface water	Alikasturi et al. (2019)
	Pseudomonas stutzeri LA3	Breaking complex pollutants into simpler form	50	–	LB broth	Palanivel et al. (2020)
	Escherichia coli	Adsorption	91.5	–	Aqueous solutions	Wang et al. (2019)

are preferred due to their higher removal efficiency and affinity for Cr(VI) (Pikna et al. 2020). This is an efficient method for recovering Cr(VI) in solid form. The method has been applied on several types of wastewaters and aqueous media such as leachate (Arroyo et al. 2009; Mahmad et al. 2016).

The mechanism of electrocoagulation depends on the generation of coagulant from the anodes due to oxidation, destabilizing contaminants, breaking of emulsions, particulate suspension, and forming flocks by aggregating destabilized phases (Arroyo et al. 2009). The iron (II) gets oxidized into iron (III) besides Cr (VI) into Cr (III) and forms oxides of iron with chromium (Pan et al. 2017). Usually, Cr (VI) can be recovered as precipitates in the EC process in the form of oxides of iron and Cr (VI) with 20% Cr by weight. The solid precipitates are mainly chromite ($FeCr_2O_4$) or their hydroxides or Cr_2O_3, $Fe2O_3$, $FeCr_2O_4$ mixtures (Arroyo et al. 2009; Pikna et al. 2020).

The parameters affecting the EC process are pH, current, and electrolyte concentration. Pikna et al. (2020) optimized Cr (VI) recovery from four steel slag leachates in 140–430 min, pH 6.0, and 0.1–0.5 A to completely remove 1 g/L of Cr (VI) (Pikna et al. 2020). Khan et al. reported a 100% removal efficiency at 1.48 A current, pH 3.0, and process time of 21.47 min (Khan et al. 2019). The iron-based anodes have superior removal efficiency at pH 7.0, while aluminum electrode is active at acidic pH (3.0) with comparatively lower removal efficiencies (Mahmad et al. 2016).

The cost effectiveness of this process should be considered as it is an energy-consuming process. The pH and electrolyte concentrations are very important in energy efficiency of EC process as pH 6.0 is efficient and higher pH (8.0) can consume more current. In contrast, low electrolytes (1000 mg/L NaCl) consume more current compared to higher electrolytes (50,000 mg/L NaCl) (Pikna et al. 2020). The energy consumed per gram Cr (VI) removed is 12.97–Watt/hour during an EC process (Khan et al. 2019).

Electrocoagulation-electroflotation (EC-EF) process was used for the removal of copper from water by using *Opuntia ficus indica* (OFI) plant mucilage. The OFI mucilage removed copper completely. Mucilage also increased the sludge settling rate. OFI mucilage which is found to be an active natural coagulant can be used for copper removal instead of chemical coagulants (Adjeroud et al. 2018). Kilany et al. 2020, developed a new electrocoagulation reactor. In a new design, a helical tube anode was placed between two (vertical cylindrical screen) cathodes. The new reactor was used for both oil and Cu removal from electroplating plant effluent. Under optimum conditions, copper and oil removal was 98% and 85%, respectively (Kilany et al. 2020). Guan et al. (2018) designed electrochemical reactor for Cu-EDTA degradation. In electrochemical reactor electro-Fenton and electrocoagulation process were used. During Electro-Fenton process, •OH radicals were generated which were responsible for Cu-EDTA destruction which releases copper ions. These copper ions were removed by using the electrocoagulation process (Guan et al. 2018). A solar photovoltaic cell (PV) was used as renewable energy source for the electrocoagulation process. This process was highly efficient for copper removal

(99.01%) and energy saving (1.039 kWh/m^3). The use of PV system with electrocoagulation process can make it a sustainable process (Thanh et al. 2019).

7.5.1.3 Membrane Filtration-Based Chromium and Copper Removal

Membrane filtration technologies are broadly divided into five major processes, i.e., microfiltration (MF), nanofiltration (NF), ultrafiltration (UF), reverse osmosis (RO), and electrodialysis (ED). The major difference in these technologies includes pore size, permeability, and operating pressure (Murthy and Chaudhari 2009). The main advantages of membrane technologies include high efficiency, complete removal of pollutants, and sometimes they consume less energy than thconventional methods (Farno et al. 2014; Marjani et al. 2012; Rezakazemi et al. 2013a; Rezakazemi et al. 2015). Due to the above-mentioned advantages, this technology was used for the removal of heavy metals from different industries wastewater (Baheri et al. 2015; Rezakazemi et al. 2012, 2013b).

Due to the simple separation mechanism of membrane technologies, they are widely used for treatment of water and wastewater (Murthy and Chaudhari 2009; Padaki et al. 2015). This separation mechanism is same for almost all membrane processes with minor exceptions. The rejection of pollutants is due to higher transmembrane pressure (Sutherland 2008). The separation of pollutants takes place with the help of semipermeable membrane. This semipermeable membrane blocks the passage of pollutants through the membrane (Sutherland 2008; Van der Bruggen and Vandecasteele 2003).

Microfiltration and ultrafiltration cannot remove dissolved Cr (VI) due to larger pore size. The removal can be enhanced by prefiltration aggregation of the Cr (VI) by various means. A surfactant-based separation process utilized the use of cetylpyridinium chloride (CPC) to create Cr (VI) micelle that further passed through titanium-based microfiltration membrane with 99% removal (Doke and Yadav 2014). Precipitating Cr (VI) into hydroxides with electric field across the microfiltration membrane reduced the membrane fouling besides removing Cr (VI) (Visvanathan et al. 1989). Similarly, biomass-assisted ceramic membrane microfiltration using baker's yeast removed 94% of 100 mg-Cr (VI)/L (Vasanth et al. 2012). A composite polyacrylonitrile electrospun membrane was effectively removing Cr (VI) and Cd (II) with nanoparticles having 90% regeneration ability (Liu et al. 2020).

A similar method can be applied for Cr (VI) removal by ultrafiltration. The polymer-enhanced ultrafiltration using chitosan, polyethyleneimine, and pectin was used to remove 100% Cr (VI) (Aroua et al. 2007). A micelle-enhanced ultrafiltration using cetyl pyridinium chloride (CPC) as surfactant was good for low concentration feed, but pressure started increasing when the concentration was increased upto 50 mM (Ghosh and Bhattacharya 2006). An indigenously prepared hydrolyzed polyacrylonitrile membrane effectively rejected 90% of ≤25 mg Cr (VI)/L at neutral pH in drinking water (Muthumareeswaran et al. 2017). Water-soluble macroligand formed complexation with Cr (VI) before ultrafiltration to achieve 95% removal efficiency (Aliane et al. 2001).

Nanofiltration is highly suited for the divalent ion removal from water. Zolfaghari and Kargar (2019), optimized the membrane filtration containing microfiltration and nanofiltration as: pH 10.0, pressure: 0.1 MPa pressure, 0.1 mg-Cr (VI)/L, and 500 mg-sulfate/L to achieve 99.8% removal (Zolfaghari and Kargar 2019). Nanofiltration membrane with enhanced negative charges showed comparatively better Cr (VI) and sulfate rejection (80%) at pH 7 than the positively charged membrane at similar permeance of 11.5 L m^{-2} h^{-1} bar^{-1} (Wei et al. 2019). Similarly, 99.7% Cr (VI) rejection was obtained using commercial nanofiltration membrane on shock absorber manufacturing wastewater (Mnif et al. 2017).

Reverse osmosis (RO) membrane selectively removes monovalent ions and utilizes the semipermeable membrane that only allows water molecules to pass under high pressure. A near 100% removal efficiency of 228 mgCr(VI)/L was reported with a polyamide reverse osmosis membrane with 30 bar pressure, 29% flux, and 95% water recovery (Piedra et al. 2015). The flat sheet polyamide RO membrane simultaneously rejected 99.7% of 5 mg/L fluoride and Cr (VI) with at 16 bar pressure and pH 8.0 (Gaikwad and Balomajumder 2017).

Bandehali et al. (2019) removed lead and copper from wastewater using modified PEI-based nanofiltration membrane. The water flux of modified membrane was higher than the PEI membrane. The lead and copper rejection of modified membrane was 85 and 86%, respectively. The lead and copper removal of this membrane was better than other membranes reported in the literature (Bandehali et al. 2019). A novel membrane using *in situ* and *ex situ* route was developed by Urbina et al. (2018) for the removal of copper from wastewater. Bacterial cellulose and chitosan were the main components of these novel membranes. The highest removal of copper was achieved with the membranes synthesiszed by using *in situ* biosynthesis. These novel membranes are easy to clean and can also be reused (Urbina et al. 2018). Recently Kanagaraj et al. 2020, used phase inversion technique for the development of a modified cellulose acetate (CA) membrane for the removal of humic acid and copper. The maximum humic acid and copper rejection was 98.5 and 99.1%, respectively. The newly developed membrane also had higher flux rate and hydrophilicity. The modified CA membrane also had better anti-fouling property (Kanagaraj et al. 2020). In a novel membrane, polyethersulfone (PES) and amine-functionalized cellulose nanocrystals (CNC) were used for Cu and dye removal from water. The surface of CNC was further modified with the help of triethoxysilane. The modified membrane was able to enhance the removal of copper and dye to 90 and 99%, respectively. The modified membrane had been found as simple and highly efficient technique for pollutants' removal (Rafieian et al. 2019). Chen et al. (2018) removed copper from wastewater by using electrospun nanofiber membrane. The maximum adsorption capacity of this membrane for copper was 120.77 mg/g. The membrane was able to prevent adsorbents' loss and aggregation. The mechanism behind copper removal followed Langmuir-type adsorption (Chen et al. 2018).

7.5.1.4 Ion Exchange-Based Chromium and Copper Removal

Ion exchange results in the interchange of ions between liquid and solid phases (Kurniawan et al. 2006). During the ion exchange process, resins remove ions from electrolytic solution and replace other ions of the same concentration. There is no structural change of resins (Rengaraj et al. 2001; Vigneswaran et al. 2005). There is also recovery of heavy metals from inorganic compounds existing in the wastewater (Damḅrowski et al. 2004). Ion exchange is an economical and efficient process for the removal of heavy metals. There is less generation of sludge during this process (Chiarle et al. 2000; Lacour et al. 2001; Lin et al. 2000; Rengaraj et al. 2001).

Ion exchange takes place in three stages. At first, there is physical adsorption followed by formation of complex between heavy metal ions and oppositely charged ions; at the end, there is hydration on the surface of adsorbents (Ferreira et al. 1999). There is reversible exchange of ions between solid and liquid phases. During the ion exchange process, strong acidic cations can effectively remove heavy metals (Kang et al. 2004).

Strong base anion exchange is an effective way to remove aqueous Cr (VI). This technology utilizes a filter bed filled with polymeric resins with functionalized surfaces (quaternary amines) (Gorman et al. 2016). These resins when completely exhausted with the pollutants can be regenerated using 4 Molar acid (Rapti et al. 2016), 15% base (Meshram et al. 2018), or 15% sodium chloride solution (Subramonian and Clifford 1988) and efficiently removes monovalent and more selectively divalent anions (Subramonian and Clifford 1988).

A novel composite metal organic framework silica gel has been reported to uptake 277 mgCr(VI)/g even in the presence of competitive ions (El-Mehalmey et al. 2018). A protonated amine-functionalized metal organic framework in a column has been reported to remove over 1000 mgCr(VI)/L at pH 3.0 and very low concentrations of 6 ppm to 47 ppb which is difficult to remove by precipitation method (Rapti et al. 2016). Hypercrosslinked imidazolium-based polyionic liquids were reported to effectively adsorb 236 mgCr(VI)/L with 84% adsorption sites as anionic exchange resin at a broad pH range (Xie et al. 2019). Similarly, a strong base anion exchange membrane (Amberlite IRA400 and IRA900) was able to achieve over 97% Cr (VI) removal of 50 ppm from aqueous solutions and real wastewater (Meshram et al. 2018).

The limitation of this technology is the generation of spent brine containing Cr (VI). Chen et al., adapted a photochemical technique with carbon-centered radicals to reduce Cr (VI) into Cr(III) precipitates in the spent brine containing Cr(VI). Acidic pH enhanced the reduction and presence of chlorides decreased the removal efficiency (Chen and Liu 2020).

Polymeric submicron ion exchange resins (SMR) were used for the removal of copper, nickel, and zinc from water. The copper removal from river water was 46%, while in wastewater copper removal was 38% (Murray and Örmeci 2019). Choi et al. 2020, removed copper from bioleached wastewater by using Amberlite IRC-86 ion exchange resin. The copper removal was pH-dependent. The maximum Cu removal was 78.9% at pH value of 5. Two-step sequential process was more effective in copper removal (Choi et al. 2020). Bispicolylamine and iminodiacetate were used as chelating resins for copper removal from water. These chelating resins required a short contact time for copper removal. These resins were reusable without a major reduction in their removal capacity (Edebali and Pehlivan 2016). Rikame et al. (2017) developed phosphorylated fullerene/sulfonated polyvinyl alcohol (PFSP) cation exchange membrane capable of not only removing copper from wastewater but also produced electricity. The cationic membrane was used in microbial fuel cell (MFC). The ion exchange capacity of the membrane was 1.67 meq/g. PFSP cation exchange membrane removed 73.2% copper from wastewater. Copper removal efficiency and electricity generation of PFSP cation exchange membrane were better than Ultrex membrane (Rikame et al. 2017). In another study, Song et al. (2018) removed copper and nickel from aqueous solution using hydrophilic nanoporous ion exchange barrier membrane. The membrane was highly selective for copper and nickel removal. Higher copper flux was observed during the separation. Stripping was the major mechanism behind copper removal. The membrane showed high stability in organic extract (Song et al. 2018).

7.5.2 Bioremediation-Based Chromium and Copper Removal

Bioremediation is the removal of pollutants with the help of microorganisms. These pollutants act as food and energy source for the microorganisms (Azubuike et al. 2016). The microorganisms break down complex and toxic pollutants into a simple and less toxic form (Ayangbenro and Babalola 2017). Microorganisms are grown in a polluted environment so that they can produce enzymes and metabolites. These metabolites are capable of breaking complex pollutants into a simpler form. During the breakdown of pollutants, energy is also released which is used by the microorganisms for their own growth (Azubuike et al. 2016). Microorganisms capable of heavy metal transformation can be isolated from both aerobic and anaerobic conditions. Mostly, aerobic microorganisms are used for bioremediation (Azubuike et al. 2016). Phytoremediation, on the other hand, is removal of pollutants with the help of plants. This technique is widely used in constructed wetlands and oil spills. It is also called green technology due to its environment friendliness, cost-effectiveness, and efficiency (Ali et al. 2013). Several mechanisms can be involved during the phytoremediation process. The major six mechanisms involved during phytoremediation are phytofiltration, phytovolatilation, phytostabilization, phytoextraction, rhizodegradation, and phytodegradation (Ali et al. 2013).

The removal or conversion of pollutants by living forms is one of the cost-effective and easy methods. Several fungal species have been reported to tolerate and reduce Cr (VI). A 1000 mgCr(VI)/L and many other heavy metal tolerating *Trichoderma lixii* was able to reduce Cr(VI) into Cr(III) under various environmental stresses (pH, temperature, tannary wastewater, etc.) by 99.4% (Kumar and Dwivedi 2019b). *Aspergillus flavus* tolerating 800 mgCr(VI)/L was also reported to reduce 89% Cr(VI) into Cr(III) (Kumar and Dwivedi 2019a). Fungi isolated from contaminated soil showed promising results of intracellular (Rhizopus sp.) and extracellular (*Aspergillus fumigatum* and *Penicilium radicum*) reduction of Cr (VI) with 95% removal efficiency in addition to the safe production of Lactuca sativa L crop by acting as in situ biofertilizer (bibi et al. 2018).

A bacterial strain *Staphylococcus aureus* could tolerate 22 mM Cr (VI) and removed 99% of 100 mgCr(VI)/L in 24h (Tariq et al. 2019). A range of Cr (VI) stress (10–500 mg/L) on *Stenotrophomonas maltophilia* with 92–100% removal efficiency at 37°C and pH 7.0. The higher ability of this strain might be associated with the chromate reductase gene *ChrR* and soluble fraction of the cell (Baldiris et al. 2018). An attempt to improve strain of *Bacillus amyloliquifaciens* by physical (UV irradiation) and chemical mutagens (acrylamide, ethidium bromide, and ethyl methane sulphonate) improved the removal efficiency of wild type (74%) to a higher level of 83% and 96% by UV irradiation and acrylamide, respectively (Tharannum 2020). Another strain of *Klebsiella* sp. also reduced 95% Cr (VI) in Luria-Bertani broth and only 63% in real tannery wastewater. This suggests that any bioremediation method utilized should be checked in real or natural conditions as well (Hossan et al. 2020).

Guo et al. (2020) recently used *Myriophyllum aquaticum* for the removal of tetracycline and copper from wastewater. *M. aquaticum* effectively removed both pollutants. In the presence of low copper concentration, tetracycline removal was higher. The role of *M. aquaticum* in the removal of tetracyclines was major as compared to the microbial biofilms (Guo et al. 2020). Eight aquatic plants were used for the removal of copper from wastewater. The copper removal was maximum in the presence of *Eichhornia crassipes* and *Pistia stratiotes*. Copper was mostly accumulated in the roots and shoots of these aquatic plants. Copper removal was affected by the presence of lignin contents in the aquatic plants. The higher the concentration of lignin in plants, the greater was the copper removal (Lu et al. 2018). Tang et al. (2020) used *Pistia stratiotes* for copper removal from distilled and surface water. *Pistia stratiotes* effectively removed copper from both distilled and surface water. The maximum removal efficiency for copper was achieved in surface water (96.38%). First-order elimination kinetics was dominant during copper removal from both types of water. The species got the ability to remove copper from both nutrient-rich and nutrient-deficient wastewater (Tang et al. 2020). Alikasturi et al. (2019) removed copper from surface, mineral, and distilled water by using *Limnocharis flava*. Maximum copper removal efficency was achieved in distilled water, i.e., 39.9%. First-order rate law model best fit the absorption process (Alikasturi et al. 2019). Palanivel et al. (2020) used *Pseudomonas stutzeri* LA3 for copper removal. The maximum copper removal efficiency was 50%. Copper removal was by adsorption and absorption process. Bacterial cell structure was also altered due to copper absorption. (Palanivel et al. 2020). Genetically engineered *Escherichia coli* cell were used by Wang et al. (2019) for copper removal from aqueous solution. The plasmid of E. coli was modified by adding a copper sensor and copper adsorbent in the plasmid. The modification enhanced the copper removal efficency of E. coli. The maximum copper adsorption was 91.5% (Wang et al. 2019).

7.6 Conclusion

Among the various oxidation states of chromium and copper, Cr (VI) and Cu (II) are the most toxic forms, and when they enters into the environment, they have negative effects on the environment (air, water, soil) as well as on the health of all living organisms. There are different methods which can be used for the treatment of both chromium and copper, like adsorption, ion exchange, membrane filtration, electrocoagulation, and bioremediation. Based on the current study, it is concluded that both adsorption and bioremediation are economical and efficient solutions for the treatment of chromium- and copper-contaminated water.

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Chapter 8
Organophosphates' Pollution Status and Their Remediation Through Microbial Interaction in the Twenty-First Century

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Abstract Organophosphorus pesticides (OPPs), being an attractive alternative to persistent organochlorine pesticides, are widely used in agriculture. The OPPs are the main components of herbicides, insecticides, and pesticides. They are derivatives of phosphoric acid having amide, ester, or thiol group possessing aliphatic, cyclic, or heterocyclic structure. The OPPs are soluble in water as well as organic solvents owing to their degradable organic nature. Currently more than 140 OPPs are being used all over the world and their careless handling, and inappropriate application contaminating environment by negatively affecting non-target species of humans, birds, animals, and plants through both systematic and non-systematic actions. The OPPs are utilized as fertilizers, agrochemicals, fungicides, pesticides, insecticides, acaricides, herbicides, plasticizers, flame retardants, plant growth

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_8

factors, chemical warfare agents in agriculture, industrial sectors, as well as for household purposes. The injudicious utilization of OPPs is casting serious threats to global environment and health of living organisms. Nervous system of aquatic and terrestrial fauna is affected due to anti-acetylcholinestrase activity of OPPs such as chlorpyriphos, dimethoate, phorate, trichlorfon, glyphosate, etc. Their soluble nature makes them part of water bodies, thus because of various biotic and abiotic factors, OPPs become part of food chain. Regarding huge devastation caused by OPPs, it is needs of time to eliminate them from ecosystem. Therefore, their detoxification from the environment is necessary. There are various chemical, physical, and biological methods which have been used to reduce OPPs. The photocatalytic degradation of various OPP compounds has been investigated using UV light and TiO_2 as photocatalyst. Chlorination of water has been reported to degrade OPPs. Bioremediation is considered as eco-friendly and economical process for the removal of these toxins as compared to other chemical and physical methods. Various microorganisms have been investigated which can degrade OPPs into less toxic compounds. Microbes use OPPs as carbon, phosphorous, and sulfur source, and electron donor by disrupting OPPs native structure, ultimately converting them to fewer toxic compounds in favourable conditions. This chapter highlights toxicokinetic study of organophosphates and their mechanism of action in living organisms. This chapter also highlights various microorganisms, i.e., bacteria, fungi, and algae, potentially involved in biodegradation of OPPs and their mechanism of bioremediation.

8.1 Introduction

The United Nations Organization for Food and Agriculture (FAO) stated that pesticides either as a single compound or in a combination of different compounds are anticipated for controlling the growth of unwanted plant species, disease-causing vectors, or pests that are causing hindrance in agricultural and food-based processes (Sancho-Martínez et al. 2012). Pesticides target the enzymatic activities of pests involved in different metabolic pathways. However, pesticides are advantageous regarding pest elimination and increasing food production. Pesticides are usually classified on the basis of (i) target pests, (ii) level of toxicity and their potential risk for human beings, and (iii) chemical structure and properties (Upadhyay and Dutt 2017) (Fig. 8.1).

Organophosphates (OPs) are extensively utilized pesticides globally. All OP compounds have a phosphate group and other organic groups depending on the nature of the compound. Such compounds are repeatedly practiced in agriculture, pharma application, cosmetics industry, etc. (Upadhyay and Dutt 2017). Considering their application in agriculture, OP compounds are largely applied as insecticides, with an estimated sale of 34% as an insecticide worldwide (Singh et al. 2006). Tetraethyl pyrophosphate, being the first OP insecticide, was developed in 1937,

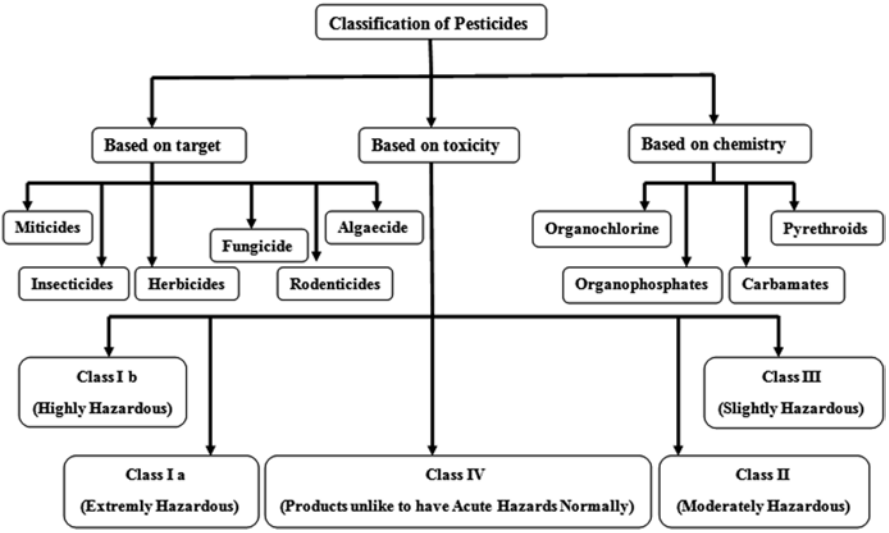
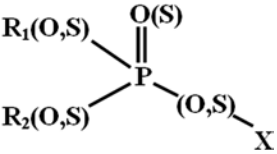


Fig. 8.1 Classification of pesticides. (Adapted from Singh et al. 2006)

Fig. 8.2 General structure of organophosphate compound. (Kaur and Goyal 2019)



leading to the worldwide production and commercialization of other pesticides for pests' control in houses and agriculture (Singh et al. 2006).

8.1.1 Characteristics of Organophosphates

Organophosphate pesticides are organic in nature with high water solubility, low persistence, and relatively easy degradation as compared to carbamates and organochlorine pesticides (Kumar et al. 2018). Structurally, these compounds are derivatives (amide, ester, and thiol) of phosphoric acid, where R1 is alkyl and R2 is aryl group bonded to phosphorus atom. They can attach to carbon through oxygen (phosphates), sulfur (phosphorothiolates or phosphorothioates), or nitrogen atom (phosphoramidates). Here, X is a variable (aromatic, aliphatic, or heterocyclic) and is called leaving group because after hydrolysis of ester it is cleaved from phosphorus (Fig. 8.2) (Sogorb and Vilanova 2002; Vale and Lotti 2015; Dar et al. 2020). The residual half-life of aryl-substituted OPs is observed more as compared to alkyl-substituted Ops, leading to their stability and more persistence in the environment. Low water solubility is found for compounds that are more complex and less polar like ethyl derivatives in relation to methyl derivatives (Chiou et al. 1979). In addition, OP pesticides have anti-enzymatic function owing to high biological actions as they can cause irreversible inhibition of acetyl cholinesterase enzyme, required for normal activity of the brain (Galloway and Handy 2003; Van der Oost et al. 2003).

8.1.2 Sources and Distribution of Organophosphates in the Biosphere

The OP pesticides are available under various trade or brand names and are widely applied that encounter different non-target living organisms. Regarding their presence in the biosphere, they are found throughout the world, such as in water bodies, sediments, in bodies of living organisms, and the atmosphere. Long-term consumption of pesticides put natural resources and biodiversity on stake due to persistent nature (Kole et al. 2001). Over and non-judicious applications of pesticides pollute groundwater reservoirs, air, and soil (Aktar et al. 2009; Schafer et al. 2012). Contamination of water bodies around agricultural land involves simple drifting, surface run-off, seepage through soil, or spillage causing considerable disturbances (Moss 2008). Owing to the cumulative and heterogeneous nature of pesticides, they find their way into food chains depending on the species, susceptibility to toxins, and their metabolic peculiarities (Wilkinson et al. 2000; Hodgson 2010). Pesticides, if used according to the standard agricultural practices, can still enter into the food chain, destroy the ecosystem balance, and cause significant ecological changes. Residues of pesticides enter into the atmosphere by means of evaporation, drift, or wind erosion and re-enter into the ecosystem through precipitation (Dubus et al. 2000; Lushchak et al. 2018). Rate of pesticide application, their half-life, disposal, and solubility are key factors that determine the impact of pesticides on soil, plants, and water resources as they are non-biodegradable and toxic (Anju et al. 2010).

8.1.3 Applications of Organophosphates

The OP pesticides are used for the prevention of crops against pests, crop management, fruits (storage, packaging, and transportation), pulses, vegetables, as well as other food supplies (Upadhyay and Dutt 2017). As many of the OP compounds are soluble in fat and readily enter the body via the skin, they are applied to control pests present on the bodies of animals. These applications are suggested due to their fast degradation rate depending on temperature, sunlight availability, and pH along with other environmental conditions (Ragnarsdottir 2000; Kumar et al. 2018). In addition, they are also practiced as chemical warfare agents, plasticizers, and air-fuel ingredients (Singh et al. 2006). Among other OPs, insecticides have replaced many compounds used earlier due to high impact on insects, adaptation of some insects to organochlorine compounds, and rapid degradation in contrast to other persistent compounds with long residual life such as organochlorines (Chiou et al. 1979).

Insecticides such as parathion applied to rice fields, fruits, cotton, and soil are biodegradable. It has been banned in some countries due to its toxic nature (López-García et al. 2003). Malathion is an active ingredient of many products including sprays and hair oils for use against head lice and fleas as well as small flying insects and mosquitoes (Aktar et al. 2009). Chlorpyrifos has been used since 1965 against termites, beetles, grasshoppers, scales, moths attacking on row crops, fruit trees, and vegetables and became the fourteenth highly used pesticide (Gomez 2009). Dimethoate is also an insecticide used against many aphids, thrips, and mites causing damage to cash crops, ornamentals, vegetables, as well as fruits (Van Scoy et al. 2016). Despite these, monocrotophos, profenofos, phorate, diazinon, and disulfoton are also used as OPPs with diverse actions (Pehkonen and Zhang 2002).

8.2 Toxicokinetics of Organophosphates

Pesticides are one of the most harmful pollutants in the environment because of their mobility and effects on living organisms (de María et al. 2006). Among the diverse groups of pesticides, the widely used OPPs affect non-target plant species and animal species found in various terrestrial and aquatic ecosystems (Blann et al. 2009). The toxicokinetics and toxicodynamics of OPPs differ with the level of exposure and the pesticide's structure (Mkandawire et al. 2014).

8.2.1 Effects on Plant Community

The OPPs adversely affect the plant community and thus the process of photosynthesis (Zobiole et al. 2012). The increasing concentration of OP insecticide dimethoate i.e., 20, 40, and 80 ppm, showed inhibition in the growth and photosynthetic activity of pigeon pea plants (Pandey et al. 2015). Foliar spray of glyphosate in velvet leaf (*Abutilon theophrasti*) decreases gaseous exchange due to decrease in stomatal conductance, which results in gradual inhibition of photosynthesis (Fuchs et al. 2002). The OPPs also affect plant mineral nutrition, carbon metabolism, nitrogen metabolism, fatty acid synthesis, and amino acid synthesis (Zobiole et al. 2010, 2011). It has been reported that chlorpyrifos applied at different concentrations on *Vigna radiata* cause reduction in nitrogen metabolism and plant growth (Parween et al. 2011). It has also been reported that OPPs affect photochemical reactions (Vivancos et al. 2011). Chlorophyll and nitrogen contents decrease with the increasing concentration of OP insecticide (Shams-El-Din et al. 1995). The OPPs reduce the germination process (Stevens et al. 2008) (Fig. 8.3). Barley (*Hordeum vulgare* L.) seeds were treated with various concentrations (0.05, 0.1, and 0.5%) of two OP

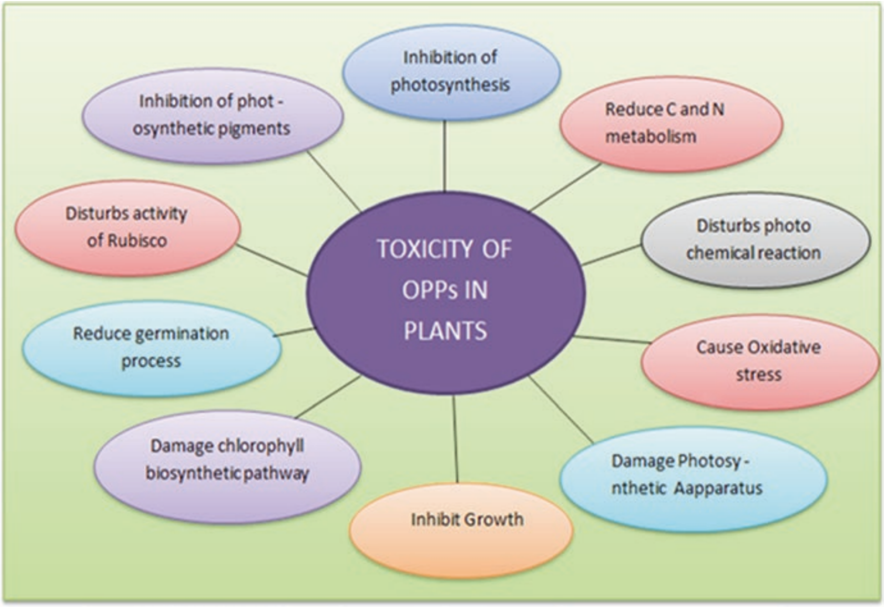


Fig. 8.3 Toxicity of organophosphates in plants

insecticides, monocrotophos and alphamethrin. These insecticides were investigated to produce chromosomal aberrations and mitotic aberrations in barley (Srivastava et al. 2008). The OPPs affect the chlorophyll biosynthetic pathway by preventing the synthesis of catalase, peroxidase, and d-aminolevulinic acids (ALA) (Barcelos et al. 2012). They change the accessibility of metal ions associated with photosystems I and II (Cakmak et al. 2009). The OPPs cause oxidative stress in plants (Vagi et al. 2017). Application of chlorpyrifos, dimethoate, and dieldrin in *Spinacea oleracea* L. disturbs the balance of reactive oxygen species (ROS), which ultimately cause oxidative damage (Singh and Prasad 2018). Glyphosate is reported to lower the level of ascorbate peroxidases and glutathione peroxidases, which play a role in scavenging ROS (Gomes et al. 2017). Glyphosate lowers the level of ribulose-bi-phosphate (RuBP) and phosphoglyceric acid (PGA); hence, it affects the activity of Rubisco (de María et al. 2006). It has been reported that dimethoate (0.06%) was sprayed on cotton and soybean. It was observed that dimethoate causes inhibition of photosynthetic pigments in cotton and soybean (Mishra et al. 2009).

8.2.2 *Effects on Animals*

The OPPs adversely affect both aquatic and terrestrial fauna by inhibiting acetylcholinesterase activity, thus affecting their nervous system (Muhammad et al. 2017). The OP fosthiazate causes acute toxicity in honeybees with small LC_{50} (Li et al.

2020). The OPs affect the social role of honeybee and cause colony collapse disorder (CCD) (Kiljanek et al. 2016). It has been investigated that dimethoate is toxic for common carp *Cyprinus carpio*. After a period of 24, 48, and 96 h, the values of LC_{50} were recorded as 84, 1.78, and 1.6 mg L^{-1}. Low rate of opercular movement, erratic swimming, and effect on maintaining normal posture were investigated (Singh et al. 2009). Dichlorvos affects the acetylcholinesterase activity in gill tissues of Pacific oyster (*Crassostrea gigas*) (Anguiano et al. 2010). The OPPs cause toxicity in *Clarias garipenus* and observed inhibition in acetylcholinesterase activities in plasma and eye homogenate by 84% and 50% (Mdegela et al. 2010). Malathion exposure to freshwater flagellate (*Euglena gracilis*) is reported to affect motility, cell shape, and cell density (Azizullah et al. 2011). Exposure of chlorpyrifos at different concentrations causes toxicity in larvae of common toad (*Dutta phrynus melanostictu*), which slows down swimming activity, decreases growth, and delays metamorphosis (Wijesinghe et al. 2011). Diazinon is reported to decrease the concentration of cholinesterase (CheS), lactate dehydrogenase (LDH), testosterone, leucocyte count (WBC), hemoglobin (Hb), and erythrocyte count (RBC) in kutum (*Rutilus frissi*) (Shamoushaki et al. 2012). Studies on rats indicated the effects of monocrotophos at various concentrations (0.625, 1.25, 2.5, 5.0, and 10.0 ml kg^{-1} body weight/day) for a period of 14 days. Liver cells of rats have shown decreasing levels of aspartate aminotransferase and ALT (alanine aminotransferase) (Sunmonu and Oloyede 2012). The OPs have been suggested toxic for algae (Ma et al. 2005). Microalgae of Chlorella were studied to evaluate the toxicity of chlorpyrifos. The EC_{50} was found ranging from 7.63 to 19.64 mg L^{-1} (Chen et al. 2016), which may dysfunction homeostatic mechanisms and may influence survival. Adult tilapia fish (*Oreochromis niloticus*) was exposed to diazinon for 30 days at various concentrations of 1.0, 2.5, 5.0, 7.5, and 10.0 mg L^{-1}. The LC_{50} for diazinon was reported to be 7.65 mg L^{-1} after 96 h. The concentrations of proteins were considerably decreased in different body parts, i.e., liver, gills, muscle, plasma, and kidney (Soyingbe et al. 2012). Diuron and diazinon cause toxicity in the embryo of zebrafish. The LC_{50} at 96 h was found to be 6.5 mg L^{-1} and EC_{50} was 4 mg L^{-1}, which changed the behavior of fish (Velki et al. 2017). The effect of diazinon at different concentrations such as 0.25, 0.5, 1, 2, 4, and 8 mg L^{-1} on the embryo of common carp has been studied. The mortality rate of embryos increases on exposure to diazinon (Aydın and Koprucu 2005). Monocrotophos cause reproductive toxicity in female Goldfish (Tian et al. 2010). The OP monocrotophos on exposure to *Cirrhinus mrigala* cause histopathological effects on gill, kidney, and intestinal tissues (Velmurugan et al. 2007; Zahran et al. 2018). The OPPs disrupt steroid metabolism as well as hepatic phosphagen system (Southam et al. 2011). The OP diazinon has histopathological effects in the spleen, intestine (lamellar fusion, curling of secondary lamellae), gills, and kidneys (glomerulus shrinking, glomerulus lesions, enlargement of space in Bowman's capsule) of Rainbow trout (*Onchorhyncus mykiss*) (Banaee et al. 2013). The OP malathion causes respiratory stress and instant death of fish (Subburaj et al. 2018).

8.2.3 Effects on Human Health

The OPs produce various types of toxicity, and their poisoning results in more than 100,000 deaths each year (Gunnell et al. 2007). The OPP common route for entry in humans is skin (Kamanyire and Karalliedde 2004). They inhibit acetylcholinesterase activity (AChE) causing changes in the peripheral, autonomic, and central nervous systems (cholinergic effects) (Ray and Richards 2001; Ross et al. 2013). The esterase inhibition occurs because OPP reacts with the active serine center by phosphorylation (Das et al. 2006). The OPs cause endocrine, metabolic, neurological, and hepatorenal disorders (De Silva et al. 2006). Monocrotophos cause neurotoxicity in human brain cells (Tripathi et al. 2017). The OPPs' acute exposure in humans results in acute cholinergic crisis, causing intermediate syndrome consisting of paralysis of proximal limbs, neck, and respiratory muscles 24–96 h after the cholinergic crisis. After 2–3 weeks of poisoning, it results in distal polyneuropathy (De Silva et al. 2006). The OPP monocrotophos cause death of children due to cholinergic syndrome (Krause et al. 2013). The OPP can cause severe poisoning and catalyze teratogenic or carcinogenic processes (Tankiewicz et al. 2010). Glyphosates are carcinogenic agents (Carvalho 2017). The International Agency for Cancer Research investigated that malathion and diazinon have probability to cause human cancer and reported parathion and tetrachlorvinphos as possible carcinogens. The OPP causes hyperactivity of *Cdk5* kinase and tau hyperphosphorylation which leads to disruption of microtubules in Alzhiemer's disease patients. Humans exposed to acute poisoning of OP display memory and learning issue (Zaganas et al. 2013; Costa 2018). The OPP causes neurodegenerative diseases, such as Parkinson's disease. Workers on exposure to OP leads to respiratory tract infections, decrease in serum, RBC, and influenza-like symptoms. Cardiac problems (hypotension, hypertension, cardiac arrest, cardiomyopathy) and hyperamylasemiais were also reported in case of long-term exposure to OPPs. Gastrointestinal problems such as diarrhea can occur through OPP ingestion. Humans on exposure to OPP may experience high fever that may last for several days. The OPPs are responsible for many psychiatric disorders because of the inhibition of acetylcholinesterase activity in farmworkers (Serrano-Medina et al. 2019). The OPPs cause myopathic disorders, i.e., muscular weakness in animals. Paralysis occurs within 24 h of OP exposure in hens. The OP insecticides inhibit the activity of several enzymes such as lipases, chymotrypsin, and trypsin by phosphorylation of these enzymes (Karalliedde and Senanayake 1989). The OPPs can cause genotoxic and mutagenic effects. It is evident from various studies that OPPs cause chromosomal aberrations and genetic mutations (Gökalp Muranli et al. 2015). The OPs damage various organs such as the liver, brain, and kidneys (Fig. 8.4). The OPP causes urinary and histopathological disorders including several diseases such as diabetes, abdominal pain, polyuria, miosis, dyspnea, bradycardia and rhinorrhoea, eczema, nausea, headache, dyspnea, and hepatitis (Azmi et al. 2006; Malekirad et al. 2013).

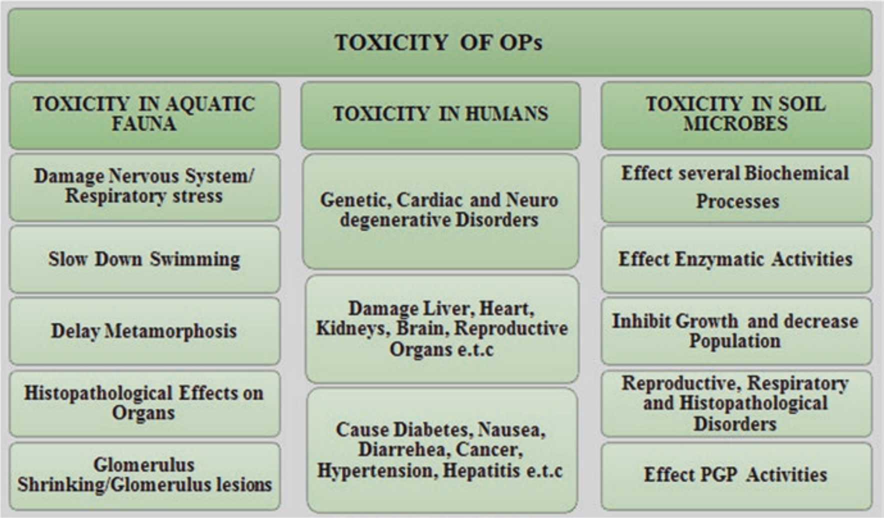


Fig. 8.4 Toxicity of OPs on aquatic fauna, humans, and soil microbes. (Ahemad and Khan 2011; Tripathi et al. 2017; Subburaj et al. 2018)

8.2.4 *Effects on Soil Biota*

Soil is a reservoir of pesticide residues and microorganisms (Jain et al. 2015). The knowledge about relationship of pesticides with soil is important to understand where soil-pesticide minerals, soil-pesticide interaction with organic matter, and related soil fertility mechanisms are of key importance (Polubesova and Chefetz 2014). In soil, the interaction of pesticides depends on four factors such as nature of solute and solvent, soil constituents, and its pH (Iovino et al. 2008). The OPPs affect biochemical processes driven by soil microorganisms such as mineralization, nitrification, denitrification, ammonification, and redox reactions (Mahía et al. 2008). The OP fungicides affect enzymatic activity phosphatase, dehydrogenase, and urease (Shukla 2000). Monocrotophos and other OPPs affect survival, growth, reproduction, and membrane permeability of algae *Scenedesmus bijuga* and *Ankistrodesmus falcatus* (Nayak et al. 1996). Cypermethrin and monocrotophos are toxic for soil bacteria and related microbes (Madhuri and Rangaswamy 2002; Survery et al. 2004). Different types of OP insecticides, i.e., dimethoate, diazinon, chlorpyrifos, quinalphos, and malathion inhibit growth and population of soil fungi, soil bacteria, and enzymes (Pandey and Singh 2004; Singh et al. 2005a). The effect of OP herbicides such as glyphosate, OP insecticide imidacloprid, and fungicide metalaxyl on PGP activities of *Mesorhizobium* sp. was studied. It was found that selected OPPs cause progressive decline in plant growth-promoting (PGP) traits of *Mesorhizobium* sp. strain MRC4 (Ahemad and Khan 2012). The OPP chlorpyrifos' effect on soil microbes was evaluated, and a decrease in the colony-forming units (CFU) of bacteria and fungi was reported (Supreeth et al. 2016). Glyphosates affect the symbiotic relationship of fungus with peanut plant (Pasaribu et al. 2013). Earthworm species were treated with different concentrations (450, 500, and 600 ppm) of OPP monocrotophos for 45 days. It resulted in reproductive toxicity and histopathological abnormalities in earthworm species (Gowri and Thangaraj 2020). Several studies revealed the effect of pesticides on soil microbial biomass and soil respiration. The decrease in soil respiration reflects decrease in microbial biomass. It was observed that dimethoate at 10 mg L^{-1} completely inhibited biological activity and growth of *Xanthobacter autotrophicus* (Hussain et al. 2009b).

8.3 Strategies to Mitigate Impact of Organophosphates

There are various strategies used for mitigation of OPs, i.e., chemical-based strategies and microbial interaction-based strategies. Different processes are involved in the remediation of OPs. Chemical methods lead to the production of less toxic compounds, while in microbial degradation methods complete mineralization of OPs can occur.

8.3.1 Chemical-Based Strategy

There are various chemical methods used for the degradation of OPs. Photocatalytic degradation and chlorination are the different methods for the degradation of OPs (Kamel et al. 2009; Sud and Kaur 2012). Chemical agents such as DS2, sodium hydroxide, and hypochlorite can be used for decontamination of OPs (Kitamura et al. 2014). The mechanism used by chemical reagents for breakdown of pesticides includes hydrolysis, oxidation, and reduction (Jacquet et al. 2016). Advanced oxidation processes constitute homogeneous photocatalysis and heterogeneous photocatalysis. Homogeneous photocatalysis includes use of various photocatalyst (H_2O_2, O_3, NaOCl) in the presence of light. Heterogeneous photocatalysis includes use of semiconductor catalysts such as TiO_2, ZnO, and ZrO_2 in combination with UV/solar radiation. The most evolving degrading technology is heterogeneous photocatalysis using TiO_2 as photocatalyst (Sud and Kaur 2012; Mirmasoomi et al. 2017). However, the mechanism of photocatalytic degradation depends on experimental conditions such as concentration of oxygen, dose of catalyst, temperature, and pH (Sud and Kaur 2012). Chlorination of water is another chemical-based method reported to oxidize OPs. It has been studied that organic thiophosphate compounds (having sulfur atom bonded to phosphorous atom) undergo oxidation process and form oxons on reaction with chlorine atom during the disinfection process. However, some pesticides become unstable in presence of chlorine atoms (Magara et al. 1994; Kamel et al. 2009). Chlorpyrifos undergo oxidation process in the presence of free chlorine and oxidize to chlorpyrifos oxon (Duirk and Collette 2006; Acero et al.

2008). Dimethoate degrades in the presence of chlorine dioxide under water treatment (Pergal et al. 2020).

8.3.2 Microbial Interaction-Based Strategy

In microbial interaction-based strategy, physical interaction between microorganisms and toxic compounds takes place that results in the production of nontoxic products. Many bacterial and fungal species have been exploited for this purpose. Several bacteria have been found in contaminated sites and that showed potential to either consume or decontaminate toxins (Silar et al. 2011; Dubinsky et al. 2013; Prakash et al. 2013; Gustavsson et al. 2016; Thakur et al. 2019). The microbial adaptability and versatility have made bioremediation a "biologically friendly" strategy to remove many toxins that are produced as a result of various anthropogenic activities. Microbial degradation usually occurs via co-metabolism or mineralization. Co-metabolism involves the conversion of parent compound into less toxic or water-soluble form. Mineralization accompanies complete conversion into nontoxic products (CO_2, NH_3, water, or inorganic compounds) (Upadhyay and Dutt 2017; Yigit and Velioglu 2019).

8.4 Importance of Bioremediation

Due to OPs' high toxicity, it is important to develop cost-effective and efficient methods for the removal and detoxification of OP residues in a polluted environment (Cycon et al. 2013). Bioremediation is promising, cost-effective, highly efficient, nontoxic, relatively simple, and eco-friendly method for the elimination and detoxification of OPs. Bioremediation involves the use of biological agents that include plants, microorganisms, or enzymes for the elimination and degradation of toxic compounds from the polluted environment (Yair et al. 2008; Hussain et al. 2009a). Diazinon treatment in soil results in significant increase in bacteria by 14% ($p < 0.05$) and *Azotobacter* by 27% ($p < 0.05$) (Singh et al. 2005b). Fungi and bacteria are well known for their phosphate solubilizing activity. The OPPs increase phosphate solubilization activity and soil dehydrogenase activity (Majumder and Das 2016). Pesticides can be harmful for a certain group of organisms and have beneficial effect on other organisms. It was investigated that pesticides' application inhibited the activity of certain fungi and increased bacterial activity (Gowri and Thangaraj 2020). The bacterial strain *Serratia marcescens* had bioremediation potential against OPPs polluted soils (Cycon et al. 2013). Bacterial species which are commonly reported for bioremediation of OP are *Bacillus* sp., *Pseudomonas* sp., *Klebsiella* sp., and *Enterobacter* sp. (Raeder et al. 2008; Singh et al. 2020). A very efficient bacteria *Paracoccus* sp. was found to degrade 92.47% of OP monocrotophos (100 mg L^{-1}) in 24 h (Jia et al. 2007). *Pseudomonas peli* can degrade

100% of OP chlorpyrifos (20 mg L^{-1}) (Hossain et al. 2015). *Pseudomonas putida* can remediate 100% of OP dimethoate (2 mg L^{-1}) within 96 h (Nazarian and Amini 2008). Different types of enzymes present in bacteria and fungi can be used for detoxification and degradation of OPs (Yair et al. 2008). The OP hydrolyzing enzymes, i.e., cell-free enzyme system, are proven to be effective for bioremediation of OP (Thakur et al. 2019). Genetically engineered enzyme was used to study OPP degradation of malathion, monocrotophos, and parathion (Qiao et al. 2003). Phytoremediation is effective for phytoaccumulation of harmful toxins and metabolic breakdown of pollutants within plant tissues. *Plantago major* L. effectively removes chlorpyrifos by 43.76% (Romeh 2020). *Lemna forma* L. has the ability to remediate OP glyphosate (Dosnon-Olette et al. 2011). Endophytic bacteria present in plants enhance phytoremediation of OP (Chen et al. 2012). Aquatic plant *Scirpus validus* removes 59.8% of 5 mg L^{-1} dimethoate in 10 days (Fu et al. 2006). OP chlorpyrifos is accumulated by *Populus* sp. and *Salix* sp. (Lee et al. 2012).

8.5 Soil Organisms Play Their Role in Biodegradation of Organophosphates

8.5.1 List of Soil Microbes Involved in Bioremediation of Organophosphate

Several organisms including bacteria, fungi, algae, etc. have bioremediation potential. However, the extensive role of bacteria has been observed among other microorganisms (Sylvia et al. 2005). Active bacterial biodegraders belong to the following classes: (i) alpha-proteobacteria such as *Sphingomonas*; (ii) Gamma-proteobacteria such as *Pseudomonas*, *Aerobacter*, *Acinetobacter*, *Moraxella*, and *Plesiomonas*; (iii) beta-proteobacteria such as *Burkholderia* and *Neisseria*; and (iv) actinobacteria such as *Micrococcus* and flavobacteria such as *Flavobacterium* (Geetha and Fulekar 2008; Matsumoto et al. 2008; Rao and Wani 2015). Nineteen bacterial and two fungal genera having the potential for degradation of chlorpyrifos are also enlisted (Table 8.1). Four bacterial and four fungal genera playing their role in degradation of monocrotophos are shown (Table 8.2). Six bacterial and two fungal genera involved in degradation of glyphosate are enlisted in Table 8.3, while seven bacterial and two fungal genera reported as efficient degraders of profenofos are also enlisted in Table 8.4.

Table 8.1 Microorganisms involved in the degradation of OP chlorpyrifos

Microorganisms	Source	Reference
Sphingobacterium sp.	Soil from paddy field	Abraham and Silambarasan (2013)
Enterobacter sp.	Soil	Singh et al. (2004)
B. aryabhattai	Soil	Pailan et al. (2015)
Providencia stuartii	Soil	Rani et al. (2008)
Stenotrophomonas sp.	Soil and sludge	Li et al. (2008) and Deng et al. (2015)
P. aeruginosa	Paddy fields and industrial soil, moist soil, field soil, soil from paddy field	Lakshmi et al. (2008, 2009), Latifi et al. (2012), and Sasikala et al. (2012)
Serratia marcescens	Agricultural soil, paddy fields, and industrial soil	Lakshmi et al. (2009) and Cycon et al. (2013)
Sphingomonas sp.	Soil and wastewater	Li et al. (2007, 2008)
Bacillus cereus	Paddy fields and industrial soil, field soil	Lakshmi et al. (2008, 2009)
Trichosporon sp., *Serratia* sp.	Sludge	Xu et al. (2007)
Enterobacter aerogenes, *P. pseudoalcaligenes*, *P. maltophilia*, *P. vesicularis*	Agricultural soil	Awad et al. (2011)
P. peli, *Burkholderia caryophylli*	Botanical garden soil	Hossain et al. (2015)
Pseudomonas nitroreducens	Effluent, storage ponds, moist soil	Latifi et al. (2012)
P. putida	Effluent, storage ponds, moist soil, soil from paddy field	Latifi et al. (2012) and Sasikala et al. (2012)
Bacillus sp.	Soil from groundnut fields, soil and industrial water, agricultural farm soil	Li et al. (2008), Madhuri and Rangaswamy (2009), and Maya et al. (2011)
Leuconostoc mesenteroides, *Lactobacillus sakei*	Kimchi (during fermentation)	Cho et al. (2009)
Brevundimonas sp., *B. diminuta*	Soil and water	Li et al. (2008) and Hossain et al. (2015)
Cupriavidus sp.	Sludge	Lu et al. (2013)
Pseudomonas fluorescence	Field soil	Lakshmi et al. (2008)
Streptomyces chattanoogensis, *S. olivochromogenes*	Soil from blueberry field	Briceno et al. (2012)
Cladosporium cladosporioides	Industrial soil	Gao et al. (2012)
Lactobacillus brevis, *L. plantarum*	Not available	Zhang et al. (2014)

(continued)

Table 8.1 (continued)

Microorganisms	Source	Reference
Pseudomonas sp.	Soil and water	Li et al. (2008), Madhuri and Rangaswamy (2009), Farhan et al. (2012), and Maya et al. (2011)
Brucella melitensis	Field soil	Lakshmi et al. (2008)
Bacillus subtilis	Field soil	Lakshmi et al. (2008)
Alcaligenes faecalis	Soil around factory	Yang et al. (2005)
Klebsiella sp.	Sludge treatment plant, soil from paddy field, paddy fields and industrial soil, field soil	Ghanem et al. (2007), Lakshmi et al. (2008, 2009), and Sasikala et al. (2012)
Pseudomonas stutzeri	Soil from paddy field, agricultural soil	Awad et al. (2011) and Sasikala et al. (2012)
Stenotrophomonas maltophilia	Riverbank soil	Dubey and Fulekar (2012)
Mesorhizobium sp.	Agricultural soil	Jabeen et al. (2015a)
Agrobacterium spp.	Soil	Maya et al. (2011)
Bacillus pumilus	Soil	Anwar et al. (2009)

Table 8.2 Microorganisms involved in the degradation of OP monocrotophos

Microorganisms	Source	Reference
Aspergillus flavus, *Macrophomina* sp., *Fusarium pallidoroseum*	Agricultural soil	Jain et al. (2014) and Jain et al. (2015)
Rhodococcus phenolicus, *Rhodococcus ruber*	Groundnut (*Arachishypogaea* L.) soil	Srinivasulu et al. (2017)
Bacillus subtilis	Vegetable and cotton fields	Acharya et al. (2015)
Starkeya novella	Soil samples of a paddy field	Sun et al. (2016)
Aspergillus sojae	Contaminated paddy field soil	Abraham et al. (2016)
Aspergillus niger, *Penicillium aculeatum*	Agricultural soil containing chickpea, pearl millet, and mung beans	Jain et al. (2015)
Bacillus sonorensis, *Pseudomonas stutzeri*, *Bacillus licheniformis*	Agricultural soil	Buvaneswari et al. (2018)
Aspergillus sp.	Gourd crop *Trichosanthes cucumerina* L. field	Anitha and Das (2011)

8.5.2 Mechanisms Involved in Bioremediation

The pesticides' removal via biodegradation has positive impact on soil fertility. The rate of degradation of pesticides depends upon their structure as some pesticides are persistent due to anionic property in their structure (Javaid et al. 2016). Major reactions considered in microbial degradation include hydrolysis, oxidation, alkylation, and dealkylation. The OP compounds may have P=O or P=S bond. They get easily

Table 8.3 Microorganisms involved in the degradation of OP glyphosate

Microorganisms	Source	Reference
Achromobacter sp.	Glyphosate-contaminated soil, methylphosphonic acid contaminated soil	Ermakova et al. (2017) and Sviridov (2012)
Bacillus cereus	Glyphosate-polluted soil in the herbicide plant	Fan et al. (2012)
C. odontotermitis	Glyphosate-contaminated soil	Firdous et al. (2017a)
E. cloacae	Rhizoplane of various plants	Kryuchkova et al. (2014)
Enterobacter sp.	Sandy soil	Benslama and Boulahrouf (2016)
G. caldoxylosilyticus	Central heating system water	Obojska et al. (2002)
O. anthropi	Glyphosate-contaminated soil	Sviridov (2012)
O. intermedium	Glyphosate-contaminated indigenous soil	Firdous et al. (2017b)
Ochrobactrum sp.	Soil	Hadi et al. (2013)
Aspergillus oryzae	Aeration tank in a pesticide factory	Fu et al. (2017)
P. chrysogenum	Soil	Klimek et al. (2001)

Table 8.4 Microorganisms involved in the degradation of OP profenofos

Microorganisms	Source	Reference
P. putida *Burkholderia gladioli*	Profenofos exposed soil	Malghani et al. (2009a)
P. aeruginosa	Profenofos exposed soil, cotton field soil, chili farm soil	Malghani et al. (2009b), Jabeen et al. (2015b), and Siripattanakul-Ratpukdi et al. (2015)
Bacillus subtilis	Grapevines or grape rhizosphere soil (culture collection of centers)	Salunkhe et al. (2013)
A. sydowii, *P. raistrickii*	Sponge Chelonaplysillerecta	Da Silva et al. (2013)
P. plecoglossicida	Chili farm soil	Siripattanakul-Ratpukdi et al. (2015)
P. suwonensis	Soil	Talwar and Ninnekar (2015)
Achromobacter xylosoxidans, *Bacillus* sp., *C. koseri*	Cotton field soil	Jabeen et al. (2015b)
Stenotrophomonas sp.	Sludge	Deng et al. (2015)

hydrolyzed due to ester bonding, thus providing several sites for hydrolysis (Briceno et al. 2007). Microorganisms generally degrade OPs through hydrolysis of P-O-alkyl or P-O-aryl bonds. It is the first step in the degradation mechanism and involves OP hydrolase enzymes (Upadhyay and Dutt 2017) (Fig. 8.5). Two hydrolases, namely OP hydrolase (OPH) and OP acid anhydrase (OPA), have been isolated from different microbes. The OPH was isolated from several *Pseudomonas* strains and found to be encoded by *opd* gene. The OPA enzyme has been isolated from *Altermonas* (bacterium) and *Pleurotus ostreatus* (fungus). Esterases such as amidases, carboxylesterases, and phosphatases catalyze hydrolytic reaction of OPs

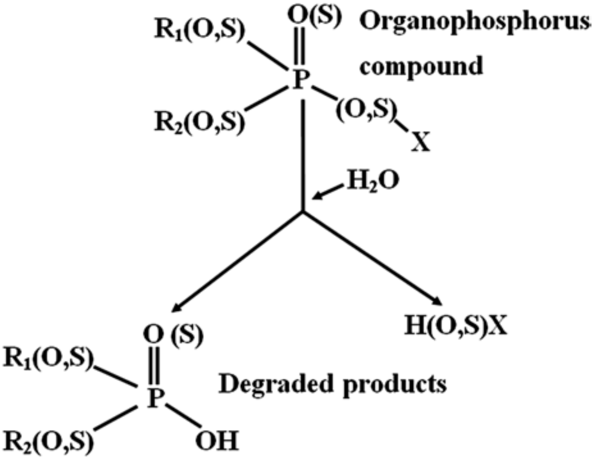


Fig. 8.5 General formula of organophosphate pesticides and their biodegraded products. (Singh et al. 2006)

(Kumar et al. 2019). Several other enzymes such as paraoxonase, phosphodiesterase, and their respective genes are efficiently playing their role in the degradation of OP pesticides. However, complete degradation of OP involves oxidation, alkylation, and dealkylation of the parent compound, resulting in the production of CO_2 and water, which is the energy source of microbes. Efficient degradation of OPs is highly based on microbial diversity along with other optimum environmental conditions (temperature, moisture content, pH, and nutrients available in soil) (Sidhu et al. 2019). Modification of different bacterial specimens through genetic engineering also enhances the potential of applied microbes (Doolotkeldieva et al. 2018).

8.6 Case Study

Considering the most widely used pesticides such as chlorpyrifos and extensively exploited microorganisms for biodegradation, this case study is divided into three parts: (i) harmful effects of OP on fauna and flora, (ii) role of microbes, and (iii) level of achievement through microbial mitigation.

(i) The World Health Organization (WHO) has classified chlorpyrifos in class II owing to its moderate toxicity (Kumar et al. 2010). It is deleterious to different organisms including soil biota, fish, birds, humans, animals, and plants. Considerable residues of chlorpyrifos have been detected in the food chain (Aysal et al. 2004). The residues of chlorpyrifos have toxic nature and property of bioaccumulation (Fang et al. 2008).

(ii) Chlorpyrifos is generally degraded into 3,5,6-trichloro-2-pyridinol (TCP) and diethyl thiophosphate (DETP) by microorganisms present in the soil. They utilize chlorpyrifos as a source of C, P, and N and finally mineralize into CO_2 and water (Singh et al. 2004; Yang et al. 2005; Yang et al. 2006; Ghanem et al. 2007). Important bacterial and fungal strains involved in the degradation of chlorpyrifos have been enlisted (Table 8.1). These strains can tolerate chlorpyrifos up to 500 ppm in soil and liquid media.

(iii) The degradation percentage of chlorpyrifos varies depending on abiotic conditions and microorganism exploitation. A *Cupriavidus* sp. was found to completely degrade chlorpyrifos within 6 h; *Cupriavidus nantongensis* has the potential to degrade 200 mg L^{-1} of chlorpyrifos within 48 h (Lu et al. 2013; Taozhong Shi et al. 2019). Several other species such as *Stenotrophomonas* sp., *Sphingomonas* sp., *Bacillus* sp., and *Brevundimonas* sp. completely degraded chlorpyriphos within 20–24 h (Li et al. 2008). Two strains of bacteria, *Achromobacter xylosoxidans* and *Ochrobactrum* sp., were reported to degrade 84.4% and 78.6% of chlorpyriphos (100 mg L^{-1}) within 10 days while complete degradation was noticed after 35 days (Akbar and Sultan 2016).

8.7 Concluding Remarks

Organophosphates (OPs) are widely used around the world, having extensive application in agricultural practices. They are highly toxic and have detrimental effects on all organisms, i.e., plants, animals, humans, and soil biota. There are various strategies which can be used to mitigate the impact of OPs, i.e., chemical-based strategies and microbial interaction-based strategies. Chemical-based strategies have drawbacks, as chemicals used for remediation have corrosive nature and they are not safe to use chemicals. Bioremediation is an eco-friendly, relatively simple, cost-effective, and efficient method for detoxification of harmful OP pollutants. Microorganisms such as bacteria and fungi have been found to be effective for degradation of OPs into less toxic compounds, and in some cases, microbes mineralize OPs into CO_2 and H_2O. There are a large group of bacterial and fungal species which have been reported for their efficient OP degradation ability. The general mechanism involved in microbial degradation of OPs includes hydrolysis, oxidation, alkylation, and de-alkylation reactions. There are various enzymes involved in these reactions such as organophosphorus hydrolase (OPH), paraoxonase, phosphodiesterase, and organophosphorus acid anhydrase (OPA). Conclusively, bioremediation is a biologically friendly method for decontamination of harmful OP pollutants from the environment. The use of recent technological approaches in the twenty-first century considering the humans, plants, animals, and soil health is important to remediate polluted sites and mitigate their negative effects for food security and quality environment.

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Chapter 9
Toxic Organic Micropollutants and Associated Health Impacts

Muhammad Ijaz, Toqeer Ahmed, and Alishbah Iftikhar Ahmad

Abstract Toxic organic micropollutants (TOMPs) are produced during any incombustion process e.g., industrial plants and road transport. These chemicals are highly toxic and some of these are carcinogens. These include poly aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), polychlorinated dibenzodioxins (dioxins), polychlorinated dibenzofurans (furans), and polybrominated diphenyl ethers (PBDEs). PAHs are emitted from municipal incinerators, coal gasification plants, aluminum industries, and coal tar and asphalt production facilities. PCBs have been used as a coolant in electric transformers and capacitors. Other uses include as a plasticizer in plastics, paints, dyes, carbonless copy papers and during heat transfer. The main sources of dioxins and furans are incinerators, industrial processes, incomplete combustion, and volcanic eruption. PBDEs are flame retardants and have been used in plastics, electronic enclosures, cell phones, personal computers, textiles, foam-based packaging, adhesives, and paint products.

There is no threshold limit for these pollutants as these can cause health damages even in small quantities. PCBs have been declared as Group I carcinogens by the International Agency for Research on Cancer (IARC). PCBs are also linked with adverse effects on kidney, liver, endocrine, and neurological systems. PAHs are genotoxins with irreversible genetic damage to humans. Exposure to PAHs leads to risk of lung, bladder, and skin cancers. Dioxins and furans cause cancer, endocrine disruption, effects on reproductive systems, and impairment of immune system.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_9

PBDEs are associated with neurodevelopment, liver and thyroid dysfunction, and endocrine disruption.

Once released into the environment, these micropollutants undergo physical, chemical, and biological processes such as atmospheric transport, volatilization, deposition, partitioning, and bioaccumulation. There is a need to implement regulatory measures for safe handling, transport, and use of organic micropollutants and to reduce the health impacts through appropriate treatment.

9.1 Introduction

Advances in evolution occur day by day. Chemical constituents are used in modern culture to furnish the requirements of humans. Some of these substances are dangerous and are detectable in various matrices such as food, soil, water, and air. Over time, organic micropollutants (OMPs) have become significant sources of pollution and pose threats to ecosystems, human health, and safety. OMPs include various classes such as microplastics, endocrine-disrupting compounds (EDCs), polycyclic aromatic hydrocarbons (PAHs), pharmaceuticals, personal care products (PCPs), agricultural products, flame retardants, and industrial chemicals (La Farre et al. 2008).

Air contamination and its unfavorable consequences for humans have become issues of great concern. There are significant sources of air poisons—for example, inorganic gases, natural impurities, and particulate matter. Even nonindustrialized nations have recognized problems with air contamination caused by traffic, development outflows, inappropriate garbage disposal and reuse, and modern and horticultural manufacturing practices (Anh et al. 2019; Bi et al. 2002).

There is an established relationship between everyday clinical manifestations of severe respiratory illnesses and concentrations of common air toxins (for example, SO_2 and NO_2), such as those seen in the metropolitan spaces of Hanoi and Ho Chi Minh City (Bohlin et al. 2008; Birgul et al. 2017). Nonetheless, more hazardous concentrates, including exceptionally harmful steady natural contaminations (POPs), in air are moderately restricted in most part because of the absence of appropriate inspecting strategies and savvy evaluation apparatuses (Bi et al. 2002; Jaward et al. 2004).

Some legacy POPs (for example, dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCBs)) are highly concentrated in the atmosphere in Vietnam and several other Asian nations (Akutsu et al. 2001). Raised concentrations of PCBs and polybrominated diphenyl ethers (PBDEs) have been measured in the air and around the people using part of the waste as recycling material in some parts of the world especially in Southeast Asia (Alaee et al. 2001). Similarly, a study reporting OMP pollution in groundwater in China screened about 1300 micropollutants in 13 samples from rural areas, although the carcinogenic risk was low, as only two samples had high micropollutant concentrations (Li et al. 2016).

9.2 Types and Sources of Atmospheric Toxic Organic Micropollutants

Harmful natural micropollutants are formed during incomplete combustion cycles, operation of chemical plants, and operation of road transport vehicles. These synthetic compounds are exceptionally harmful, and some (such as PCBs, polychlorinated dibenzodioxins (PCDDs, or dioxins), PAHs, polychlorinated dibenzofurans (PCDFs, or furans), and PBDEs) are cancer-causing agents (Li et al. 2016).

PAHs are emitted from metropolitan incinerators, coal gasification plants, aluminum smelters, and coal tar and asphalt production facilities. In industry, PCBs have been utilized as coolants in electric transformers and capacitors. Their different utilizations include plasticizers in plastics, paints, dyes, carbonless copy paper, and heat transfer (Huang et al. 2006).

The main sources of dioxins and furans are incinerators, industrial processes, incomplete combustion, and volcanic eruptions. PBDEs are flame retardants and are used in plastics, electronic equipment, cell phones, personal computers, textiles, foam-based packaging, adhesives, and paint products (Gouin et al. 2005).

During thermal and combustion processes, dangerous OMPs (such as PAHs, PCBs, furans, and dioxins) are formed (Gevao et al. 2006). Because they are semivolatile, they occur in gaseous form or are associated with particulate matter in the atmosphere. When these compounds are released in atmosphere, they can be transferred or accumulated to the terrestrial as well as aquatic environment through deposition (wet and dry) (Chen et al. 2017b).

The zone of influence is a major issue associated with emission of the compounds mentioned above, and this determines whether such emissions have mainly local or regional impacts, or whether they influence global background pollution levels. The existence of these compounds (PCBs, PAHs, dioxins, and furans) was recently investigated in the Eordaia basin in northwest Greece, where intensive coal burning takes place for power generation (Chen et al. 2017b; Hien et al. 2007).

Toxic organic compounds were formed by the burning of materials such as quantities of transformer oil, mineral oil and plastic wires etc. in a closed room. Similarly, indoor concentrations of semivolatile organic compounds in gas phase, settled dust, and airborne particles has been detected (Blanchard et al. 2014; Schröder et al. 1997).

Plastics play significant roles in overall advancement of human well-being—for example, by enabling creation of disposable clinical equipment and expansion of food handling. However, plastic waste entering the environment may have the opposite impact—for example, by creating conditions conducive to disease transmission, encouraging breeding of mosquitoes, obstructing water drainage, and causing flooding. Lack of appropriate waste management is believed to have resulted in accumulation of over 250,000 tons of floating plastic pieces in the seas (Rappe et al. 1986).

It was estimated that coastal nations discarded 4.8–12.7 million metric tons of plastic into seas in 2010 (Eriksen et al. 2014). In the environment, plastic waste (which frequently originates as consumer goods waste that has been disposed of

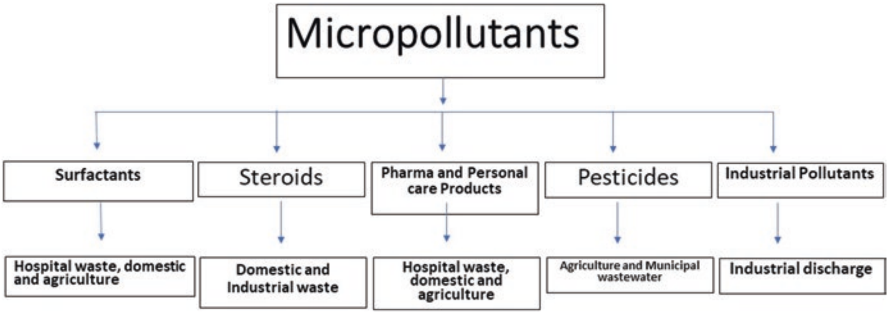

Fig. 9.1 Types of toxic organic micropollutants and their sources

inappropriately) undergoes slow degradation via photodegradation, thermo-oxidation, and (to a lesser degree) biodegradation, degrading the integrity of the materials and causing them to disintegrate into parts less than 5 mm in size, which are known as secondary micropollutants (Brown et al. 2001; Rappe et al. 1986). When plastic particles of small sizes are purposely created to be utilized in consumer goods (such as makeup, exfoliants, or toothpaste) or commercial applications (such as air blasting), they are called essential microplastics.

Microplastics are now found in seawater in concentrations of up to 102,000 particles per cubic meter and are additionally responsible for contaminating freshwater (Vickers 2017; Zagorski et al. 2003) and even staple commodities such as beer, sea salt, and tap water (Sakurai et al. 2000).

The pervasive presence of microplastics in the environment and in consumer goods prompts inevitable human exposure to these particles. The results of this exposure are not yet fully known. The current evidence regarding the impacts of environmental exposure to microplastics on human well-being has been explored to some extent, giving rise to theories regarding the mechanisms of exposure and the extent of microplastic toxicity, and providing a basis for additional research. However, the available data on the effects of microplastics on humans are limited because of ethical issues, the strict biosecurity measures required when performing research involving human subjects, and restrictions on the locations where such research can be conducted (Birnbaum and DeVito 1995).

Different types of toxic OMPs and their sources are shown in Fig. 9.1.

9.3 Health Effects of Toxic Organic Micropollutants

There is no known safe concentration of these toxins, as they can damage human health even in small quantities. PCBs are classified as group 1 carcinogens by the International Agency for Research on Cancer (IARC) and are associated with harmful effects on the kidneys, liver, endocrine system, and neurological system. PAHs are genotoxins and cause irreversible genetic damage in humans. Exposure to PAHs poses risks of lung, bladder, and skin cancers (Kouimtzis et al. 2002).

Dioxins and furans cause malignancies, endocrine dysfunction, effects on reproductive systems, and immune system impairment. PBDEs are associated with endocrine, neurodevelopmental, liver, and thyroid dysfunction (Lee et al. 1999).

After these micropollutants are delivered into the environment, they go through physical, chemical, and organic processes such as volatilization, atmospheric transport, distribution, and bioaccumulation. There is a need for appropriate measures to manage transport and utilization of natural micropollutants safely and to decrease their impacts on health through suitable treatment (Mandalakis et al. 2002). Different types of toxic OMPs, their transport media, and their associated health influences are listed in Table 9.1.

Table 9.1 Types of organic micropollutants, their transport media, and associated health impacts

Organic micropollutants	Transport media	Adverse health impacts	References
Microplastics	Water, soil, air	Disruption of photosynthesis in primary producers; reduced food intake and energy levels; disturbances producing inflammation and oxidative stress in higher vertebrates; cell damage and inflammatory and immune reactions	Revel et al. (2018) and Vethaak and Legler (2021)
Pharmaceuticals (β-blockers, anti-inflammatory drugs, antibiotics, neuroactive compounds)	Water, soil	Toxic effects on biota, harming aquatic and terrestrial environments	Larsson et al. (2007) and Manzetti and Ghisi (2014)
PCPs (e.g., antiseptics, fragrances)	Water, soil	Breast cancer; asthma; autism; reproductive problems; other health issues	Paulsen (2015)
EDCs	Water, soil, air	Endocrine disorders (e.g., adrenal disorders); neurodevelopmental dysfunction in children; endocrine-related cancers; bone and metabolic disorders; male and female reproductive disorders	Meek et al. (1994), International Agency for Research on Cancer %J Lyon (2010), Grob, (2015), and Chávez-Mejía et al. (2019)
PAHs	Water, soil, air	Effects on reproduction, development, and immunity in terrestrial invertebrates; carcinogenic effects (e.g., benzo[*a*] pyrene is a group 1 carcinogen); mutagenic effects, posing serious threats to human health; increased risks of lung cancer	humans (2010), Latimer and Zheng (2003), and Kim et al. (2013)

(continued)

Table 9.1 (continued)

Organic micropollutants	Transport media	Adverse health impacts	References
Agricultural waste (pesticides)	Water, soil, air	Harmful effects through antagonism or mimicking of natural hormones in the body, as well as hormone disruption; immune suppression; diminished intelligence; cancers; reproductive abnormalities in humans; adverse health effects of pyrethroid pesticides (e.g., immunotoxicity, teratogenicity, carcinogenesis, mutagenicity)	Aktar et al. (2009) and Zhou et al. (2019)
Flame retardants	Air, dermal contact, dust ingestion	Ripple effects on wildlife and the environment; minor respiratory irritation; BFRs affect the endocrine, neural, reproductive, immune, and cardiovascular systems	Feiteiro et al. (2021)
PCBs	Water, soil, air	Skin and eye irritation; decreased pulmonary function; decreased birth weight in offspring of occupationally exposed mothers; variable effects on cancer formation; altered reproductive and thyroid function in both males and females	Safe (1994), Ross (2004), and Carpenter (2006)
PCDDs, PCDFs	Air, soil, food	Adverse effects on the immune, nervous, and endocrine systems with long-term exposure; impaired reproductive function; high TCDD levels cause dermal problems with acne-like lesions (chloracne) on the face or upper body; reduced motility, abnormal morphology, and reduced capacity of sperm to penetrate oocytes, resulting from ingestion of PCDDs or PCDFs in food	Guo et al. (2000) and Zheng et al. (2008)

BFR brominated flame retardant, *EDC* endocrine-disrupting compound, *PAH* polyaromatic hydrocarbon, *PCB* polychlorinated biphenyl, *PCDD* polychlorinated dibenzodioxin, *PCDF* polychlorinated dibenzofuran, *PCP* personal care product, *TCDD* 2,3,7,8-tetrachlorodibenzodioxin

9.4 Toxic Organic Micropollutant Exposure

Micropollutants are far-reaching foreign substances. Exposure of the human body to micropollutants occurs through ingestion of food containing toxic substances, inhalation of micropollutants in the surrounding air, and also skin contact with particles contained in items, materials, or dust (Nakao et al. 2002). Possible effects of exposure to toxic OMPs on human health are shown in Fig. 9.2.

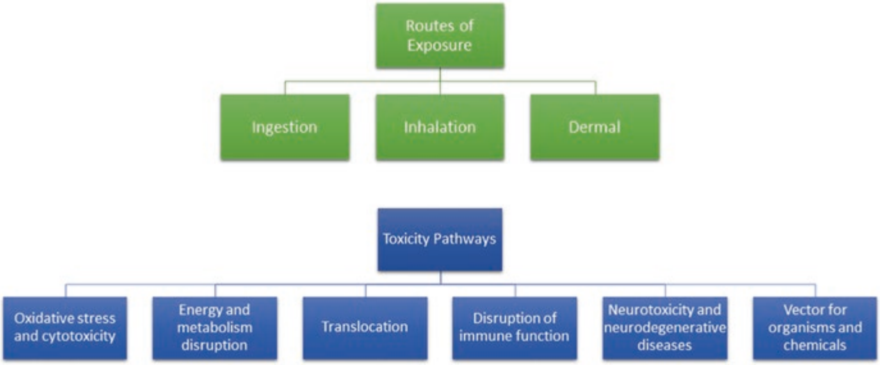

Fig. 9.2 Routes and effects of exposure to toxic organic micropollutants on human health. (Revel et al. 2018)

9.4.1 Inhalation Exposure

Micropollutants are delivered into the air by various sources, including manufactured materials, scraping of materials (for example, vehicle tires and structures), and resuspension of micropollutants from surfaces. One study of atmospheric micropollutants measured outdoor concentrations of 0.3–1.5 particles per cubic meter and indoor concentrations of 0.4–56.5 particles per cubic meter (33% from polymers), including particles of inhalable sizes. It has been estimated that, on average, an individual person inhales 26–130 airborne micropollutant particles per day (Dayan and Koch 2002).

According to an atmospheric examination utilizing a life-sized model, it is common for a male individual performing light movements to inhale 272 micropollutants during each day. Various assessments have focused on the influences of variations in aspects such as space use factors, cleaning processes, furniture materials, exercise, and seasons. The properties of molecules, such as their size and thickness, influence their effects on the respiratory system; smaller and thinner particles are breathed into deeper parts of the lungs than larger or thicker particles (Carroll 2001).

There is evidence that macrophage activation or movement of particles into the circulation or the lymphatic system may lead to transport of microparticles within the body. The huge surface areas of tiny particles in the respiratory system may elicit major chemotactic responses, inhibiting macrophage movement and increasing the ability of particles to penetrate different tissues and cause persistent irritation, known as residue overburden (Wobst et al. 1999).

In one study, the presence of polystyrene nanospheres (64 nm in size) prompted neutrophil convergence and aggravation in the lungs of rodents. Moreover, proinflammatory responses were observed in epithelial cells as a result of greater oxidant activity brought about by the huge surface area of the nanospheres (Brown et al.

2001). In an in vitro study, polyvinyl chloride (PVC) particles (2 μm in size) created by emulsion polymerization caused hemolysis and critical cytotoxicity in rodent and human airway cells (Su and Christensen 1997).

Respiratory symptoms that have previously been linked to increases in aviation and interstitial lung disease have also been associated with exposure to airborne micropollutants in factory workers, workers managing livestock, and workers in PVC production facilities, with the same effects being replicated (Barboza et al. 2018; Agarwal et al. 1978).

Filaments 205 nm in size have additionally been identified in human lung biopsies and associated with malignant growths, although causation has not yet been demonstrated. All things considered, under conditions of high fixation or individual susceptibility, airborne micropollutants can injure the respiratory system (Donaldson et al. 2000).

9.4.2 Dermal Exposure

Dermal contact with micropollutants is considered a less critical means of exposure, although it has been postulated that nanoparticles (<100 nm in size) could cross the dermal barrier (Barboza et al. 2018).

This route is regularly associated with exposure to monomers and plastic substances such as bisphenol A, phthalates, and EDCs via daily utilization of common equipment. The likelihood that nanoparticles do cross the dermal barrier and cause harm should not be discounted without confirmation. The presence of plastics in medications can cause minor inflammatory responses, as well as less common reactions such as fibrosis. However, in one study, sutures utilizing interlaced polyester and monofilament polypropylene were found to cause more minor reactions and fibrosis than silk after 21 days (Vickers 2017; Eriksen et al. 2013). In a study using mice, different types of plastic plates 10 mm in size were implanted subcutaneously and then removed after 98 days. Polyethylene plates were found to cause the least aggravation, but PVC plates stabilized with organo-tin or plasticizers caused toxic effects, with moderate degeneration and rot, perhaps due to leachate toxicity (Canesi et al. 2015). Although microparticles and nanoparticles may cause aggravation and unusual bodily reactions, differences in surface properties could elicit particular results. Human epithelial cells have been shown to exhibit harmful effects with exposure to micromaterials and nanomaterials (Frias et al. 2010).

Accordingly, the known adverse effects of nanoparticles and inevitable dermal exposure to plastic particles (for example, from engineered strands, dust, and microbeads in cosmetic products) support the requirement for further research in this area.

9.4.3 Oral Exposure

Ingestion is viewed as one of the most significant routes of human exposure to micropollutants. In view of the widespread utilization of these substances (for example, in food packaging), it has been estimated that each person ingests 39,000–52,000 micropollutant particles per year (Cole et al. 2013).

Particles may enter the gastrointestinal system through mucociliary clearance after inhalation, and they may cause major inflammation, increased tissue penetrability, and changes in gut microorganism populations and digestion (Karami et al. 2017). The presence of micropollutants has been documented in food items such as mussels, fish, table salt, sugar, and filtered water. In Europeans, exposure to micropollutants via bivalve consumption has been estimated to be 11,000 particles per year (Saravia et al. 2014). Moreover, it has been estimated that each year, Europeans ingest 37–100 micropollutant particles per capita through consumption of table salt.

However, some researchers have suggested that settling of micropollutant residue on dinner plates may be a more significant source of micropollutant consumption than the presence of these pollutants in the food itself (Furukuma and Fujii 2016). Incidence of dementia are higher while living near highways as compared to Parkinson's disease and multiple sclerosis (Chen et al. 2017a).

Particles of insoluble substances may infiltrate digestive fluid through an increase in their dissolvability via adsorption of a "crown" of intestinal substance or because of their small sizes, so it was observed that particles present in rodent intestinal segments are of polystyrene latex with a size range of 14 nm to 415 nm (Sternschuss et al. 2012).

Another possible means of infiltration of these particles is persorption, with paracellular movement of particles through a single layer of intestinal epithelium. Micropollutants would be exposed to these equivalent systems according to their toxic nature especially in circulatory system. This has been demonstrated in vivo after oral administration. For example, in a study of rodents, 6% of polystyrene particles (0.87 mm in size) entered the circulation within 15 min of oral administration. In another study, oral administration of 1.25 mg kg of polystyrene particles 50 nm in size resulted in 34% absorption, perhaps via transport through the mesentery lymph system into the circulatory system prior to accumulation in the liver (MohanKumar et al. 2008).

Polystyrene nanospheres were delivered by human colon fibroblasts across the cell layer. After disguising by human gastric adenocarcinoma cells, these polystyrene particles influence the quality of articulation, hinder cell viability and initiate provocative reactions (Li et al. 2016).

Humans are exposed to micropollutants through inhalation and ingestion because our environment is now significantly contaminated with micropollutants. However, the dangers associated with bodily contamination by micropollutants are not yet adequately understood, because of a lack of research assessing general human exposure and its consequences (Saravia et al. 2014).

9.5 Conclusion

Polyaromatic hydrocarbons, polychlorinated dibenzodioxins, polychlorinated biphenyls, polychlorinated dibenzofurans, and polybrominated diphenyl ethers are highly toxic substances emitted from incinerators, coal gasification plants, the aluminum industry, and coal tar and asphalt production facilities. There is an urgent need to reduce the presence of these toxic pollutants in the atmosphere and in the environment. The following are important recommendations to help achieve this goal:

1. Open burning of garbage should be limited (especially in periurban areas), and emissions from chimneys and brick kilns should be permitted only under strictly controlled conditions.
2. Use of older vehicles should be banned, especially those that have been running for more than 20 years and those with outdated engine, because road traffic emits toxic lead and other pollutants, which can impact not only human health but also the health of plants and trees growing along roadsides.
3. Industries should be required to limit their waste, and there should be appropriate mechanisms for waste management, especially in the steel and plastic industries.
4. Policies regarding emissions should be enforced strictly, and action should be taken against anyone violating these policies or polluting the environment.
5. Activities should be undertaken to increase awareness of environmental pollution and discourage it at all levels.

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Chapter 10
Impact of Aerial Fungal Spores on Human Health

Sadia Alam, Maryam Nisar, Syeda Asma Bano, and Toqeer Ahmad

Abstract Fungal spores are present in almost all types of environments and prevail in certain environmental conditions. The composition of aeromycoflora of a particular area plays an important role in the spreading of many respiratory allergies. The indoor and outdoor aerial fungal spores may be different due to many factors. The aerial fungal spores play an important role in public health as many fungal spores are potent allergens for human population. These fungal spores may also cause some important mycolic infections. Indoor environments are possible sources of fungal spores which can be injurious to human health. These fungal spores can endure for months in suitable conditions. Many environmental factors such as high temperature, high humidity, dampness physical activity, and the wind speed play effective role in the release and distribution of fungal spores in air and which can impede wellness of local population. Aerial fungal spores are the major cause of allergic diseases and infections in immunocompromised patients in many parts of the world. The aerial fungal spores of *Alternaria, Aspergillus, Cladosporium, Candida, Curvularia, Epicoccum, Fusarium, Geotrichum, Helminthosporium, Mucor, Penicillium, Rhizopus, Trichoderma*, and *Trichothecium* were found as dominant in the air of many cities of the world. Variations in composition of aerial fungal spores occur due to environmental and meteorological factors. Some fungal spores are seasonal, and therefore, these spores are linked with some seasonal mycotic infections. They are also established to cause Type I hypersensitive diseases with IgE-mediated response. Fungal spores are present in both outdoor and indoor environments and behave as suspended bio pollutants of the air. Many aerial

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fungal spores are found as main cause of respiratory tract allergies. Many fungal spores can penetrate in lower respiratory airways of human lungs and intercede allergic reactions. These fungal spores can be a serious health hazard for immunocompromised persons. The sensitization to fungal spores may cause some fungal allergies in local population. The seasonal data of aerial fungal spores and their pattern of distribution can help to prevent fungal allergies and mycotic diseases.

10.1 Introduction

10.1.1 Composition of Aeromycoflora

Fungi are omnipresent in the world's environment and are an integral part of airborne microbiome. Particulate matter dispended in air includes bacteria, fungi, clay, and sand particles of 10 μm or smaller to below 0.1 μm and gases including ozone (O_3), nitrogen dioxide (NO_2), and sulfur dioxide (SO_2) (Ministry of Environmental Protection of the People's Republic 2017). *Alternaria* is the most common fungus present in outdoor and indoor environment. Indoor environment also contains *Aspergillus fumigatus* and *Alternaria* spp. Both species have positive impact on developing asthma (Shabankarefard et al. 2017). Humans are continuously affected by aerosols because of domesticated animals, plants, plumbing systems, heating and cooling systems, and saprophytic molds along with suspended dust particles that contribute to a type of airborne fungus. Yamamoto et al. (2015) detected different types of yeasts in classroom environment including *Rhodotorula*, *Candida*, *Cryptococcus*, *Malassezia*, and *Trichosporon.* Certain researchers have indicated that most of the fungi found in indoor environment comprise of the genera prevailing in outdoor environment (Barberan et al. 2015). Goh et al. (2000) studied library environment and found that indoor fungi concentration was 50 times less than that of outdoor environment.

10.1.1.1 Allergenicity of Airborne Fungal Spore

The huge diversity of fungal kingdom is well known. A variable lot of fungal species exist; some of them disseminate airborne spores, conidia hyphae, or other fragments that are inhaled by human beings. Three taxonomic groups of fungi and their 112 fungal genera including Basidiomycota, Ascomycota, and the Deuteromycota release those allergens which spread allergic diseases. Associated components of fungal conidia are unlike any other bio aerosol in that these are heterogeneous; those which have pathogenic and inflammatory properties are actively secreted by biological dynamic particles. In several multi-studies sensitization of fungi has been identified which is considered to be a risk factor for severe asthmatic patients. The hypersensitivity to fungal allergens ranges from as low as 2% to as high as 90% (Arbes et al. 2005; Zureik et al. 2002), and it was reported that sensitization of fungi is dependent on different exposure as with most allergens just like source and commercial skin test extracts, based on selection criteria of test subject and analysis methods. There are several subject methods which are used to measure exposure such as spore count, endure assessments of visible growth of fungi, and this procedure is also used to understand the relationship of exposure to clinical outcome. Fungi including *Aspergillus*, *Cladosporium*, *Penicillium*, and *Alternaria* species have been investigated for human exposure. These genera have been found in abundance and a cause of maximum human exposure to airborne fungal spores. These have been detected in vast geographic area and can be detected through various diagnostic means (Cruz et al. 1997).

10.1.1.2 Fragments of Fungi in the Environment

Indoor environment is polluted by airborne fungal spore which is characterized by numerous diagnostic methods. The particulate matter in air have been studied rarely for personal exposure. Many studies' procedures have been promulgated to verify presence of hyphal fragments in indoor environment that indicates the amount of particles in air amounting to 6–56% of total fungal particles (Li and Kendrick 1995; Foto et al. 2005). These fragments of aerosols actually originate from indoor polluted surfaces, and these particles may even persist in indoor environment for quite long in viable form thus aiding to fungal dispersion (Madelin and Madelin 2020). It has been detected from different epidemiological studies that multitudinous fragments of fungal hyphae are associated with acute high expiratory flow rates (Delfino et al. 1997).

Submicron Fungal Fragments

Those particles which are derived for intracellular and extracellular structure are known as submicron fungal fragments that have been aerosolized from fungal colony (Górny et al. 2002). Their usual size is around 1mm and they lack morphological features. Reports related to submicron fungal fragments are few as it is a bit difficult to collect and identify fungal fragments from polluted environment and its isolation is totally based on experimental conditions (Gorny et al. 2002; Gorny 2004; Cho et al. 2005). Dr. Tinna Reponen and Rafal Gorny developed aerosolization chamber, and its purpose was to assess gradual release and collection of bio aerosols. Aerosolization of submicron fungal fragments studied by different authors from culture medium vessels, building internal tiles were found polluted with *Aspergillus versicolor* (Górny et al. 2002, 2003). An aerosolization chamber was designed by researchers group of Dr. Tinna Reponen and Rafal Gorny, and different researchers found different fungal species involved in formation of submicron fragments on internal tiles of buildings and culture vessels. The species involved were *Aspergillus versicolor*, *Penicillium melinii*, *Cladosporium cladosporioides*, and *Stachybotrys chartarum*. The small hyphal segments related to these species have been indicated in aerosols with spores but to large concentration (320–514 times higher). These findings depict that colony structure, desiccation stress, air velocity, degree of vibration, and moisture conditions may all affect aerosolization rate (Górny et al. 2002; Górny 2004). Various study methods have investigated respiratory disposition of submicron fungal fragments and inflammation. All are based on computer-based models. Cho and colleagues currently explained that the presence of *S. chartarum* fragments is in higher concentration than spores, but in case of *A. versicolor*, a total count 230–250 was similar to the spore. The model was utilized to predict infants' environment, and it was known that sedimentation rate was a 4–5 times multitude of the value associated with young ones (Cho et al. 2005). Further investigation is needed to determine personal fungal exposure from a clinical point of view.

Larger Fungal Fragments

Conidia in broken form and visible septate hyphae or mycelium are considered as larger fungal fragments. Their size exceeds 1mm and comprised of fragmented hyphae (Green et al. 2005). As compared to submicron particle, these fungal fragments are larger in size, easier to be visualized by light microscopy and environmental air samples. In some geographical locations, their concentration can range up to 56% of the total aerospora (Li and Kendrick 1995). Larger fungal fragments related research is scarce as compared to submicron fragments in aerosols. But it is evident that their presence is based on a number of similar variables including substrate disturbance, wind, speed, and wind direction (Green et al. 2005). Filamentous fungi reproduce through hyphal fragmentation. Fragmentation is continued by vacuole formation following a reduction in nutrients that may be induced by environmental stress (Papagianni et al. 1999; Paul et al. 1994). This stress and nutrient depletion zone proceeds towards hyphal separation at septal junctions, and their dissemination is made through wind blowing (Marfenina et al. 1994). The process of conidial fragments formation has not yet been investigated thoroughly and remains undiscovered. It is considered that multicellular conidia get rupture near cross walls of hyphae due to different osmotic potential or when they differ in moisture content (Taylor and Jonsson 2004; Schäppi et al. 1999).

10.1.2 Taxonomy of Allergic Fungi

Kingdom fungi have huge diversity of eukaryotic organisms including mushrooms, molds, bracket fungi, puffballs, smuts, plant rusts, and yeast. Fungi contain different metabolic processes which differ from animals to plants. They secrete enzyme into environment, and their function is also to absorb the breakdown product of enzyme action. Some of these enzymes are also well-classified allergens. Phylogenetic relationships were unclear among different classes of fungi, but currently its classification is based upon morphological characterization and sexual state. Deuteromycetes or fungi imperfecti at fungal phyla are resolved by DNA sequencing. On the basis of DNA sequencing, it has been found out that three fungal phyla are mostly associated with important aeroallergens; Basidiomycota, Ascomycota, and Zygomycota. Many fungal allergens have been categorized. Specific immunoglobulin E (igE) level in individuals sensitized to fungi has a close relationship between fungal phylogeny, and this is a great benefit from this study. This strong correlation between molecular fungal systematics and IgE sensitization gives a strong evidence about cross reactivity of fungal allergens with human immunity response (Levetin et al. 2016).

10.1.3 Common Fungal Aeroallergens

Aeroallergens are the substances that are dispersed in air as spore or pollens and are able to cause an allergic reaction.

10.1.3.1 Pollens

Aeroallergens are found in certain seasonal plants, and when pollens acting as aeroallergens cause sensitivity reactions in patients, the response is called "hay fever." Because it is the most common illness during haying season in summer months of May and June in Northern areas, some individuals may suffer from this seasonal allergy throughout the year. Hay fever caused by pollens differs from region to region and person to person; small, hardly visible pollens of wind pollinated plants are the main cause of hay fever. The insect pollinated plants have larger pollens that are much larger to remain in air and cause no risk. The plants responsible for pollen allergy or hay fever include trees: alder (*Alnus*), birch (*Betula*), hornbeam (*Carpinus*), cedar (*Cedrus*), hazel (*Corylus*), willow (*Salix*), olive (*Olea*), poplar (*Populus*), linden lime (*Tilia*), horse chestnut (*Aesculus*), and plane (*Platanus*). Grasses [family Poaceae] especially ryegrass (*Lolium* sp.) and timothy (*Phleum pratense*) are involved in causing allergies. An estimated proportion of 90% of hay fever sufferers are allergic to grass pollens. Plantain (plantain), ragweed (ambrosia), nettles/*Parietaria* (Urticaceae), fat hen (*Chenopodium*), sorrel/dock (*Rumex*), and mugwort (*Artemisia*) also cause allergic immune sensitivity.

Ranging from the mid spring to early summer, the pollen count is the highest in a year. The pollen-sensitive patients may anticipate at the onset of the season and when the season ends.

10.1.3.2 Spores

Both sexual and asexual spores in many fungi actively spread by strong ejection from their reproductive structure or sporangium, which spread through the air to distant area. Many fungi have special physiological and mechanical processes as well as spore structure and surface structure formation like hydrophobic characteristics for spore ejection. This process consists of strong discharge of ascospores enabled by structure of ascus and accumulation of solutes causing osmotic potential in the fluid that push the spores towards dispersal at high velocity into the air (Trail 2007). When single spores get discharged, this process is known as ballistospore dispersal and involves small water droplet formation (Buller's drop), which when link with spore it moves toward projectile ejection with a starting acceleration rate of more than 10,000 g. Other fungi depend on alternative mechanisms for spore ejection which include mechanical forces like puffballs.

Peanuts and other food material may become airborne thus causing allergic reactions in disease-prone individuals like children, immunocompromised people, pregnant women, and elderly adults. Currently concern has been raised about peanuts protein related allergens in the air that may cause a full-blown anaphylaxis and in the result respiratory exposure can occur. In schools setting as a protein food for children, even in well-ventilated restaurants, when airborne peanut protein exposure occurs, different allergic responses were explored. Children have been detected with peanut-associated allergic reaction. No peanut allergen was found in air after subjects consumed peanut (Perry et al. 2004). Dr. Michael Young (2006) reported that peanut allergy may result in life-threating anaphylactic response, but its association with airborne allergy is unconfirmed. Eosinophilic gastroenteritis is an uncommon and heterogeneous condition involving eosinophilic infiltration of gastrointestinal tissue first described by Kaijser in 1937 (Whitaker et al. 2004).

The stomach is the type of organ which is mostly affected followed by the small intestine and colon. Eosinophil is commonly found in gastrointestinal mucosa, like a part of host immunity mechanism; its finding in deeper areas is mostly pathologic. Pathogenic mechanism of disease occurs. Viable IgE and food allergy correlation have been observed in some patients. Eosinophilic aggregation in tissue for inflammation is a complicated process which occurs by different processes of accumulation of cytokines. Cytokines IL 3, IL 5, and granulocytes macrophages colony stimulating factor [GM –CF] are involved in activation, and it has been observed in histological examination of the intestinal wall. Stomach/intestinal allergies are treated by corticosteroids, and its response rate is much positive.

10.1.4 Respiratory Disease Caused by Aeromycoflora

Fungal flora is found everywhere in the environment. Mycopathogens are omnipresent in the environment. Serological reports have revealed that major human population proportion have been affected with fungus respiratory diseases during their life span. Even symptomatic infections by these fungi are infrequent in healthy and vigorous individuals. This indicates the possible hazard of developing a respiratory system disease.

10.1.4.1 Histoplasmosis

Histoplasmosis is a respiratory disease caused by fungal pathogens and commonly occurs in the South America, Africa, Australia, Asia, and Mississippi Valley of the United States. *Histoplasma* is a dimorphic fungus that grows in the environment as a filamentous mold, but during human infections they occur as budding yeast. Soil is the primary reservoir of this fungal pathogen, especially in location rich in bird and bat feces. *Histoplasma* is not transmitted from human to human, and its acquisition is made through inhalation of microconidial spores in the air. In endemic areas, histoplasmosis is high, and the 60–90% of population harbor anti-*Histoplasma* antibodies depending on the locating habitat, but few individuals experience symptoms. Young ones are most likely to be affected and immunodeficient adults. The disease pattern of histoplasmosis is similar to tuberculosis in many ways. Following inhalation this disease gets symptoms similar to tuberculosis because spores go to the respiratory organs and are engulfed by alveolar macrophages. Fungal cells increase in number and sustain even after being engulfed by these phagocytes. Granulomatous lesions caused by focal infections are similar to the Ghon complexes of tuberculosis even in symptomless conditions. Histoplasmosis can become severe and reactivate and spread to other areas of the body such as the spleen and liver. Symptoms and signs of histoplasmosis contain headache, fever, chest discomfort, and weakness. Initial diagnosis of this disease depends on cultures grown on fungal-selective media (Sabouraud Dextrose Agar) and chest radiographs. Giemsa staining and direct fluorescence antibody staining technique can also be utilized for detection of the disease. In some conditions this infection may be restricted and antifungal therapy is not necessary. Yet in case of complexities, the disease is treated by antifungal agents like ketoconazole and amphotericin B; in immunocompromised patients, itraconazole is more effective.

10.1.4.2 Coccidioidomycosis

Coccidioidomycosis infection is caused by dimorphic fungi known as *Coccidioides immitis*. This disease is sometimes mentioned as valley fever because it is endemic to the San Joaquin Valley of California. Same infection is found in arid and semiarid area of southwestern United states, central and South America, and Mexico. Coccidioidomycotic infection is caused by inhalation of fungal spores. In epidemiology of this disease, the arthospores are produced when the fungal hyphae breaks into fragments. When fungus gets entry in host cells, it is distinguished into spherules filled with endospore. Some *C. immitis* infections are self-limiting and asymptomatic. Yet, the infection can be chronic for immunocompromised patients (Fig. 10.1). Endospore may be elated in the blood, spreading the infection and formed granulomatous lesions on the nose and face. In chronic situation some other organs can be infected and cause serious complex diseases such as untreatable meningitis. This disease can be diagnosed by isolation of fungal pathogens from clinical specimen. *C. immitis* can be cultured on Sabouraud Dextrose Agar when incubated

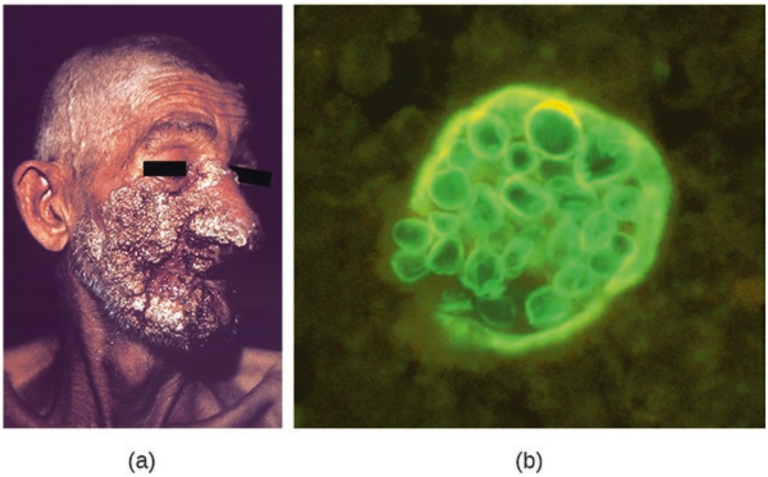

Fig. 10.1 (**a**) The patients have facial lesion due to *Coccidioides* infection. (**b**) The fluorescent micrograph shows a spherule (Source: http://www.cdc.gov/fungal/diseases/coccidioidomycosis/index.html)

at 35 °C. It is very dangerous to grow in laboratory environment because it is the most infectious mycopathogens capable of surpassing human immune system in the laboratory. This pathogen is rendered as Risk Group 3 agent and can be experimented only in BSL-3 lab facility. The serology of patient may be utilized for its diagnosis through presence of antibody against the pathogen in the patient serum. Though minor cases do not require thorough treatment, but severe pathologies can be treated with **amphotericin B.**

10.1.4.3 Blastomycosis

Another dimorphic fungus *Blastomyces dermatitidis* causes disease termed as blastomycosis. Like *Coccidioides* and *Histoplasma*, *Blastomyces* spread through soil, and fungal spores can be breathed with dust from eroded soil. Symptoms and signs of blastomycosis are mild flu-like and treat with time without medication. It can spread in immunocompromised people and is able to produce severe cutaneous disease with underlying skin lesions on the hand and face. These abrasions are ultimately converted into discolored and crusty surface and can cause deforming scars on skin. Systemic blastomycosis is uncommon, but when it is left untreated, it always results in fatality. Urine antigen tests are now available for diagnosis of pulmonary blastomycosis. Further tests include serological assays such as EIA or immunodiffusion tests. **Ketoconazole** or **amphotericin B** are used for the treatment of blastomycosis.

10.1.4.4 Mucormycosis

The diversity of fungi in the order Mucorales causes disease termed as **mucormycosis**, uncommon mold infection. These include bread molds, like *Mucor* and *Rhizopus*, generally related species is *Rhizopus arrhizus (oryzae)*. In immunocompromised patients, these fungi can establish itself in many different organs but cause infection in the sinuses, respiratory organs, and human dermal region. From the environment the spores enter through breathing in spore-laden air, but spore can also infect the derma layer through gastrointestinal tract if ingested or wound. Sever infection can occur in immunocompromised individuals such as a patient who had a transplant or with cancer. When spores are inhaled into the host's tissue, the fungi grow by spreading hyphae. Infection causes disease in both lower and upper respiratory tracts. In some severe cases the host brain and sinuses are also affected, and the disease is rhinocerebral mucormycosis. Its pathological manifestations are pyretic response, headache, congestion, and tissue death resulting in formation of black lesions in the oral cavity and facial swelling. Infection of the lungs is termed as pulmonary mucormycosis; symptoms include shortness of breath, fever, chest pain, and cough. In chronic cases, the pathogen may disperse to the central nervous system paralyzing the patient in coma and cause death. Currently, for diagnosis there are no PCR-based or ELISA available for detection of pathogens in medical specimens. Tissue biopsy specimens is the only detection strategy to assess the presence of the fungal pathogens. Infections are treated by intravenous administration of **amphotericin B,** and surgical procedures are utilized for removal of superficial infections.

10.1.4.5 Aspergillosis

Aspergillus is a fungus having a mycelial mat comprising of large filaments found in organic debris and soils. This fungus is the most common fungal pathogens; however rarely people become sick. *Aspergillus* may colonize the host and cause infection called aspergillosis. In immunocompromised patients, when its spores are inhaled, the patient can develop allergic asthma-like reactions. Clinical manifestations commonly include wheezing, flue, coughing, headaches, and shortness of breath. Aspergilloma or fungal balls are formed when colonies of hyphae are accumulated in the lungs (Fig. 10.2). In the lungs the *Aspergillus* mycelium damages the host tissues and causes pulmonary hemorrhage and bloody cough. When the infection worsens, the disease becomes fatal because of disseminated fungal mycelium, and it may take the patient to unrecoverable stage of brain hemorrhages and pneumonia. Laboratory diagnosis mostly requires radiography of chest and microscopic testing of tissues and respiratory samples of fluid. *Aspergillus* antigens are identified from serological test. If a person is exposed to fungus, skin test can also be performed for its determination. These tests are similar to that performed for tuberculosis.

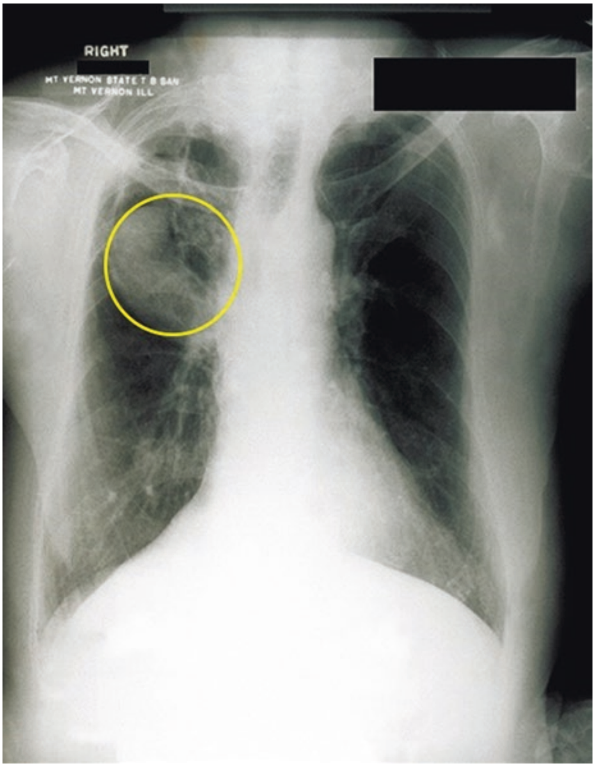

Fig. 10.2 An Aspergilloma (fungal ball) can be observed in the upper lobe of the right lung in this chest radiograph of patients with aspergilloma (Source: Modified image by Centers for Disease Control and Prevention)

10.1.4.6 *Pneumocystis* Pneumonia

Pneumocystis pneumonia (PCP) is a type of pneumonia caused by *Pneumocystis jirovecii*. Initially supposed to be a protozoan, this microbe was previously classified as *P. carinii,* but after genetic analyses and biochemical tests it is regrouped as a fungus (*Pneumocystis jirovecii*) (Fig. 10.3). Immunodeficiency syndrome (AIDS) patients acquire *Pneumocystis* pneumonia, and some of premature infants may get infected also. When lungs are infected shortness of breath is inevitable with cough and fever. These infections are difficult to diagnose. The pathogen is normally identified by slide identification under microscope. Usually fluid and tissue samples from the infected organ are used. Molecular detection may also be used using PCR assay to probe *P. jirovecii* in symptomless patients with immunodeficiency disease. A combo drug **trimethoprim-sulfamethoxazole** is successfully utilized for treatment of the disease.

10.1.4.7 *Cryptococcosis*

Cryptococcosis infection caused by encapsulated yeast termed as *Cryptococcus neoformans. This fungus mostly resides in soil and can be detected in avian feces. If inhaled basidiospores found in air the spores may cause disease in infected*

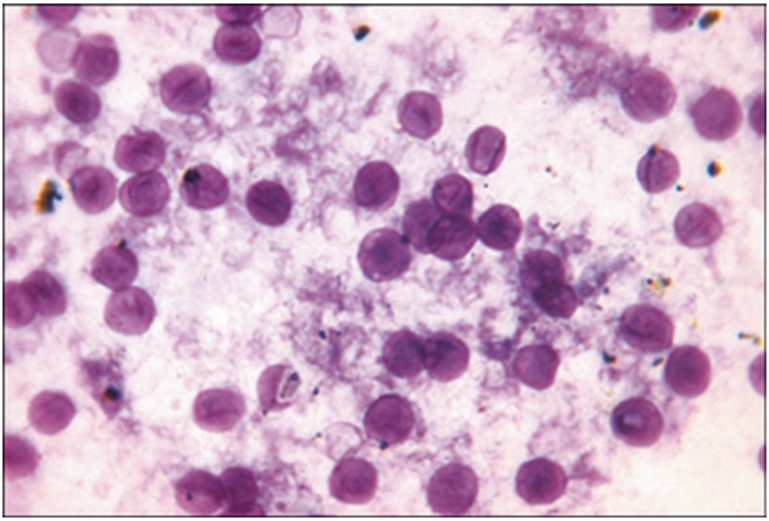

Fig. 10.3 A light micrograph of smear containing *Pneumocystis jirovecii* obtained from human lungs tissue (Source: Modified image by Centers for Disease Control and Prevention)

immunocompromised patients. This microbe is surrounded by thick polysaccharide capsule and enables them to evade the response of alveolar macrophages. Early manifestations of infection include a dry cough, malaise, and fever. Pulmonary infection is often disseminated to the brain in immunocompromised patients. The resultant **meningitis** produces confusion, sensitivity to light, and headaches. This infection is diagnosed on the basis of microscopic examination of cerebrospinal fluids or lung tissues. Indian ink can be used to locate the capsules bordering outer wall of the fungal pathogen. ELISA technique is also performed to endorse the detection. For the initial treatment of pulmonary infection, **flucytosine combination with** Amphotericin B can be used. Amphotericin B is a broad-spectrum drug against fungus that targets cell membranes of fungus. In immunocompromised and those with AIDS patients, cryptococcal infections are more common.

10.1.4.8 Dermatophytes

Dermatophytes are fungi able to cause contagious diseases of the skin, hair, and nails. The disease is termed as dermatophytosis. Dermatophytes have enzymes that can degrade keratin proteins of the scalp, hair, nails, feathers, horns, and hooves. Dermatophytes are mostly soil resident microorganisms and decompose the organic matter. The decomposing ability also enables these microbes to infect hosts when alive. Some dermatophytes (anthropophilic species) are habituated and are transmissible to person to person. When dermatophytes are habituated to animals, these are zoophilic species. A few (geophilic) species frequently reside in the environment and can be parasitic when these get the opportunity. Zoonotic transfer of some of the zoophilic and geophilic species may also occur. There is also evidence of reverse zoonosis, i.e., human to animals route of disease transmission is also noted. The epidermis, nails, and hair of living host are the target residing areas for dermatophytes. The infection may limit itself, but sometimes the illness may cause facial or tissue impairment and discomfort, when spread widely. Economic effects, such as damage to obnubilate, are additionally consequential in livestock. Infrequently, dermatophytes may invade subcutaneous tissues and (very infrequently) other sites, especially in immunocompromised hosts (Cafarchia et al. 2004).

Tinea capitis Most often children get infection on the scalp and hair, and it is known as tinea capitis. The disease is caused by diverse groups of pathogens like *M. canis*, a zoophilic species causing the same infection in continental Europe, while *T. tonsurans* is mostly associated anthropophilic infection in human population of the USA and the UK. Variable pathogenic organisms have been isolated and include *T. violaceum*, *M. audouinii*, *T. schoenleinii*, and *T. soudanense*. Some fungi are zoophilic only and include *T. mentagrophytes*, *T. verrucosum*, and *M. persicolor*. *M. gypseum* and *M. nanum* (uncommonly) have been detected as geophilic species in some the infection in some area. Tinea capitis is manifested when scaly, erythema and baldness grow rapidly on the scalp. Some human-residing dermatophytic species may result in bald crusts with slight inflamed tissue at follicle point. Dermatophytes associated with animals are able to cause swelling in the infected area called kerions. “Favus” is an infective manifestation of anthropophilic *T. schoenleinii*. This a chronic infection and hairs are surrounded by yellow crusts. When untreated the disease may last up to years (Nweze and Okafor 2005).

Tinea corporis or ringworm occurs on the main body and in extreme parts of the body including face sometimes. Neck and hand wrists also get infected more often from children to adults. Human-infecting microbes are *T. rubrum* and *E. floccosum*. Both of these infect the skin only. The other causative agents are *M. audouinii*, *T. schoenleinii*, *T. tonsurans*, and *T. violaceum*. The fungal pathogens causing this dermatophytic infections in animals are mostly *M. canis*, *T. verrucosum*, *T. equinum*, *T. mentagrophytes*, and *M. persicolor*. The geophilic pathogenic flora comprised of *M. gypseum* and *M. nanum*. Tinea corporis may be characterized by one or more lesions of pink or red or even scaly with annular ring appearance. The ring borders may have follicular papules or vesicles mostly when the infecting pathogen is zoophilic or geophilic in origin. The zoophilic fungus *Trichophyton quinckeanum* can form yellow crusts on the skin called scutulae. Itching gets started in lesions. The remedial measures include treatment with corticosteroids. Tinea corporis may take few months to be cured naturally if left untreated.

Tinea faciei and tinea barbae are dermatophytic face infections, and the causative agents are usually acquired from pets or livestock. The target area for fungal pathogenesis includes the scalp or torso. Tinea barbae include fungal infection in hair and skin of beard or mustache. The victims are usually men. *Trichophyton rubrum* is the causing agent, and follicular pustules are formed along with scaling and redness of skin. The cattle associated pathogen *T. verrucosum* and *T. mentagrophytes* may have a large inflammation of infected area with pustular folliculitis or kerions. The other fungal species involved include *M. canis*, *T. tonsurans*, *T. megnini*, and *T. violaceum*. Tinea barbae is sometimes considered as a similar condition as tinea faciei by some researchers. Tinea faciei is visually perceived on the hairless facial area. The causing pathogens are *T. rubrum*, *T. tonsurans*, *T. schoenleinii*, *T. mentagrophytes*, *M. canis*, and *T. erinacei*. The itching sensation increases when skin is exposed to sunlight and even burning starts. In some cases this condition resembles tinea corporis.

Tinea cruris Anthropophilic fungal dermatophytes infect groin and groin associated area. *T. rubrum*, *T. mentagrophytes* var. interdigitale, and *E. floccosum* are common causative agents. The clinical manifestations include itching, burning, pruritus, and formation of red lesions with clear centers. The edges of the ring are sharp and raised. Vesicles or pustules may be formed that may exude out and are moist when macerated. The moist acute cases may resemble eczema while dry pustular forms of lesions are chronic in nature. As the lesion increases, in size hyperpigmentation occurs in the central part. Both tinea cruris and tinea pedis are conditions caused by the same fungal pathogen and can occur simultaneously.

Tinea pedis and tinea manuum *T. rubrum*, *T. mentagrophytes* var. interdigitale, and *E. floccosum* cause tinea pedis infection mostly, and these pathogens are anthropophilic. Interdigital tinea pedis (athlete's foot) is an infection of the foot, characterized either by dryness, fissures, and scales or white, moist macerated lesions in some or all of the spaces between the toes. Tinea pedis also exists in the chronic, erythematosquamous type. This condition is evident when scales appear on the feet; swelling and dryness are also visible on the feet. Another form of tinea pedis appears on feet soles and manifests itself in the form of redness and withdrawal of foot nails. **Tinea manuum** is a dermatophytic fungal pathologic reaction condition on human hands. When these fungi infect hands, palms become dry; red coloration due to erythematous response and scaling also occurs. Anthropophilic dermatophytes are mostly isolated for tinea manuum condition (*T. rubrum*), zoophilic fungi *M. canis*, *T. mentagrophytes*, *T. verrucosum*, and *T. erinacei*, or the geophilic organism *M. gypseum* are also isolated in some cases. **Tinea unguium** (or onychomycosis) is a condition when nails are infected with dermatophytic fungus. Its manifestation is evident when nail shape is distorted and the color is changed (Microsporum 2004).

10.1.4.9 Allergen in Respiratory Allergic Patients

At the start of the eighteenth century, it was detected that fungi in air environment cause many respiratory ailments (Huber 2006). Sir Floyer in 1726 has mentioned a patient with an astringent asthmatic attack who visited a brewery where fermentation was going on. After a century, Blackley detected that chest tightness and bronchial catarrh were caused by *Penicillium glaucum* spores were inhaled (Blackley 1873). Storm van Leeuwen was the scientist who declared that asthma is also caused by fungal spore inhalation. The initial discovery of fungi as respiratory allergen was made 300 years ago, but the disease could not be studied much (Crameri et al. 2014). Presently enormous data is available where fungi as respiratory allergen have caused several ailments both in indoor and outdoor environments. Many asthmatic patients are prone to aeromycoflora and develop infections when exposed to fungal spores, and some patients may become asthmatic even if they were previously not (Jo et al. 2014). Home dampness, visible mold magnification, and moldy odor are indication of huge fungal load inside homes and are the main causes of asthmatic reactions in children and elderly (Meng et al. 2012). A correlation exists between fungal spores load and asthmatic reactions in patients. Mortality may be caused when asthma patients are not treated within time. It was noted in Chicago that double deaths from asthma occurred on days when fungal spores in air were more as compared to days when fungal spores load was less (Targonski et al. 1995). In rural areas when crops ripen the spores load in air is also increased. This increase is further augmented when crops are harvested and stored (RodrÍGuez-Rajo et al. 2005). Respiratory ailments associated with fungi mostly belong to Ascomycota and Basidiomycota group (Pulimood et al. 2007).

The allergic response was indicated in experiment when IgE-mediated reactions were increased. The histamines in basophils were released in sensitive patients. This was detected by skin testing (Fadel et al. 1992). Earlier bronchial and nasal challenge experiments for spores and mycelia inhalation concluded that it may produce rhinitis, asthma, and eosinophilic infiltration reactions (Licorish et al. 1985). There is evidence that fungal spores and mycelium both have certain components that can cause allergic reactions. *Alternaria alternata* allergen (Alt a 1) is present in both spores and mycelium of fungus and detected by electron microscopy (Twaroch et al. 2016). Fungi have the ability to activate further the innate immune system which may result in inflammation enhancement by other allergens like pollens.

It is a prerequisite if patients are tested in hospital environment for sensitization against fungal allergens. Air is always laden with fungal spores, and it is almost unavoidable to find a fungal spore-free environment. Different sizes of fungal air contamination have been investigated in recent years, and several fungal species have been identified (Oh et al. 2014). DNA sequence analysis of different fungal abundant species in air and dust particles in different seasons were studied. It was found that fine particles contain more fungal allergens than coarse particle which in turn harbored more human pathogens (Oh et al. 2014). There are certain other factors that influence fungal allergen presence in air. These include climatic factors like temperature, precipitation, wind, and moisture content in air. Sunlight is also an important factor that affects fungal spore presence in air (Kilic et al. 2010). The spores level increases in hot months and autumn season and greatly reduces when winter approaches. If we note daily variation in spores count early evening and afternoon have more spores load.

Collectively the human body is exposed to fungal spores through air inhalation, skin exposure, or when ingested with contaminated food. The lungs route is most prominent route for getting fungal allergens of various shapes and sizes. Usually 2–250 μm spores are able to cause respiratory allergic reactions. Certain small spores get entry to the lower respiratory part of lungs. The threshold level for each allergen is different to start sensitizing symptoms like in *Alternaria* 100 spores/m^3 are able to induce allergic manifestations, whereas in *Cladosporium* 3000 spores/m^3 are needed to create allergic symptoms. Halogen Immunoassay (HIA) is used to quantify fungal fragments and submicron fungal particles (Green et al. 2006). It is generally found that large fungal fragments and submicron particles colonize air more than spores. It is also detected that air allergens are not necessarily dependent on spores number or fragments count (Brito et al. 2012). Major *Alternaria* allergen Alt concentration varies with developmental stage of producing pathogen.

10.1.5 Prevalence of Sensitization

Fungi are omnipresent in all types of environment, and this characteristic creates fungal sensitization everywhere in the earth environment. A range of 3–10% population is affected by fungal sensitivity reactions globally. Similarly atopic patients' response to the atmospheric fungus was found magnified (Park et al. 2014). A study conducted in different European countries indicated *Alternaria* and *Cladosporium* sensitive allergy in a population of children and adults of 5–60 years of age with rhinitis and/or asthma. A estimate of 9.5% patients were sensitive to either *Alternaria* or *Cladosporium* species as detected by skin prick method. Spain had maximum sensitization (20%) while Portugal had minimum values (3%) (D'amato et al. 1997). Rivera-Mariani et al. (2011) reported that Early Aversion of Asthma in Atopic Children (EPAAC) surveyed infant population of 10 European countries, Australia, and South Africa, for IgE antibodies against aeroallergens. Data from the USA indicated 12.9% of the population developed *Alternaria alternata* sensitivity. Another study showed allergic response against *Ganoderma applanatum* with the prevalence of 30%. On the basis of different studies conducted, it is evident that fungal sensitivity is also an age-dependent phenomenon and individual immunity plays a main role. Children particularly infants are more susceptible to get aeromycoflora infection (Moral et al. 2008). IgE antibody levels against *Alternaria* increase with age, and after a certain age their titer in blood is decreased with growing age. Fungi do not cause monosensitization, and polysensitization is observed usually. A study by Cantani and Ciaschi (2004) has revealed involvement of genetic factors in population for molds sensitization. Aeromycoflora is usually identified on the basis of spore morphology as time consuming and an expert is required for the identification. IgE level and skin tests of allergic patients do not sufficiently depict exact prevalence of aeromycoflora influence on respiratory allergies. Fungal allergens extraction is also a bit difficult task as pure form of the allergen is seldom extracted (Kespohl et al. 2013).

10.1.6 Fungal Detection in Air

Usually culture techniques are used to isolate air fungus. Different fungal media are used to isolate on Potato Dextrose Agar and Sabouraud Dextrose Agar. Czapek dox agar is also utilized to grow air fungus. The petri dish containing sterilized medium is exposed for 5 minutes in air and then closed with lid and incubated. These cultured fungi are identified through microscopy. This method is time consuming, and a special expert is required to identify the culture. DNA sequencing is another method to detect exact species through molecular technique using 18srRNA analysis. This technique is quite expensive and lengthy. Present-day researchers identify fungal species in air samples or clinical samples on the basis of molecular analysis. Suchorab et al. (2019) have devised an E nose containing gas two sensors for detection of fungi in air. The air samples are collected through polyamide tubes. Clinical diagnosis of fungal allergen is usually symptoms based and clinical manifestations are categorized. Skin test and in vitro tests (particularly the RAST) are utilized to assess fungal allergens. Usually people are allergic to different allergens along with the fungal allergens. This makes it difficult to exactly identify the fungal allergens. It is different to extract the fungal allergen in pure form, but still *Alternaria alternata*, *Aspergillus fumigatus*, and *Cladosporium herbarum* have been characterized and can be utilized for rapid detection of fungal allergy. Further studies should be conducted to characterize different fungal allergens.

10.1.7 Prevention and Control of Fungal Ailments

Microclimate plays a significant role in fungal growth on walls of the buildings, bio-deterioration, and contamination of indoor environments. Fungal contamination of buildings not only deteriorate buildings and their indoor environment but also poses serious health risks to the inhabitants as they produce both allergens and toxins. About 200,000 species of fungi and microbes are known, but 60–100 are significant pathogens in indoor environment. Among these pathogens, mold is the most important contaminant having relation with sick building syndrome symptoms which is mostly present in water leakage and areas having relative humidity above 70% or condensation (Straus, 2009). Fungi have some useful or beneficial impacts (Hyde et al. 2019), but due to infections and damaging impacts, it's important to control the fungal growth in the environment. It has been observed that tensile strength and weight loss/durability of building may decrease more than 80% which can increase the biodeterioration of buildings (Kazemian et al. 2019). It is important to address the fungal growth on both indoors and outdoors of buildings to minimize the general public health, occupational health, and economic loss. Prevention and control of molds and mycotoxins in food can be minimized by adopting the various preventive measures which depend on the type of food, storage time, and techniques (Northolt and Bullerman 1982). There is no direct method to completely eliminate fungi from the environment, but surveillance methods on regular intervals and sterilization methods can inhibit the fungal growth and can decrease the chances of infections in the medical environment (Araujo and Cabral 2010; Caggiano et al. 2014). However, correlation between fungal infections and fungal contamination through genetic analysis is suggested (Caggiano et al. 2014). Molecular techniques can be helpful in differentiating the medical and environmental strains and their pathogenicity. Preventive measures include early detection of different body parts by routine cultural through direct microscopy, histopathology, antigen detection, and serological tests (Rodrigues and Nosanchuk 2020; Seeliger and Schroter 1984). Different types of measures are adopted to control the fungus-related ailments and allergies including environmental, meteorological, and chemical treatments which are discussed in more detail:

10.1.7.1 Environmental Controls

Virtuous air quality can help in controlling the fungal growth in the more important environments like hospitals where chances of fungal growth are more, kitchens in the homes, and humid offices (Munoz et al. 2001). High Efficiency Particulate Air (HEPA) filters are recommended to install at the incoming air to maintain good quality of air. Similarly, surveillance at regular time interval for maintaining good air quality can help in controlling the fungal infections.

10.1.7.2 Meteorological Factors

Climatic factors like temperature and humidity play an important role in growth of fungi and spreading infections in the different environments. Fungi can easily adopt themselves with the changing climate, and it is important to understand the mechanism at molecular level as highlighted earlier (Hernandez and Martinez 2018). For safety and durability of food, both water activity and moisture contents are important. Water activity (aW) is defined as the ratio of the water vapor pressure of sample to be tested to the water vapor pressure of pure water under the same conditions. Water activity is important for the growth of microbes as they will not grow below a certain limit (Northolt and Bullerman 1982). For example, a_w of 0.70 is required for mold spoilage and 0.60 for all other microorganisms. Similarly, pH, temperature, oxygen contents, and many other factors can also influence the growth of microbes (Mermelstein 2009). Another study reported aW for different molds ranges between 0.6 and 0.95 like xerophilic molds have aW 0.6 and most molds 0.80 and some yeasts have 0.95 (Stanaszek-Tomal 2020).

10.1.7.3 Chemical Use

Cleaning of kitchen sinks, cabinets, and showers with detergents is recommended as these areas in homes, offices, and especially in the hospital environment can cause the growth of *A. niger*, *A. terreus*, and *Fusarium* spp. Paints can play important role in the growth of fungus as they prevent the growth of *Aureobasidium pullulans*, while *Aspergillus* and *Penicillium* species can grow quickly on paints (Nielsen 2003). In some cases, depending on the nature of the solvents, fungi may grow on water-based or solvent-based paints. Natural preservatives like chitin, chitosan, and its derivatives are recommended for food preservatives alternative to chemical preservatives like fungicides to control the growth of post-harvest fungus. It is reported that chitosan has triple effect (De Oliveira Junior 2016). Similarly, pH, O_2, and CO_2 have influence on growth of molds but extent varies. CO_2 at 20% in air depresses mold growth and aflatoxin production and markedly depresses mold growth (Northolt and Bullerman 1982). Hot water with temperature of 70 °C for 1 h contact time is an effective disinfectant as reported. Use of hot water and steams requires no chemical for fungal growth control. Other chemical treatments include hydrogen peroxide, sodium hypochlorite, and peracetic acid, and quaternary ammonium compounds (quats) at concentration of more than 0.5% are effective against bacteria and fungi (Wolf et al. 2021). Different fungicides are also used to inhibit and kill the fungus by damaging cell membranes or by stopping energy production mechanism (NPIC 2019).

Diverse range of products are used as fungicides like ethanol, vinegar, tea tree oil, etc. A study reported that tea tree oil has the greatest inhibitor effect against Aspergillus fumigatus and Penicillium chrysogenum isolated from air samples while vinegar inhibited against P. chrysogenum and no inhibitory effect has been observed against 70% ethanol (Rogawansamy et al. 2015). Herbal medicine treatment is effective against the control of skin infection, e.g., mustard oil is effective against dermatophytes. A study reported mustard essential oil effectiveness against molds by inhibiting their growth (Mejia-Garibay et al. 2015). Similarly, another study reported the effectiveness of natural oil like cinnamon leaf, bay, clove, mustard, lemongrass, thyme, orange, sage, and rosemary and concluded that effectiveness depends on method of application (Suhr and Nielsen 2003). Nonchemical method includes genetically modified and resistant crop varieties that can combat fungal and other diseases (The Bichel Committee 1999).

10.1.7.4 Public Awareness

Fungal infections are more severe and difficult to manage because both the host cells and fungi are Eukaryotes. Public awareness about the growth and related infections is highly important to address the issues. As most of the people are unaware about the causes, spread, and control of infections (Brandt and Park 2013), public awareness about the types of fungus, their pathogenicity, and control of its spread is mandatory to save both health and food. Fungal diseases are seldomely reported on the TV talk shows or print media. Although most of the food is spoiled by growth of Aspergillus and other fungal genera, public awareness is scanty. It is treated as neglected disease as compared to other infections. It is recommended to allocate more funding for the control of fungal infections (Rodrigues and Nosanchuk 2020).

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Chapter 11
Health Risks Associated with Arsenic Contamination and Its Biotransformation Mechanisms in Environment: A Review

Muhammad Hamza, Sadia Alam, Muhammad Rizwan, and Alia Naz

Abstract Contamination is the presence of specific or nonspecific substances in high concentration in a given environment which may or may not be harmful for society. Pollution is the slow and continuous introduction of toxic elements into the environment which may lead to toxicity. A survey conducted by World Health Organization reported that more than one billion people lack healthy air to breath and only air pollution is responsible for annual three million deaths globally. Among pollutants, arsenic is the most toxic element detrimental to multicellular living organisms in contrast to many single-cell or unicellular microorganisms as these utilize arsenic as a respiratory metabolite. In the periodic table, arsenic is placed in group 15 and has atomic number 33. Arsenic toxicity depends on its physical and chemical forms, valence state, route of transmission to body, toxicity dose, and duration of exposure of body to arsenic. Arsenic toxicity leads to carcinogenicity and mutagenicity. The Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances has placed arsenic as group 1 human carcinogenic element. Humans are exposed to arsenic through drinking water contaminated with arsenic; the water from the wells, which are drilled into arsenic-rich ground strata; or leaked water pipes or wells or by industrial or agrochemical waste. Humans may come in contact with arsenic by inhalation of dusts, fumes, or mists contaminated with arsenic. Food with pesticides residues and grown in arsenic rich soil or irrigated with contaminated water also harbour arsenic. The order for toxicity of

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arsenicals is: MMA (lll) > Arsenite (lll) > Arsenate (V) > MMA (V) = DMA (V). Arsenic is an agent that induces mutation and affect the genetic makeup of human being; it also increases the risk of cancer in multiple organs including the skin, kidney, lung, and urinary bladder. Earth crust has 2–5 mg/kg arsenic richly deposited in igneous and sedimentary rocks like shale and coal. Arsenic exists as organic and inorganic forms. Organic As (V) are relatively less toxic than inorganic arsenicals. Microorganisms have the ability to bioremediate the arsenic by active uptake (*bioaccumulation*) and or passive uptake (*adsorption*), an enzymatic process in which organic arsenicals are converted into inorganic arsenicals and in result form volatile arsenic. In this process, As (V) is reduced into As (III) in which a series of methylation reactions involve. Arsenic contamination risk should be assessed on a regular basis and management measures should be implemented accordingly.

11.1 Introduction

11.1.1 Pollution and Contamination

Contamination is the presence of specific or nonspecific substances in high concentration in a given environment that may be detrimental to the community or otherwise. While pollution is the slow and continuous addition of toxic elements into the environment, the addition takes place as a result of human activity which may lead to toxicity. Contaminants are produced through various natural and anthropogenic activities, such as production of chemicals in a larger scale, the methods of handling and other processing techniques also add up the contaminants release in surroundings. The level of pollution throughout the globe is gradually increasing, and it gives a red light indicator to all the developed and developing countries.

Pollution is a worldwide problem and disseminates everywhere regardless of political borders and geographical boundaries.

11.1.2 Pollutants and Their Impact on Environmental Health

According to the World Health Organization survey, more than 1 billion people all over the world do not breathe fresh air, and the annual death rate due to air pollution is 3 million (WHO 2006; Schwela et al. 2006).

Each year due to pollution, more than 1 million seabirds and thousands of sea mammals become extinct around the globe. In the United States, about 1.2 trillion gallons of unprocessed industrial and sewage wastes are thrown in the water bodies. Due to various environmental pollutions, more than 3 million infants are killed annually (USEPA 2006).

Accelerated population rate, human-induced activities, and a shift from rural to urban areas are the factors which increased the pollutant level to its peak.

Industrialization has brought about daily use of more than 60,000 chemicals in the form of fuels, consumer products, industrial solvent drugs, pesticides, fertilizers, and food products. Microorganisms are ubiquitous and act as the backbone for the entire biosphere. Microorganisms play a key role in extreme environmental conditions (such as frozen environment, acidic lakes, fissures of the earth's surface, deep sea beds) to the small intestine of animals and also regulate the biogeochemical cycles. Global biogeochemical cycles include carbon cycle, nitrogen cycle, methane metabolism, and sulfur metabolism, which are regulated by microorganisms (Das et al. 2006). Microorganisms are able to produce metabolic enzymes that are responsible for specific and safe removal of contaminants or toxic materials, through different processes, such as degradation or destruction of chemicals or through indirect transformation into another safe or less toxic compound (Dash et al. 2013).

11.2 Heavy Metals

All heavy metals are toxic, having little beneficial characteristics. Metal toxicity leads to serious health conditions and causes high morbidity and mortality in the community.

Salts of heavy metal are soluble in wastewater, and as a result, they contaminate the soil and drinking water. Through ordinary physical methods of separation, the soluble heavy metals are not separated or isolated (Hussein et al. 2004). When the concentration of heavy metals is very low, in such case the physicochemical methods are ineffective and cost-effective. At low concentration the effective and cheap methods applied for its removal are biological methods such as bioaccumulation and biosorption (Kapoor and Viraraghavan 1995; Hansda and Kumar 2016).

For safe removal of heavy metals and to re-establish the natural condition of soil, remediation agents like microorganisms and plants are used. Modification occurs in the microbial community when soil is exposed to heavy metals. The growth of microorganisms is extremely important when the concentration on heavy metal is low in soil (Jansen et al. 1994). Microbial communities respond against the heavy metals variably. Their response is based on several factors, such as concentration and availability of heavy metals. It is a complex process which is controlled and regulated by multiple factors, including the kind of metal, nature of the medium used for processing, and microbial species, which is a key factor (Coblenz and Wolf 1994). Rocks and soils have abundant concentration of elements like iron, arsenic, and manganese and ions like chloride, fluoride, sulfates, and radionuclides. These compounds pollute water when diffused in it and affect the quality of the groundwater (Hashim et al. 2011). The natural sources of pollutants which are able to release are volcanic eruptions, forest fire, and cosmetic dusts. They are also a key source for many noxious heavy metals like cadmium, lead, mercury, etc. (Timmreck 2012). Several man-made activities such as quarrying, energy release, combustible production, lamination, handling of aqueous waste refuse, nuclear fuels, and agriculture waste are responsible for the release of heavy metals into the environment and become an environmental pollutant.

11.3 Arsenic

Arsenic (As) is a conspicuously noxious metalliform element abundant in aqueous and soil medium naturally. Human-induced ventures like drilling, use of pesticides or herbicides that contain arsenic, and fields flushing with arsenic-polluted water add up to heavy contamination of arable land (Williams et al. 2009).

Arsenic is contemplated as the most widely distributed element found in the environment. It is known to be as the twentieth most commonly available trace element in the earth's crust, and 14th in seawater, while in the human body, it is twelfth. As^{75} is the stable isotope of arsenic found in natural form. Several other radioisotopes were synthesized (Jomova et al. 2011).

The most common environmental toxic substance is arsenic; it enters into the environment through geologic and chemical derivation on earth and also through human-induced activities. The Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances places arsenic as group 1 human carcinogenic element (Abadin 2013). Arsenic transformation by microorganism generates a global arsenic bio-geocycle (Zhu et al. 2014). Both environmental and human health are the main factors that raise the importance of arsenic. Humans get exposed to arsenic through contaminated drinking water, the water taken from the wells that are drilled into soil horizons rich in arsenic, or through leaked water pipes or wells polluted with industrial effluents or chemicals used for agricultural purposes (Hughes et al. 1988). Arsenic may be inhaled when in dust, fumes, and mists. Arsenic based pesticides also add this contagion to the food grown thus contaminating the food chain. Arsenic exposure can occur when people consume food contaminated with pesticides or the food grown in arsenic-rich soils or water contaminated with arsenic (Nriagu 1990). Arsenic is known as protoplastic poison because it affects the sulphydryl group of living cells which directly disturbed the function of enzymes in the cell, cell respiration, and its somatic division known as mitosis.

Arsenic is toxic to multicellular living organisms but many single cell or unicellular microorganisms utilize this element as a respiratory metabolite. Key pollution issues related to arsenic are groundwater contamination. Arsenic toxicity depends upon several properties such as its physical and chemical forms, valency, transmission pathway to the human body, toxic concentration, and exposure duration to arsenic (Hughes et al. 2011). Arsenic is the major toxic element that affects the water quality throughout the world (Nordstrom 2002; Smedley and Kinniburgh 2002). Many commercial uses of arsenic lead to the magnification of a toxic environmental pollutant. They are mainly used as alloying agents in lead solder, lead shot, grids of battery, sheath of cables, and in the pipes of boiler. The waste of paints and pharmaceutical industries highly discharge arsenic which directly meets the oceanic and groundwater. Report on seawater shows the concentration of arsenic is about 0.002 ppm (Maher and Butler 1988).

Toxicity of arsenic mainly leads to carcinogenicity and mutagenicity (Ratnaike 2003).

Arsenic has ionic characteristics, which make it complex than other heavy metals. Arsenic form compounds like cationic and ionic and also transform ion into neutral atoms. Many oxidation states of arsenic are found in the natural system, like 2III, 0, 1III, 1V, 1III, and 1V, which are the most prevalent arsenic states in nature.

The most commonly available valence states of arsenic are Arsine (−3), elemental arsenic (0), arsenite (+3), and arsenate (+5). Arsenite (A_{III}) is the dominated form under reducing condition, while oxygenated state support to dominate arsenate (As_{V}) in various environments.

Formation of elemental arsenic occurred in hydrothermal deposits at low temperature (50–200 °C) and oxygen-deprived soils, and a bit sulfur conditions are required to complete its formation.

Physical characteristics such as brittleness, non-ductile, and water insolubility are adopted by solid elemental arsenic.

Arsenic adversely affects human health more than any other contagion. Consumption of arsenic-contaminated water affects vital organs and causes different types of cancers (IARC 2004; Yuan et al. 2010). Chronic respiratory ailment results from arsenic exposure of lungs (Smith et al. 2006; Von Ehrenstein et al. 2005), and reproductive aberrations and fetal developmental anomalies have also been observed (Smith and Steinmaus 2009; Vahter 2009).

Based on the toxicity of arsenic, 2III is the extremely toxic state of arsenic and rarely found in nature. Due to the use of arsenic in various industries and in agriculture sectors, it enhances its toxicity to the environment and becomes toxic environmental pollutant. Currently, it is a hot topic to understand the natural transformation of arsenic, its migration, and circulation cycle in the natural system to protect the environment from contamination of arsenic. Natural and anthropogenic activities are the main sources that elevate arsenic level in aquifers. In the earth's crust, the average abundance of arsenic is between 2 and 5 mg/kg and is richly deposited in igneous and sedimentary rocks like shale and coal.

Not only geological sources are responsible for the contamination of groundwater, but also environmental conditions which control the chemical and biological conversion of the material play an important role to contaminate groundwater.

Inorganic arsenic is also known as Class 1 carcinogen agent most likely to induce cancer in living cells. Geological horizons of Asian continent contain elevated Arsenic levels in drinking water. The regions include the densely populated floodplains and South and Southeast Asia deltas (Tripathi et al. 2007; Zhao et al. 2010).

Chronic and epidemic complications on the health of humans, animals, and plants are the highlighted factor which increases the importance of arsenic day by day (Hughes et al. 2011). The uptake of arsenic by many plants such as rice pollutes and disturbs the food chain (Zhao et al. 2009, 2010).

11.3.1 History of Arsenic Use

11.3.1.1 Origin of Arsenic

In 1250, Albertus Magnus was the first to document the element arsenic (Jomova et al. 2011).

The name Arsenic is basically derived from the Persian word az-zamikhor, and there are several other modifications of the root word "Zar," which means yellow or golden orpiment (like deep yellow-orange color) (Jomova et al. 2011; Meharg 2005). In Syria, ancient people used the term zamika for arsenic. In contrast, the Greeks gave the name *Arsenikon*, which is translated as *Arsenicum,* and they believed that metals and other substances have gender-specific properties. So they regarded arsenic as Arrsenikos Orarsenikos (masculine) as it had yellow- orange orpiment pigment characteristics (Meharg 2005).

The word arsenic is first used by Latin and French, while in other languages like Russian, Spanish, and Chinese, arsenic is named as Ars'enico; in German it is Arsen and in Italian it is Arsenico. As European chemists began to differentiate elements and compounds, the name arsenic was strictly referred to element no. 33. Arsenic is the twentieth most abundant element on the surface of the earth, and it has adverse effects on human health, and also it affected the natural environment (Cullen and Reimer 1989; Adriano 2001).

11.3.2 History of Arsenic

Arsenic is also known as "poison of kings," a name that describes its historical use and hazardous effect. In the past, it has affected human lives more than any other noxious element. As a result, ratios of death in human civilization are drastically associated with arsenic. The historical poisoning epidemics included arsenic use in most of the cases. Its use in present day life is also threatening and it is suspected to continue in future if not restricted (Kretsinger et al. 2013).

11.3.3 An Old Remedy

The elemental form of arsenic was isolated about seven centuries ago. Chinese and Greek healers used and utilized compounds of arsenic as medicines for more than 2400 years ago. Besides the poisonous and carcinogenic effects of arsenic, physicians and scientists used arsenic to treat various diseases and conditions successfully (Chen et al. 2011; Zhu et al. 2002).

Hippocrates (460–370 BC) was the pioneer who used arsenical such as realgar and pastes of orpiment to treat ulcers. Chinese Nei Jing Treaty (263 BC) reported the use of arsenic pills to cure the periodic fever associated with malaria.

Centuries ago (100 BC), realgar-containing pastes were used to cure certain dermal complications like carbuncle. From 40 to 90 AD, Dioscorides analyzed that use of arsenicals can cause loss of hair, but on the other hand, it would also clear lice, scabies, and many skin outgrowth. Malaria was treated by using medicine which is composed of realgar, arsenic trioxide, and orpiment, and the drug was formulated by Si-Miao Sun (581–682 AD). Pharmacopoeia of Shi-Zhen Li in the Ming Dynasty (from 1518 to 1593 AD) reported that various diseases were successfully treated by using arsenic trioxide (As_2O_3). In Europe Avicenna (980–1037 AD) and Paracelsus (1493–1541 AD) introduced therapy based on using arsenic (Kretsinger et al. 2013).

From the eighteenth to twentieth century, compounds of arsenic such as neosalvarsan, arsphenamine, and arsenic trioxide were used as drugs (Antman 2001; Zhu et al. 2002).

Lefebure in 1700 discovered a paste-containing arsenic which is used as a remedy to treat all kinds of cancer. Fowler's solution, invented by English scientist Thomas Fowler, consists of arsenic trioxide and potassium bicarbonate (KH_2AsO_3, 1%w/v) that may be used to treat asthma, cholera, eczema, pemphigus, and psoriasis. In the nineteenth century, ulcers and cancer were treated by using external pastes of arsenides and arsenic salts; it may also be applied as antiperiodics, antifebrile, disinfectant, spasmolytics, scathing agent, stomachic carminative, depilatories, iron-increasing agent, tranquillizers, and stimulants. Administration of drugs is done through different manners such inhalation of drug vapors and muscular and intravenous injections. In 1887, chronic myelogenous leukemia (CML) is treated using Fowler's solution through which white blood cells count was reduced. In 1931 studies reported the remarkable effectiveness of Fowler's solution while treating nine patients of chronic myelogenous leukemia (CML) successfully. Chronic effects of arsenic, such as busulfan (drug used in chemotherapy), was reported in the 1950s.

In 1910, Paul Ehrlich, a physician, Noble laureate, and father of chemotherapy, discovered salvarsan, also known as arsphenamine, an arsenic-based organic compound which was effective against syphilis and tuberculosis and was screened from almost 500 organic arsenic compounds. Some arsenic-based compounds were used to cure sleeping sickness or trypanosomiasis such as melarsoprol. The Discovery of novel drugs and the toxic effect of arsenic are the key factors which cause decline in the usage of arsenic (Kretsinger et al. 2013).

11.4 Occurrence of Arsenic

Arsenic is counted as one of the most abundant elements on the earth's crust. It is found in more than 320 various minerals more likely in arsenopyrite (Foster 2003).

Windblown dust is the source which contaminates air, water, and soil with arsenic; also it may enter into water through leaching. The most common and prominent atmospheric source of arsenic is volcanic eruptions. Arsenic also enters into the environment through smelting and mining of ores containing arsenic as co-element. Studies reported that igneous activities are the ultimate source of arsenic on the earth's crust (Nriagu 1994).

The earth crust surface contain very low concentration of arsenic ranging, from 0.1 to 1000 ppm (mg kg^{-1}), or more. The range of arsenic in atmospheric dust is 503,400 ppm. Marine water harbors a mean of 2.6 ppb, while in stream water, the range may get reduce to 0.4 ppb. A sufficient level of arsenic is circulating us through different sources (Mukhopadhyay et al. 2002).

Anthropogenic activities play a key role in the distribution and contamination of arsenic because a variety of arsenic compounds, that is, both inorganic and organic, are supplied into the atmosphere and environment via anthropogenic and geogenic sources (Nordstrom 2002).

Different biogenic or biological sources also play an important role to distribute a small amount of arsenic in the soil and water. Recent studies on arsenic groundwater contamination in Bangladesh and West Bengal acknowledge that geological activity is the source for the arsenic dissemination. The sedimentary rocks of Himalayas have dispersed it the time span of ten thousand years. In oxidizing conditions, at low pH, arsenate is dominant, while at high pH arsenite is dominant. Under reducing environment uncharged arsenite $As(OH)_3$ is predominant, and it is highly hazardous and quite strenuous to remediate (Smedley and Kinniburgh 2002). It is associated with some noncorrosive minerals, such as sulfide mineral and release into the environment in large amounts (Duker et al. 2005). Some key sources which increase the level of arsenic on land are coal ash (22%), commercial wastes (40%), mining industry (16%), and steel industry (13%) (Eisler 2004).

Some arsenic compounds such as arsenic trioxide (As_2O_3) are frequently used in the synthesis of different items like ceramic, glass, electronics, antifouling agent and pigment production, cosmetics, fireworks, and copper-based alloys (Leonard 1991).

Arsenic in combination with copper and chromium is used for the preservation of wood, such chromated copper arsenate (CCA). Sodium arsenite is used to control the growth of aquatic weeds, which has contaminated ponds and lakes in many regions of the United States (Adriano 2001).

Studies reported that soil is probably contaminated by the usage of arsenical pesticides to control the growth and production of tick, fleas, and lice in sheep and cattle dips (McLaren et al. 1998).

A New South Wales study indicated 11 dip sites containing significant amount of arsenic in the soil. The study results depicted that top 0 to 10 cm soil contains 37–3542 mg/kg of Arsenic. Variation was observed in down soil profile as aresenic concentration was 57–2282 mg.kg at 20–40 cm depth (McLaren et al. 1998).

Phosphatic fertilizers are also source of arsenic contamination in soil that may indirectly contaminate the food chain via uptake by plants (Peng et al. 2011).

Effluents of timber treatment in New Zealand are key in contaminating aquatic and terrestrial environments with arsenic (Bolan and Thiagarajan 2011). Ores of sulfide such as Pb, zinc, Au, and copper contain a rich concentration of arsenic which can be released into the environment during the process of mining and smelting.

Dust particles stuck with the dress of smelters can also contaminate the nearby ecosystems with toxic metals or metalloids such as arsenic (Adriano 2001). Gaseous arsenic as well as bottom and fly ash containing a significant amount of arsenic are the products of coal combustion. Dust banning of these toxic materials containing arsenic can lead to soil and water contamination (Beretka and Nelson 1994). Many herbicides, pesticides, and fertilizers contain arsenic.

Agricultural soil may be contaminated through a variety of agricultural practices and fertilizers containing arsenic as a key component, such as pesticides, herbicides containing arsenic, manure of pig, and phosphorous fertilizers, can raise the level of arsenic in soil, thus endangering human health (Li et al. 2016).

Solid wastes released from industries like pesticide- and herbicide-manufacturers contain arsenic leading to contaminate the soil and water reserves. Chatterjee and Mukherjee (1999) reported that the release of industrial effluents of the product name Paris green pesticide [$Cu(CH_3COO)_2 \cdot 3Cu(AsO_2)_2$] increases the level of arsenic in groundwater and soil of urban areas of Calcutta, India. Pesticides such as lead arsenate ($PbAsO_4$), Paris green [$Cu(CH_3COO)_2 \cdot 3Cu(AsO_2)_2$], zinc arsenite ($ZnAsO_4$), magnesium arsenate ($MgAsO_4$), and calcium arsenate ($CaAsO_4$) are used as horticultural pesticides and have great part in contaminating soil all over the world (Peryea and Creger 1994).

Studies reported that organoarsenical herbicides such as disodium methanearsonate (DSMA) and monosodium methanearsonate (MSMA) also increase the level of arsenic and the chance to contaminate the soil (Peryea and Creger 1994).

Agriculture soil containing arsenic is also distributed in some soil components like iron (Fe), organic component matter, manganese oxide carbonates, and sulfides also, and such kind of distribution can disturb characteristics such as mobility, bioavailability, and toxicity of arsenic (Islam et al. 2004; deLemos et al. 2006).

Microorganisms can take part in the process of distribution and redistribution of arsenic; they can perform arsenic transformation and act as arsenic absorbents (Oremland and Stolz 2003, 2005; Islam et al. 2004).

Studies reported that some microorganisms induce the release of arsenic to the groundwater, which can increase the risk of diseases in millions of people of Bangladesh, West Bengal, and some parts of China (Smith et al. 2006).

Groundwater contaminated with arsenic can also transfer it into crops and aquatic ecosystems through the irrigation system. Arsenic-contaminated irrigation water can reduce crops yield and may have a negative impact on health when such crops are consumed as food source. Limited studies were reported on agricultural soil contaminated with arsenic as compared to that of contaminated groundwater, but only some studies explained the mechanism of uptake of arsenic in different plants (Correll et al. 2006).

Qualitative and quantitative effects of arsenic on crops such as rice, which is irrigated mostly by groundwater are becoming a major issue confronted by the world nowadays (Meharg and Rahman 2003).

A study conducted by the British Geological Survey and Department of Public Health Engineering (2001) groundwater and the area under shallow tube well irrigation concluded that every dry season of each year, about 1000 mg of arsenic is cycled with irrigation water (BADC 2005; Saha and Ali 2007).

Annually 1 kg/ha of arsenic is donated to the agriculture soil fed with 1000 mm of water contaminated with arsenic (100 ppb). Studies concluded that the range of arsenic in soil from 25 to 50 mg/kg is the safe limit for rice cultivation (Saha and Ali 2007). The ability to release the arsenic into the environment through anthropogenic activities is greatly dependent upon chemical nature and bioavailability in nature.

Ore dressing, smelting, mining, smelting of non-ferrous metals, production of arsenic and manufacturing of arsenic-based compounds, petro-chemical industries, pesticides, beer, table salt, tap water, paints, pigments, cosmetics, glass, manufacturing of mirror, antifungal compounds, insecticides, treated wood and contaminated food, dye stuff, and tanning industry use arsenic in different concentrations (Hasanuzzaman and Fujita 2012).

Arsenic compounds especially orpiment (As_2S_3), realgar (As_4S_4), and arsenolite (As_2O_3) were consumed and utilized by humans in different forms of domestics and daily usage of products such as pigments, medicines, manufacturing of alloys, pesticides, herbicides, glassware, embalming fluids, and as a depilatory in leather manufacturing (Eisler 2004).

11.4.1 Soil Microorganisms and Arsenic

Soil microbes can convert arsenic into volatile derivatives and thus wipe it away from the surface of the earth. Microfloras of soil and bacterial species isolated from the soil are reported which show the characteristic of biological volatilization. The phenomenon of arsenic volatilization is done by both oxic and anoxic microorganisms including bacteria and unicellular mycoflora (Edvantoro et al. 2004; Meyer et al. 2008).

In the United States, both types of organic and inorganic arsenic are used in agriculture. Inorganic arsenic is converted into methylated arsenic, such as monosodium methyl arsenate (MSMA) and are still used as pesticides/herbicides. Monosodium methyl arsenate (MSMA) is used to maintain the turf of golf courses and is also used in sod farms and in cotton fields to control weed production (Matteson et al. 2014).

The pentavalent aromatic arsenicals like roxarsone [4-hydroxy-3-nitrophenylarsonic acid, Rox (V)] are used to control coccidioides infection and improve weight gain, feed efficiency, and also meat pigmentation in poultry and in swine. It is used as an antimicrobial growth promoter (Bednar et al. 2004; Stolz et al. 2007).

11.4.2 In Rock

Volcanic and industrial activities with arsenic pollute the environment. Some of the major anthropogenic activities such as mining and smelting of nonferrous metals and combustion of fossil fuels increased the level of arsenic contamination in soil, air, and water. Pesticides containing arsenic increase the arsenic amount in agricultural soil. Use of arsenic as a preservative for timber can also pollute the environment (WHO 2000, 2001). Naturally, arsenic occurs mostly in sulfide form and is associated with certain minerals, such as silver, copper, lead, nickel, antimony, cobalt, and iron. More than 200 species of minerals contain arsenic. High concentration of arsenic is mostly associated with deposits of sulfide, while terrestrial abundance is about 5 mg/kg.

The level of arsenic is detected approximately 2900 mg/kg in sedimentary iron, manganese ores, and phosphate rock deposits (WHO 2001). Both natural and anthropogenic activities are the key sources that release arsenic into the atmosphere. Natural sources accompanied about 1/3 of the world's arsenic atmospheric flux (7900 tons/year).

Soil and sediments contain different ratios of arsenic ranging from 1 mg/kg to as high as 40 mg/kg. Human activities may contribute to several grams of arsenic in soil. According to WHO (2001), arsenic concentrations may vary from 5 to 3000 mg/kg contributed by anthropogenic activities.

11.4.3 In Groundwater

Through water, arsenic is transported from anthropogenic and natural sources. Factors that affect the form and concentration of arsenic are as follows (WHO 2000, 2001):

- Conditions of water such as reducing promote the predomination of arsenites.
- Level of biological reactions like biological conversion of inorganic arsenic to methylated arsenic acids.
- Water type such as seawater to that of freshwater versus groundwater.
- Reservoirs of water near sources such as soil and rocks contain a high level of arsenic and also anthropogenic sources.

Studies reported that less than 10 μg/L of arsenic is detected in freshwater sources such as river and lakes, while this concentration varied up to 5 mg/L when water source is located near high anthropogenic sources which carry rich content of arsenic.

Comparative studies concluded that an average concentration of arsenic in seawater and groundwater is 1–2 μg/L, while concentration of arsenic is detected up to 3 mg/L in those areas that have volcanic rock and where high deposits of sulfide mineral are found (WHO 2001).

11.4.4 Arsenic in Overall Environment

About 24,000 tons per year of arsenic has been added into environment through anthropogenic activities such as mining and smelting of parent metals and burning of fuel (brown coal) and pesticides containing arsenic. Volcanic activity may also boost up the level of arsenic in the environment through different ways such as low temperature volatilization, vegetative exudates, and dusts containing arsenic elements blown by the wind (WHO 2000, 2001).

Inorganic arsenic (a mixture of both As_{iii} and As_{v}, predominant by pentavalent) is present in the atmosphere of urban, suburban, and industrial areas. Methylated arsenic is considered as the smaller component of arsenic in the atmosphere (WHO 2000). In remote and rural areas, the concentration of arsenic in air ranges from 0.02 to 4 ng/m^3, while in urban areas this concentration exceeded up to 3–200 n^{3}g/m^3. More than 1000 ng/m^3 of arsenic has been reported from industrial sources such as smelting of nonferrous metals and burning of coal containing a high concentration of arsenic in power plants (WHO 2001). Many decades have witnessed groundwater pollution with arsenic particularly in China, Taiwan, and some Central and South American countries. The natural geological formations that have reservoir of arsenic exist in West Bengal (India), Bangladesh, some parts of Argentina, Chile, Mexico, Thailand, Brazil, etc. Groundwater generally has As (V). Methylated arsenic compounds also exist in groundwater (IARC 2004).

11.5 Applications of Arsenic

11.5.1 Arsenic Used as Biotic Weapon

The United States released more than 1.2 million gallons of DMAs (V) during Vietnam War. It is also known as agent blue and is one of the rainbow herbicides used to destroy crops such as rice bamboo, and banana (Stellman 2003).

Recently in the United States, agent blue was used as herbicides on the cotton field and courses of golf. In Florida, diphenylated arsenic compounds such as Clark I (diphenylchloroarsine) and Clark II (diphenylcyanoarsine) were synthesized and used in World War I and World War II. After the war these chemicals are deposited in land and seawater. After that, deposited arsenic compounds are degraded by bacteria into inorganic forms, and the species of bacteria were isolated from the contaminated sites (Harada et al. 2010).

Different processes of various industries contributed to elevate the level of arsenic in water, soil, and air. Uses of various chemicals and agricultural pesticides which contain arsenic as a major constituent can increase the chances of environmental contamination.

Decades ago, inorganic arsenic compounds were excessively consumed as wood anti-decay agents, pesticides, weedicides, and colorants, and now its use is abandoned in agriculture for its hazardous effects. Some arsenic (organic) compounds are used as pesticides such as disodium methyl arsenate (DSMA), monosodium methyl arsenate (MSMA), and cacodylic acid, while some are used as additives in the feed of animals. To improve the properties of a mixture of metals or alloy, a small amount of elemental arsenic was added to it and used in certain product,s such as lead-acid batteries, light-releasing/light-emitting diodes, and semiconductor (Oremland and Stolz 2003)

11.5.2 Useful Effects of Arsenic

In oral administration, arsenic was used as Fowler's solution in curing mixtures and also used for the treatment of certain diseases like asthma and leukemia and different malignancies (Leslie and Smith 1978). In the past, arsenic was used as a remedy to treat syphilis, topical eosinophilia, trypanosomiasis, lichen planus, verruca planum, and psoriasis. Arsenic is used for domestic, industrial, and agriculture purposes such as in the form of insecticides, weed killers, and rodenticides (Thorburn 1983; Antman 2001; Çöl et al. 1999; Saha et al. 1999). Arsenic is also used as wood preservative and also utilized as an active ingredient of anti-spirochetal and anti-protozoa medicines. Chromated copper arsenate was used in residential wood furniture but is banned since 2003 in the United States and Canada. Disodium methanearsonate in small amounts was applied as herbicides in cotton fields, but the Environmental Protection Agency banned its use since 2009. Roxarsone, arsanilic acid, and derivatives are commercially utilized in poultry feed to increase biomass, improve feed efficiencies, and cure poultry disease (FDA 2008). Arsenic along with lead is used to make an alloy. Alloys are used in lead-acid batteries. Electronic industries also use arsenic in making conductors and semiconductors as gallium arsenide. It is also utilized in making microwave and milliwave devices. Arsenic is used in making fiber optics and computer chip crystals (IARC 2006). Pigments, antifungal compounds in wall paints, different soaps, ceramics, and electrophotography have arsenic as a prime ingredient. Arsenic is also used as a foul smell removing agent in wall paints.

11.6 Organic and Inorganic Arsenic

11.6.1 Arsenic in Periodic Table

Arsenic is an element found in the periodic table. It is placed in group 15 and has atomic number 33. In elemental form, arsenic is symbolized as (Adriano 2001). Group XV contain semimetallic element, but here arsenic was also reported as metal contaminant. Along with arsenic, other elements such as nitrogen, phosphorus, antimony, and bismuth are also placed in the same group.

Arsenic has four valence states:

1. 3 (*arsenides*)
2. 0 (elemental)
3. +3 (trivalent, *arsenites*)
4. +5 (pentavalent, *arsenates*)

The atomic mass of arsenic is 74.921 and has 60 atomic mass units (amu), and its atomic number is 33, denoted by Z, which shows the number of protons present in nucleus of each atom of arsenic (Carter et al. 2003).

11.7 Physical Characteristics of Arsenic

11.7.1 Arsenic Forms

Arsenic is metallic gray and yellow in color. Metallic gray is the stable form of arsenic. Precipitation occurs whenever arsenate (AsO_4^{3-}) and its various protonation types such as H_3AsO_4, H_2AsO_4, $HAsO_4^{2-}$, and AsO_4^{3-} were exposed to metal cations. Under acidic or moderate reducing conditions, arsenate coprecipitate or absorb into the iron oxyhydroxides. Mobility of coprecipitation is reducing under acidic and moderate reducing conditions. pH is directly proportional to arsenic mobility, so as pH increases mobility of arsenic is also increased (Evanko and Dzombak 1997). Arsenic is predominantly present in anionic form because it does not create complexes with other anionic elements and compounds such as Cl^- and SO_4^2 (Evanko and Dzombak 1997). Absorptive ability of arsenic is privileged to soils, and therefore in groundwater and surface water, they may travel very limited distance. Arsenite (AsO_3^{3-}) and its protonated form such as H_3AsO_3, $H_2AsO_3^-$, and $HAsO_3^{2-}$ are dominated in high reducing conditions. Arsenite has strong binding affinity to sulfur compounds and can absorb or coprecipitate with metal sulfides (Evanko and Dzombak 1997). **Methylation** of arsenic may result to the generation of methylated compounds of arsine such as trimethyl arsenic acid (CH_3) and dimethylarsine HAs $(CH_3)_2$, AsO_2H_2, and dimethylarsenic acid $(CH_3)_2$ AsO_2H. The phenomenon is named as biotransformation (Evanko and Dzombak 1997). Previous studies suggested that arsenic load can be reduced through absorption and coprecipitation with hydrous iron oxides, and the suggested techniques are very effective to remove these hazardous materials. Arsenate can be leached from the soil having a low amount of reactive metals (Evanko and Dzombak 1997). Generation of arsenite (AsIII) can be promoted in the presence of organic and reducing conditions, that is, alkaline and saline. These two factors create compound units with arsenic (Evanko and Dzombak 1997). Arsenide binds to gallium and forms gallium arsenide. Gallium arsenide has alloy-like or intermetallic-like characteristic which is further used in semiconductor industry (Carter et al. 2003). Arsine has −3 valence state, found in the form of a colorless gas. Arsine is used in several industrial processes and is harmful to humans because it is a potential hemolytic agent (Carter et al. 2003; Klimecki and Carter 1995). Arsenic makes covalent bond with hydrogen, sulfur, and oxygen, and it self-creates inorganic arsenicals. When it binds with carbon, it forms organoarsenicals.

11.8 Arsenic Toxicity

11.8.1 Division of Arsenic According to Their Toxicity

The biotransformations such as redox cycles occur between the harmless or less toxic pentavalent arsenate As (V) and highly toxic and carcinogenic trivalent arsenite As (III) (Oremland and Stolz 2003).

Inorganic arsenite (As III) is less toxic than MAs(III), and it generates variation in the hepatocytes of hamsters and humans (Petrick et al. 2000, 2001).

Biological methylation is the initial process through which various toxic arsenic species are detoxified or deactivated. MMA (V) and DMA (V) are the end product of methylation which act as biological marker for chronic arsenic exposure, and excluding MMA (III), others are excreted through urine. The intermediate product of methylation is MMA (III).

The leakage level of lactate dehydrogenase, leakage level of potassium, and mitochondrial metabolism of tetrazolium salt in human hepatocyte cells determined the species and toxicity of the arsenicals like arsenite (III), arsenate (V), MMA (V), DMA (V), and MMA (I) (Petrick et al. 2000, 2001).

The following order determined the toxicity of arsenicals according to their species:

MMA (lll) > Arsenite (lll) > Arsenate (V) > MMA (V) = DMA (V)

The MMA (III) (monomethylarsonic acid) is the intermediate product of biological transformation of arsenic. MMA (III) is more toxic with respect to other arsenical species, and it is the only species of arsenic responsible to induce cancer and other health problems. So methylation is the process that activates the toxicity of arsenic, and it is not being considered as the detoxification process (Styblo et al. 2000).

11.8.2 Effect of Arsenic on Living Cells

Arsenic is an agent that induced mutation and affects the genetic makeup of human beings; it also increases the risk of cancer in multiple organs, including the skin, kidney, lung, and urinary bladder (Karagas et al. 1998). Arsenic is accumulated inside the different parts of plants; whenever the same plant is consumed, arsenic is transmitted to the human or animal body and causes serious health-related complications (Peng et al. 1994; Abedin et al. 2002).

More than 200 enzymes were hunted by arsenic, but mostly it will affect cell metabolic pathways, DNA replication, and repairing, and also it replaces phosphate in high compound, that is, adenosine triphosphate. **Peroxidation** of lipid and damage to DNA are caused by induction of reactive oxygen intermediates, during redox cycling and activation of metabolic pathways (Cobo and Castiñeira 1997). Arsenite binds to thiol or sulfhydryl groups present in tissue proteins of organs such as the liver, spleen, lungs, kidney, lungs, GIT mucosa, and keratin-rich tissues such as the skin, hair, and nails (Ratnaike 2003).

Cellular biochemical functioning is disturbed when arsenic reacts actively with proteins and enzymes. Several processes such as photosynthesis, transcription, respiration, and metabolism of plants were heavily affected by the toxicity of arsenic (Meharg and Hartley-Whitaker 2002).

Arsenic creates reactive oxygen species (ROS) generation inside the cell and oxidizes proteins. Lipid peroxidation also occurs, and cell organelles are damaged. DNA is also harmed through ROS (Finnegan and Chen 2012).

11.8.3 Arsenic Exposure

11.8.3.1 Biogeochemical Cycle and Arsenic

The process in which three different systems (geological, biological, and chemical) interact for an element is known as the biogeochemical cycles of that element. The biogeochemical cycle includes mobilization and transport of elements in different systems from living to nonliving and vice versa or ability of a living organism to degrade or increase the concentration of elements in an environment. Volatilization of the element is a rapid and faster method, in which the element directly evaporates from soil or water and enters the atmosphere (Brown 2008; Bundschuh and Bhattacharya 2009).

Under steady-state conditions, the ratio of total mass of a chemical in a specific system to that of total emission rate or total removal rate is known as atmospheric residence. Heavy metals such as mercury and lead have a higher residence time in the atmosphere to that of other heavy metals. Microbial diversity plays a key role in biogeochemical cycles because microbes are able to change the residence time and half-life time of chemicals, a phenomenon known as acclimatization, “in which certain kind of microbial population are continuously exposed to specific chemical, which results, rapid transformation or degradation or detoxification of that chemical.” Two antagonistic processes are bioconcentration and biodegradation in which the living organisms especially microorganisms are involved. A bioconcentration is a process in which the concentration of living organism (microorganism) is higher to that of chemical in the environment or atmosphere, while biodegradation is a process in which biological transformation of a substance occurs into a new substance or compound by the help of microorganisms (Centeno et al. 2006).

11.8.3.2 Exposure Pathway

Sources of Exposure

Food and water are the major route for arsenic exposure to human, animals, and plants. Exposure to arsenic also occurs through air by inhaling contaminated air or through dermal contact when the skin encounters or is exposed to arsenic-contaminated accessories.

Rocks are the main natural source, from which arsenic is released and added to environmental assets like food and groundwater. Arsenic contamination is a major global issue, and US EPS enlisted arsenic as one of the most toxic elements in the world. Humans and especially animal models are used to study the complete metabolism (i.e., oxidation, reduction, and alkylation) of inorganic arsenic. Under certain enzymatic processes, the As (III) is converted into As (V). Monomethylarsonate (MMA) or dimethylarsinate (DMA) is formed by a process known as methylation. Various arsenic forms exist inside the human body; out of the total arsenic, 20% is methylated arsenic (in which 14% is MMA and 6% DMA). 78% of As (III), and at last 2% of As (V). Level of methylated arsenic is increased, when the body is exposed to As (III) and As (V) for long term (Aposhian et al. 2004). There are many sources through which arsenic is exposed to a body (living or nonliving); they may be natural, industrial, and administrated or accidental source. Self-administered and unintentional or accidental consumption of arsenic occurs in adults or children. Adults mainly consume arsenic for suicidal or homicidal purposes, and in that case, arsenic causes acute poisoning (Fuortes 1988). Humans are exposed to arsenic whenever they consume water contaminated with arsenic. The water may be taken from the wells that are drilled into arsenic-rich ground strata or water pipes that are contaminated by industrial or agrochemical wastes or effluents (Hughes et al. 1988). Arsenic contaminated dusts, fumes, and mists, food contaminated with arsenical pesticides or the food grown with arsenic contaminated water or soil rich in arsenic are the hazard sources for humans (Nriagu 1990). Community-based study was conducted and reported that children poorly metabolize arsenic than women. The arsenic metabolism rate in children is DMA (47%) and inorganic As (49%) while women are able to metabolize DMA (66%) and inorganic As (32%) (Concha et al. 1998). Aromatic arsenicals are exposed and introduced to environment when chicken litter is applied as fertilizer to farmlands (Bednar et al. 2004).

Organic As (V) are relatively less toxic than inorganic arsenicals (Bednar et al. 2004; Stolz et al. 2007). Degradation of aromatic and methylated arsenicals results in the production of more toxic inorganic arsenicals (Feng et al. 2005). Microorganism is able to degrade or bioremediate the arsenic which gives possible advantage and importance to microorganism. Microorganism provides a cost-effective technology and environmentally friendly way to remove heavy and toxic metal from the environment (Valls and De Lorenzo 2002). A natural process known as bio-volatilization is applied to remove arsenic from soil and water, which is also considered as a tool of bioremediation. Several factors are involved in the volatilization of arsenic from the soil or water; these factors are arsenic valence forms, its concentration, moisture content in soil, temperature, organic materials, several other elements, growth rate of microbes, and volatilization capacity of arsenic (Edvantoro et al. 2004; Gao and Burau 1997).

Arsenic is one of the natural elements present in sediment, soil, and rock. Human may happenstance with arsenic from two sources that may be natural or anthropogenic or both. The quantity as well as quality of arsenic is mainly dependent upon geological antiquity of the area (Fowler 2013; Nordberg et al. 2014).

In the United States level of air contaminated with arsenic in rural areas ranges from <1–3 ngm^{-3}, while in urban areas the level is quite deviated and ranges from 20–30 ngm^{-3} (ATSDR 2007).

According to the World Health Organization, the level of inorganic arsenic contamination in fresh water such as surface water and groundwater ranges from 1 to 10 gL^{-1} (WHO 2001).

Nordstrom in 2002 revealed that in some areas of the globe, the level of arsenic in drinking water is high as >100 gL^{-1} (Nordstrom 2002).

11.9 Transfer of Arsenic to Body

Arsenic is an ordinary element of the human body. The soluble form of arsenic is absorbed through the gastrointestinal tract. About 40–100% for arsenic was absorbed by humans. Due to low reactivity with the epithelial membrane of GIT, the absorptive ability of both inorganic and organic arsenate (As V) is higher than arsenite. Arsenate is the most common form of arsenic that is present and contaminates the drinking water. Arsenic absorbs through intestine and becomes part of the blood. The disseminated form of arsenic is MMA which is distributed into the whole body. Concentration of arsenic in the blood and soft tissue of nonexposed individual is 1–5 μg/L and 0.01–0.1μg/L. Arsenic accumulates in nails and hairs, and highest recorded level is from 0.1 to 1μg As/g. The metabolic pathway of arsenic in humans is divided into two processes.

The reduction process can reduce arsenate into arsenite when it enters into the periphery of the cell. Inside the liver cells, arsenite is methylated and forms MMA and DMA. The mechanism of trimethylarsine oxide production is not yet observed in the human body. Mechanism of actions of both inorganic arsenate and arsenite acts differently (Abernathy et al. 1999). Arsenate acts like phosphate because it replaces phosphate during cellular reactions. Arsenite may react with thiol (-SH) groups that are present inside proteins and lead to inactivate a variety of enzymes. Cellular processes convert arsenate into arsenite. Arsenate induces similar biological effects as arsenite inside drinking water. Inorganic arsenic makes a strong bond with molecules of humans. Acute toxicity of MMA and DMA is less that in inorganic arsenic form. Toxicity of inorganic arsenate is quite higher than MMA and DMA, and one-tenth is the ratio of toxicity between inorganic arsenate and arsenite. Direct absorption or excretion of inorganic arsenic is not done immediately, but there are several types of detoxification mechanisms that occur through the process of methylation. The actual chronic effects of DMA and MMA are not known yet, but still some studies evaluate that the toxic mechanism of DMA induces due to chronic exposure. The rate of arsenic excretion can significantly define the type of arsenic to which the body is exposed. Kidneys filter some types of inorganic arsenic and release it into urine. DMA and MMA generated after the process of methylation can also be excreted through urine. In two to four days, about 50–90% of arsenic is removed from blood containing arsenic, and the remaining were removed very slowly with the passage of time.

11.9.1 Acute Toxicity

11.9.1.1 Acute Poisoning

Acute poisoning mostly occurs by accidental ingestion of insecticides or pesticides and mostly in the case of suicide attempt. Vomiting and diarrhea may occur when a small amount, less than 5 mg, of arsenic is ingested, but complications may resolve in 12 h, and no treatment prescription is reported for this condition (Kingston et al. 1993). For arsenic the lethal dose for acute illness ranges from 100 mg to 300 mg. According to Risk Assessment Information System Database, 0.6 mg/kg/day of inorganic arsenic is denoted as acute lethal dose for humans. Here are some examples of acute lethal dose which may lead to death of individual: A 23-year-old young male ingested 8 gm of arsenic, and he survived for only eight days.

The American Association of Poison Control Centers reported 898 cases of non-pesticidal and pesticidal exposure of arsenic, of which 21 were intentionally exposed. This case resulted in death of one affected. Frequency of pesticidal exposure is lower as compared to non-pesticidal; here 338 cases were reported out of which two cases were intentionally exposed to arsenic and no mortality was reported (Bronstein et al. 2007).

A student got a dose of 30 gm of arsenic; after 15 h of ingestion, he was treated with British anti-lewisite (an arsenic antidote) and hemodialysis, but he expired within 48 h. The severity of illness depends upon the dose of ingestion, but death usually occurs within 24 h to 4 days. Primary complication of acute poisoning is mostly related to the gastrointestinal system, such as nausea, vomiting, colicky abdominal pain, excessive salivation, and watery diarrhea. The abdominal pain is severe. Acute psychosis, diffuse skin rashes, toxic cardiomyopathy, and seizures are other complications related with ingestion of arsenic. Diarrhea is one of the prominent illnesses which enhances the permeability of blood vessels. Stools in cholera are described as rice water, but in the case of acute arsenic poisoning, the blood has also been released with stool, so they are known as bloody rice watery diarrhea. Due to massive fluid loss from the gastrointestinal tract, reduction in blood volume occurs, and circulatory collapse may lead a person to death. Esophagitis, gastritis, and hepatic steatosis are some of severe complications which were detected by post-mortem examination. Other complication such as hemoglobinuria, intravascular coagulation, bone marrow depression, severe pancytopenia, normocytic normochromic anemia, and basophilic stippling are listed as hematological abnormalities. Four to eight sailors were exposed to arsenic and developed renal failure. Some other complications such as respiratory failure, pulmonary edema, and peripheral neuropathy (which may last for two years) were also observed in acute poisoning. Long-term peripheral neuropathy leads to conditions like severe ascending weakness as in Guillain-Barré syndrome which requires mechanical ventilation. The most common neurological disorder due to exposure of arsenic is encephalopathy, which is mostly caused when arsphenamine is administrated intravenously, and the encephalopathy is thought to be due to hemorrhage complications. Other complications related to acute poisoning of arsenic are metabolic disturbance, hypoglycemia, and acidosis which has also been reported in a single patient (Hughes and Kitchin 2006).

Some other laboratory tests such as blood count and comprehensive metabolic panel may also be recommended for arsenic quantification. Removal of the source of exposure, loss of fluids, and use of chelators such as dimercaprol or 2,3-dimercaptosuccinic acid were recommended to treat acute poisoning. Hemodialysis is recommended in the case of renal failure (Morales et al. 2006; B'hymer and Caruso 2004; Flora and Pachauri 2010; Kalia and Flora 2005).

11.9.2 Chronic Toxicity

11.9.2.1 Chronic Poisoning

Multiple organ defect is mainly caused due to chronic ingestion of inorganic arsenic. High level of arsenic in drinking water causes serious health-related complications including skin ailments, vascular disease including arteriosclerosis, peripheral vascular disease, ischemic heart disease (ISHD), renal disease, neurological effects, cardiovascular disease, chronic lung disease, cerebrovascular disease, reproductive effects, and cancers of the skin, lungs, liver, kidney, and bladder. Non-insulin-dependent diabetes mellitus is associated when the body is exposed to high concentration of arsenic (Wang et al. 2003; WHO 2001).

11.9.2.2 Respiratory Effects

Both occupational and tubewell-contaminated water exposure were reported to cause disease of the respiratory system. Occupational inhalation of arsenic from different sources such as mining and milling ores and from several industrial processes induces severe clinical complications such as irritation of mucus membrane which further leads to laryngitis, bronchitis, rhinitis, tracheobronchitis, stuffy nose, sore throat, hoarseness, and prolong cough. Highly and unprotected occupational exposure causes perforated nasal septum within 1–3 weeks of exposure. Clinical complications such as tracheobronchial mucosal and submucosal hemorrhages with sloughing mucus, hemorrhages of alveoli, and pulmonary edema are caused due to inhalation of arsenite. Other complications such as chronic asthmatic bronchitis and asthma was caused due to consumption of arsenic-contaminated groundwater. Studies conducted in West Bengal, India, report diseases such as restrictive and obstructive lung disease. Skin lesions are an associated disease with respiratory disorder caused due to chronic arsenic exposure. The same disease association was found among children of Chile. In Taiwan, blackfoot disease is the most common with bronchitis.

11.9.3 Gastrointestinal Effect

GIT effects were mostly observed during acute exposure of arsenic. Nausea, vomiting, and diarrhea were observed in occupational exposure to dust or fume containing arsenic.

Complications such as burning of lips, painful swallowing, thirst, and severe abdominal colic were observed due to acute poisoning of arsenic. Pathogenic mechanism of arsenic affects the epithelial cells of GI tract and leads to irritation. Efficiency of water solubility of arsenic was detected in the absorption of inorganic arsenic through GI tract.

11.9.4 Cardiovascular Effects

Prolonged exposure of arsenic through drinking water leads to induce cardiovascular complication (Wang et al. 2007). Several epidemiological studies suggested that mortality rate of cardiovascular diseases due to inhalation of arsenic trioxide increases day by day. Antofagasta, Chile, witnessed a causality of 17 deaths under 40 in 1980 due to myocardial infarction, and it was linked with arsenic-contaminated water use. Food and water contaminated with arsenic are the only sources for consuming arsenic which affects cardiovascular system (main paper). Cardiovascular disease is enlisted as the major leading cause of death throughout the world. Epidemiological analysis shows that dose-response relationship is the way to induce cardiovascular disease (Balakumar and Kaur 2009). Atherosclerosis and abnormalities of electrocardiogram were enlisted as subclinical disorders and caused to prolong exposure of arsenic-contaminated drinking water (Wang et al. 2007). Damaging of blood vessels or the heart is caused due prolonged exposure to inorganic arsenic (paper reference). Children who are exposed to drinking water contaminated with arsenic concentration of 0.6 mg/L were followed by myocardial infarction and thickening of arterial walls. Voluntary consumption of arsenic causes acute poisoning, and the following complications were observed: hypercontracted fibers in muscles, myofibrillar disruption, and mitochondrial abnormalities and vacuole formation inside the cytoplasm. Myocardial depolarization and cardiac arrhythmias are caused due to both acute and chronic exposure to arsenic which leads to failure of the heart. Peripheral vascular disease (PVD), ischemic heart disease (IHD), and cerebrovascular disease (CVD) are the clinical complications due to chronic exposure of arsenic. Diseases are discussed below.

11.9.4.1 Peripheral Vascular Disease

An ecological study was conducted in southwest Taiwan, and the aim of that study was to show the relationship between mortality rate of PVD and arsenic exposure in drinking water. The standard mortality rate shows that male (3.56) is greater than that of female (2.3) (Tsai et al. 1999). Reduction in mortality rate was observed when study population were exposed to drinking water that have a low level of arsenic (Yang 2006). The peripheral vascular system is affected by blackfoot disease (BFD), and in the southwest coast of Taiwan, the disease adopts the shape of endemic (Tseng et al. 2005). Progressive arterial occlusion is mostly observed in lower extremities. Initial symptoms include numbness and coldness in the highly affected areas of the body; also the absence of peripheral pulsation was detected. These symptoms further progress into ulceration, gangrene, and spontaneous amputation of high affected areas of the body. In the mid-twentieth century, the level of incidence increased and ranged from 6.5 to 18.9 out of 1000 individuals (Tseng 2008).

11.9.4.2 Ischemic Heart Disease

Deprived supply of oxygen to myocardium may lead to develop ischemic heart disease. Ecological studies were conducted in several arsenic endemic villages of Taiwan which show that mortality rate of IHD may increase with increasing level of arsenic exposure. Relationship between level of arsenic exposure and mortality rate is shown as that the rate of mortality is 3.5% when range of exposure is <0.1 mg/L and the mortality rate is 6.6% when level of exposure is >0.6 mg/L (Chen et al. 1996). A cohort study was designed by Chen et al. (1996) in which a comparison of cumulative mortality due to IHD was found out between two residents such as affected and unaffected by this disease, but both were living in the same area. The annual increase in arsenic exposure can increase the mortality rate due to IHD (Thurston et al. 2016).

11.9.4.3 Cerebrovascular Disease

Areas of Taiwan have a high level of arsenic in drinking water in which the risk of cerebrovascular disease is ranging from 1.2 to 2.7 in 1000 exposed versus nonexposed individuals (Navas-Acien et al. 2006). An ecological study was conducted by Tsai et al. (1999) in southwest Taiwan in which relative risk for cerebrovascular disease was determined between male and female. The risk of CVD in male (1.14) is relatively lower than that of female (1.24).

11.9.4.4 Atherosclerosis

Atherosclerosis is a pathogenic response of the tunica intima of the arterial vessel walls to noxious stimuli. Atherosclerosis is characterized by the deposition of lipids in the walls of vessel, due to which the wall of vessels becomes narrowing. The above complication at the end leads to IHD. The prevalence of carotid atherosclerosis is increasing as the level exposure of arsenic in drinking water increases. It is also a dose-response relationship. A cross-sectional study was conducted by Wang et al. (2002) on a population of southwest Taiwan that lives in an arsenic endemic area. Individuals were screened by using duplex ultrasonography, and results show increase in prevalence of carotid atherosclerosis. After adjusting other risk factors (smoking, alcohol consumption, serum cholesterol, and others), the risk of atherosclerosis was measured as 1.8 and 3.1.

11.9.4.5 Hypertension

Hypertension is associated with chronic exposure of arsenic (Chen et al. 2007). A cross-sectional study was conducted by Chen et al. (1995) which shows that frequency of hypertension was increased in two relative population such as 5% increase in control population and 29% increase in the population that have highest cumulative exposure to arsenic (18 mg/L/year). Chen et al. (2007) performed an occupational study which shows that prevalence of arsenic is quiet low in the population, which are not exposed to high level of arsenic. A cross-sectional study in China was conducted by Kwok et al. (2007) in which 8790 pregnant women were exposed to arsenic-contaminated drinking water, but the level was not equal to that drinking water consumed by the localities of arsenic endemic areas of southwest Taiwan. After controlling other relative factors (age, body weight, etc.), rise in systolic blood pressure has note as 1.9 mm mercury at arsenic level 12–50 g/L, 3.9 mm mercury at arsenic level 51–100 g/L, and 6.8 mm mercury at arsenic level 51–100 g/L. Variation in systolic blood pressure is due to exposing body to different concentrations of arsenic. So it has also effect on diastolic blood pressure but in little extent.

11.9.5 Endocrine

Type 2 diabetes (insulin independent) is a clinical complication that arose due to chronic exposure of arsenic (Chen et al. 2007). Several epidemiological studies were conducted and reported this disease in Taiwan and Bangladesh (Lai et al. 1994; Tseng et al. 2000). The frequency of diabetes mellitus is twice higher in the villages ingesting contaminated water with inorganic arsenic than that of consuming water free of arsenic contamination (Lai et al. 1994). The relative risk of diabetes mellitus was found with multivariate adjusted ratio between some risk factors like exposure to arsenic, BMI, and physical activity. Results indicated that risk factor BMI and Physical activity show 6.6 and 10 relative risk for diabetes while in case of arsenic exposure (more than 15 mg/L/year) the relative risk for diabetes is 0.1–15. A cohort study was conducted on the occurrence of diabetes which shows that the disease was associated with BMI, age, and continuous exposure to arsenic (Tseng et al. 2000). The relative risk of diabetes due to cumulative arsenic exposure (>17 mg/L/year) was 2.1, when other factors such BMI and age were adjusted. In 2006, a systematic review of experimental and epidemiological data of Bangladesh and Taiwan shows that the risk for the development of diabetes mellitus due to cumulative exposure of arsenic is 2.5 (Navas-Acien et al. 2006).

11.9.6 Hepatic

The hepatic complication arises due to arsenic exposure that is known for over a century. Use of arsenic in therapeutics may develop ascites in patients. Prolonged use of Fowler's solution (used as tonic containing 1% potassium arsenite) may lead to complications such as noncirrhotic portal hypertension (Huet et al. 1975). Arsenicosis was reported in the localities of West Bengal, India, because of consumption of water contaminated with arsenic, and about 77% of patients may also develop hepatomegaly (Mazumder 2005).

It was the first chemical agent which caused liver disease in humans. Due to multiple times of exposure for months or years, arsenic accumulation starts and induces chronic complication. Initial symptoms are bleeding of esophageal varices, ascites, jaundices, and at last hepatic lesions caused due to long time usage of medicines containing arsenic (Saha et al. 1999). Clinical symptoms indicated tender and swollen liver. Blood tests show high level of hepatic enzymes. About 0.02–0.1 mg/kg/day is enough to generate chronic clinical complication. Arsenic disturbed mitochondrial functionality and also affects the metabolism of porphyrin. Studies suggested that patients use Fowler's solution face following clinical complications such as cirrhosis and hepatic fatty infiltration of the liver (Saha et al. 1999). Final stage clinical complications include noncirrhotic portal fibrosis and cirrhosis with liver failure which results to jaundice, ascites, and coma (Saha et al. 1999).

After liver function tests, serum enzyme elevation was observed in patients who have hepatomegaly. The results of Mazumder's (2005) epidemiological survey indicated that population developed hepatomegaly when consumed arsenic concentration of 50g/L or more. The incidence of hepatomegaly was higher in male than in female, and also study shows dose-response relationship (Abdul et al. 2015).

11.9.7 Neurological

Neurological disorders such as impaired intellectual functions, peripheral neuritis, and neuropathy are caused due to lifelong exposure to arsenic. Several nervous disorders were observed in smelter workers, beer consumer in England, and children in Bangladesh consuming arsenic-contaminated water (Wasserman et al. 2004). Sensory and motor fibers are counted in peripheral neuropathy, and illustrious characteristics are axon dying back with segmental demyelination. In the nineteenth century, a case of peripheral neuritis was observed due to consumption of beer contaminated with arsenic. Sulfuric acid was used to prepare sugar for the process of brewing, and that acid was originated from arsenical pyrites. Initial complications include needling in the finger and toes, painful walking, pain, and weakness in highly exposed parts of the body. The intelligence ability of children of Bangladesh was decreased due to consumption of drinking water contaminated with arsenic that have concentration greater than 50 g/L (Wasserman et al. 2004). As mentioned in the cardiovascular section, arsenic can damage both peripheral and central parts of the nervous system. Encephalopathy is due to exposure to arsenic at a concentration of 1 mg/kg/day. Other symptoms related to encephalopathy are headache, lethargy, mental confusion or hallucination, seizures, and coma. Continuous and repeated exposure to arsenic induces complications such as contract sensorimotor polyneuropathy and a systematic disorder which resembles Landry-Guillain-Barre syndrome. Axonal degeneration was observed within 1–5 weeks of acute exposure to arsenic. The neurological disorders include persistent headache, short-term memory loss, memory disorders, distractibility, irregular irritability, tired sleep, loss of libido and increased urgency of urine. A detecting technique known as electromyography was used which shows variation in the velocity of nerve signal.

11.9.8 Skin

Skin lesions are the primary and harsh effects of the body associated with exposure of arsenic. In the late eighteenth century appearance of lesions due exposure to arsenic was observed by physicians (Yoshida et al. 2004). Appearances of lesions were due to usage of inorganic arsenic for various ailments after that their effect was observed in patients (Yoshida et al. 2004).

Hyperpigmentation is a most common skin-related complication caused due to exposure to arsenic or arsenic-contaminated water. The appearance of pigmentation is due to hyper melanin production in the melanocytes. Body parts such as areola or groin have hyperpigmentation, and in some individuals the appearance of hypopigmentation (like raindrops) has also been observed on the face, neck, and back. Hyperkeratotic papules, warts, or corns are formed on the palms and soles of people who consumed arsenic-contaminated water. Other complications such as hyperkeratotic papules are observed in patients' palm and sole, who consume water contaminated with inorganic arsenic. White horizontal lines in the nails, called Mees' lines, are also observed (Rossman et al. 2004).

11.9.9 Developmental Disorders

Inorganic arsenic can create developmental abnormalities in the fetus when transmitted from mother (Vahter 2008). Administration of inorganic arsenic to female rodents can transmit to offspring through placenta and generate serious complications in newborns, such as malformations, principally tube effects. Malformation was not observed in the rodent and rabbits that were orally administered (Desesso 2001). Recent studies show that exposure of pregnant rats to nontoxic doses of arsenite through contaminated drinking water leads to certain clinical complication like fetal brain developmental defects and behavioral changes (Chattopadhyay et al. 2002). Adverse effects such as spontaneous abortion, stillbirths, premature births, low bodyweight, and high mortality rate were induced whenever pregnant women were exposed to water contaminated with arsenic (Ahmad et al. 2001). In Bangladesh a cross-sectional study was conducted to evaluate the effect of arsenic on pregnant women. The results indicated adverse pregnancy effects at concentration level >0.05 mg/L for maximum five year (Ahmad et al. 2001). Previous studies show the relationship between arsenic and infant mortality.

Miscarriages were reported in several pregnant women working in semiconductor industries.

11.9.10 Hematological Disorders

Long- and short-term exposure of arsenic affects the hematopoietic system. Clinical abnormalities including anemia and leukopenia are caused due to acute, intermediate, and chronic oral exposure to arsenic. These effects were induced by arsenic due to direct cytotoxic or hemolytic effects on blood cells and also due to erythropoiesis suppression. Other complications such as depression of bone marrow has also been observed due to consumption of high dose of arsenic-contaminated drinking water. Anemia and leucopenia were observed in the adults consuming arsenic-contaminated soya sauce that has concentration of 3 mg As/day. Death occurred within hours when individual consumed arsine (10 ppm). The red blood cells lysis occurred at this concentration. If concentration is slightly lower such 0.5–5.0 ppm then the above complications will approach in a few weeks and in working place the acceptable concentration for arsine is 0.5 ppm/L. Renal disorder was counted as a secondary complication in which the clogging occurs between nephrons and hemolytic debris. Arsine shows more hemolytic activity than that of mono-, di-, and tri-methyl arsines. In the absence of proper therapy, exposure of body to arsine becomes fatal because inside the body arsine is converted into inorganic and methylated derivatives of arsenic.

The in vivo study on mice and rats revealed the actual mechanism behind the hemolysis that whenever blood is exposed to arsenic it reduced the level of intracellular GHS. It results in sulfhydryl group oxidation of hemoglobin and conversion of ferrous into ferric. The capability of cells to uptake oxygen was reduced when hemocyanin is combined with arsenic (Saha et al. 1999).

11.10 Genotoxicity Effects

Smelter workers may inhale arsenite, which may lead to increase in the prevalence of chromosomal aberrations in the peripheral lymphocytes. During the gestation of female mouse, the same effects were also observed on its liver that was exposed to high concentration 22 mg As/m. These studies determined the clustogenic effects of arsenic. Arsenic cannot cause point mutation in the cellular system. A study shows that arsenic induces inhibition of DNA repair system after incision step in the cells of Chinese hamster V79.

11.10.1 Mutagenic Effects

Mutagenesis is known as damage to chemical and structural properties of DNA and alteration of genetic material that may be categorized into form base pair mutation to whole chromosomal deletions or clastogenesis. Some genetic changes may be transmitted to the next generations and become a hereditary disorder. Some of these induce cancer. Direct genetic mutation was not observed due to arsenic. Basic mechanism for comutagenicity and co-carcinogenicity of arsenic was caused due inhibition of DNA repair system. Comparative analysis between pentavalent and trivalent was done which is needed to evaluate the prevalence of chromosomal aberration and also to check more potential and genotoxic species of arsenic. Resultant of this comparative analysis shows that trivalent is more potential toxic than pentavalent. Dismutase and catalase are the enzymes that hunt free radical oxygen which may directly help to protect DNA damage induced due to arsenic.

11.10.2 Biochemical Effects

In both animals and humans, outsized important enzymes were inhibited by arsenic compounds. The activity of glucose transport is blocked by phenylarsine oxide (PAO), which can affect the uptake of glucose by inhibition of insulin activation and also inhibit the signal transmission by blocking vicinal thiol which is present ion

3T3-L1 adipocytes. The mechanism was observed inside muscles of rats. Rapid accumulations of arsenite in the liver of body cause inhibition of NAD-linked oxidation of pyruvate or a-ketoglutarate.

11.10.3 Renal Effects

The kidney is the main organ that detoxifies the blood and removes toxic material. Renal complications were generated due to repeated exposure to arsenic. Kidneys are the main and only organ of the human body that covert arsenate from low to high toxic and less soluble form of arsenite. Capillaries and glomeruli tubules were mainly affected due to arsenic exposure. A severe condition proteinuria and casts are induced when proximal tubular cells were damaged. In case of severe acute arsenic exposure, the risk to renal failure increases. Destruction of mitochondria was observed in tubular cells. Dialysis is the only effective way to overcome these effects. Arsenic-induced hemolysis occurred which leads to a sever complication known as tubular necrosis and at the end complete renal failure. Hemodialysis is used to remove hemoglobin-bound arsenic.

11.10.4 Other Human Health Effects

Visual perception of children is affected when they consume drinking water having high concentration of arsenic, and it will not affect visual motor integration. It was confirmed by two diagnostic methods: visual motor integration test (VMIT) and motor visual perception test (MVPT) (Siripitayakunkit et al. 2000). In Bangladesh, a study reported that children exposed to high level of arsenic in drinking water will have a reduced intellectual function. A comparative study shows the dose-response in two groups of children: Children who consumed water containing high concentration of arsenic (>50 g/l) had low intellectual function than those who consumed water with less amount of arsenic (>5.5 g/l) (Wasserman et al. 2004). Growth retardation in children is also associated with arsenic. Children's height is reduced when drinking water is polluted with arsenic. Results of a comparative study between two groups show that children having high concentration of arsenic in hair have height less than those children having less concentration of arsenic in their hair (Siripitayakunkit et al. 2000). Birth defects such as spontaneous abortion, stillbirth, and infant mortality are also associated with drinking water contaminated with arsenic.

Consuming high concentration of inorganic arsenic-contaminated water can affect the respiratory system and cause bronchiectasis (Mazumder 2005). Bronchiectasis is a clinical complication which is characterized as dilation of bronchi and bronchioles due to obstruction. Other complications such as hematological, reproductive, and immunological disorders were also reported (ATSDR 2007; WHO 2001).

11.10.5 Carcinogenic Effect

Different public health and regulatory organizations all around the world categorized inorganic arsenic as carcinogen to humans. Epidemiological data act as a base for such classification. Generalized and occupational studies conducted in Taiwan show that localities of Taiwan were exposed to high concentrations of arsenic. Recent studies which were conducted in particular countries such as Bangladesh, Mexico, and Chile show that the most common source of arsenic to which humans were exposed is drinking water, which is naturally contaminated with high concentration of arsenic. Skin, lung, and bladder are the most sophisticated organs of human which tend to induce tumor after exposure to high concentration of arsenic. Liver, kidney, and prostrate are enlisted as related organs which were also affected (Agency for Toxic Substances and Disease Registry (ATSDR) 2007; World Health Organization (WHO) 2001. Studies show that arsenic induces leukemia and lung cancer in model or experimental animals. Humans exposed to water or wine/beer naturally or intentionally contaminated with high concentrations of arsenic can induce skin complications such as precancerous dermal keratosis, epidermoid carcinoma, and lung cancer. Diseases like blackfoot disease, Bowen's disease, and skin cancer show correlation with arsenic-contaminated drinking water, and they were reported in countries such as Argentina, Chile, and Canada.

Cancer of the Skin

Bowen's disease and squamous and basal cell carcinoma are the most common arsenic exposure-associated skin cancers (Maloney 1996). An exposure of 6–20 years with a mean latent period of 14 years causes these ailments. The most common form of skin carcinoma induced by arsenic is known as Bowen's disease or carcinoma in situ (Maloney 1996). Appearance of lesions is solitary, randomly distributed, and has multifocal opening. Lesions are mostly from 1 mm to 10 cm in size and have sharp demarcated round or irregular plaque-like appearance (Shannon and Strayer 1989). Arsenical keratosis may lead to developing squamous cell carcinomas. These cells show more aggression than hyperkeratotic cells. The development of squamous cell carcinoma is mostly observed on extremities or highly exposed areas (Shannon and Strayer 1989). Basal cell carcinoma is induced due to arsenic exposure. Skin cancer is more prevalent in males than females. Prevalence of skin cancer is directly proportional to age. Studies also reported the dose-response relationship in skin cancer patients. Duration of exposure to contaminated drinking water, cumulative exposure to arsenic, average exposure of arsenic, and period of localities living in the endemic areas are main factors that contribute to increase in the prevalence of skin cancer.

Cancer of the Lung

Several studies claimed that inhalation of inorganic arsenic increases the chance of lung cancer (Agency for Toxic Substances and Disease Registry (ATSDR) 2007; World Health Organization (WHO) 2001). Occupational exposures to arsenite are mostly reported in most studies. Process of ore smelting contaminated air with arsenic trioxide. Some other studies reported that lung cancer is developed in workers who work with arsenic-containing pesticides.

Not a specific type of cellular carcinoma is induced in the worker exposed to arsenic. Several kinds of cellular carcinomas were observed due to arsenic inhalation such as epidermoid carcinoma, small carcinomas, and adenocarcinoma workers (Agency for Toxic Substances and Disease Registry (ATSDR) 2007; Arain et al. 2009).

Individuals working on smelting of nonferrous metals, pesticides spray production, and gold mining workers inhale inorganic arsenic that induce cancer of respiratory systems.

Body Enzymatic System

Compounds of arsenite are mainly absorbed through the elementary canal of the human body, and these compounds start their deposition in various cells of the body. The deposition of arsenic in body cells disturbs the body's enzymatic system, after which cell death occurs.

11.11 Mechanism of Arsenate Toxicity

Step 1

The first step starts with the breakdown of pyruvic acid (obtained from glucose inside the mitochondria of cell) through a specialized type of enzyme. A complex of pyruvate oxidase is needed for oxidation decarbonylation of pyruvate, which produced acetyl coenzyme A and carbon dioxide before entering to TCA cycle (tricarboxylic acid cycle). Several enzymes and cofactor collectively create an enzyme system. Single protein molecules of an enzyme contain one lipoic acid, and there are two sulfhydryl or thiol groups present in one lipoic acid. They are essential to maintain proper workability of cell. If the body cell is exposed to arsenite (trivalent arsenic), then attached to it are two hydrogen of thiol group with sulfur molecule that create dihydrolipoyl-arsenite chelate complex. This complex prevents reoxidation of dihydrolipoyl group, which is necessary for the continuation of enzymatic activities. So, enzymatic activity stops. As a result of this enzymatic inactivation, the level of pyruvate increases in the blood, while in contrast cellular energy becomes lower, which leads to death of cell. Arsenic can also affect workability of another enzyme name as succinyl coenzyme A, which may reduce the level of cellular energy (ATP) (Saha et al. 1999).

Step 2

The inorganic form of arsenate is available in the environment. It blocks the mitochondrial enzymatic activity of eukaryotic cells but in different manner. In the process of oxidative phosphorylation, phosphate-deficient ADP gets inorganic phosphate and becomes ATP. This inorganic phosphate is replaced by arsenate. Arsenate is attached with ADP and forms an unstable arsenate ester bond that rapidly hydrolysates. As a result, the level of ATP inside the cell is continuously reduced, and it also disturbs the transfer of electron between inorganic phosphorus and ATP. In the presence of arsenate, the high energy bond of ATP cannot be conserved, and the process is called arsenolysis. Two different ways that were adopted by arsenic to affect the functionality of mitochondria:

- Trivalent arsenic seize the reduction of nicotinamide adenine dinucleotide by deactivating enzymes in Krebs cycle.
- Pentavalent arsenic breaks the chain of oxidative phosphorylation by a process of arsenolysis.

Compounds of arsenate also disturbed the reaction of succinate and succinic acid during the generation of ATP (Saha et al. 1999).

11.11.1 Mechanism of Trivalent Arsenic Toxicity

The activity of trivalent arsenic is mostly related with enzymes loaded with specialized functional groups like thiols or vicinal sulfhydryls. In vitro study shows that trivalent arsenic reacted with thiol which contains GSH and cysteine (Scott et al. 1993; Delnomdedieu et al. 1993). The affinity of trivalent arsenic is higher toward dithiols than monothiols, and arsenite may transfer from (GSH)3- arsenic complex and combine with dithiol 2,3 dimercaptosuccinic acid. Toxicity caused by arsenite is induced when it builds complex with thiol groups and leads to blocking important biochemical processes.

A multiple subunit complex such as pyruvate dehydrogenase (PDH) requires cofactor lipoic acid (dithiol) to perform enzymatic reaction appropriately. Now arsenite binds with moiety of lipoic acid and inhibits the functionality of pyruvate dehydrogenase (PDH) (Hu et al. 1998). Pyruvate dehydrogenase has a key role in the generation of ATP because it converts pyruvate into acetyl CoA, which acts as a precursor molecule in the citric acid cycle and also as an electron transporter. Due to inactivation of PDH, reduction is observed in the production of ATP. Methylated trivalent arsenicals are highly active than arsenite MMAV and DMAV (source reference). Arsenite bind to sulfhydryl group and reduce the metabolic activities such as glucose uptake, gluconeogenesis, fatty acid oxidation, and glutathione production. These activities were induced by inhibiting relevant enzymes of each metabolic process, after that the cellular redox status is reduced and generates cell cytotoxicity.

Metabolism

The valence state of arsenic determines its metabolic pattern in mammals. As (III) and As (V) are the two most common inorganic arsenic valence forms responsible for human exposure. These two forms are readily interconvertible. Arsenic is methylated in the body by alternating reduction of pentavalent arsenic to trivalent and addition of a methyl group from *S*-adenosylmethionine (toxic and widely distributed in the environment. Most microorganisms have evolved mechanisms to use methylarsenicals as weapons in microbial warfare (Zhang et al. 2015; Chen and Rosen 2020).

11.12 Arsenic Removal Technologies

1. **Adsorption**
2. **Electrocoagulation**
3. **Ion exchange**
4. **Membrane technologies**
5. **Phytoremediation**

11.12.1 Adsorption

Adsorption is the accumulation of adsorbate (liquid) on the surface of adsorbent (solid), and there is the formation of a film. Adsorption is of two types, that is, physisorption (physical) and chemisorption (chemical). Physisorption is the adsorption in which van der Waals forces are involved. Chemisorption creates a strong chemical bond (ionic or covalent) between adsorbent and adsorbate. Physical adsorption is weak and reversible, while chemisorption is strong and irreversible; the heat range (kJ/mol) for physisorption is low, and chemisorption is high (Singh and Gupta 2016). Adsorption is an effective and low-cost technique for heavy metal removal for wastewater. The adsorption technique is simple and flexible, capable of high-quality treatment. Adsorption is reversible which can regenerate adsorbents as well (Fu and Wang 2011). There are some important factors which influence the heavy metals adsorption process, for example, adsorbent dosage, initial concentration of heavy metals, temperature, pH, mixing speed, and contact time. Adsorption generally increases with the increase in the above factors (Agarwal and Singh 2017; Sahu et al. 2009).

Some recent studies on adsorption of arsenic from water are shown in Table 11.1. Uppal et al. (2019) synthesized zinc oxysulfide (ZnO_xS_{1-x}) for arsenic removal by using facile chemical method. The adsorbent was highly effective in arsenic removal with maximum removal efficiency of up to 99.9%. The maximum removal capacity of arsenic was 299.4 mg/g. ZnO_xS_{1-x} was found to be highly stable and was reused successfully up to five cycles (Uppal et al. 2019). The zirconium metal-organic frameworks (UiO-66 and UiO-66(NH_2)) were used for the removal of arsenic (III and V) from polluted water. The framework effectively removed both Ar III and V from wastewater. The maximum removal capacity for As III and V was 205.0 and 68.21 mg/g, respectively. This framework is highly stable and low cost and had high adsorption capacity for arsenic (He et al. 2019). Coprecipitation-hydrothermal method was used by Yin et al. (2019) for the synthesis of activated charcoal-coated zirconium-manganese nanocomposite. The novel nanocomposite effectively removed arsenic III and V from synthetic wastewater. The maximum adsorption capacity of arsenic III and V was 132.28 and 95.60 mg/g, respectively. The Zr/Mn/C nanocomposite emerged as a green, low-cost adsorbent capable of effectively removing arsenic from wastewater (Yin et al. 2019). Kang et al. (2019) removed arsenic from synthetic wastewater using adsorbent powder trapped in alginate beads. These beads were further calcined. The surface area of adsorbent was enhanced by 100 times after calcination. The calcined beads proved to be effective in arsenic removal within a short period of time (Kang et al. 2019). A composite of alum sludge and melamine was co-pyrolyzed and used for arsenic removal. The composite effectively oxidizes arsenic III to arsenic V. This green composite effectively oxidized arsenic and also adsorbs arsenic from wastewater in the presence of light. The mechanism behind adsorption was chemisorption (Kim et al. 2020).

11.12.2 Electrocoagulation

Electrocoagulation (EC) is a highly effective and simple process used for the treatment of different types of wastewaters. EC effectively removed pollutants from industries such as poultry slaughterhouse (Kobya et al. 2006), electroplating (Adhoum et al. 2004), restaurant (Chen et al. 2000), and laundry wastewater (Janpoor et al. 2011). EC when combined with other treatment technologies can effectively remove pollutants from wastewater. EC is 100 times a more effective adsorbent than the conventional coagulation technique (Mollah et al. 2004). The flocs formed during EC are highly stable and can be easily removed by filtration. EC is a low-cost and highly efficient process. It requires simple equipment and can be used for treatment of wastewater at the industrial scale. This process does not require any chemicals; therefore there are no secondary pollutants that are produced during EC process. EC process can operate at low current, so its sustainability can be achieved by combining it with renewable energy sources, for example, solar, wind, and biofuels (Zaroual et al. 2006). The process does not require additional reagent and chemicals which make this process environment friendly. The absence of chemicals in EC process also reduces the quantity of sludge produced.

Table 11.1 shows a few recent studies on electrocoagulation of arsenic from different water systems. López-Guzmán et al. (2019) simultaneously removed arsenic and fluoride from well water using electrocoagulation process. Iron and aluminum electrodes were used during electrocoagulation. The process was highly effective for the removal of both arsenic and fluoride. The maximum arsenic and fluoride

Table 11.1 Technologies used for arsenic removal

Technology	Type	Mechanism	Removal efficiency	Adsorption capacity	Medium	References
Adsorption	Zinc oxysulfide (ZnO_xS_{1-x})	Electrostatic interaction	99.9%	299.4 mg/g	Aqueous	Uppal et al. (2019)
	Zirconium metal-organic frameworks (UiO-66 and UiO-66(NH_2))	Chemisorption	–	205.0 mg/g	Wastewater	He et al. (2019)
	Activated charcoal-coated zirconium-manganese nanocomposite	Chemisorption and physisorption	–	132.28 mg/g	Synthetic wastewater	Yin et al. (2019)
	Calcination of sodium alginate and polyvinyl alcohol	Chemisorption	–	–	Synthetic wastewater	Kang et al. (2019))
	One-step fabrication of alum sludge and graphitic carbon nitride (g-C_3N_4)	Outer sphere complexation and physisorption	–	–	Synthetic wastewater	Kim et al. (2020)
Electrocoagulation	Iron and aluminum	Oxidation	100%	–	Well water	López-Guzmán et al. (2019)
	Iron electrodes	Oxidation	–	–	Drinking water	Banerji and Chaudhari (2016)
	Aluminum electrodes	–	≥90%	–	Drinking water	Silva et al. (2018)
	Iron (Fe) plate bipolar electrodes	Oxidation	96%	–	Raw groundwater	Mohora et al. (2018)
	Fe(0)-based Electrochemical technology	Reactive Fe(III) precipitates to bind As	≥90%	–	Groundwater	Roy et al. (2020)

Technology	Type	Mechanism	Removal efficiency	Adsorption capacity	Medium	References
Ion exchange	Novel chelating ion exchange resins		63.5%	–	Saline geothermal water	Çermikli et al. (2020)
	Amine-doped acrylic ion-exchange fiber	Pseudo-first-order kinetics	83%	205.3 ± 3.6 mg/g	Synthetic water	Lee et al. (2017)
	Ion exchange/electrodialysis (IXED) process	As(V) ions in the solution are exchanged by OH_	–	–	Synthetic water	Ortega et al. (2017)
	Fe_3O_4/halloysite nanocomposite	chemical process	99.62%	427.72 mg/g	Synthetic water	Song et al. (2019)
	La(III)-montmorillonite hydrogel beads	Hydrogen-bond and electrostatic interactions	–	58.75 mg/g	Synthetic water	Yan et al. (2020)
Membrane filtration	Novel adsorptive nanocomposite membrane	Chemisorption and Physisorption	–	41.09 mg/g	Water system	Nasir et al. (2019)
	High-flux ultrafiltration membrane	–	–	–	Contaminated water	Bahmani et al. (2017)
	Composite membranes	Bayerite arsenic adsorption	60%	–	Synthetic water	Salazar et al. (2016)
	Ultrafiltration hollow fiber membranes	–	41%	–	Synthetic water	Kumar et al. (2019)
	Hydrophobic kaolin hollow fiber membrane	–	100%	–	Synthetic water	Hubadillah et al. (2019)

(continued)

Table 11.1 (continued)

Technology	Type	Mechanism	Removal efficiency	Adsorption capacity	Medium	References
Phytoremediation	*Pteris vittata*	Absorption	≥95%	–	Groundwater	Yang et al. (2017)
	Lemna valdiviana	Absorption	82%	1190 mg/kg	Synthetic water	de Souza et al. (2019)
	Vallisneria natans	Oxidation, methylation, absorption	73.24%	–	Synthetic water	Li et al. (2018)
	Echinodorus cordifolius, Arthrobacter creatinolyticus	–	96 ± 3%	–	Synthetic water	Prum et al. (2018)

removal was 100% and 85.68%, respectively. Electrocoagulation using iron electrodes (ECFe) was used for the removal of arsenic from drinking water. Iron electrodes caused the oxidation of arsenic which resulted in high arsenic removal. The presence of phosphate in drinking water had negative impact on arsenic oxidation and adsorption. The maximum removal of arsenic was achieved at low current and pH7 (Banerji and Chaudhari 2016). Silva et al. (2018) removed arsenic, fluoride, and iron from drinking water using the electrocoagulation process. There was positive effect on arsenic removal in the presence of iron. However, fluoride had a slight negative effect on arsenic removal. The arsenic removal was above 90% in the presence of iron. All three pollutants were completely removed within 1 h (Silva et al. 2018). Horizontal continuous flow EC reactor was used for arsenic removal from raw groundwater. The reactor used bipolar iron electrodes. The optimum current density, flow rate, and charge loading for the EC reactor were 1.98 A/m2, 12 L/h, and 54 C/L, respectively. The maximum arsenic removal was 96% (Mohora et al. 2018). Roy et al. (2020) recently developed integrated system consisting of arsenic oxidizing bacteria and iron electrocoagulation (bio-FeEC). The bio-FeEC effectively reduced arsenic from 150 to 10 μg/L. This integrated system produces less sludge and also consumes less energy than the conventional FeEC. The bio-FeEC emerged as a promising technology for arsenic removal (Roy et al. 2020).

11.12.3 Ion exchange

Ion-exchange technology is proved to be effective in treating water polluted with heavy metals. The major advantages of ion-exchange technology include high removal efficiency, fast kinetic rate, and high treatment capacity (Kang et al. 2004). Ion-exchange resin is capable of replacing the cations with the targeted heavy metals in the wastewater. Ion-exchange resins are either natural or synthetic. Most commonly synthetic resins are used due to their high efficiency and wide range (Alyüz and Veli 2009). The cationic exchange resins mostly used for heavy metals removal are either strongly acidic resins containing sulfonic acid groups or weak acid resins having carboxylic acid groups. These strongly acidic and weak acid resins have hydrogen ions which are exchanged with the metal ions. When the metal ion solution is passed through the ion-exchange column, the hydrogen ions on the resin are exchanged with the metal ions.

Recent ion-exchange technologies used for arsenic removal from water are summarized in Table 11.1. Çermikli et al. (2020) used novel chelating ion-exchange resins for the removal of arsenic and boron from geothermal wastewater. They used a hybrid method (adsorption-membrane filtration) for this treatment. The hybrid process was effective in boron removal; however arsenic removal was also good. The maximum arsenic and boron removal were 63.5% and 86%, respectively (Çermikli et al. 2020). The ion-exchange acrylic fiber was doped in amine for the removal of arsenic (V) from water. The novel fiber was efficient in arsenic removal. The maximum adsorption capacity for arsenic was 205.3 ± 3.6 mg/g. The maximum removal efficiency of arsenic was 83%. The fiber can be used as a low-cost and reusable ion-exchange medium (Lee et al. 2017). A hybrid anion exchange electrodialysis process was used for treating arsenic-polluted water. The OH- ions generated in the electrodialysis process were replaced with arsenic ions. The hybrid process efficiently removed arsenic at different concentrations ranging from 2.1 to 15 mg L^{-1} (Ortega et al. 2017). A novel cactus-like Fe_3O_4/HNTs magnetic nanocomposite was developed by Song et al. (2019) for the removal of arsenic (III and V) from wastewater. The maximum removal efficiency of cactus-like nanocomposite from arsenic III and V was 98.56% and 99.62%, respectively. The maximum adsorption capacity for arsenic III and V was 408.71 mg/g and 427.72 mg/g, respectively. The nanocomposite was highly reproducible (Song et al. 2019). In a recent study Yan et al. (2020) removed arsenic from water using montmorillonite hydrogel beads containing lanthanum. The addition of lanthanum increased the surface area of hydrogel beads. The major mechanism behind arsenic adsorption was ion exchange, complex chelation, and electrostatic forces. The maximum adsorption capacity of hydrogel beads was 58.75 mg/g (Yan et al. 2020).

11.12.4 Membrane Technology

Different types of porous and thin-film composite membranes are used for wastewater treatment. These membranes include those requiring low pressure, for example, microfiltration, ultrafiltration, and distillation. Membranes requiring high pressure, for example, nanofiltration and reverse osmosis. Membrane derived by osmotic pressure includes liquid membranes, forward osmosis, and electrodialysis. The major factors effecting the efficiency of different types of membranes in wastewater treatment and heavy metal removal include pore size and their distribution, flow rate, hydrophilicity, surface charge, and functional group presence (Abdullah et al. 2019).

Recent membrane technologies for arsenic removal are given in Table 11.1. A novel adsorptive nanocomposite membrane was used for arsenic removal from the water system. The novel membrane was highly effective in arsenic removal from water. The removal of arsenic was by both chemisorption and physisorption. The maximum adsorption capacity of the nanocomposite membrane for arsenic was 41.90 mg/g (Nasir et al. 2019). High-flux ultrafiltration membrane was used for the removal of arsenic from aqueous solution. The membrane shows high flux (172–520%) than the conventional ultrafiltration membrane. The efficiency of this membrane in rejecting arsenic was also higher (1.1–1.3 times) than the conventional ultrafiltration membrane (Bahmani et al. 2017). Salazar et al. (2016) prepared composite membrane by using solvent casting for arsenic removal from aqueous solution. The composite membrane was highly stable. The addition of bayerite particles into the composite membrane improved arsenic adsorption. The maximum arsenic rejection was 60% achieved within one hour (Salazar et al. 2016). Dry-wet phase inversion technique was used for the synthesis of cellulose acetate/polyphenylsulfone ultrafiltration membrane. The fabricated membrane was used for arsenic removal. The polyphenylsulfone ultrafiltration membrane was more effective in arsenic removal as compared to conventional hollow fiber membrane. The maximum removal percentage for arsenic was 41% (Kumar et al. 2019). Phase inversion/sintering technique was used for the preparation of low-cost hydrophobic kaolin hollow fiber membrane. The low-cost membrane was used for arsenic removal from synthetic wastewater. Fluoralkylsilane agent was used for the surface modification of modified membrane. The modified membrane showed excellent arsenic removal as the arsenic removal was 100% (Hubadillah et al. 2019).

11.12.5 Phytoremediation

Phytoremediation is the absorption of pollutants from water and soil by the roots of green plants (Sharma et al. 2015). Phytoremediation can be used for the removal of both organic and inorganic pollutants from water, soil, sediments, and sludge (Bauddh et al. 2015; Bhatia and Goyal 2014). Several plant species were successfully used for the removal of pollutants from water and soil (Sharma et al. 2015). The plant species used for phytoremediation should be native, have high growth rate, and should be adaptable to different environments, strong root system, and high pollutant accumulation (Valipour and Ahn 2016). The important factors which affect plant growth and phytoremediation are temperature, light, pH, and salinity. The availability of nutrients also affects plant growth and phytoremediation (Gupta et al. 2012).

Table I summarizes a few recent arsenic phytoremediation studies. Phytoremediation of arsenic from groundwater was done by using *Pteris vittata*. The effect of phosphate mineral on arsenic remediation was also studied. The presence of phosphate enhanced the arsenic removal potential of *P. vittata. Pteris vittata* has been able to reduce the concentration of arsenic from 200 μg L^{-1} to <10 μg L^{-1}. The maximum absorption of arsenic was ≥ 95% (Yang et al. 2017). de Souza et al. 2019 used *Lemna valdiviana* for arsenic phytoremediation from synthetic wastewater. The effect of pH, phosphorus, and nitrogen on the performance of *L. valdiviana* was also studied. Optimum conditions for arsenic adsorption were pH 6.3–7.0, phosphorus 0.0488 mmol L^{-1} (P-PO_4), and nitrogen 7.9 mmol L^{-1} (N-NO_3). The maximum arsenic accumulation was 1190 mg kg^{-1}. The maximum absorption of arsenic was 82%. *L. valdiviana* was proved to be a promising macrophyte for arsenic phytoremediation (de Souza et al. 2019). *Vallisneria natans* was used for arsenic removal from water. *V. natans* first oxidized arsenic III to arsenic V and then methylated to dimethylarsinate (DMA). Maximum arsenic accumulation was in roots ((≥95.65 ± 0.10%). The maximum arsenic removal by *V. natans* was 73.24%. *V. natans* showed great potential for phytoremediation of arsenic from contaminated water (Li et al. 2018). In a study, Prum et al. (2018) used a combination of *Echinodorus cordifolius* with *Bacillus subtilis* and *Arthrobacter creatinolyticus* for arsenic removal from water. The combination of *E. cordifolius* and *A. creatinolyticus* resulted in enhanced arsenic removal. The maximum arsenic removal was 96 ± 3% (Prum et al. 2018).

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Chapter 12
Mycotoxins in Environment and Its Health Implications

Sadia Alam, Sobia Nisa, and Sajeela Daud

Abstract Mycotoxins are secondary metabolites produced by toxigenic molds under suitable conditions such as high temperature, moisture, etc. Stored foods are more susceptible to fungal growth and subsequent mycotoxins contamination. Mycotoxins are mutagenic, carcinogenic, immune-suppressive, and make the host susceptible to infectious diseases. Several methods can be used for mycotoxin detection, but enzyme-linked immunosorbent assay (ELISA) is proved to be the cost-effective method. Management strategies are very important in reducing the mycotoxicosis risk. This threat can be reduced by mitigation measures such as chemical methods, antagonistic activities, biodegradation, irradiation, heat, etc. Aflatoxin is one of the most hazardous and widespread mycotoxins contaminating foodstuffs. It is produced by different strains of *Aspergillus* species in a variety of products, such as cereals, pulses, coffee, wine, grape juice, and dried fruits. Mycotoxins monitoring in food and feed stuff fruits has become an important issue worldwide because of both the impact on human health and the high economic losses that is associated with crop production. Mold growth of *A. flavus* and *A. parasiticus* is stimulated to produce aflatoxins in conditions of high temperature, high humidity level, pest invasion, drought, high water activity, and adverse weather conditions in field as well as in storage godowns. Food commodities susceptible to mycotoxins contamination include wheat, rice, barley, maize, milk, peanuts, almonds, figs, pistachios, dried apricots, mulberries, dates, walnuts, spices, meat, etc. These toxins may persist in cereals even after mold destruction. However, the amount of toxin is reduced by several processes up to 20% including thermal food processing. Exposure to these chemicals causes wide variety of human disorders such as birth defects, reproductive disorders, mental problems, kidney and liver

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dysfunction, and immune system suppression. Diet is one of the main routes of exposure to these toxic chemicals. Mycotoxin contaminates the food commodities which is the major public health threat. These toxins are usually transferred during the processing of contaminated ingredients or seeds. So they bind to the plasma proteins of human body and persist there.

12.1 Introduction

12.1.1 Turkey X Disease and Discovery of Mycotoxins

The term mycotoxicology refers to the toxic effects caused by fungal mycotoxins. Modern mycotoxicology started with the discovery of aflatoxins in the early 1960s when the peanut-based feed caused the Turkey X disease and more than 10,000 turkeys and chickens were found dead in England (Blount 1961). It was then named as Turkey X disease and is considered as a turning point for the use of the term mycotoxins. Early investigations on Turkey X disease revealed neurological symptoms followed by coma and finally death in chickens intoxicated by eating mycotoxin-contaminated meals (Wannop 1961). The original description of Turkey "X" disease by Blount (1961) was that the turkeys in England dying of intoxication exhibited both clinical and gross pathologic signs. Catarrhal and hemorrhagic enteritis was a major sign along with the characteristic position assumed by poults dying, as described by Blount (1961), that the neck of poult would be tilted and the head flown back (opisthotonus) and legs would be sprawled completely toward the back (Richards 2008).

As studies were carried out to identify the etiology of Turkey "X" disease in England, no significant organisms were isolated from Brazilian groundnut meal; instead, microscopic examination revealed the presence of some fungal elements. However, a similar outbreak like Turkey "X" disease was reported from Kenya shortly thereafter by eating Ugandan groundnut meal. Investigations on Ugandan groundnut resulted in isolation of *Aspergillus* species that later on identified as *Aspergillus flavus*. The causative agent of Turkey X disease was then determined as aflatoxin. There is an array of highly cogent carcinogens being produced by the most abundant fungi like *A. flavus* and *Aspergillus parasiticus*. Further studies revealed isolation and identification of major aflatoxins, B1, B2, G1, and G2, using thin-layer chromatography (Armbrecht et al. 1963).

Afterward, many new fungal contagions were identified and characterized. Mycotoxins are secondary metabolites of fungi. Many genera of fungi have the potential to produce mycotoxins like *Aspergillus*, *Penicillium*, and *Fusarium* spp. Mycotoxins contaminate about 25% of agricultural commodities globally. Mycotoxin contamination is a worldwide issue occurring in both tropical and temperate regions of the world. Mycotoxigenic fungi colonize cereals in the field and after harvest; thus, they harbor a mixture of many toxins. Crops when kept for storage are also prone to fungal attack and may be polluted with mycotoxins during storage. Major food crops being infected by fungi and then intoxicated by mycotoxins include cocoa, coffee, cereals, oil seeds, spices, nuts, dried fruit, dried peas, beans, and fruits. The production of mycotoxins also depends on environmental factors during plant growth and then on the storage conditions of food (Fiers et al. 2013; Ameye et al. 2015). Mycotoxins can exhibit acute and chronic toxicity, mutagenic, and teratogenic effects. Humans may encounter severe health hazards or high mortality rates in countries with poor management programs. Toxic effects of mycotoxins depends on the nature of mycotoxins and their mode of action ranging from deterioration of the liver or kidney function and interference with protein synthesis leading to extreme immunodeficiency. Some mycotoxins are neurotoxic, and higher doses can lead to brain damage and death.

12.2 Origin and Chemical Nature of Mycotoxins

Mycotoxins are fungal metabolic compounds produced secondarily, capable of causing disease and death in humans and other animals. During ancient times, many major epidemics have been observed in humans and animals due to mycotoxin intoxication. Alimentary toxic aleukia (ATA) and ergotism are examples of dreadful mycotoxicosis instances that resulted in the death of thousands of people in Europe and Russia.

Mycotoxicosis is the term used to describe the toxic effects caused by mycotoxins. The toxic effects of mycotoxins depend on the duration of the exposure, health, age, and sex of the exposed individual. On the other hand, many factors like alcohol abuse, vitamin deficiency, and dietary status can also effect the severity of mycotoxin poisoning. Mycotoxins are manufactured from some general metabolic compounds and through a channel of various pathways (Bennett and Bentley 1989). The chemical nature of mycotoxins varies from alkaloids, sesquiterpenes, polyketides, derivatives of phenylalanine, and macrocyclic acid lactones (Ibrahim and Menkovska 2019). A wide variety of mycotoxins are known today, but most concerns are those causing severe health risk to both human and animals. They also impact nutrition and food security due to lack of access to safety and healthy foods (Bryden 2012).

12.3 The Mycotoxins

Filamentous fungi are common in the environment and can produce thousands of toxic compounds. However, mycotoxins produced by fungi are important as they are toxic at low concentration.

Exposure to mycotoxins in diet can cause vomiting, abdominal cramps, pulmonary edema, convulsions, coma, and death. *Aspergillus*, *Penicillium*, *Fusarium*, and *Claviceps* are the common species that produce more important toxins. From

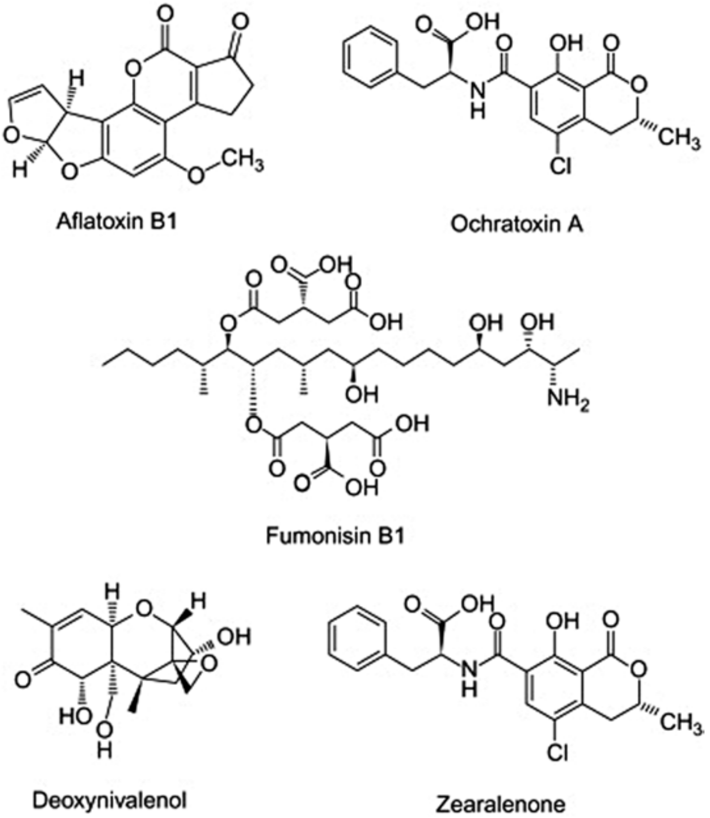

Fig. 12.1 Common types of mycotoxins (Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC164220/)

toxicity and clinical manifestations point of view, the mycotoxins of foremost significance are aflatoxins (AFs), ochratoxin A (OTA), deoxynivalenol (DON), nivalenol (NIV), fumonisin (FUM), ergot alkaloids, zearalenone, T-2 toxin, and patulin (CAST 2003). The chemical nature and toxic impacts of different mycotoxins are explained below in Fig. 12.1.

12.3.1 Aflatoxins and Types of Aflatoxins

Aflatoxins are widely spread in food and feed supply chains. They are toxic chemicals produced by different species of *Aspergillus*, especially from *A. flavus* and *A. parasiticus* (Cotty and Jaime-Garcia 2007). Fungi-producing aflatoxins have been found in corn, peanuts, peanut products, cotton seeds, peppers, rice, sunflower seeds, pumpkin seeds, and tree nuts. Contamination of aflatoxins is most common in countries with warm and humid climates like Africa, Asia, and South America and in temperate areas of Europe and North America. When agriculture crops contaminated with mycotoxins are used as green produce in foods and processing of animal feed, it results in contamination of final food products implicating severe health hazards to both humans and animals.

There are about fourteen chemical structures of aflatoxins being produced as secondary metabolites by *Aspergillus*, and the major groups of aflatoxins are aflatoxins B1, B2, G1, G2, M1, and M2. The B-type aflatoxins have distinct cyclopentane ring. These compounds have a blue fluorescence under long wavelength of UV. Aflatoxin B1 is the most toxic and potent carcinogen found to be correlated with hepatotoxicity and liver cancer. On the other hand, aflatoxin B1 has the ability to penetrate through the skin and cause health risk (Boonen et al. 2012). G-type aflatoxins have a xanthone ring instead of the cyclopentane. These compounds produce green fluorescence under UV. Other members of the aflatoxin family are originally isolated from bovine milk. These include M1 and M2 which are hydroxylation products of AFB1 and AFB2, respectively (Songsiriritthigul et al. 2010).

Poultry and farm animals fed on aflatoxin-contaminated feed produce contaminated meat, eggs, milk, and milk products. Human intake of these aflatoxin-contaminated products may result in liver damage and cancer. Children are more prone to develop toxicity to aflatoxin contamination, whereas adults are affected when doses exceed a certain amount (Gong et al. 2004). Aflatoxins have been found to be associated with changes in reproductive structures and hence the reproductive potential of human males (Kasturiratne et al. 2008). In food and animal feed, acceptable aflatoxin levels ranged from 20 to 300 ppm to prevent toxicity from a higher dose of aflatoxins (Stoloff et al. 1991). Permissible levels of mycotoxins in different food commodities as given by the FDA (Food and Drug Administration) are provided in Table 12.1.

Table 12.1 FDA regulatory guidance for mycotoxins in food and food commodities for human and animal use

Sr. no	Intended use	Food or food commodities	Permissible level of aflatoxins
1	Human consumption	Milk	0.5ppb
2	Human consumption	Foods, peanuts, peanut products, and nuts	20ppb
3	Immature animals	Animal feed, peanut products, and corn	20ppb
4	Dairy animals	Corn, animal feed and ingredients	20ppb
5	Breeding cattle and mature poultry	Corn and peanut products	100ppb
6	Beef, cattle, and poultry, regardless of the status of age or breeding	Corn and peanut products	300ppb

12.3.2 Ochratoxins

Ochratoxins are a group of compounds produced by a number of fungi like *Aspergillus* and *Penicillium* species, particularly *Aspergillus ochraceus* and *Penicillium cyclopium*. There are three types of ochratoxins, namely, A, B, and C. All types of ochratoxin have same basic structure, but R side chains may be variable. Ochratoxin A (OTA) is the most toxic and commonly detected as compared with other types of ochratoxins. *A. ochraceus*, *Aspergillus carbonarius*, and *Penicillium verrucosum* are major producers of ochratoxin A (Hassan and Mathesius 2012). These fungi are widespread in nature, as they can survive in a wide range of conditions (temperature, substrate, pH, and moisture). *A. ochraceus* is widespread in tropical regions, while *P. verrucosum* dominate temperate regions like Europe, Canada, and South America (Ruan et al. 1995). OTA are common contaminants of grains such as corn, oats, barley, rye, and wheat, whereas contamination of other plant products like coffee beans, nuts, spices, olives, beans, grapes, and figs has also been reported (Khan et al. 2003; Turra and Di Pietro 2015).

Investigations on the chemical structure of ochratoxin A revealed that it is a pentaketide derived by coupling of dihydrocoumarins family with β-phenylalanine. It has been found to be associated with contamination of water and house heating ducts, hence responsible for environmental and health hazards for human and animals (Hope and Hope 2012). Ochratoxin A can be absorbed by human and animal bodies on ingesting food and animal feed contaminated with ochratoxin A. After ingestion through food, it can be detected in host tissues, blood, organs, and breast milk of human and animals. It can cause renal tumors and nephrotoxicity (Bui-Klimke and Wu 2015).

Ochratoxin A is a stable molecule. It is fat soluble and cannot be readily excreted; hence, its uptake means its deposition in tissues of infected organisms which is directly proportional to the uptake of ochratoxin A. In animals, the main reason for ochratoxin A contamination is feeding on mold-contaminated fodder.

12.3.3 Fumonisins

Fumonisins (Fm) are toxic secondary metabolites produced by *Fusarium verticillioides*, *Fusarium proliferatum*, and some other Fusaria. Fungi producing fumonisins are found in grains, such as rice, sorghum, etc. *F. verticillioides* and *F. proliferatum* cause corn disease, namely, fusarium ear rot (Parsons and Munkvold 2012). More than 28 fumonisins have been isolated and are classified into four groups (A, B, C, and P). Fumonisin B1 (FB1) is the most abundant toxin contributing 70–80% to the total fumonisin group.

The chemical structure of fumonisin indicated their polyketide nature. Fumonisins consist of a 20-carbon aliphatic chain with two side chains which are linked to ester and hydrophilic in nature. Thus, they resemble sphingosine that is an essential phospholipid in cell membranes. Gelderblom and coworkers were the first persons to isolate fumonisin B1 and fumonisin B2 from cultures of *F. verticillioides* (Gelderblom et al. 1988). The discovery of fumonisins go back to late 1980s where it is linked with many years of study on the disease known as equine leucoencephalomalacia (ELEM). Equine leukoencephalomalacia (ELEM) is commonly known as "moldy corn poisoning." It is a disease of the central nervous system affecting horses, mules, and donkeys with symptoms of blindness staggering, drowsiness, and liquification of brain tissues (Wilson et al. 1990). Disease is linked with feeding animals on moldy corns for a duration of several days to weeks.

Mycotoxin fumonisins specially produced by two species of *Fusarium*, that is, *F. verticillioides* and *F. proliferatum*, can cause esophageal cancer in human. Incidence of high rates of human esophageal cancer associated with fumonisins has been reported from China, Southern Africa, and Italy (Li et al. 1980; Marasas 1996; Franceschi et al. 1990). In other experimental studies, fumonisins were found to be involved in the inhibition of cell growth and induction of apoptosis *in vitro* (Tolleson et al. 1996). As per the directions of Food and Drug Administration (FDA), the permissible limit of fumonisins in human food should not exceed 4ppm/kg, whereas in animal feed, the level of fumonisin should not be more than 5–100 ppm/kg depending upon different types of farm animals (FDA 2001). This level can be achieved by good farming practices and better control of fungal growth.

12.3.4 Trichothecenes (TCTCS)

The term TCTCs is derived from trichothecin, the first isolated compound in this group. Many species of *Fusarium* produce TCTCs when infects corn, wheat, barley, and rice. TCTCs are also produced by fungi such as *Myrothecium*, *Trichoderma*, *Trichothecium*, *Cephalosporium*, *Verticimonosporium*, *and Stachybotrys*. Toxicogenic *Stachybotrys chartarum* can proliferate in humid storage environment and thus can cause environmental health hazard for residents (Hardin et al. 2003).

The Trichothecene family has been classified into A, B, C, and D types. All of the types have common sesquiterpene nucleus with epoxide ring and side chains of hydroxyl, methyl, or acetyl. All the types of trichothecenes are very stable and survive during various processes like milling or cooking and during storage of finished products (Widestrand and Pettersson 2011). Types A and B of trichothecenes are of utmost concern for consideration as causing harmful effects to both humans and animals with type A being more hazardous than type B. Subclasses of type A trichothecenes are Don, 3-ADon, 15-ADon, Niv, T-2, HT-2, and 4, 15 Das. These subclasses have same trichothecene nucleus but are varied in side chains. On the basis of toxicity, of the type A subclasses, T-2 trichothecene is the most toxic and at a concentration of 1 mg/kg body weight can inhibit translation in eukaryotic cells, thus leading to lethality (Ueno 1984). Dermal exposure to subclass T-2 trichothecene can initiate skin burning pain, redness, and appearance of blisters. Oral ingestion of T-2 trichothecene can cause vomiting, diarrhea, nasal irritation, and cough.

Table 12.2 Toxic effects and permissible levels of most toxic groups of trichothecenes

Toxic groups of trichothecenes	Subgroups of most toxic trichothecenes	Toxicogenic fungi	Toxic effects	Permissible level
Trichothecenes Type A	T2 HT2	*Fusarium langsethiae*, *Fusarium poae*, *Fusarium sporotrichioides*, *Fusarium equiseti*, and *Fusarium acumninatum*	Growth retardation, myelotoxicity, hematotoxicity, necrotic lesions on contact sites	100 ng/kg b.w./day
Trichothecenes Type B	Nivalenol (NIV), DON 3-ADon 15-ADon Fusarenon-X	*Fusarium graminearum* and *Fusarium culmorum*	Vomiting, hemorrhagic diarrhea, anorexia, suppression of body weight gain, hepatotoxicity, dermatological problems, and altered nutritional efficacy	1µg/Kg b.w/day to 1 mg/kg b.w./day for various derivatives

It can also affect vision, leading to blurred vision (Adhikari et al. 2017). Due to its high toxicity, this toxin is also produced by fungal fermentation and can possibly be used as biological warfare agent (Venkataramana et al. 2014).

Trichothecene (type B) is further classified into deoxynivalenol (Don), nivalenol, Fusarenon-X, and trichothecin. All have the same basic structure but vary in their side chains. The most frequently found toxin from type B trichothecene is the deoxynivalenol, also known as vomitoxin, due to the its ability to induce vomiting episodes when ingested. *F. graminearum* and *F. culmorusis* are the main producers of deoxynivalenol. They are plant pathogens causing fusarium corn blight in corn and fusarium head blight in wheat (Kim et al. 2016). Mycotoxicoses caused by trichothecenes affect many organs including the gastrointestinal tract and hematopoietic, cardiovascular, immune, and hepatobiliary systems. Initially, they can inhibit protein synthesis by binding with eukaryotic ribosomes. On the other hand, they can induce toxicity by deregulation of calcium homeostasis, impairing membrane functions and thus altering intercellular interactions. Higher doses of trichothecenes can cause rapid leukocyte apoptosis, leading to immunosuppression (Ueno 1983). They are also associated with reduced growth rate due to feed refusal and lost reproductive potential (Table 12.2).

12.3.5 Zearalenone (ZE)

A variety of Fusarium species, for example, *F. graminearum*, *F. culmorum*, *F. cerealis*, *F. equiseti*, *F. crookwellense*, and *F. semitectum*can, produce zearalenone (ZE). These species of *Fusarium* are common inhabitants of soil and are also known as plant pathogens. High moisture contents and low temperature favor the growth of *Fusarium* species and hence production of zearalenone (Bennett and Klich 2003). ZE is resistant to high temperature treatment and can be detected in various cereal crops like maize, barley, rice, oats, and sorghum (Tanaka et al. 1988).

The chemical structure of Zearalenone is a macrocyclic β-resorcylic acid lactone, mimicking the reproductive hormone estrogen (Shier et al. 2001). This structural similarity to estrogen may cause early puberty in individuals. ZE binds with estrogen receptor and stimulates protein synthesis. Therefore, it is called phytoestrogen due to its hyperestrogenic effects and premature onset of puberty in female animals (Collins et al. 2006). ZE can also interact with immune system, resulting in immunosuppression (Berek et al. 2001). Zearalenone and its analogues can indicate clinical manifestations in both animals and human with major symptoms of enlarged uterus and mammary glands, swelling of vulva and vagina, and abortion in some cases. As zearalenone is heat stable and can withstand food processing like milling, grinding, heating, and cooking, its presence in food and food commodities should be controlled. As per FDA and WHO the maximum acceptable daily intake level of zearalenone to human and animal should be below 0.5 μg/kg body weight (Zinedine et al. 2007).

12.3.6 Patulin

Various species of *Penicillium*, *Aspergillus*, and *Byssochlamys* can produce a toxic metabolite named patulin (Ozsoy et al. 2008; Puel et al. 2010). *Penicillium expansum* is a famous patulin-producing species that is commonly present in rotten apple. It is also known as blue mold and attacks pear, cherry, grapes, and oranges. Chemically, patulin is a water-soluble lactone and is classified as polyketide. It was initially isolated in the 1940s as a broad-spectrum antifungal compound. It is known by different names like clavacin, expansin, clavatin, and gigantic acid as it was co-discovered by various groups who gave them different names (Goyal et al. 2017).

Patulin can cause DNA damage and is known as immunotoxic, genotoxic, carcinogenic, neurotoxic, and teratogenic. It can affect cells by formation of free radicals, leading to caspase-3 activation, leading to apoptosis (Saxena et al. 2009). Due to associated health risks, FDA regulated the patulin levels as 50 μg/kg in all squashes and 25 μg/kg for natural unprocessed apples, and it should not exceed 10 μg/kg in children's apple food products (EC 2006; Unusan 2019).

12.3.7 Ergot toxin

Outbreak of ergotism was noticed earlier in Middle Ages and France. Ergotism was then called St. Anthony's fire due to the burning sensation felt in limbs. It is caused by eating grains of rye or wheat contaminated with ergotamine, that is, a mycotoxin produced by fungus *Claviceps purpurea*. Ergotamine causes vasoconstriction. This mycotoxin is extremely toxic. In recent years, different studies reported its toxic effect on human including hallucinations, gangrene, and even loss of limbs in humans or hooves in cattle (Klotz 2015). These toxic effects are induced by antagonism of neurotransmitters, like dopamine, norepinephrine, and serotonin, resulting in long-term vasoconstriction, leading to reduction of blood flow and related side effects. Ergot alkaloids have a number of applications in medicine from promoting labor pain, reducing uterine hemorrhage to treating migraines and endocrine disorders like parkinsonism (De Groot et al. 1998; Burn 2000; Crosignani 2006).

12.3.8 Sterigmatocystin

Sterigmatocystin (STE) is synthesized by many genera of fungi including *Aspergillus*, *Chaetomium*, *Bipolaris*, *Emericellai*, *Podospora*, *Fusarium*, *Farrowia*, *Humicola*, *Moelleriella*, *Monocillium*, and *Eurotium* (Rank et al. 2011). It was first time isolated in 1954 from cultures of *Aspergillus versicolor* (Castillo-Ureuta et al., 2011). STE is an antecedent compound of aflatoxin B1 (AFB1), and there is similarity between chemical structures and properties of both STE and AFB1. STE also exhibits hepatotoxic and carcinogenic effects like AFB1. STE is known to cause several toxic effects by interacting with the cell cycle, leading to DNA damage and cell cycle arrest. It can also induce apoptosis and hence cell death (Cui et al. 2017).

12.3.9 Nitropropionic acid (NPA)

A. flavus, *A. oryzae*, and *A. wentii* produce nitropropionic acid, which causes fatal food poisoning in human, congestion of liver and lungs, convulsion, and apnea. NPA can cause poisoning of livestock when they are fed on plants contaminated with NPA (Johnson et al. 2000). Consumption of contaminated foodstuffs can also cause toxicity in human. Even low doses of NPA can lead to acute encephalopathy and dystonia (Liu et al. 1992).

12.4 Other Mycotoxins

Penicillium also produces many other less common mycotoxins such as cyclochlorotine, rugulosin (RS), and luteoskyrin (LS). These toxins mainly affect the liver. Some other toxins produced by *Penicillium* are penicillic acid (PA), citrinin (CT), xanthomegnin, citreoviridin, and cyclopiazonic acid (CPA). *Alternaria* species also produce various toxins including alternariol, alternariol monomethyl ether (AME), altertoxin I, tenuazonic acid, alternaric acid, dehydroaltenusin, altenusin, and alteriusol that contaminate common edible items such as vegetables, fruits, etc.

12.5 Detection of Mycotoxins

To minimize the exposure of human beings and livestock to mycotoxins, efforts should be directed to monitor and control the level of mycotoxins in foodstuff. Various countries have launched surveillance programs for the detection of mycotoxins to reduce their consumption risk.

Various techniques have been used for rapid detection of mycotoxins as a single method cannot serve the purpose due to differences in chemical nature, molecular mass, and functional groups of mycotoxins.

12.5.1 Traditional Techniques for Detection of Mycotoxins

Various chromatographic techniques are being used for detection and quantification of mycotoxins from cereals. Thin-layer chromatography (TLC), ultraviolet coupled with high-performance liquid chromatography, gas chromatography–mass spectrometry, and fluorescence are some of common techniques that are used for detection of mycotoxins. In addition, immunometric assays like ELISAs and membrane-based immunoassays are also commonly used to detect the presence of mycotoxins. TLC method is simple and cost-effective for detection of mycotoxins, but it has low sensitivity and accuracy. The limited length of TLC plate and the effect of temperature and humidity on separation of mycotoxins are some other limitations of TLC method; hence, modern methods involving quantification of mycotoxins are preferred. Liquid chromatography coupled with mass spectrum and fluorescence detectors are benchmark methods to detect mycotoxins (Cirlini et al. 2012). Due to ion suppression and matrix effects, LC-MS can give unsatisfactory results for the quantification of mycotoxins. In such cases, tandem mass spectrometry is preferred over fluorescence due to its ability to identify both nonfluorescent and fluorescent toxins.

Immunological assays, like ELISA, gained popularity for the detection of mycotoxins as they can directly be applied and no cleanup procedure is required. This method provides rapid and economical measurements, but at low concentration, it lacks precision. Other drawbacks in the method are time consumption, requirement of specialist plate reader, and inability to be used for field testing. Another immunochromatographic method is lateral flow strip assay. Antigen–antibody reactions are also used for quick analysis of mycotoxins with high specificity and sensitivity. This assay has been developed on commercial basis for the detection of many mycotoxins like DON and aflatoxins (Xu et al. 2010).

12.5.2 New Methods for Detection and Quantification of Mycotoxins

With the advancement in technology, various detection technologies have been developed for the detection and quantification of mycotoxins in recent years. Some of these techniques are ultrafast liquid chromatography connected with tandem mass spectrometry (UFLC-MS/MS), fluorescence polarization immunoassay, nanoparticle-based methods of detection, and implementation of chip-based method for detection of mycotoxins in foods. Other techniques such as biosensor and capillary electrophoresis are in progress. The presence of mycotoxicogenic fungi in food can also be detected by PCR. In short, a number of sensitive techniques are available for the detection of mycotoxins, but the selection of method should be based on objective of detection, sample size, nature of sample, and facilities available in laboratory (Singh and Mehta 2020).

12.5.3 Management of Mycotoxin Contamination

There are different ways which are developed for management of mycotoxin contamination in crops. These methods are given below.

12.5.4 Control of Mycotoxin Production

Preharvest control involves growing fungus-resistant crops, crop rotation with resistant varieties, control of insect pests using registered insecticides, and use of atoxigenic biocompetitives (such as control of aflatoxin contamination in crops by using native *A. flavus* strains which compete with toxin-producing strains) (Magan et al. 1984). Humidity and temperature have great influence on production of mycotoxins by toxicogenic fungi. Storage practices also play important role in the production of mycotoxins; hence, environmental factors like temperature, moisture level, and humidity of warehouses play important role in mycotoxin production.

12.5.5 Removal of Secreted Mycotoxins from Food

Secreted mycotoxins in food and feed can be eliminated by a variety of ways such as physical separation, filtration, and solvent extraction. Physical separation includes removing mold damaged seed and mold-damaged kernel by air blowing and density and floatation separation; that is, depending on the density of mycotoxins, they float and hence separated. Moreover, filtration involves using activated charcoal, clays, and filter pads on which mycotoxins are adsorbed and hence separated. Moreover, solvent extraction, drying, washing, milling, boiling, irradiation, microwave heating, and peeling are also used as methods to remove secreted mycotoxins (Shi et al. 2018; Sarrocco and Vannacci 2018).

12.5.6 Detoxification of Mycotoxins

Different physical, chemical and biological methods have been designed to inactivate mycotoxins in food crops and feed. Physical destruction includes processes like gamma irradiation (World Health Organization, Food irradiation 1988). Some chemicals are also suggested to inactivate mycotoxins from food. These chemicals include acids, bases, aldehydes, and oxidizing gases. Biological methods that are formulated to destroy mycotoxins include enzymatic digestion and fermentation. Various reports are available regarding the use of microorganisms like bacteria and yeast and to degrade mycotoxins in food (Ben Taheur et al. 2019; Xia et al. 2017; Wang et al. 2019). Detoxification by biological means is considered as efficient approach as fewer and nontoxic end products are obtained. In vitro studies involving the use of microbial strains for detoxification produced significant results.

12.5.7 Elimination of Mycotoxins by Food Processing

Mycotoxins are usually not destroyed by cooking, but some mycotoxins may be inactivated by other types of food processing. Processing techniques cannot completely destroy the mycotoxins but can reduce their concentration (Neme and Mohammed 2017). Softening can be used to reduce the level of mycotoxins in food commodities as fungi accumulate on the surface of the granules. Although mycotoxins are compounds stable at higher temperature, still their concentrations can be reduced by using frying and baking methods at above 100°C. Similarly, under certain conditions, fumonisin B1 is reduced by sugars such as fructose to lose its hepatocarcinogenicity.

12.5.8 Dietary Modifications

Metabolism, distribution, and adsorption of mycotoxin are greatly affected by dietary modifications. For example, carcinogenic effects of AFB1 are inhibited by ascorbic acid and green tea. Similarly, toxic effects of ochratoxin A and fumonisin B1 are inhibited by vitamin C and vitamin E (Atanda et al. 2013, Karlovsky et al. 2016). Mycotoxin binders can be used that inhibit the absorption of mycotoxins by binding to mycotoxins. They do not allow mycotoxins to enter into the bloodstream from the intestine. Commonly used adsorbent materials are activated carbon, complex nondigestible carbohydrates, aluminosilicates, and cholesterol. Although dietary modifications can reduce the risk of mycotoxins, further studies are required to ensure food safety.

12.6 Toxicology

Mycotoxins are known to cause several kinds of acute and chronic illnesses in humans and animals (Beardall and Miller 1994). Toxic effects of mycotoxin exposure in humans are associated with ingestion of contaminated food and water and inhalation of aerosols (Babič et al. 2017; Kumar et al. 2017; Viegas et al. 2017). Since a substantial number of agricultural products are contaminated throughout the world, food ingestion is found to be the main route of exposure, especially in humans, although inhalation of aerosolized particles is a conceivably important route of exposure principally in certain working areas, such as product processing plants, and spaces where there are chances of high airborne concentration (Hooper et al. 2009; Ferri et al. 2017).

Comparable to all infectious agents, mycotoxin exposure can result in a spectrum of medical disorders, affecting organ systems and superficial skin and inducing allergic reactions such as asthma, sinusitis, pneumonitis, and hypersensitivities (Bossou et al. 2017). Mycotoxin exposure can also result in conditions such as vomiting, abdominal cramps, edema, convulsions, and even death. Long-term toxic effects of mycotoxins can cause physiologic decompensation for an individual such as cancer and immune deficiency (CAST 2003; Lewis et al. 2005).

The mycotoxins of foremost importance are "AFs, ochratoxin A (OTA), deoxynivalenol (DON), fumonisins (FUM), nivalenol (NIV), ergot alkaloids, T-2 toxin, patulin and zearalenone" arranged in the order of severity of disease they cause (CAST 2003). Co-occurrence of mycotoxins has also been observed. These mycotoxins sometimes are exposed in combinations, for instance, AFs and FUMB1, and vomitoxin and zearalenone are found to co-occur in the same corn. When more than one mycotoxins are consumed in combination, response to such exposure can be classified into following categories: (i) additive, when the interactive effect can be measured by individual consideration of each mycotoxin; (ii) antagonist, if the effect is lower than the anticipated from each mycotoxin individually; or (iii) synergic, if the response of one toxin is augmented by the presence of second toxin; synergistic effects are more pronounced than additive and antagonist (Paterson and Lima 2010; Gil-Serna et al. 2014).

Potential toxicological effects of mycotoxins are acute, chronic, mutagenic, hemorrhagic, hepatotoxic, nephrotoxic, and neurotoxic effects on multiple systems, leading to death sometimes. These toxicological effects happen due to interference in the vital processes like protein synthesis and DNA replication causing necrosis, lung infection, and weakened immunity and can also result in mutagenic and teratogenic effects (Omotayo et al. 2019).

12.6.1 Hepatic Effects

The liver is known to be a biologically active organ in performing vital activities: metabolism, excretion, and detoxification (Surai 2005, Shaker et al. 2010). The liver is known to be the foremost target organ for mycotoxin toxicity and carcinogenicity, especially aflatoxins. Aflatoxins perform their mechanism of action by interrupting the immune function. Aflatoxins interfere with nucleic acids and protein synthesis, causing toxicity in targeted organs (Afsah-Hejri et al. 2013). When mycotoxins are absorbed in the digestive tract, they are transferred to the liver, thereby causing damage to the liver (Dalezios et al. 1973).

Hepatocellular carcinoma is considered to be the most commonly occurring disease and is the fourth leading cause of deaths worldwide (Eaton and Groopman 1994). It was estimated that there is a high correlation between the incidence of hepatocellular carcinoma and the presence of aflatoxin B1 (Henry et al. 2001). Notably, it is reported that aflatoxin consumption is responsible for 530% of liver cancer (Liu and Wu 2010). Incidence of carcinoma of liver cancer is estimated to be around 40 percent. Approximately 80% carcinoma cases are reported from developing countries with the highest outbreak in Africa, approximately 40% cases and 55 % from China (Liu and Wu 2010; Chhonker et al. 2018). In this regard, as the level of aflatoxin intake is increased, the incidence of liver cancer is logarithmically elevated (Henry et al. 2001). Several studies have suggested there is synergistic effect of aflatoxins and hepatitis B and C virus in the etiology of the liver cancer (Wu and Santella 2012; Palliyaguru and Wu 2013).

Furthermore, several studies have demonstrated that mycotoxin exposure causes changes in hepatic histopathology, including bile duct proliferation, periductal fibrosis, and cholestasis (Javed et al. 1993). The effects of mycotoxins (aflatoxins and ochratoxins) on hepatic histopathology have been studied in broilers by Bakeer et al. (2013). From that experiment, it was found that aflatoxin exposure amplified Kupffer cell activation, sinusoidal dilation, and periacinar hepatic necrosis and hepatocellular vacuolations. Additionally, Ortatatli et al. (2005) reported that if the concentration of aflatoxins in diet is around 100 ppb, they can cause hydropic degeneration and fatty vacuoles in hepatocytes. Also, Krishnamoorthy et al. (2007) demonstrated that exposure of T-2 toxin results in enlargement of the liver, hepatocyte necrosis, and hyperplasia of the bile duct.

Furthermore, ochratoxin A has been estimated to be teratogenic in experimental animals, where it interferes and inhibits hepatic mitochondrial transport systems and causes injury to the liver, and various studies suggest that OTA is excreted in milk of affected animals (Chhonker et al. 2018).

12.6.2 Neurotoxic Effect

Likewise, other organs mycotoxins induce etiology in neuronal tissue, but there are only few surveys reported for such toxicity. Among several mycotoxins, T-2 toxin, macrocyclic trichothecene, fumonisin B1 (FB1), and ochratoxin A (OTA) are considered to have the ability for causing neurotoxicity (Uetsuka 2011). During neurotoxicity, immune responses damage neurons, and the overall CNS damage is amplified by astrocytes and endothelial cells (Karunasena et al. 2010). Low concentration of T-2 toxin can cause alterations in the metabolism of brain biogenic monoamines in experimental model, and intake of T-2 toxin results in altered permeability for amino acids. T-2 toxin if reaches the fetal brain causes fetal death and fetotoxicity primarily in the CNS. Study suggests that T-2 toxin-induced effects may be the outcome of oxidative stress (Uetsuka 2011).

Ergot exposure can induce convulsions and hallucinations. Neurologic effects can be induced by volatile organic chemicals (VOCs). Kodua poisoning is caused by cyclopiazonic acid and 3-nitropropionic acid produced by *Arthrinium* species and *Penicillium* and *Aspergillus* species, respectively. Symptoms include dystonia, convulsion, and carpopedal spasm.

Mycotoxins produced by *Penicillium* and *Aspergillus* species are “tremorgenic” and known to cause tremors, ataxia, and convulsions (Fung and Clark 2004). FB1 has the potential to cause cerebral cortex neuronal degenerations, concurrent with inhibition of ceramide synthesis. OTA induces acute deficiency of striatal dopamine and its metabolites, followed by substantia nigra, striatum, and hippocampus neuronal cell apoptosis (Uetsuka 2011).

12.6.3 Renal Toxicity

Long-term exposure to mycotoxins causes nephropathies and urinary tract tumors (Jahanian 2016). AFB1 is considered to be nephrotoxic because toxin targeting kidney induces various effects (Madhavan and Rao 1967; Akao et al. 1971), and in kidney, these mycotoxins reduced the rate of glomerular filtration, tubular reabsorption, and the tubular transport. But it increases the rate of excretion of Na and K and gamma-glutamyltransferase (Grosman et al. 1983). Renal cortex of albino rats demonstrated that AFB1 induces degeneration and necrotic changes and enlargement of glomeruli (Grosman et al.1983).

Various renal cell lines were used to demonstrate renal toxicity. The renal toxicity study established that cell multiplication was decreased in renal cell lines. Fetal kidney cells were reported to be more sensitive to the cytotoxic effect (Yoneyama et al. 1987). AFB1 and AFM1 toxicities were assessed on HEK293 cells and CD-1 mice. The two mycotoxins, individually or in combination, caused the formation of ROS, leading to kidney damage with a considerable decrease in L-proline and proline dehydrogenase (Li et al. 2018).

Occurrence of ochratoxin A in the serum in high levels indicates chronic nephropathy (Abid et al. 2003). Ochratoxin A binds to low molecular weight macromolecule in serum inducing nephrotoxic effects when accumulated in the kidney (Stojković et al. 1984; Ali and Abdu 2011), demonstrating ochratoxin A effects on rats' kidney. They reported that ochratoxin A treatment decreased kidney weight and increased the levels of serum urea and creatinine. Furthermore, animal study showed that ochratoxin A treatment induced proximal tubular atrophy and cortical interstitial fibrosis (Bayman and Baker 2006).

12.6.4 Effect on Gastrointestinal Tract

GI tract is the first physiological barrier against contaminated food products and the first target for mycotoxins too. When intestinal mucosa is contracted by such contaminants and toxins, they exert their deleterious effects on gastrointestinal tract (Pinton and Oswald 2014; Akbari et al. 2017). Ingestion of mold-contaminated food items and beverages and potential mycotoxins exposure produce symptoms such as nausea, vomiting, abdominal pain, and diarrhea. The mechanism of toxicity is associated with direct toxic effects on gastrointestinal mucosal surfaces. Mushroom toxicity causes similar toxic effects on GIT (Fung and Clark 2004). Mycotoxins, primarily aflatoxins, ochratoxin, and deoxynivalenol (DON), have been demonstrated to alter intestinal permeability in different species (Moldal et al. 2018).

The health and performance of an individual are correlated with intestinal microbiota. Intestinal microflora competitively inhibits colonization of the intestinal epithelium by foreign pathogens modulating the gut-associated lymphoid tissue (GALT). Recent study revealed that ochratoxin A (OTA) occurrence in the colon significantly decreased concentrations of acetic, butyric, and total short-chain fatty acid (SCFA), indicating that OTA can alter composition and metabolism of the colonic microflora (Broom 2015).

There is a correlation between the intestine and ingested mycotoxins and their deleterious effects in an individual. Mycotoxins exert negative effect on intestinal health, for instance, declined intestinal cell viability and decreased concentrations of short-chain fatty acid (SCFA). Beneficial bacteria are eliminated, and increased expression of genes is increased related to inflammatory response and counteracting oxidative stress. These negative effects will lead to recurrent intestinal infections and impaired digestion process and absorption of nutrients (Liew and Mohd-Redzwan 2018).

12.6.5 Mutagenic Effects

Mycotoxins are considered to be mutagenic, carcinogenic, and teratogenic because they interact with nucleic acid (DNA) and other macromolecules (Paterson 2008). Mutagenic effects exerted by mycotoxins can be direct or indirect; these can either change bases (direct) or inhibit enzymes (indirect) involved in stabilization of nucleic acids (Paterson 2008; Paterson and Lima 2009). Carcinogenic mycotoxins include AFs, sterigmatocystin, OTA, FUMs, zearalenone, citrinin, luteoskyrin, patulin, and penicillic acid. All of these function by damaging DNA except for FUMs, which interferes in signal transduction pathways (Gacem et al. 2020).

High levels of ROS resulted in neuronal stress, when neuronal cell line (Neuro2a) was exposed with OTA. Furthermore, other events also lead to mutagenic effects: mitochondrial membrane lost, DNA damage, and higher gene expression of neuronal biomarker inducing apoptotic cell death. In SH-SY5Y neuronal cells, OTA increased dose-dependent cytotoxicity levels with concurrent caspase-9 and caspase-3 activation in rat embryonic midbrain cells (So et al. 2014).

Co-occurrence of T-2 toxins and aflatoxin B1 makes them the strongest mutagens. Sehata et al studied the alterations in gene expression induced by T-2 toxin in the fetal brain of pregnant rats. T-2 toxin treatment upregulated gene expression for oxidative stress (heat shock protein) and apoptosis (caspase-2). In another study, it was reported that deoxynivalenol treatment (2501000 ng/mL) could cause an increase in interleukin-8 mRNA. It was indicated that the ochratoxin A treatment increased gene expression for apoptosis, inflammation, and oxidative stress in rat kidney (Jahanian 2016).

12.6.6 Other Effects

Since ZEA are present in the air, they are thought to cause pulmonary and cardiovascular toxicity. In one study, human bronchial epithelial cells (BEAS-2B) were treated with 40 mM ZEA; as a consequence, mycotoxin caused DNA damage, cell cycle arrest, and downregulation of inflammation (Ben Salem et al. 2017). Outcome of ZEA interaction with H9c2 cardiac cells caused oxidative stress (Sharma 1993).

The immune system is known to be an important defensive system against foreign pathogens and invaders (Pestka 2008). Specialized immune cells interact with each other to give off desired consequence (Turner et al. 2003). Mycotoxins either exert suppressive or stimulatory effect on immune system (Girish and Smith 2008). Previous study has reported that aflatoxin exposure induces immunosuppression, indicating that the susceptibility to infections is increased with AF intake. Girish and Smith (2008) found that immunosuppression is induced by several mechanisms, as depicted by the decreased antibody production, the delayed hypersensitivity response, the decreased bacterial clearance from systemic route, the declined lymphocyte proliferation, the suppression of macrophage phagocyte ability, and the changed CD4+/CD8+ ratio.

Aflatoxin B1 exerts their action on biomolecules such as DNA, changing their actions (Bhat et al. 2010). Mycotoxins always lead to inhibition of protein synthesis; consequently, they impair immune cell proliferation. But mycotoxins are also known to adversely affect the surface receptors of macrophages, neutrophils, and lymphocytes; consequently, miscommunication between defense cells led to immunosuppression.

It has been also demonstrated that mycotoxins also cause suppression of humoral immunity. In this concern, ochratoxin A is known to suppress natural killer cell activity by inhibiting interferon production (So et al. 2014).

12.7 Mycotoxin Management and Degradation

Several factors influence mycotoxin production from respective fungal species such as temperature, moisture, existing nutrients, humidity, and some others (FAO 2002). Fungal growth and mycotoxin production can be prevented by employing good agricultural and manufacturing practices. Developing countries suffer more from mycotoxin presence in agricultural products, whereas developed countries have opted for modern technologies and good control (FAO 2002). The Hazard Analysis and Critical Control Point (HACCP) system also has significant role in mycotoxin prevention and management (Kabak et al. 2006; Stove 2013), though several strategies like good agricultural and manufacturing practices can prevent the mycotoxigenic fungal and mycotoxin development. However, once food has been contaminated with mycotoxins, postharvest detoxifying strategies are needed to manage contaminants in feed and food.

However, it is not possible to always avoid mycotoxin contamination during preharvest, postharvest, and storage, requiring detoxification of feed and food. Therefore, several detoxification processes are employed for prevention of mycotoxin exposure and the effects produced by them. Detoxification of mycotoxins in such cases can be accomplished by either removing or eliminating the contaminated products or inactivating the mycotoxins present in food or feed by physical, chemical, or biological methods (Beretta et al. 2000).

12.7.1 Physical Methods

Several physical strategies are employed for elimination and inactivation of mycotoxins in food commodities.

Sorting and Segregation Mycotoxins can be removed from food commodities by means of sorting and removal. It has been found that patulin levels are reduced up to 99% by sorting and segregation of rotten and poor-quality fruits or trimming of decayed sections of fruits (Scudamore and Banks 2004; Broggli et al. 2002). Fumonisin and aflatoxin contamination in corn can be reduced by sorting and segregation (Peraica et al. 2002).

Heat Treatment Many mycotoxins are heat stable so they are not easily destroyed within normal temperature (80–121 °C) range of food processing; boiling, frying, and pasteurization. Factors such as moisture content, ionic strength, and pH of food are known to affect the sensitivity of mycotoxins. Aflatoxins are degraded within temperatures range 237–306 °C. Aflatoxins can be decomposed when food commodities contain higher moisture content (Beretta et al. 2000).

Irradiation Radiation has been proven useful in control of aflatoxins, T-2 toxin, or deoxynivalenol in grains and was also found effective on OTA decontamination in poultry feed which can be achieved by UV radiation for one hour (Gul Ameer et al. 2016; Avantaggiato et al. 2004).

Filtering and Adsorption Mycotoxin adsorption decreases aflatoxin, patulin, ZEA, DON, and nivalenol residues by activated charcoal addition due to its porous nature (Liu et al. 2011; Magnoli et al. 2011). Mycotoxin adsorption by bentonite clay effectively eliminates aflatoxin B1 from aqueous environments, and it has been found that bentonite clay helped in removing aflatoxin M1 from milk (Venter 2014).

12.7.2 Chemical Methods

Several chemical agents have been proven to successfully decontaminate and inactivate mycotoxins and have been investigated for their effectiveness in mycotoxin decontamination, namely, bases, oxidizing agents, organic acids, and other agents.

Bases (Ammonia, Hydrated Oxide) Ammonization of grains helps mycotoxin control, preventing fungal growth and reducing aflatoxins, fumonisins, and OTA levels. However, this detoxification method is not acceptable for human food in the European Community (EC) (Peraica et al. 2002). Recently, a mixture of glycerol and calcium hydroxide was shown to have a powerful detoxification effect for mycotoxins. A mixture of 2% sodium bicarbonate solution and potassium carbonate reduces OTA contamination in coco shells (Federal Register 2003).

Oxidizing Agents (Hydrogen Peroxide, Ozone) Ozone has been approved for effective decontamination of mycotoxins (Agriopoulou et al. 2016). Ozone degraded patulin, aflatoxins, and zearalenone. The decontamination of aflatoxins AFB1, AFB2, AFG1, and AFG2 was achieved with ozone (Quintela et al. 2012).

Organic Acids Several organic acids successfully degraded ochratoxin OTA. Egg albumin efficiently reduced OTA levels without affecting total polyphenols (San'Ana et al. 2008).

12.7.3 Biological Methods

Various physical and chemical detoxification methods have been developed to control mycotoxin contamination and fungal growth. However, not all of them are not permitted due to their biosafety concerns and high cost.

There is a need to devise appropriate biological detoxification strategies for ensuring food safety (Walter et al. 2015; Petchkongkaew et al. 2008). Numerous bacteria, molds, and yeasts can biodegrade mycotoxins in food for human consumption.

Bacterial Strains Several scientists reported that *Bacillus* and *Brevibacterium* species in their interaction with mycotoxins can detoxify them. *Bacillus licheniformis* isolated from soybean removed OTA efficiently, with efficiency of 92% with 48 h treatment at 37 °C (Cho et al. 2010).

Bacillus natto and *Bacillus subtilis* were shown to remove zearalenone from liquid medium: up to 75% zearalenone could be degraded after incubation. In another study, was degraded by this *B. subtilis* strain interaction biodegraded up to 99% of zearalenone (Moss and Long 2002; Tinyiro et al. 2011). Recent studies have indicated probiotic potential of different Lactobacilli to degrade fungal toxins (Zada et al. 2021).

Yeast Strains Yeasts can efficiently inhibit mycotoxigenic fungal growth and to prevent mycotoxin synthesis. *Saccharomyces cerevisiae* decreased patulin contamination during fermentation of juices: patulin could be removed completely after 2 weeks' yeast fermentation (Gromadzka et al. 2009).

Molds In addition to bacteria and yeasts, molds can also biocontrol mycotoxins; molds such as *Aspergillus*, *Rhizopus*, and *Penicillium* spp. can also effectively detoxify mycotoxins. *Clonostachys rosea* effectively detoxify mycotoxins in cereals (De Felice et al. 2008). OTA accumulation and aspergillosis occurrence are inhibited by *Aureobasidium pullulans* and therefore used as a biocontrol agent in fruits or in wine grapes (De Felice et al. 2008).

12.8 Climate Change and Increased Mycotoxin Production

Climate change is an inevitable probability as assessed by prominent researchers. Conducive temperature and water activity are pivotal for fungal growth and production of noxious fungal metabolites. Climate change is depicted by three major factors: (i) temperature rise, (ii) increase in CO_2 concentration, and (iii) drought stress (Medina et al. 2016). The rise in global temperature will raise mycotoxin ratio in temperate regions, and food security in these countries may become prone to increased aflatoxin production. Preharvest fungal infection of crops may prevail, and the outcome may be increased mycotoxin production in the field. There may be increased incidence of ochratoxin A, patulin, and *Fusarium* toxins. The European Food Safety Authority has reported that earlier ripening of crops in central and southern Europe will enhance pests and occurrence of diseases. Conventional fungal species may diminish in tropical regions; hence, mycotoxin production may decrease (Paterson and Lima 2010).

It has been suggested that climate change may induce a 1/3 of yield variability in major food commodities globally (Ray et al. 2015). It has been noted that Serbian maize was devoid of any aflatoxins during 2009–2011, but 69% maize was affected by aflatoxins in 2012 when temperature was increased (Kos et al. 2013). Dobolyi et al. (2013) have also observed similar findings in Hungary.

The estimates indicate increased atmospheric CO_2 concentration in the coming 25 years up to 350–400 versus 650–1200 ppm (Medina et al. 2016). CO_2 increase with elevated temperature and water stress condition will modify the growth of toxigenic fungi and pattern of mycotoxin production.

Studies are lacking in revealing the acclimatization ability of fungal species to climate change. The optimum temperature required for growth of toxigenic fungus differs from the temperature at which toxin is produced. The raised temperature may induce production of different toxin as indicated in a study when *Alternaria alternata* capable of producing alternariol (AOH), alternariol monomethyl ether (AME), and altenuene (AE) produced AOH at 21°C at 0.95aw but at higher temperature produced increased concentration of AME (Vaquera et al. 2017). Three-factor interaction was investigated by Medina et al. (2016) under elevated temperature, drought stress at 37 °C, and increased CO_2 concentrations (650 and 1000 ppm). Molecular studies related to aflatoxin gene expression also concluded same findings.

12.9 Future Prospects

The presence of these noxious contagions in food, feed, and the environment is of great concern due to their association with a multitude of detrimental health effects. The human population is more exposed to other contaminants including pesticides, heavy metals, and other pollutants. Recent studies have revealed their presence in human blood and urine (Arce-López et al. 2020). Humans are often concurrently exposed to heterogeneous mixtures of mycotoxins provoking a public health perspective. Actual exposure to mycotoxins based on food consumption is quite difficult to assess, and detection of mycotoxins bound to organic molecules has also become problematic. Climate change perspective urges for great concern on mycotoxin increase in environment and food commodities, ultimately affecting human health. These factors compel for managing the risk associated with mycotoxins and taking preventing measures to control the growth of mycotoxigenic fungi. Some novel approaches are need of time to combat the risk of increased mycotoxins in the environment to assure food safety.

12.10 Conclusion

Mycotoxin contamination is a worldwide problem as they are the most toxic and dangerous toxins linked with food safety. They have diverse chemical structures having various effects on human and animal health. They adversely affect the quality of agricultural products and are responsible for significant economic losses. Efforts should be made to control mycotoxin production at preharvest stage and detoxify them to minimize their exposure. Effects of climate change on mycotoxin production should also be studied in current scenario of elevated temperature, increased CO_2 concentration, and the expected drought in tropical region. There is a need to constantly monitor the quantity of mycotoxins in food commodities to cope with the demand for healthier foods.

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Chapter 13
Antibiotics: Multipronged Threat to Our Environment

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Abstract The use of antibiotics in different fields of human societies is increasing since the discovery of penicillin, the first antibiotic discovered in 1928. Initially, they were used to treat human ailments; later, they found their way in industry, horticulture, animal husbandry, honey production, fish farming and aquaculture, ethanol production, antifouling paints, disinfectants, and food industry. This unprecedented use of naturally occurring and synthetic antibiotics led to the development of broad-spectrum resistance in the bacterial communities against the commonly used antibiotics. As the exposure of antibiotics to our environment is increasing, so is the development of antibiotic-resistant bacterial communities not only in the medical settings and industry but also in our environment. There is a concern that increased presence of antibiotics in the environment can contribute to the recruitment of resistance factors from the environmental resistome to human pathogens which may further complicate the issue of resistant pathogens. In this chapter, we will discuss about different routes and sources responsible for the antibiotic pollutants and their environmental consequences and evaluate different management strategies for their control to reduce the risk associated with the presence of antibiotics in our environment.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_13

13.1 Introduction

Antibiotics are undoubtedly one of the most effective drugs being utilized for human and animal therapy. They are not only used for preventing and treating different infectious diseases in humans and animals but also for agricultural and farming purposes. There is an increasing concern over the past years about the effects of irrational use of antibiotics and their disposal on both human and environment health. Environmental media which include air, soil, and water act both as a transmission medium and reservoir for antibiotic-resistant bacteria. The worrisome aspects regarding the ever-increasing use of antibiotics in the environment are that the drug-resistant bacteria may proliferate and make their way to the food chain and that they may wipe out trophic levels entirely in some of the ecosystems. These fears are being realized globally now, and since the awareness of the impacts of antibiotic pollution in the environment, the scientific community has recognized the importance of devising strategies to regulate this phenomenon. The coming sections explain about our current knowledge of the presence of antibiotics in the environment and its widespread consequences and also highlight the measures to protect human and environmental health.

13.2 Routes of Antibiotics Contamination to the Environment

Antibiotics enter the environment through different routes (Fig. 13.1). Antibiotics are usually partially metabolized in humans and animals after their administration (Kümmerer et al. 2009b) and are excreted through urine, stool, and sweat and enter into the sewerage system. Sewage treatment plants, hospital waste, inappropriate disposal of unused and expired drugs, animal husbandry, and aquaculture are the major sources that contribute to the environmental load of antibiotics (Harris et al. 2012). The active substances in these antibiotics end up in various environmental compartments such as water and soil since most of them are water soluble and are therefore not likely to be degraded (Jianan Li et al. 2015). Antibiotics used in human medicines enter sewers from households and healthcare facilities. From there, they enter wastewater treatment plant without any pre-treatment, and via treated wastewater they finally enter drinking water. When sewage sludge gets applied to soil from the wastewater treatment plants, active substances from antibiotics make their way to fields. Antibiotics may enter groundwater through soil or from streams, lakes, and rivers. Antibiotics may enter the environment directly via wastewater that is discharged from the facility where antibiotics are formulated or indirectly through the wastewater treatment plant (Küster and Adler 2018). The routes of antibiotics' entry into the environment are linked with the excretion of manure from livestock where a major portion of antibiotics is discharged into the environment in an active form. The overuse of antibiotics as feed additives in aquaculture has aggravated the

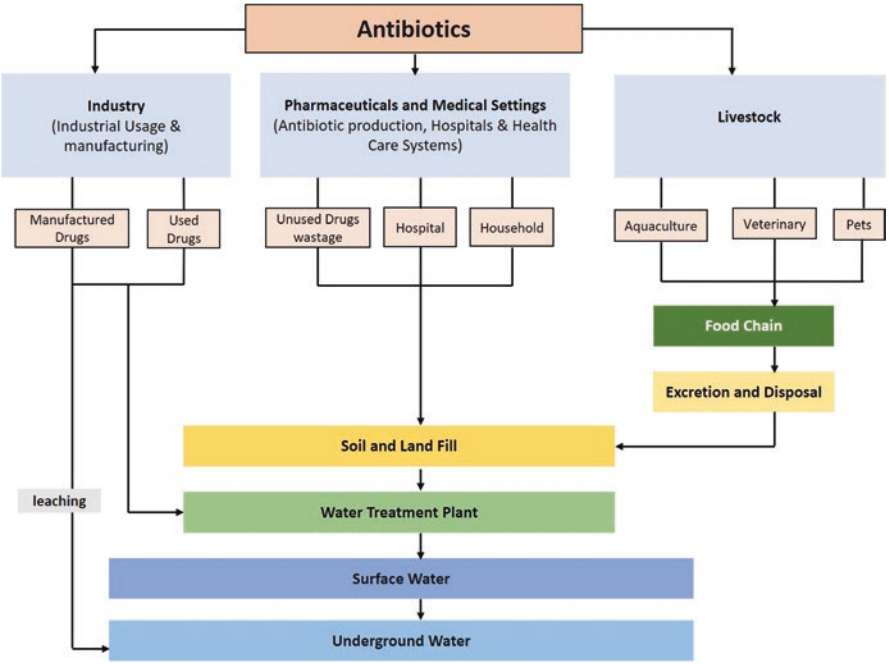

Fig. 13.1 Routes of antibiotic entry into the environment

problem of antibiotics contamination in the environment. Antibiotics get orally administered to the patients where they get partially metabolized along with their misuse in the hospitals due to which huge amounts of antibiotics are released in the hospital waste. Moreover, the detection of high concentrations of antibiotics in effluents from antibiotics manufacturing facilities has contributed to environmental contamination. The wastewater treatment plants represent a major source where sludge as well as treated wastewater are prominent pathways. Mutual interactions take place between all the entry routes that generate novel threats of spread of ARGs and ARB to humans as well as animals.

13.2.1 Antibiotics from Poultry, Veterinary, and Aquaculture

It has been speculated that in Europe, nearly two-thirds of all the antibiotics present are used in human medicine whereas one-third is employed for veterinary purposes. Recent reports estimate that in the United States, livestock producers use antibiotics nearly 11,200 tons for objectives other than therapy to promote growth of livestock and poultry (Whitacre 2015). The administration of antimicrobials in livestock depends on the reason of usage. Antibiotics are orally administered via drinking water or feed, whereas they are administered through injections for therapy (Pareek et al. 2015). Antibiotics are used in the livestock to treat diseases, prophylactically at subtherapeutic doses to alleviate infection by bacteria and to promote growth (Chee-sanford et al. 2009). Antimicrobials are routinely added to drinking water as well as animal feed as growth promoters and are an important part of swine production since the 1950s (Cromwell LG 2001). Some antibiotics get sprayed on crops; all the spray does not remain on the plant, but rather major portion is washed into soil and thereby reaches groundwater (Pareek et al. 2015).

Coccidiostat are found in broiler rations that are broad-spectrum antimicrobials like ionophores as well as sulfonamides. Antimicrobials such as chlortetracycline, bambermycin, bacitracin, penicillin, and virginiamycin get incorporated in the food of turkeys as well as broilers for increase in growth. Bacitracin is an antimicrobial drug which is not only used for promoting growth but also to control necrotic enteritis, which is an intestinal infection caused by *Clostridium perfringens*. Virginiamycin is another such drug used for the same purpose. The old drugs like tetracyclines are now unsuccessful due to the rapid increase in antibiotic resistance. Because of this, modern antibiotics such as fluoroquinolones are used for curing *Escherichia coli* diseases that are frequently prevalent in poultry (Wiedner and Hunter 2013). For controlling the mortality rate of the poultry, fluoroquinolones are the only effective drugs for the cure of some infections, specifically the *E. coli*.

The application of antibiotics in animals causes their release into the environment since majority of these antibiotics are designed in a way that they get quickly excreted from the treated animals (Burkholder et al. 2007). In 2006, the production of agricultural waste in the United States exceeded 200 million tons (Graves et al. 2011). Antimicrobials can be excreted as urine or feces in both unchanged form of the drug and parent form like drug metabolites, prodrug, and active compound (Bártíková et al. 2016). Furthermore, antibiotic metabolites may be modified back to the biologically active form even when they were excreted in an altered and inactive form. For instance, *N*-4-acetylated sulfamethazine, which is in fact a sulfamethazine metabolite, gets easily converted to its active form in liquid manure (Sarmah et al. 2006). Many different antibiotics have the ability to persist in the environment, and their presence may be easily detected not only downstream of the wastewater treatment plants but also in the adjacent fields receiving animal wastes. Moreover, in spite of the antibiotic remains, even a huge number of antibiotic resistant bacteria colonizing the gut of animals treated with antibiotics may be discharged into the environment. Commensals being the important carriers of antibiotic-resistant genes can act as a reservoir of such genes that flows across the entire microbial ecosystem. These microbes particularly bacteria harbor ARG and mobile genetic elements in agricultural effluents that promote it while exchanging among bacteria (Finley et al. 2013).

The role of veterinary antibiotics for the risk in the environment needs to be addressed. The burial of dead animals on the farm highly contaminates groundwater by nitrogen species as well as dissolved organic matter. The extent of the risk it poses to human and environmental health depends upon the quantity of dead animals buried as well as the site's hydrogeological conditions (Feeds et al. 1980).

Effluents from veterinary clinics also contribute to antibiotic pollution. Hotspots for occurrence of ARB include livestock keeping and farms. From here, ARB gets introduced to the environment through wastewater or via spread of sewage sludge or fermentation residues. Aquaculture is another pathway where antibiotics are overused. When medicated foods are used by fisheries, antibiotics are released directly into the surface water (Whitacre 2015). Antibiotics may enter the environment by animal farming when manure is used as a fertilizer.

It is known that antibiotics get poorly metabolized in animals' guts. Consequently, large amounts of active substances are excreted. Mainly excrements get stored as slurry (mixture of urine and feces), and small amounts mixed with straw get stored as manure. Antibiotics are indirectly incorporated when manure or slurry is used as a fertilizer. Through runoff and leaching, the antibiotics get introduced to the soil from slurry/manure storage. Antibiotic degradation takes place in the soil due to which groundwater and surface water might contain antibiotic residues. This entry of antibiotic residues in the soil affects soil microbiota (Van De Vijver et al. 2016). Plants take up some of these compounds; thus humans and animals that consume these plants get affected.

Development of the antibiotic-resistant bacteria is associated with indiscriminate use of antibiotics. Livestock can carry antibiotic-resistant bacteria as a result of antibiotics being directly administered and development of antibiotic resistance after administration as well. Other ways of developing antibiotic resistance include intake of the contaminated feed and breathing of the air containing resistant bacteria. The natural reservoirs present in the environment can be a source of further spread of antibiotic resistance.

13.2.2 Administration of Antibiotics in Humans for Cure

Antibiotics get administered in humans for treatment of several bacterial infections. About 40–90% of the administered antibiotics get actively excreted as parent compound in the urine and feces, ultimately reaching the environment, contaminating soils and water (Polianciuc et al. 2020). The major classes of antibiotics used for the treatment of bacterial infections worldwide are quinolones. These antimicrobials are significant for treatment against both gram-positive and gram-negative bacteria. These antibiotics work much effectively against the anaerobic bacteria especially the ones resistant to sulfonamides and β-lactams, making them important for therapy. The therapeutic action of quinolones is critical in the infections by organisms resistant to other antimicrobials. The most commonly used antimicrobials in human medicine are **ofloxacin** and **ciprofloxacin**. They are widely used in treating tuberculosis, joint infection, typhoid fever, and sexually transmitted diseases. Recently introduced antibiotics such as gemifloxacin, gatifloxacin, and moxifloxacin are used in treating chronic bronchitis, urinary infections, cystitis, acute sinusitis, pyelonephritis, and gonorrhea. Increased antibiotic consumption is considered to cause treatment failures in human medicine thus leading to an increase in illness duration, morbidity, as well as mortality (Merlin 2020). Unregulated antibiotic consumption causes increased levels of antibiotic residues as well as transformation products in the environment.

13.2.3 Antibiotics from Hospitals and Other Medical Settings

Hospitals are important sources for the discharge of antibiotics in municipal wastewater. Hospitals are focal points for spread of many antibiotic-resistant bacteria. The transmission occurs from patient to patient through contact with patients, healthcare workers, and contaminated objects. Pathogens carrying antibiotic resistance genes can epidemically spread between patients, or the genes can be transmitted via horizontal gene transfer (Whitacre 2015). The transmission of antibiotic-resistant bacteria in hospitals is further driven by antibiotic pressure (Almagor et al. 2018). Selection density has an important influence regarding antibiotic pressure in hospitals. Selection density refers to the amount of antibiotics used per person in an area. The selection density is high in a hospital where the number of antibiotics in the formulary is small and gathering of few patients in a small space like ICU also contributes to high selection density. Colonization pressure influences the transmission of microorganisms in hospitals. Higher colonization pressure increases the spread of multidrug-resistant organisms in the hospitals (Cantón et al. 2013). Increasing use of antibiotics in the medical settings since the last decade has been observed which has reached about 200,000 tons per year, making them potential environmental contaminants because of their synergetic and prolonged effects when they enter into the environment (Wise 2002).

13.2.4 Medical Waste, Hospital Wastewater, and Spread of Antibiotic Resistance

Intensive care units and hospitals are significant breeding grounds for the development and dissemination of antibiotic-resistant bacteria. Around 10% of generated hospital waste is pathogenic and infectious, which can cause great hazards to the public (Chartier et al. 2014). Hospital wastewater acts as a rich reservoir for antibiotic resistance as well as other genetic influences that foster the extension of antimicrobial resistance to the environment (Berendonk et al. 2015). This takes place since the hospitals receive vast amounts of antimicrobial substances and human pathogens. A study got conducted in Singapore to assess antimicrobial resistance in hospital wastewater by analyzing the presence of antibiotic resistance factors in hospital effluents such as resistant bacteria, antibiotic residues, and genetic determinants. Levels of trimethoprim, azithromycin, clarithromycin, sulfamethoxazole, and ciprofloxacin were quite reduced (around tenfold) as compared to those reported in another research study (Rodríguez-Blanco et al. 2012). Bulk of antibiotics deployed in hospitals gets discharged into wastes, and thereby a selection pressure on bacteria is generated. As a result, bacteria depicting resistance become prevalent in hospital wastewater at such concentrations which are capable enough to terminate susceptible bacterial growth (Beyene and Redaie 2011). Therefore, hospital wastewater may enhance level of microbes depicting resistance in recipient sewers through selection pressure as well as introductory channels (Stalder et al. 2014). The environmental exposure with the resistant pathogens may cause crucial health concerns because of the existence of transmittable genes. Resistant pathogens may also function as a reservoir of resistance genes that lead to serious health concerns (Keen and Patrick 2013). *Campylobacter, Clostridium, Salmonella, Pseudomonas aeruginosa, Shigella, Vibrio, Staphylococcus aureus,Leptospira, Enterobacter, Klebsiella*, and *E. coli* are the most prevalent bacteria in hospital wastewater (Arshad Sid 2017).

Studies have shown that limiting the use of antibiotics could increase or decrease the phenomenon of antibiotic resistance depending upon the antibiotic class. Treatment of antibiotics may accelerate the dissemination of drug-resistant bacteria in multiple ways. Firstly, commensal flora that protects against invading bacterial colonization gets disrupted by antibiotics, making patients more vulnerable to acquire new bacterial strains. Thus, patients exposed to antibiotic resistant bacteria after or during antibiotic treatment are more likely to become colonized. Secondly, antibiotics have the potential to remove competing commensal bacteria in patients whom antibiotic resistant bacteria have already colonized which allows overgrowth of the bacteria that are resistant. This enhanced load of antibiotic-resistant bacteria may lead to greater shedding and hence greater contagiousness (Kraemer et al. 2019). Consequently, superbugs are becoming common and claiming lives. The most prevalent among them are **CRE**, **MRSA**, **ESBL-producing** *Enterobacteriaceae*, **VRE**, multidrug-resistant *Acinetobacter*, *Pseudomonas aeruginosa*, and *Klebsiella*. Interventions to limit the use of antibiotics can potentially reduce the spread of antibiotic resistance. CDC's Antimicrobial Resistance Threat Reports 2019 include the recent death as well as infection estimates that highlight the urgent threat of antibiotic resistance in the United States. It has been stated that around 2 million people in the United States acquire an antibiotic infection and around 23,000 people die each year (Table 13.1).

13.2.5 Disposal of Unused and Expired Antibiotics

Antibiotic consumption has been reported to be increased in 76 countries (Klein et al. 2018). The increased antibiotic consumption is greater among the low- as well as middle-income nations as compared with the higher-income countries. The inappropriate disposal of unused and expired antibiotics is much often ignored driver of AMR. The vast majority of the drug users do not know how to properly dispose unused and expired antibiotics and simply throw away their unwanted medications. This improper disposal of antibiotics leads to their piling up in the landfills, drains,

Table 13.1 Bacteria listed in antibacterial resistance threat report in 2019 (Biggest Threats and Data | Antibiotic/Antimicrobial Resistance | CDC, n.d.)

Serial no.	Name of bacteria	Estimated cases in 2017	Deaths in 2017
1.	Carbapenem-resistant *Acinetobacter*	8500	700
2.	*Clostridioides difficile*	223,900	12,800
3.	Carbapenem-resistant *Enterobacteriaceae*	13,100	1100
4.	Drug-resistant *Neisseria gonorrhoeae*	550,000	–
5.	Drug-resistant *Campylobacter*	448,400	70
6.	ESBL-producing *Enterobacteriaceae*	197,400	9100
7.	Vancomycin-resistant *Enterococcus*	54,500	5400
8.	Multidrug-resistant *Pseudomonas aeruginosa*	32,600	2700
9.	Nontyphoidal *Salmonella*	212,500	70
10.	Drug-resistant *Shigella*	77,000	Less than 5

and water supplies that leads to both environmental contamination and toxicity to human, animal, and aquatic life. The disposed of drugs when not properly removed during wastewater treatment process thereby reach surface water and are ultimately released into the aquatic environment (Anwar and Saleem, 2020). The concentration of these antibiotics has sufficient capability to promote resistance by target modification or by HGT. Host genomes get repositioned and thereby function as vehicles for acquiring resistance and dissemination. Therefore, the indiscriminate discharge into the environment compromises the antibiotics' effectiveness as well as augments resistance as less harmful microbes mutate to deadly pathogens (Anwar et al. 2020). As a result, the same bacteria when spread to humans are already resistant to those antibiotics causing increased mortality and morbidity.

13.2.6 Industrial Discharge of Antibiotics from Drug Manufacturing Facilities

Industrial discharge of antibiotics from drug formulation facilities is considered a crucial risk factor leading to antibiotic resistance dissemination. Detection of high levels of antibiotics (mg/L) specifically fluoroquinolones, tetracycline, and penicillin in effluents from antibiotics manufacturing bodies in India and China highlights the significance of analyzing and monitoring the results of the high selection pressure on the microbial communities (González-Plaza et al. 2019). Enhanced level of antibiotics in the environment can foster the development of ARGs because of natural selection and may help establish environment as a reservoir for further proliferation of antibiotic resistance genes to microbes through water and food webs. These industrial discharges which pollute receiving aquatic bodies are recognized to lead to an enrichment of ARGs, accelerating their dissemination. The practice of discharging hazardous industrial waste from drug manufacturing facilities is not limited to only Asian countries but can be observed around world. Industrial discharge of antibiotics from drug formulation facilities is considered a substantial point source with levels higher than other routes (Khan et al. 2013).

13.2.7 Municipal Sewage, Wastewater, and Sewage Treatment Plants

The traditional wastewater treatment plants have been designed to effectively remove certain pollutants and pathogens but are not effective in eliminating antibiotics or antibiotic resistance genes. Wastewater treatment plants serve as hotspots for the spread of antibiotic resistance genes. Antibiotics get discharged into WWTPs from hospitals, pharmaceutical industries, and households. Antibiotic residues from households enter together with sewage to wastewater treatment plants. Sewage microbiota consists of human commensal microbiota which gets mixed with bacteria that colonize the sewage system. The fraction of antibiotic-resistant bacteria in sewage can reach more than 50% in a given group like *Enterobacteria*. Leachate from municipal solid waste pollutes environment by antibiotics thrown into household rubbish bins.

Wastewater from wastewater treatment plants contains a significant load of antibiotics. Tetracyclines, β-lactams, quinolones, sulfonamides, and macrolides have frequently been detected from emissions of WWTPs. The biological treatment processes create favorable conditions for the development of antibiotic resistance genes and horizontal gene transfer under sub-inhibitory concentrations of antibiotics. Variations in the concentrations of antibiotics in wastewater are due to several reasons: the size of wastewater treatment plant, seasonal fluctuations, and antibiotics usage patterns. Activated sludge is an important wastewater treatment process for controlling pollutants and it serves as an important route for the spread of antibiotic resistant genes in the environment. Antibiotic resistant bacteria present in the activated sludge go down into the water of aeration tank and sedimentation tank and get released with the effluent. These bacteria can potentially contaminate soil when the activated sludge is used as a fertilizer. Moreover, the antibiotic resistance genes in the treated water are released through effluent into the surrounding water (Gupta and Singhal 2018).

13.2.8 Antibiotics from Surface Treatment Compounds in the Environment

Contaminating bacteria can sustain for long time periods on any surface exhibiting resistance to the applied disinfectants. Nosocomial pathogens may survive on dry surfaces for weeks, but some pathogens, including *Acinetobacter baumannii* and

P. aeruginosa, require humidity for their survival. These pathogens can easily transmit if disinfection is not done properly. The multidrug-resistant bacteria *Klebsiella pneumoniae* and *E. coli* survive for several weeks on steel surfaces according to a study. Research has shown that horizontal gene transfer of β-lactamase genes occurs when recipient and donor cells are mixed upon steel. The study shows the potential of bacteria to retain on touch surfaces plays a vital role in horizontal gene transfer of resistance genes. Recent reports demonstrate that biofilm producing strains of *A. baumannii* can persist on the inanimate surfaces longer than the non-biofilm producing ones (Cantón et al. 2013). Excessive and inappropriate use of antibiotics in this situation may contribute to the persistence of antibiotic resistant bacteria. Inappropriate control of infection can propagate the antibiotic resistant bacteria and can further lead to endemics. The used antibiotics in hospitals get discharged into aquatic environment through wastewater leading to an increase in the rate of antibiotic resistance in the environment (Kraemer et al. 2019).

13.2.9 Antibiotics from the Aquatic Environment

Antibiotics are discharged into the aquatic environment through wastewater effluents and improper disposal from livestock and humans. Antibiotic resistance genes have been frequently detected in surface river water, municipal wastewater, water supply reservoirs, and drinking water (Huerta et al. 2013). Runoff from agriculture and damaged sewage pipes are responsible for the entry of antibiotic resistance bacteria into groundwater. Antibiotic concentrations in untreated wastewater were measured in the United States according to a report. The estimated concentrations ranged from 4 ng/L to 27,000 ng/L. The basis of this estimation was the number of administered antibiotic prescriptions. It was found that the major classes of antibiotics present in the aquatic environment were quinolones, sulfonamides, and macrolides. Among quinolones and sulfonamides, ciprofloxacin and sulfamethoxazole were the most prevalent in municipal water effluents, and sulfamethazine was the most prevalent in farm runoff (Huang et al. n.d.). Antibiotic concentrations were much lower in the effluents of highly advanced treatment processes because of significant eradication of antibiotics by these processes. Levels of antibiotics in drinking water are mostly reported to be minute when compared to the high levels in surface waters, agricultural runoff, and wastewaters.

13.2.10 Antibiotics from Sediments

Sediments often contain antibiotic-resistant bacteria because of the unmonitored application of antibiotics in aquaculture. Substances used in aquaculture may directly enter the sediments from water without any pre-treatment process. This leads to high concentration of antibiotics in sediments. Sulfonamides, tetracyclines, and quinolones get readily adsorbed in sediments. Antibiotics have both quantitative and qualitative effects on the microbial communities residing in sediments. The excess use of antimicrobials for treatment of bacterial diseases in aquaculture has led to antibiotic resistance development in *Aeromonas salmonicida*, *Vibrio anguillarum*, *Pasteurella piscicida*, and *Aeromonas hydrophila*. Therefore, the high antibiotic load in sediments is strong enough to inhibit bacterial growth for aquaculture (Kümmerer et al. 2009a).

13.3 Airborne Antibiotic Resistance Genes in the Environment

The airborne bacteria in healthcare environment are mostly multidrug resistant and hence pose a threat to humans even outside medical settings through airborne transmission. Antibiotic resistance genes have been reported from air samples collected wastewater treatment plants (WWTPs), livestock, and hospitals. Airborne particles in highly contaminated places provide greater number of adhesion sites which facilitates microorganisms to suspend with increased stability in air. Airborne transmission plays an important role in the environmental dissemination of antimicrobial resistance. Distribution pattern of airborne drug-resistant bacteria depends on physiochemical factors, bacterial communities, meteorological parameters, antibiotic usage, and air quality (Jing Li et al. 2018). Detailed information on airborne pathogens and their impacts on human and environmental health is unfortunately not enough, and further research is required in this domain.

13.4 Hazardous Consequences of Antibiotics in the Environment

There is a great concern about the deleterious effects of antibiotics on our environment over the last few years; therefore much is not known about the hazards of antibiotics entering the water sources. Moreover, the concentration of the antibiotics present in waters is generally very low due to which it cannot be reliably measured by common analytical methods. Although individual concentrations of antibiotics in waters are low, but a large number of antibiotics when combined can cause serious environmental and health problems (Kümmerer et al. 2009a). Horizontal gene transfer between bacterial species in wastewater may be fostered by rich nutrient content and high density of bacteria in the biofilms. Co-selection through substances like heavy metals and biocides that are present in sewage sludge, wastewater, and fermentation residues is another mechanism via which antibiotic-resistant bacteria occur in the environment (Gupta and Singhal 2018). Effluents from veterinary clinics and hospitals also contribute to antibiotic pollution. Hotspots for the occurrence of antibiotic-resistant bacteria include livestock keeping and hospitals. From here, antibiotic-resistant bacteria get introduced to the environment through wastewater or via spread of sewage sludge or fermentation residues. Aquaculture is another pathway where antibiotics are overused. When medicated foods are used by fisheries, antibiotics are released directly into surface water (Whitacre 2015). Antibiotics may enter the environment by animal farming when manure is used as a fertilizer. Some antibiotics get sprayed on crops; all the spray does not remain on the plant rather major portion is washed into the soil and thereby reaches groundwater (Pareek et al. 2015). Leachate from municipal solid waste pollutes the environment by antibiotics thrown into household rubbish bins. Antibiotic resistance genes (ARGs) have been observed in the air samples from places that are around WWTPs. Mutual interactions take place between all the entry routes that generate new threats of spread of ARGs and ARB to humans and animals through airborne aerosols and dust. Some of the major hazards regarding the antibiotic presence in the environment include elimination of the entire trophic levels in ecosystems and entry of multidrug-resistant bacteria into the food chain. Microbial communities are complex and have the major task of nutrient cycling. Cycling of the nutrients is important for maintaining quality of soil and for sustainable agricultural land use. Nitrogen is one such essential nutrient, and two main genera of gram-negative bacteria drive its cycling that are **Nitrosomonas** and **Nitrobacter**. Broad-spectrum antibiotics like tetracyclines and sulphonamides at high concentrations disrupt the nitrification process and inhibit nutrient cycling significantly (Frade et al. 2014). Antibiotics primarily affect microorganisms like bacteria, fungi, and microalgae. Sensitivity of microalgae varies to antibiotics. For example, cyanobacteria (blue-green algae) show sensitivity to sarafloxacin. Antibiotics exposure to the environment influences the early life stages of various organisms and exhibits adverse effects on reproduction (Pareek et al. 2015). Behavior of the aquatic organisms is also impacted by antibiotics exposure to the environment (Fig. 13.2). One such example is that the antibiotics impact locomotion (phototaxis) of the aquatic organism *Daphnia magna*. Primary antibiotic resistance is present naturally in microorganisms. Secondary resistance on the other hand develops when microorganisms encounter antimicrobial drugs during therapy. Through horizontal gene transfer or conjugation, the plasmid mediated resistance is easily transferred between microorganisms. Resistance then reaches the environment with the ability to adversely affect terrestrial and aquatic organisms. Important examples are methicillin-resistant *Staphylococcus Aureus* (MRSA) and vancomycin-resistant *Enterococci* (VRE). The drug-resistant bacteria can get transferred to humans when manure is used as a fertilizer or when plants get watered with surface water (Küster and Adler 2018). The problem of antibiotic resistant bacteria is accelerating, and tools to combat this problem are decreasing in power.

13.5 Effect of Irrational Use of Antibiotics on Human Health

Misuse of antibiotics in humans in therapeutic regimens ultimately develops antibiotic resistance (Animals et al. 1999). Two main human health consequences of increased AMR due to misuse of antibiotics are rise in foodborne diseases and

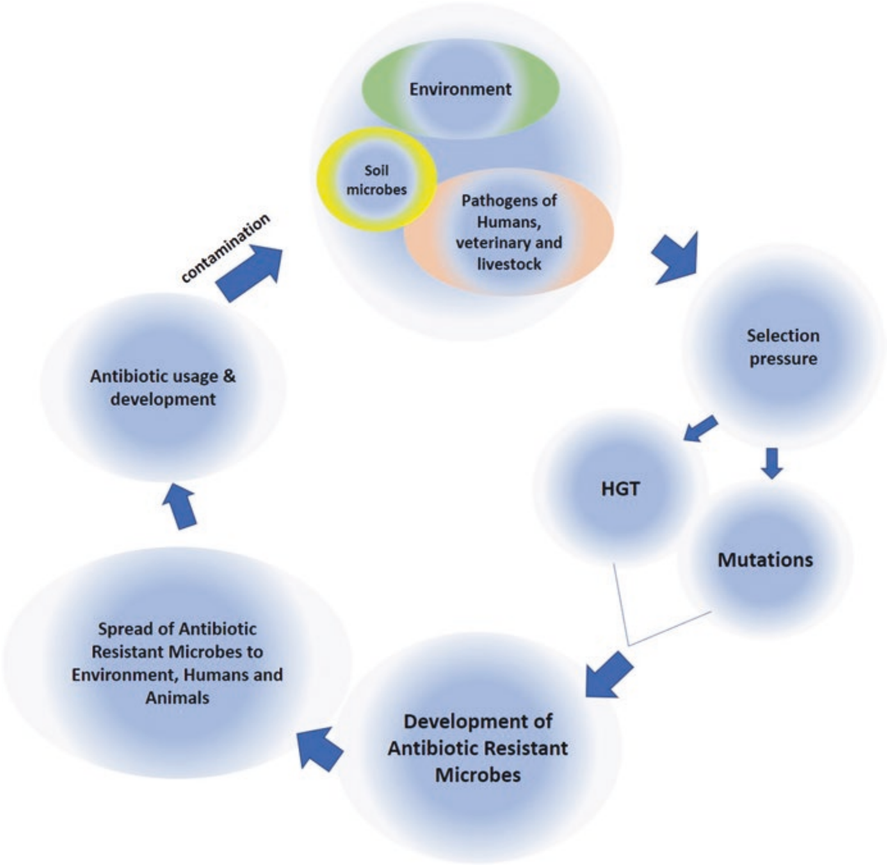

Fig. 13.2 Environmental hazards of antibiotics

increased cases of treatment failures (de Kraker et al. 2016). Increased human infections by resistant bacteria from food take place as there is rise in the prevalence of antibiotic resistance because of increased human exposure to antibiotics (Smith et al. 2005). Consuming an antibiotic can reduce the infectious dose for *Salmonella*, if the bacteria is resistant to that antibiotic, and the same goes for other foodborne bacteria. Several analyses of outbreaks of antibiotic-resistant *Salmonella* have shown that prior exposure to antibiotics may result in a huge number of cases as compared to the cases that would have taken place if a sensitive strain had caused the outbreak (Mølbak 2005). It has been observed in the case of *Salmonella* outbreaks that unrelated previous treatment with an antibiotic can predispose humans to infection with susceptible or resistant *Salmonella*. As bacteria become more and more resistant, treatment of patients with antibiotics for whatever reason enhances risk for patients to develop subsequent infections caused due to resistant bacteria. Thereby the public health impacts are increased cases of infections and larger outbreaks (Anderson et al. 2003). In addition, increasing AMR in bacteria can lead to treatment failures if the bacteria are resistant to an antibiotic used for treatment.

An example of treatment failure is a case in Denmark where an AMR *S. typhimurium* **DT104** outbreak due to contaminated pork got traced back to a swine herd (Mølbak et al. 1999).

13.6 Management Strategies for Control of Antibiotics Release in the Environment

The deaths estimated per year because of antibiotic resistance are approximately 70,000 globally (Kraemer et al. 2019), which makes its management crucial. Dissemination of antibiotic resistance can be effectively controlled by the application of appropriate measures for improving wastewater treatment processes as well as by restricting the antibiotic use in livestock as well as agriculture. "One Health Model" which connects animal, human, and environmental health domains should be applied to resolve this issue worldwide. Understanding antibiotic resistance and antibiotic pollution as one health approach may help in creating more effective policies. Little has been known about the fate, occurrence, risks, and effects linked with the discharge of antibiotics and antimicrobials into the environment. There must be fundamental data on the fate, sources, and effects of antibiotics in the environment for appropriate risk management. The discharge of antibiotics into the environment should be greatly reduced, and for this purpose, the unused drugs should never be flushed down the drains (Kraemer et al. 2019). The misuse of antibiotics by the general public should be stopped by making people aware that the antibiotics only help against the bacterial diseases and not against the viral diseases. There should be procedures to regulate suppliers in the pharmaceutical industry to make sure that antibiotics do not get released into surrounding waters during their production (Fig. 13.3). Future antibiotic interventions should be "targeted antimicrobials" with a narrow spectrum of activity to facilitate early responses instead of broad-spectrum agents. Furthermore, the usage of these antibiotics should be implemented with antimicrobial susceptibility testing. Moreover, the usage of biomarkers should be encouraged to pinpoint when any antibiotic is essentially required and also when antibiotic treatment should be terminated. Resultantly, the selection impact would be lower on the microbiota (Cantón et al. 2013). Societies should publish proper guidelines for appropriate antibiotic use and to reduce the antibiotic resistance in the environment. These guidelines must include coordination between clinicians, infection control teams, pharmacists, microbiologists, and drug-use prescribers. A collaboration between the disciplines of epidemiology, microbiology, nursing, pharmacy, and infectious diseases could result in an efficient program to mitigate antibiotic pollution in the environment.

Fig. 13.3 One health approach to combat antibacterial resistance

13.7 Conclusion

Antibiotic pollution has not only contributed to antibiotic resistance but also directly affected human and environmental health. However, little information is present on the sources, occurrence, fate, effects, and risks associated with antibiotic consumption globally.

There is a significant gap in understanding the interactions between antibiotics and their metabolites and development of antibiotic resistance after their discharge in the environment. Multiple approaches should be considered to reduce release of antibiotics in the ecosystem for appropriate risk management. Currently, no proper regulations are present for antibiotics monitoring in surface water, drinking water, or groundwater. The scientific community has started to realize the significance of designing plans to regulate antibiotic pollution in the environment in the past few decades. New policies should be implemented locally to restrict the dissemination of antibiotic resistant bacteria and antibiotic resistance genes through environmental routes.

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Chapter 14
Remediation of Plastic Waste Through Cohesive Approaches

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Abstract Growing volume of environmental plastic waste has generated global concerns because of its persistence in the environment. Plastic is one of the main environmental problems because of its slow degradation rate or organic matter's non-biodegradability in natural conditions. Plastic contamination and global warming are caused not only by increasing the issue of waste disposal and landfilling but also by burning CO2 and dioxins. Not only the environment is contaminated, but plastic also poses health risks to wildlife. Plastic waste burning produces poisonous gases that pose a health hazard after inhalation causing cancer and lung diseases. Biodegradation of plastics by microbes is one possible solution to this problem. Plastic waste has not been much treated so far by means of combination of biological along with the physicochemical methods; this chapter explores the potential of cohesive methods for remediation of plastic waste. Main benefits of plastic are lightweight, inertness, toughness, strength, and low cost, but it also has the disadvantages such as recalcitrant biodegradation and difficult to naturally degrade. This chapter highlights the effect of cohesive methods on the plastic degradation by potential microbes. PET type of plastic was treated biologically by various microbes including microalgae, lichens, fungi, and bacteria subjected to either pretreatment or not. It is concluded from the different review studies that pretreatment had marked effect on the cracking and alteration of plastic polymer which helped to grow microbial species on the cracked surface.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_14

14.1 Introduction

Plastic consumption is increasing day by day, and plastic pollution has amplified manifold (Haward 2018). About 100 million tons of plastics are manufactured around the world every year (Payne et al. 2015). The use of the synthetic polymers is part of our daily life; polythene and plastics are widely used as packaging, food, medicine, clothing, shelter, transport, industry, and agriculture in not only rural but also urban areas since the last few decades (Cragg et al. 2015). This causes waste disposal and contamination due to extensive use of polythene and plastics. The best (Eichinger et al. 2005) way to degrade water treatment and remove pollutants from the environment is through biodegradation (Sanchez et al. 2015). Biodegradation is the degradation of the natural and artificial polymers by different microorganisms (fungi, bacteria) (Sanchez et al. 2015).

Plastic pollution is increasing at such an alarming rate that plastic disposal seems very difficult due to limited dumping sites (Restrepo-Flórez et al. 2014). In all economic sectors, plastic polymer has been widely used for manufacturing various useful products. Because of being versatile, elastic, durable, and recalcitrant, it has brought quality to life as it acts as an outstanding barrier to external stress (Singh and Sharma 2008; Alimi et al. 2018). Moreover, it has unique mechanical and thermal properties: cost-effective, low-weight indestructible, and highly moldable, and is widely used at industrial and household levels. Plastic polymer like polyethylene is a man-made polymer which has high molecular weight and greatly hydrophobic in nature (Ahmed et al. 2014). It causes adverse impact to the environment because of its recalcitrant nature and extensive use in the production of grocery bags, conveyance material, and beverage bottles and in making of electrical and medical appliances (Krupp and Jewell 1992).

Polythene is sustainable and will require up to 1000 years for natural environmental degradation (Sangale et al. 2012). Plastic is one of the main environmental problems because of its slow degradation rate or organic matter's non-biodegradability in natural conditions. Ali et al. have clarified in 2009 that improper disposal of waste and landfilling are not the only cause of plastic contamination and global warming, but other activities like burning carbon dioxide as well as carcinogenic hydrocarbons called dioxins are also contributing to it. Burning of plastic waste produces poisonous gases that pose a health hazard after inhalation causing cancer and lung diseases (Pramila and Ramesh 2011). The accumulation of synthetic polymers in the environment is mostly because of the unavailability of effective methods of disposing these polymers and thus increasing the environmental hazards to plants and animals (Barnes et al. 2009).

The main characteristics of plastic are lightweight, inertness, toughness, strength, and low cost, but it also has some drawbacks, like it is intractable to degradation and very hard to decay naturally (Leja and Lewandowicz 2010). The best (Eichinger et al. 2005) way to degrade water treatment and remove pollutants from the environment is by biodegradation (Sanchez et al. 2015). Biodegradation is the method of degrading natural polymers like cellulose, lignin, and artificial polymers like polystyrene and polyethylene by the enzymatic activity of microbes such as fungi and bacteria into metabolites such as H_2O, CO_2, CH_4, biomass, etc. (Sheel and Pant 2018).

14.2 Plastic as Source of Pollution

The amount of plastic deposition in the environment is evident that environmental contamination is caused by plastic. Around 10% of global waste disposal is reported to be plastic (Lebreton and Andrady 2019). According to a general estimate, the annual production of plastic has reached to approximately 52 million tons and is increasing day by day and contributes to almost 60% of ocean debris, and it is estimated that total accumulation of plastic will be reached to 250 million tons till 2025. Plastic contamination has been described as a global concern in freshwater and marine environment. Plastic waste is estimated to account for 60–80% of marine debris, exceeding 90–95% in some areas (Kibria 2017). Eighty percent of the total plastic waste is from sources that are land based, while the remaining 20% has ocean origin, which includes different sources like ropes and nets used for fishing (Van Sebille et al. 2016). Plastic debris is an increasing pollutant which does not degrade easily, but remains for long periods in the aquatic ecosystem. An estimated 5 trillion fragments of plastic float in the oceans of the planet (Tunçer et al. 2019).

The plastics are manufactured at a large scale because it is used in textile industry, food synthesis, construction activities, and for the synthesis of carrying and conveyance material. The accumulation of plastic in the water bodies is considered a major problem and may undergo mechanical and chemical breakdown, causing water pollution and threat to aquatic life (Eriksen et al. 2014). Its direct contact to the ultraviolet rays from sunlight and disintegration by the ocean waves breaks plastic into micro and nano forms which more toxic and easily become the part of the food chain. The studies suggest that the plastic present in the oceans is difficult to degrade due to pertaining environmental conditions (i.e., exposure to UV radiations and its conversion into micro and nano form) (Cole et al. 2011). The high-density polyethylene usually sinks down into water, undergoing torpid degradation and changing into microplastics, causing huge threat to marine biota (Andrady 2017), while the low-density polyethylene and polypropylene floats on water surface (Alimi et al. 2018). Dangerous waste has been exposed to the natural environment. In many areas, the local environment has been destroyed by major disasters including oil spills every year, and the unnecessary use of plastics has degraded soil and water. Million tons of polythene are produced worldwide. It is used in the development of plastic films to make containers and other products like cups. Polythene waste also causes damage to the health of fish, birds, goats, deer, and other animals (Lora and Andrade 2009). Plastic pollution emerges as a threat to global ecology, as it is resilience to degradation (Saxena et al. 2009). The continuous plastic pollutant flow is sustained by two means: deliberately by unsafe domestic and industrial waste disposal and by improperly contained static and transported waste directed by the weather; land-based plastic waste migrates to the oceans, where it is further introduced by the dumping or destruction of underwater ships and offshore oil platforms. Such pollution has a number of deleterious consequences. Plastic waste in the marine environment is the cause of numerous dangerous and environmentally harmful effects. Plastic remains pose a direct threat to wildlife, with many and varied species recognized as having an undesirable impact on plastic objects (Mussgnug et al. 2010).

The one main source of environmental pollution is LDPE (Romero Saez et al. 2017). High-density polyethylene generally sinks into water undergoing degradation and converting into microplastics (Andrady 2011), and the low-density polyethylene and polypropylene floats on the surface of water (Alimi et al. 2018).

The key risks coupled with plastic objects to animals are the entanglement and ingestion of such objects (McKendry 2002). Not only the environment is contaminated, but also plastic poses health risks to wildlife. The improperly disposed and utilized plastic bags don't allow air and water to enter the earth which leads to exhaustion of fresh water and is also an ultimatum to a creature's life. Direct contact to ultraviolet rays from sunlight degrades plastic into small toxic parts, which can be easily entered into the food chain by ingestion of especially aquatic animals (Denuncio et al. 2011). A wide range of humans have been noted to have negative impacts on plastic wreckage, ocean birds, sea turtles, cetaceans, filter feeders, fur seals, and sharks (Srirangan et al. 2012). Marine birds are particularly prone to plastic items through ingestion, which they mistake for food (Sims et al. 2006). Furthermore, plastic contamination annually records higher amounts of marine mammal death approximately 1 lakh and seabirds deaths up to 1 million (Kedzierski et al. 2018).

Plastic eaten or taken up by these animals does not digest and contribute to decrease stimulation of the diet and blocking of gastro intestine, reduce secretion of gastric enzymes, and lower the steroid hormone level and raising reproductive problems (Horton et al. 2017). Plastic particulates in the ocean were shown to retain very high concentrations of organic toxins. Harmful chemicals like polychlorinated biphenyls (PCBs), nonylphenols (NPs), organic pesticides including dichlorodiphenyltrichloroethane (DDT), polycyclic aromatic hydrocarbons (PAHs), polybrominated diphenyl ethers (PBDEs), as well as bisphenol A (BPAs) have been consistently found across oceanic plastic wreckage (Sharma et al. 2019).

The existence of these substances even further raises the risk involved with the consumption of plastic debris by wild animals (Kurian et al. 2013).

14.3 Nature and Kinds of Plastics

Plastics are synthetic long-chain polymeric particles and are considered very resilient toward environmental changes (Kumar et al. 2017). Plastics can be defined as long-chain polymers, which can occur naturally or synthetically (Ghosh et al. 2013). Natural plastics consist of polymers that include chitin, lignin, starch, etc., whereas synthetic plastics are generally derived from petrochemicals such as polyethylene, polystyrene, silicone, nylon, etc. (Narwal and Gupta 2017). Polymers are mainly petrochemical in nature and have semisynthetic organic compounds and high molecular weight which can be molded into different shapes like bags, household items, wires, packaging and wrapping material (40% consumption), agriculture mulch, pipes, and electronics (Accinelli et al. 2012). Monomers of ethylene form the polyethylene, which is an organic polymer, nonpolar, porous, high molecular weight hydrocarbons formed primarily by cracking ethane and propane, naphtha, and gas oil (Khoddami et al. 2013). High-density polyethylene (HDPE) and low-density polyethylene (LDPE) are the two most common types of polyethylene. Polyethylene is completely linear and available from 0.91 to 0.97 g/cm^3 with elastic thickness range. Furthermore, high-density polyethylene is additionally linear with marginal splitting resulting in high packing density (Kigozi et al. 2013).

Basically, polyethylene is an organic polymer which is made up of long-chain monomers known as ethylene (C_2H_4) molecules. Polythene is produced by ethane degradation or cracking propane and gas oil (Sangale et al. 2012). The general formula of polyethylene is C_nH_{2n}, and the n is the number of carbon. Polythene compounds have two types that are most common which include HDPE and LDPE (Romero Saez et al. 2017). Polyethylene having little density is completely linear and accessible from 0.91 to 0.97 g/cm^3 with elastic thickness range. High-density polyethylene is additionally linear with marginal splitting resulting in high packing density (Kigozi et al. 2013). Polyethylene (HDPE, LDPE, LLDPE, and MDPE), polystyrene (PS), polypropylene (PP), and polyvinyl chloride (PVC) have been classified as commonly used plastics (Muhonja et al. 2018).

Plastic is composed of different elements like oxygen, nitrogen carbon, hydrogen chloride, and silicon. Coal and hydrocarbons are used in extracting the fundamental plastic material (Ali et al. 2016). Therefore plastics are classify into two various types, that is, thermoset and thermoplastics. Thermoplastics are classified as non-biodegradable, and these are generally allowed for their hardening and softening to cool and heat repetitively. On the other hand, thermoset plastics have a strong cross-linked structure, and they are considered linear solids (Bardají et al. 2020).

14.4 Uses of Different Plastic Types

Food, cosmetics, pharmaceutical chemicals, and detergents are packed mostly by using synthetic plastics. Thirty percent of plastics have their usage in packaging worldwide. Plastic's usage is increasing at a rapid level of 12% annually (Sabir 2004). The most commonly used plastics in packaging are polyethylene (HDPE, LDPE, LLDPE, and MDPE), polyethylene terephthalate (PET), polystyrene (PS), polypropylene (PP), polyvinyl chloride (PVC), polyurethane (PUR), polybutylene terephthalate (PBT), and nylons which are shown in Table 14.1 below. The major use of plastics is not restricted to their mechanical and thermal characteristics but depends on the durability and stability of plastics.

Table 14.1 Table showing different uses of plastics (Shah et al. 2008)

Plastic	Uses
Polyethylene	Plastic shopping bags, food packaging film, bottles of milk and water, toys, pipes used for drainage and irrigation purposes, bottles of motor oil
Polyethylene terephthalate (PET)	Bottles of carbonated soft drink, packages of processed meat, jars of peanut butter, filling of sleeping bags and pillows, textile fibers
Polystyrene	Disposable items, packaging, laboratory and electric products
Polyvinyl chloride	Automobile seat covers, shower hangings, raincoats, bottles, visors, soles of shoes, garden hoses, and electricity pipes
Polyurethane	Tires of automobiles, gaskets, automobile bumpers, insulation of refrigerators, cushioning of furniture, and life jackets
Polypropylene	Bottle caps, drinking straws, medicine vials, seats, batteries and bumpers of automobiles, disposable syringes, and carpet backings
Polycarbonate	Making nozzles on papermaking machinery, streetlights, safety wires, car's rear lights, baby feeders, housewares, skylights, and greenhouse roofs and sunrooms
Polytetraflouroethylene (PTFE)	Industrial applications, that is, chemical plant, electronics, and bearings. Coatings on nonstick saucepans and frying pans

14.5 Plastic Waste Disposal

Plastic disposal is a global issue. Around the world, the most widely plastic disposal methods are recycling, landfilling, and incineration (Silva et al., 2020).

14.5.1 Combustion of Plastic

Combustion of plastic products also produces gases as by-product, and these released gases are hazardous as their inhalation by living organisms especially humans can lead to several respiratory disorders and in some cases can also cause cancer (Pramila and Ramesh 2011). The plastic waste is mainly burned in landfills, this threatens Natural environment due to emission of toxics gases from it causing air pollution and ozone layer depletion, in addition to this dioxins release that have potential of causing various anthropogenic problems like hormonal abnormalities (Raziyafathima et al. 2016). The aromatic rings, chains, and bonds make the plastic polymer resistant to microbial degradation, thus persisting for centuries and affecting the natural environment, causing serious air, water, and soil pollution (Eriksen et al. 2014).

14.5.2 Landfilling

Around 60% of plastic waste is discarded in a landfill, which is known to be one of the best methods of disposing of solid waste material. It's a widely used method for disposal of plastic, but the main drawback of this approach is that on the open land, the dumped plastic is not quickly degraded (Qasaimeh et al. 2016). Plastic litter, which is dumped openly or in sanitary landfills, produces harmful leachate. In addition, disposing plastic in landfills results in land degradation and also increases the chance of plastic ingestion by animals. Ultimately, the release of plastics into aquatic environments leads to their intake by aquatic animals which causes death of such organisms and creates a high risk of biomagnifications and bioamplification of harmful plastic substances (Denuncio et al. 2011).

14.5.3 Recycling

It is essential to have proper treatment as well as disposal options for plastic waste treatment. Recycling plastic is a better disposal option, but this method has its drawbacks since it can no longer be recycled at the end of the life of products. The production and use of biodegradable plastics is another method (Al-Salem et al. 2009).

14.6 The Assessment of Biodegradable Nature

The assessment of the biodegradable nature of plastic can be done by measuring the structural changes under the microscope or by evaluating the growth of microorganisms after the biological and enzymatic action along with the evolution of carbon dioxide (Kissi et al. 2001; Ahmed et al., 2018). Plastics are of numerous kinds such as polystyrene (PS), polyethylene (PE), polyurethane (PU), polypropylene (PP), poly(vinyl chloride) (PVC), and poly(ethylene terephthalate) (PET). Plastic polymers basically comprise of hydrocarbon monomers created by natural and synthetic organic and inorganic raw material. Generally, there are two main kinds of plastic, that is, thermoplastics and thermoset plastics. Thermoplastics are long linear carbon chains, having different molecules which are joined end to end. Among different kinds of plastics, the microplastic is more dangerous (Cole et al. 2011) as it is difficult to identify and tracked (Kutten, 2019) and is accumulating inside the body of different organisms causing severe anomalies resulting visible decline in abundance and diversity of fish and coastal birds.

14.6.1 Factors Affecting Biodegradation of Plastics

The effects of the biodegradation process are also depending on some main factors like characteristics of the polymers and the condition of the environment. The characteristics of the polymer include functional group, morphology, molecular weight, stability, crystalline nature, additives, cross-link, and copolymers. Low molecular weight polymers are favorable for biodegradation (Varjani and Upasani 2017), and environmental conditions like temperature, ultraviolet radiations, pH, hydrophobicity, salinity, presence or absence of O_2, etc. also affect the biodegradation of plastics (Gu 2003). In the formation of polymers, stabilizers and antioxidant are used which drop off biodegradation time, and also it can be harmful for microbes (Kale et al. 2015). In addition to all listed above, the structural factors (linearity and polymer branching; bonding type, such as C-C, amide, and ester), the polymers' molecular composition, and physical structure such as powder, films, pellets, and fibers can also affect the polymer's biodegradability. The rate at which the polymer degrades eventually depends upon the procedure of decaying and speeding of process.

14.6.2 Different Steps of Biodegradation Mechanisms

Biodegradation is a process of degrading complex organic polymers into simpler forms by using microbes (Restrepo-Flórez et al. 2014). Processes causing alterations in polymer functions or properties due to chemical, physical, or biological reactions ultimately result in bond breakage. Chemical alterations have been categorized as polymer degradation (Ghosh et al. 2013). Optical mechanical or electrical properties of a substance or material change due to degradation through cracking, crazing, erosion, discoloration, or phase separation. The changes comprise bond breakage and chemical transformation, and new functional groups are also formed (Nigam 2013).

Degraded particles are again scattered in the environment, and those particles are generally nontoxic. For biodegradation, microbes form the catalytic enzymes in nature (Hadad et al. 2005). Through various enzymatic activities and cleavage of bonds, the degradation process is achieved by microbes (Pathak and Navneet 2017). The degradation process occurs in sequential phase's bio-deterioration (changing the the physicochemical characteristics of the polymer), bio-fragmentation (breakdown of polymers into simpler form through enzymatic cleavage), assimilation (microbes uptake the molecules), and mineralization (after the degradation, oxidized metabolites such as CO_2, H_2O, and CH_4 are produced, which are shown in Fig. 14.1).

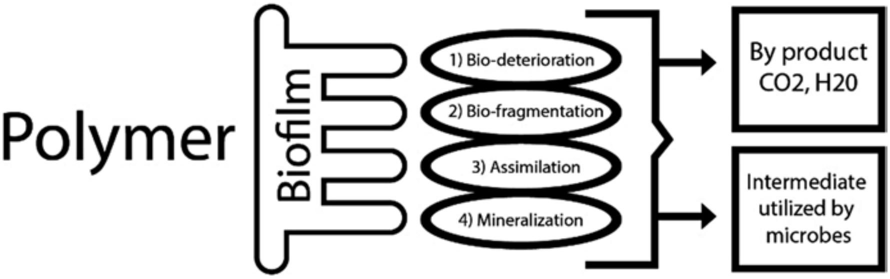

Fig. 14.1 Different steps of microbial polymer degradation

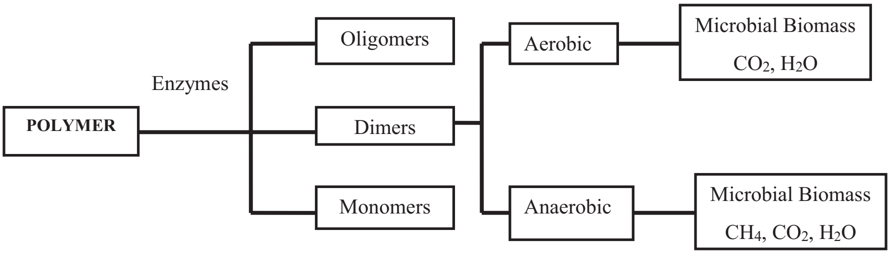

Fig. 14.2 Polymer degradation by aerobic and anaerobic condition

14.6.3 Aerobic and Anaerobic Degradation of Polymers

Degradation of polymers depends on polymers' physicochemical properties. The weight and crystalline nature are the main properties of polymers which affect the efficiency of microbial degradation. The polymer degradation enzymes are divided into two types, that is, extracellular depolymerase and intracellular depolymerase (Gu 2003). In the degradation of complex polymers into simple units such as monomers and dimers, exoenzymes are generally involved. They are also used as carbon and energy sources by microbes. During or at the end of processes, polymer degradation (mineralization) produces new products, for example, CO_2, H_2O, or CH_4 (Gu 2003). On the availability of oxygen, this degradation process is dependent. In both aerobic and anaerobic cases, mineralization of polymers takes place. Polymers are converted into simple form by using microorganisms, and mineralization produces CO_2 and H_2O in the presence of oxygen, while in anaerobic conditions, it produces organic acids like CH_4 and H_2O which are shown in Fig. 14.2. Biodegradation is an efficient way to clean up the waste of plastic with the help of microbes (Kumar et al. 2011). Enzymes of microbial species are used for pollution control and contribute to the creation of an environment that is friendly (Gu 2003). Various types of microbes are known to be used through the process of mineralization.

14.7 Major Properties Affecting Plastic Biodegradation

14.7.1 Characteristics of Plastics

Plastic products take hundreds of years to degrade naturally, and the material only partially degrades after that. It is important to know the structure and characteristics of polymers that change with external environmental factors according to the life cycle of the material. Weight reduction is an important parameter that helps to measure the degradation rates. This section describes some of the important properties that assist in indicating the rate of degradation (Artham and Doble 2008).

14.7.2 Weight of Plastic Films

Plastic film is preferred as it is Light weight, durable nature, and low cost. Therefore, due to these properties of plastic it is used in the world for many applications and mostly in packaging (Kumar et al. 2013). Plastic is not easily degraded because they are durable and made up of such a strong C-H bond. One way for the degradation of plastic is to degrade plastic biologically, which is commonly known as biodegradation (Moharir and Kumar 2019). Some researchers have placed the films of plastic in the soil to analyze the rate of biodegradation of plastics (Chiellini et al. 2003). The loss of plastic film rate before and after the study is used as a degradation rate parameter with some other relevant parameters. Weight loss of plastic film is the indicating parameter of degradation. Therefore the essential parameter to be considered is the weight of plastic films before and after the process of degradation (Hadad et al. 2005).

14.7.3 Thickness of Plastic Films

Any plastic material strength is related to the thickness of material similarly thickness of plastic shows its strength, thicker film will be more strength and vice-versa. In plastic film degradation studies, it is one of the most significant parameters that must be taken into account. The degradation rate of thicker plastic films is slow, and a thinner plastic film will degrade quickly. The thickness of plastic depends on the application in which they are used (Moharir and Kumar 2019).

14.7.4 Density of Plastic Films

Types of plastic are categorized by their densities. With the range of thickness, every plastic has its density. It is an important parameter to count the viability of a film, and it plays an important role in which the transparency of the film is a key factor needed for certain applications (Gulmine et al. 2003).

14.7.5 Mechanical Properties of Plastics

Plastic's mechanical and elastic properties are useful in identifying the plastic strength that would be useful for any further research to be carried out and used in particular applications (Gerald 2000). Stress increases as these polymers distort under pressure, and it relies on the polymers' structure and mechanical characters, and some of the main polymer mechanical properties are as follows.

14.7.6 Tensile Strength of Plastic Films

The Tensile strength is a significant mechanical character that shows the durability, strength, and rigidity of the polymers (Ferreira et al. 2005). In many applications, various thickness levels of polymers are tested in for tensile strength to know the effectiveness in resisting external loading. The tensile test is performed to control tension till the failure stage to understand the strength and capability of the polymer.

14.7.7 Plastic Film Elongation

Elongation is another important character. The breakpoint of polymers can be identified by performing this test that will help to understand the efficiency of material breakage at a particular length (Pedroso and Rosa 2005). Some external factors such as temperature, sunlight, and UV radiation can affect the elongation of the polymer.

14.7.8 Young's Modulus of Plastics

Now the term Young's modulus is replaced by the elastic modulus. For determining any solid, material stiffness is measured by Young's modulus. The linear elasticity of materials basically defines the solid material stiffness. With different temperatures, Young's modulus varies. Young's modulus of polymers is measured to analyze its elastic behavior. The stress-strain relationship is defined by this mechanical property (Pedroso and Rosa 2005).

14.8 Potential Degradation Procedures

A process which causes the breakage or splitting of complex or larger fragments into simple and small size particles is known as degradation; degradation of these polymers into monomers can be done as a result of any physical and chemical changes; in the degradation process, a lot of procedures are involved. The plastic degradation includes all processes (either natural or synthetic) accounting for changing plastic properties (Yousif and Haddad 2013). Depending upon composition and type, the degradation time of plastics varies like plastic bottles require 400–500 years and grocery bags require 10–1000 years to degrade (Eriksen et al. 2014). Plastics can be degraded by a number of physical, chemical, and biological methods. Physical degradation includes polymer recrystallization or denaturation of protein structures and exposure to ultraviolet rays which refer to the polymer breakdown by photooxidation, releasing different chemical compounds and radicals, decreasing molecular weight leading to polymer destruction, and converting it into a more hazardous form. Several procedures like photochemical and thermal degradation can be used for the biodegradation of polythene (Lu et al. 2009). Plastic accumulation in our environment is a very serious concern, and its accumulation in the environment is causing long-term problem to living organisms and their habitats. It is actually destroying the natural habitat of flora and fauna, especially those in the aquatic environment (Restrepo-Flórez et al. 2014). Degradation of plastic mainly occurs by three processes which are physical, chemical, and biological degradation process (Yousif and Haddad 2013). The biodegradation of plastics occurs actively, depending on their properties, under different conditions, and degrading microorganism varies from one another and has its own optimum soil and water growth conditions. Ecological factors such as humidity, pH, temperature, salinity, aerobic and anaerobic conditions, solar light, water, pressure, as well as plant environment not only affect the degradation of polymers but also have a critical impact on the microbial community and enzymatic activity (Nigam 2013).

Plastic biodegradation requires adherence of the microbes to the polymer layer, microorganism growth by using the polymer as the origin of carbon source, and polythene degradation (Gunatillake et al., 2006). The biological decomposition of plastic, extracellular depolymerization and intracellular metabolism, involves at least two forms of enzymes (Tilman 1977). From the previous work, it is observed that UV due to the synergistic effect of nitric acid and microbial action encouraged an oxidation reaction that improves and increases the rate of LDPE biodegradation (Egli 1995).

14.9 Properties and Applications

PET is semicrystalline thermoplastic polyester (Harrison and Wren 1976). It is produced by different companies under separate trade names. PET is strong and durable, stable both chemically and thermally with low gas permeability, and easy to handle and manage (Ingram et al. 1999). This combined effect of properties makes PET a valuable product for a variety of applications and a considerable component of global plastic usage (Chen et al. 2011). More than 50% of the synthetic fabrics generated globally consist of PET, and global usage of PET has been reported to exceed $17 billion per year (Chen et al. 2011). The Sheets, films, fabrics, food and beverage packaging (especially soft drinks and water bottles), appliances, auto parts, home appliances, lighting products power tools, sports goods, photography devices, X-ray sheets and textiles are products based on the actual use and the desired properties of PET. By controlling the polymerization conditions, PET can be manufactured to specifications (Nigam 2013).

14.10 Pretreatments for Plastic Degradation

It was anticipated that physical treatment may enhance the biodegradation rate (Arkatkar et al. 2009). Physicochemical treatments of the polymer by microbes like fungus lead to oxidation and further breakdown. Thus physicochemical pretreatment of polymers helps in easy assimilation by the microbes (Arkatkar et al. 2009). The oxidized polymer helps in adhesion of microorganisms and easily adheres to the oxidized polymers surface, which become less hydrophobic and it the prerequisite biodegradation.

14.10.1 Physical Methods

The physical treatment strategies involve decreasing the plastic waste through physical methods like crushing (Al-Salem et al. 2009), incineration, and pulverizing. Some of the other treatments of physical mode include thermal treatment, treatment with ultraviolet rays, photooxidative degradation, etc. In addition, these types are responsible for altering the polymer's nature, shape, and structure to some extent (Mohan et al. 2016). Plastic modifications are identified by surface splitting, cracking, polymer disintegration, degradation, decreased polymer weight, discoloration, and gaps on the polymer surface, also referred to as aging.

Mechanical stress is provided by giving high speed or stirring and powdering, splitting, mixing, chopping, crushing, etc.; this mechanical strength breaks the polymer and decreases its molecular bulk (Ahmed et al. 2018). Plastic polymers is complex compounds and microorganisms cannot ability to utilized it directly. The oxidation process reduces the long chain of plastic polymers and make availability to microorganism by reducing its hydrophilic level. It also included UV exposure and provides temperature.

14.10.2 Photodegradation

In order to degrade the larger and complex molecules into simple, smaller particles, high-intensity photon particles are used like ultraviolet radiations to react with the photo reactive groups, so the chains of polymers cleave in a proficient way. Photodegradation is a polymer degradation process that includes placement of films under the sunlight or ultraviolet rays and photodegrade them with time (Moharir and Kumar 2019). Strong bond of polymers is hard to disrupt, but this kind of pretreatment will increase the rate of biodegradation.

14.10.3 Thermal Degradation

Thermal degradation is similar to the photodegradation (Ray and Cooney 2018). Photodegradation includes chemical reactions occurring on the outer surface, while thermal degradation occurs on the greater surface of the polymer (Ray and Cooney 2018). Thermal degradation occurs with heat treatments such as incineration, pyrolysis, and gasification, but treatments such as incineration emit toxic gases, like dioxins and furans which are known to be the main hazards to humans and to the environment as well (Erceg et al. 2018).

14.10.4 Chemical Degradation

Chemical treatment methods depend on different chemicals usage that have capability of splitting plastic polymer's chain and converting it into forms which are nontoxic in nature (Lin and Yang 2009). These methods cannot be used on large scale due to the problem of disposing these chemicals that are used in these methods. Treating plastic polymer with nitric acid enhances the rate of biodegradation (Leja and Lewandowicz 2010). Many previous investigations also reported that providing pretreatment enhanced the rate of biodegradation (Ahmed et al. 2018). Pretreatment may enhance the breaking of polymer bond due to oxidation, and it also improved the hydrophilic level and converted plastics into a more available form which can be easily assimilated by microorganisms (Vimala and Mathew 2016). UV, nitric acid, and temperature exposure are the best ways for physicochemical degradation as reported by Ray and Cooney (2018).

14.10.5 Biological Degradation

Biodegradation is another method for the disposal of plastic waste, it is an environmental friendly technique, and it is more suitable than physical and chemical degradation (Shah et al. 2008). Latest developments have advocated that many organisms (bacterial and fungal species) have the ability to degrade plastics, and in this process, by-products are produced that are nontoxic in nature (Restrepo-Flórez et al. 2014). As no secondary contaminants are produced like landfilling and incineration, this method of treatment is cheap, efficient, and profitable that can be applied on large scale in reactor operation for organic waste treatment (Michaud et al. 2007). Ethanol and biofuels are useful end products of microbial degradation of pollutants (Iranzo et al. 2001). But this technique is not practically applied at commercial scale (Shah et al. 2008).

The natural process of organic and inorganic degradation by microbes into nutrients is known as biodegradation. Degradation is conducted by different organisms (bacteria, algae), insects, and those organisms which eat dead matter and recycle it into new forms. All naturally produce plastic like cellulose, chitin, and PHAs which can be completely broken down by microorganisms. Under natural conditions, polyethylene degrades slowly, or it is nonbiodegradable, and this causes major environmental problems. Nondegradable solid waste such as polyethylene is most commonly used, and increasing the amount of waste in the environment has been a threat to the world (Arkatkar et al. 2009). Decaying of polymer or plastic means any type of physicochemical changes in the plastic construction and nature results from the ecological factors, like light, heat, humidity, biological activities, or any chemical condition (Nigam 2013). Polymeric substances are the potential carbon and energy sources for heterotrophic microorganisms, including bacteria and fungi, in many respects (Ghosh et al. 2013). Biodegradation is defined as the decaying or dissolution of pollutant molecules by microbial actions and secretion of enzyme. Microorganisms biodegrade the polymers which are natural or synthetic. The making alterations mostly deteriorate the sturucture/function of the polymers like bond breakage having biological, physical and chemical reactions and are categorized as polymer degradation processes. (Ghosh et al. 2013). These degradation processes bring changes in the optical mechanical or electrical characteristics, crazing, cracking, discoloration, erosion, or phase separation. The changes comprise bond scission, chemical transformation, and the formation of new functional groups (Nigam 2013).

Biodegradation refers to the degradation or deterioration of complex organic polymer into simpler components by the help of microbes (Restrepo-Flórez et al. 2014). Biochemical or microbial degradation is a novel concept which involves living microbes in the degradation process by expending the enzyme produced by these organisms. In the complete process, these microbes utilize these polymers as their carbon and energy source (Nigam 2013).

Biodegradation happens by enzyme activity and chemical degradation by living organisms. Initially, the breakdown of polymers into smaller molecules, that is, monomers, is through abiotic reactions such as oxidation (Patel and Bhaskaran 2016). Photo degradation also known as hydrolysis, or biotic reactions such as microorganism degradation during this many microbes are active in the presence of oxygen or in the absence of oxygen (Zheng et al. 2005). Environmental factors such as light, temperature, humidity, and chemical conditions also help in plastic degradation. Breakdown of polymers by means of microbes, that is, algae, fungi, and bacteria, is actually chemical degradation material, that is, polymer degradation, so it is a type of degradation involving biological activity (Patel and Bhaskaran 2016). It generally denotes the degradation and accommodation of polymers by living microorganisms to produce degradation products. Biodegradable polymer is then degraded, and carbon dioxide, methane, and biomass are the end products (Zheng et al. 2005).

This is comparatively more suitable method than physical and chemical degradation as it has less or no hazardous impacts and has relatively fast and efficient degradation potential and is an environmentally friendly technique, but yet not practically applied at commercial scale (Shah et al. 2008). Polymer conversion is done by microbes by mineralization, and under aerobic conditions mineralization produces carbon dioxide and water, while in the absence of oxygen, it forms methane and carbon dioxide (Singh and Sharma 2008). In our natural environment, the biodegradation process is performed by different microbes, but their polymer consumption rate is slow (Shah et al. 2008). It is evident that some microbial strains have the potential to degrade the plastic; thus such strains can be employed in the degradation of polymer by providing appropriate controlled environment (Zheng et al. 2005). Both natural and artificial plastic can be utilized effectively by different microbial strains. Degradation is a very complex and slow process. It doesn't start by direct action of microorganisms but is highly influenced by ecological factors, that is, pH, temperature, and UV. The biological degradation is accompanied by solubilization, dissolution, charge formation, enzyme-catalyzed degradation, and hydrolysis (Singh and Sharma 2008).

Microbes are present in all kind of environments where life exists. Different organisms mainly fungi bacteria produce variety of enzymes they also differs between the similar species, and these enzymes also help in degradation of polymer (Zheng et al. 2005). Microbes have special plan for the utilization of plastic as it acts as a carbon and energy source for them. Degradation of plastic waste by means of microbes is the most expedient method of degradation. It is generally based on 2 steps, in the first step adhering of enzyme substrate(polyethylene) occurs and causes hydrolytic cleavage, fungus and bacteria that produces intra and extracellular enzymes and further cause the degradation of polymer (Singh and Sharma 2008).

The most prominent microbes that have the capability of polymer degradation are fungi and bacteria, but both have quite different mechanisms of degradation, and both require different conditions for their growth (Anthony 2016). The assessment of biodegradable nature of plastic can be done by performing the measurement of structural changes by microscope observation or by evaluating the growth of microorganisms after the biological and enzymatic action along with the evolution of carbon dioxide (Anthony 2016). Many microorganisms (bacteria, fungus, and algae) have been isolated with the ability to grow on polyethylene. The effects of these microbes have been described on the physiochemical properties of these polymers, including changes in crystalline, molecular weight, sample topography, and functional groups found on the polythene layer. While several scientists have demonstrated the biodegradation of polyethylene, the enzymes involved and the mechanisms associated with these phenomena remain unclear (Restrepo-Flórez et al. 2014).

Biodegradation is influenced by various factors, including the features of plastic, the type of pretreatment, and the type of organisms. The characteristics of polymers like mobility, tacticity, crystalline nature, molecular weight, the form of functional groups and substituents present in their structure, and the added plasticizers or additives to the polymer all play an important role in their degradation (Hu et al. 2019). Microbes are present in every environment where life exists; different organisms mainly fungi and bacteria produce a variety of enzymes, and they also differ between similar species, and these ten enzymes also help in the degradation of polymer (Zheng et al. 2005). The most prominent microbes that have the capability to degrade polymers are fungi and bacteria, but both have quite different mechanisms of degradation, and both require different conditions for their growth.

14.11 Enzymatic Degradation by Microbial Agents

Different microbial species excrete different enzymes for LDP degradation, such as bacterial enzymes which include laccases, peroxidases, lipases, hydrolases, and glycosidase and fungal enzymes which include catalases, proteases, ureases, hydrolases, laccases, peroxidases, and lipases (Bhardwaj et al. 2013). Different enzyme like Lignin that is a degrading enzyme produced by fungi and manganese peroxidase, that is partially purified from the strain of *Phanerochaete chrysosporium* also aids in the degradation of high molecular weight polyethylene under carbon limited and nitrogen-limited conditions (Restrepo-Flórez et al. 2014).

14.12 Mechanism of Enzymatic Degradation

14.12.1 Lignin-Degrading Enzymes

A number of enzymes are involved in hydrolysis of polymers. These enzymes are laccase, manganese peroxidase, glycol oxidase, lignin peroxidase, sugar oxidase, alcohol oxidase, and quinone oxidoreductase (Martínez et al. 2005). Lignin-degrading fungi release more than 100 laccases to date and can range in size from 60 to 70 kDa (kilo Dalton) (Baldrian 2006). Laccases are copper-containing oxidases that catalyze the electron oxidation of primarily phenolic and lower-redox potential compounds, although they can oxidize non-phenolic compounds in the presence of mediators, such as 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (Martínez et al. 2005). Glycol oxidase, sugar oxidase, and alcohol oxidase are a diverse group of enzymes that also take part in lignin degradation. These enzymes produce H_2O_2, a vital product in ligninase activity through the oxidation of ligninase enzymes (Martínez et al. 2005). Lignin is a plant woody biomass organic aromatic polymer and intransigent to nature degradation. White rot fungi have been widely studied for plastic degradation as the most effective lignin degrading microbes. Polyethylene membrane degradation by lignin-degrading fungus. Under various nutrient conditions, *Phanerochaetechrysosporium, Trametesversicolor,* showed that manganese peroxidase (MnP) is the primary enzyme in polymer degradation.

In the presence of Tween 80, Mn (II) and Mn (III) chelators, partially distilled MnP used for polyethylene surface treatment led to major degradation (Iiyoshi et al. 1998). Four groups, CHO, NHCHO, CH_3, and $CONH_2$ were formed through nuclear magnetic resonance (NMR) examination of bio-degraded nylon-66 with fungus IZU-154 that decay lignin also showed that the nylon66 was decayed oxidatively (Deguchi et al. 1997).

Lignin-degrading fungi primarily secrete laccases, where the oxidation of various polyaromatic compounds is catalyzed. Laccase is also known for nonaromatic substrate degradation (Mayer and Staple 2002). Laccase can also perform oxidation of polyethylene's hydrocarbon backbone. There will be reduction of 20% and 15%, respectively, of the average molecular weight and molecular number of polyethylene when we incubate cell-free lacquers with polyethylene (Bhardwaj et al. 2013). The degradable polymer (comprising pro Oxidant and 6% starch) was allowed to treat with *Phanerochaete chrysosporium, Streptomyces viridosporus* T7A, *S. badius* 252, *S. Setonii*75 Vi2 among them *Streptomyces viridosporus* T7A treated plastic showed a 50% decline in tensile strength.

The ability of *Pleurotus ostreatus* to break down oxo-biodegradable plastics without prior physical intervention, such as UV or thermal heating, racks, and small holes was formed on the surface of plastic from the formation of OH groups and C-O bonds after the incubation period of 45 days. In fact, the dye deterioration in such bags has been noted. La and MnP enzymes secreted by polyethylene can be degraded through *Chaetomium globosum* fungus (Sowmya et al. 2015). Various biological mechanisms such as chemical, thermal, photo, and biodegradation play their role in polyethylene deterioration (Shah et al. 2008). Microbes as part of secondary metabolism have a natural capability to convert or absorb mass of substances, including hydrocarbons (PAHs), pharmaceutical products, and metals. Plastic polymer build functional groups by solubilizing through enzymes to enhance hydrophilicity, and the main polymer chains are weakened, which results in bad mechanical properties and in low molecular weight polymers which makes them more available for further microbial incorporation (Shah et al. 2009).

Biodegradation of plastics often contributes to the breakdown of polymers by certain enzyme systems into oligomers and monomers or further transformation into organic intermediates (such as acids, alcohols, and ketones) (Arkatkar et al. 2009). Microbial cells absorb these water-soluble cleaved products where they are metabolized. After aerobic metabolism, CO_2 and water formed, while anaerobic metabolism produced carbon dioxide, water, and methane as end products. The polymers mechanically breakdown through dome physical variables like pressure, temperature, and humidity by which the process is stimulated by biological agents such as enzymes as well as other metabolites.

Plastic biodegradation due to difficulties in penetrating extracellular enzymes into the plastic polymer is usually called surface degradation, therefore acting only on the surface of the plastic polymer. Plastic degradation is when the pro-oxidants catalyze the formation of free radicals in polyethylene that react to the polyethylene matrix with molecular oxygen. The enzymatic hydrolysis degradation of plastic polymers is a two-step process: Initially, the enzyme attaches to the substratum of the polymer and then catalyzes a hydrolytic cleavage. Intracellular deterioration is the hydrolysis of an endogenous carbon supply by the growing microbe itself, whereas extracellular degradation does not necessarily require the use of an exogenous carbon source. La and MnP enzymes secreted by *Chaetomium globosum* fungus were responsible for the degradation of plastic polymer (Sowmya et al. 2014).

14.12.2 Laccases

Laccase enzyme is a benzene diol, a multi-copper enzyme and one of the three main ligninases. Laccase catalyze the oxidation of wide range of phenolic substrates including diphenols, polyphenols, substituted phenols, diamines, and aromatic amines, with the reduction of molecular oxygen to water. Laccase is widely present in the number of bacterial fungal and plant species as well. Laccase is involved in the degradation of lignocellulose substances, plant pathogenesis, and pigment production; they also act as oxidizing agent for variety of inorganic and organic compounds like aromatic amines, substituted phenols, diphenols, polyphenols, and diamines with associated reduction of molecular oxygen to water; in recent studies laccases are also being used in industrial applications like biopolymer modification, bioremediation, bleaching agent in textile industry, detoxification of effluent, and pulp lignification. For industrial application discovery of novel laccases with variety of substrate specifications is very important that makes them highly useful biocatalysts for various biotechnological applications.

14.13 Plastic Biodegradation Analysis Techniques

Biodegradability of polyethylene can be described through tracking the modification of CO_2, the intake of O_2, improvements in the attribution of polymers (physicochemical), and the maturing of species. Several experiments could be carried out to assess plastic degradation for the mentioned purposes (Mohan and Shrivastava 2010). Loss of weight may be caused by chemical leaching, including plasticizers. The degradation of polymers having low molecular weight fraction without degrading long chains can result in the development of carbon dioxide. Very minor changes in the chemical composition or skipping any additives of plastics affect the quality of plastic. To check the level as well as nature of decaying, there are a number of techniques that are available.

14.13.1 Mechanical Properties

The Tensile strength-Elongation at fail and modulus of the plastic polymer is mostly examined by dynamic mechanical Analysis (DMR).

14.13.2 Physical Properties

Morphology, that is, micro cracks, are analyzed by scanning electron microscope (SEM).

14.13.3 Chemical Properties

Chemical properties are determined by Fourier transform infrared spectroscopy (FTIR).

14.13.4 Molecular Weight

The thin layer Chromatography (TLC), Chemilluminesence, Gas Chromatography-Mass Spectrometry (GC-MS), Gas Chromatography (GC), Nuclear Magnetic Resonance (NMR), Matrix Assisted Laser Desorption Ionization-Time of Flight.

14.14 Mechanism of Plastic Biodegradation

Different microorganisms like algae, fungi, and bacteria produce different chemicals like mucilaginous substances by algae, while bacteria and fungi produce laccases, hydrolases, PETases, peroxidases, and lipases which help in cleaving the polymer structure into simpler and available form for microbes as reported by Bhardwaj et al. (2013). Lignin-degrading fungi secrete laccase enzyme having capability to break the complex structures like aromatic and polyaromatic compounds. Meanwhile, laccases are also involved in degradation of nonaromatic compounds (Restrepo-Flórez et al. 2014).

Different microorganisms produce a variety of enzymes, and they also differ between the similar species, and these enzymes also help in the degradation of polymers like plastics (Zheng et al. 2005). Microbes have a special plan for the utilization of plastic as it acts as a carbon and energy source for them. Degradation of plastic waste by means of microbe is the most expedient method of degradation. It is based generally on two steps; in the first step adhering of enzyme to substrate (polyethylene) occurs, and the second involves the hydrolytic cleavage as fungus and bacteria produce intra- and extracellular enzymes that further cause the degradation of polymer (Singh and Sharma 2008). Recently, it has been reported (Kumar et al. 2017) that the most dominant microalgae were S*cenedesmus dimorphus* (green microalga), *Anabaena spiroides* (blue-green alga), and *Navicula pupula* (diatom). It was shown that polyethylene sheet showed the proliferation of microalgae in both outer and inner sides, and the erosion cum degradation was obvious.

14.14.1 Microbial Growth and Plastic Degradation

It was evident that the microbial species produced biofilms on the surface of PET plastic during the current study and the growth of microbes on plastic films was efficient when provided with pretreatment. The growth of various microbial species like bacteria, fungi, microalgae, and lichens on plastic was regarded as a milestone in plastic biodegradation. It was evident from compound microscopy and scanning electron microscope (SEM) analyses that microbes were able to grow on cracks and fishers created during pretreatment. Very few literature is published on the PET biological degradation or its utilization to support microbial growth. Rare examples are members of the filamentous fungi *Fusarium oxysporum* and *F. solani*, which have been shown to grow on a mineral medium with PET yarn (although growth rates have not been given). Once identified, microorganisms with the enzymatic machinery needed to break down PET could serve as an environmental remediation strategy as well as a breakdown and/or fermentation platform for the biological recycling of PET waste products. The use of PCL as a selective isolation substrate deserves a comment. Cutinase, a serine esterase secreted by many phytopathogenic fungi, including *F. solani f. sp. pisi* (Murphy et al. 1996), may have a low substrate specificity. Certain cutinases hydrolyze cutin and can also degrade PET (Lin and Kolattukudy 1978). Cutinase is induced by cutin or suberin (Murphy et al. 1996) and can be repressed by glucose (Lin and Kolattukudy 1978). On this general basis, PCL hydrolysis has been used as an initial screen to study fungal isolates that produce enzymes that may be active on aromatic synthetic polyesters such as PET. Esterases and cutinases from various fungi and bacteria can hydrolyze ester bonds in PET (Muller et al. 2001; Nimchua et al. 2007).

Regarding PET degradation by microalgae, a recent report showed that diatoms (a group of microalgae) have the ability to degrade PET through the production of the enzyme PETase under eosinophilic marine conditions (Moog et al. 2019). Another aspect of the biodegradation of plastic is the development of efficient closed or open loop recycling strategies for TPA (and EG) in order to synthesize new PET from its own degradation products through to further metabolism.

Engineering microalgae metabolism to create cells that can fully metabolize PET and use it as a carbon source (Moog et al. 2019). The same authors suggested that physically treated PET can be efficiently biodegraded by enzymes such as PETase, which are produced by microalgae such as diatoms. Once an enzyme such as PETase or laccase has started to break down PET, it is speculated that its by-products may be further affected by some other enzymes produced by other microbial consortia in the same environment. down PET, it is speculated that its by-products may be further affected by some other enzymes produced by other microbial consortia in the same environment.

14.14.2 Products of Microbial Degraded or Treated Plastics

Previous research has demonstrated that carbon dioxide is the prime product released through polythene biodegradation. The production of aldehydes, ketones, and carboxylic acids was reported in LDPE film extrusion smoke in the extrusion coating. *Rhodococcus rubber* (C208) generated polysaccharides and proteins using polythene as a carbon source in another study. *Rhodococcus rhodochrous* ATCC29672 (bacterium) and *Clados* produced polysaccharides and proteins. *Rhodococcus rubber* (C208) formed polysaccharides and proteins using polythene as a carbon source (Sivan et al. 2006). In one more study, *Rhodococcus rhodochrous* ATCC29672 (Bacterium) and *Cladosporium cladosporioides* ATCC 20251 (fungus) utilized polythene to generate polysaccharides and proteins, while *Nocardia asteroides* GK911 (bacterium) generated proteins only.

14.15 Conclusion

Different pretreatment and cohesive methods with the most effective species are very helpful in the degradation of plastic. The use of different efficient species on different types of plastic and examine which plastic type can be more easily degraded. In order to understand the complete process of biodegradable plastics over a longer period of time, prolonged biodegradation studies on plastics using selected microorganisms should be carried out.

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Chapter 15
Treatment Technologies for the Environmental Micro-pollutant

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Abstract Advance studies related to MPs contamination along with their metabolites are detected in the aqueous environment throughout the world. Their biological nature and continuous emission render them as "prospective pollutant" or "emerging pollutants." The major categories of MPs are divided into eight groups. For the absolute removal of MPs and their metabolites, there is no specific technique and is quite difficult and somewhat impossible because of their distinctive properties. The emission of MPs in large amounts in different aqueous bodies in different parts of the world renders a serious threat to the aquatic as well as human ecosystem. So, the most applicable methods used for MPs are activated carbon absorption, coagulation-flocculation, advanced oxidation process, and ozonation membrane bioreactor and membrane process. The typical WWTPs cannot provide the expected results for the elimination of significant MPs. However, with little efforts, upgrading and optimizing the current protocols in the WWTPs is all set to crucially decrease the loading rates of MPs. Besides all the conventional techniques and processes, advanced oxidation processes (AOPs), activated carbon adsorption (granular activated carbon and powdered carbon), coagulation-flocculation, membrane bioreactor, and membrane process are also applied for the removal of MPs. Among all these persistent treatment methods, advanced oxidation processes and membrane systems are the most efficient techniques and come to the forefront. For both removal of micro-pollutant and inhibiting the production byproducts and metabolites and other pollutants, a combined treatment should be preferred to achieve the desired results.

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants,*
Health Impacts and Allied Treatment Technologies, Emerging Contaminants and
Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5_15

15.1 Introduction

Among different pollutants micro-pollutants (MPs) are defined as anthropogenic chemical compounds that mainly occur in the aquatic environment quite above the natural substantial background level mainly because of urbanization and human activities in modern as well as developing worlds but with concentrations so minute that is found to be in trace levels (i.e., up to μg/L range). Therefore, MPs are specifically defined by their occurrence in low concentration level and anthropogenic origin. Billions of natural as well as anthropogenic chemicals fall into this group of pollutant. Few decades back, the occurrence and concentration level of MPs in the aquatic environment have become an alarming global issue of increasing ecological concern. MPs are also termed as emerging contaminants, engulfing a vast and expanding category of natural as well anthropogenic substances (Stamm et al. 2016). As of today, majority of the countries in the First World have successfully been able to reduce the overall level of MPs in the aquatic environment by legalizing and adopting appropriate effective measures. Consequently, the focus has been shifted to this emerging class of contaminants because of their hazardous nature to the elements of the biotic sphere. Ample of research found that it is not only the pollutants that have been introduced into the environment most recently but also the advancement in the development of analytical techniques and protocols that made it possible to detect such substances despite their minute concentration in the aquatic environment (Brack et al. 2015; Gavrilescu et al. 2015; Guibal et al. 2015).

The significance of MPs in the environment is not essentially due to persistency but because of their biological nature and continuous emission render them as “prospective pollutant” or “emerging pollutants.” Advance research found that billions of MPs along with their metabolites have been detected in aqueous bodies all around the world (Escher et al. 2014). Meanwhile the existence of these MPs is very low in the aqueous environment and unlikely results into acute toxicity, but it is concluded that their long-term presence may cause chronic health conditions (Schriks et al. 2010). One study conducted in Germany detected the concentration up to several μg/L of about 55 active pharmaceuticals with nine metabolites in the wastewater of about 49 sewage treatment plants. Similarly, wastewater of several European treatment plants was analyzed, and the result detected about 27 pharmaceutical compounds and four metabolites, with the highest average concentration of about 1.0 μg/L (Larsen et al. 2004). Many of the detected MPs were active pharmaceutical components, additives, excipients, and EDCs. These concluded results are alarming, but the situation is even worse in the developing countries, where the concentration and the number of many MPs have been detected exceedingly high. This can be mainly attributed to the fact that in the developing countries, the majority of these MPs are being sold as off-exchange products, consequently resulting in increasing levels in the aqueous environment (Garcia-Galan et al. 2016). At the end, the widespread scientific viewpoint concluded that a more advanced management approach should be developed and implemented all around the globe (Brack et al. 2015). Yet precise management approach and legislation regulation for the safe permissible level of MPs in the environment needs a further understanding of their fate and distribution, and concerning their harmful effects should also be characterized. This may include the transformation mechanism of several MPs in the environment, the level of toxicity they cause in living organisms, and significant effect on the ecosystem along with the remediation strategies.

15.2 Transport and Sources of MPs in Environment

Micro-pollutants accumulated in the waterbody have a diverse origin, among which the domestic waste effluents are the main source from surface water. In the aquatic environment, pharmaceuticals which are detected frequently mainly originated from convenience stores, drug stores, and hospitals. The main drawback of such chemicals is that they are available without a prescription (i.e., ibuprofen, aspirin, naproxen, acetaminophen). However, these medicines are mainly produced for healthcare purposes for humans and animals, but they are not completely metabolized in the body (Thomas and Foster 2005). Both the residual medicine and their metabolites are excreted by animals and humans into the wastewater. Moreover, the source of waste can be from the manufacturing industries and also expired medicines. Pathways and sources of PMs in the urban water cycle are shown in Fig. 15.1.

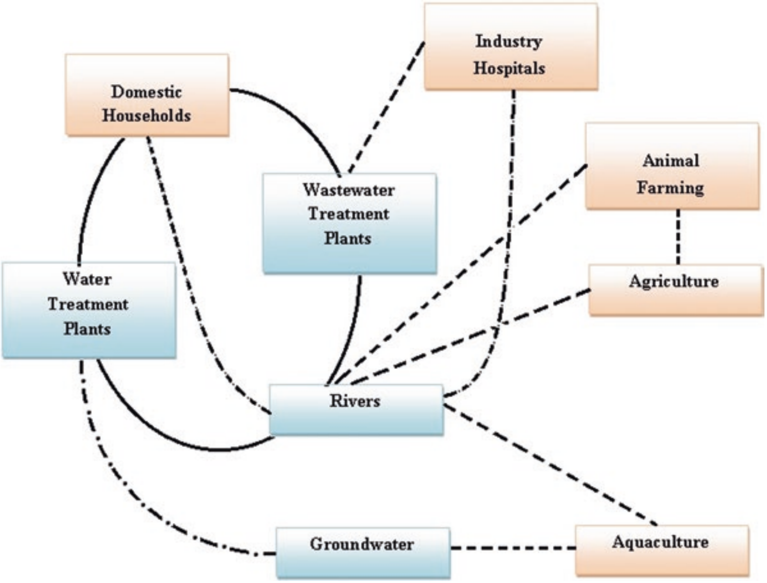

Fig. 15.1 Pathways and sources of PMs in the urban water cycle. (Ellis 2006)

EDCs consist of natural hormones, nonylphenol, insecticides, and bisphenol A, considered as significant MPs. Release of such compounds is from raw materials like flame retardants and plastics. But these compounds can also directly be generated by humans (Poulsen et al. 2005; Prevedouros et al. 2006). These compounds have hormone-like properties, and these EDCs have adversely affected the human health (Sonnenschein and Soto 1998; Ellis 2006). Excretion of these compounds from the human body into the sewage is directly discharged into the water system nearby like lakes and rivers. Therefore, waste from sewage is commonly considered a major source of MPs.

The physical and chemical properties and the bioavailability can influence the existence of MPs in the aquatic environment. A study conducted by Caliman and Gavrilescu evaluated and categorized the elimination and generation of MPs based on some significant factors, that is, environmental factors, physicochemical properties, accumulation and transformation, retention, and transport (Caliman and Gavrilescu 2009).

Moreover, it has been observed that the physical properties of MPs can influence the mobility of pollutants from one phase to another (e.g., soil-water movement). Precipitation, sorption, colloid formation, and complexation all contribute to the retention of MPs. The significant mechanisms of transport consist of dispersion, diffusion, active transport, and advection. The transformation processes, also called the decomposition of the parental compounds as a byproduct, are ineffective to prevent the complete reaching of MPs into the natural environment. In the application of adequate conversion processes to treat the wastewater, it is very difficult to control the concentration of MPs in the marine environment to be accumulated and emitted (Moon-Kyung and Kyung-Duk 2016).

15.3 Categories of MPs in Aquatic Environment

The major categories micro-pollutants in the aquatic environment are divided into eight groups, that is, personal care products (PCPs), agriculture, detergents, and perfluorinated compounds (PFCs), additives, flame retardants, new class, human pharmaceuticals and veterinary drugs, and endocrine disruptive chemicals (EDCs).

15.3.1 Personal Care Products (PCPs) (Table 15.1)

Table 15.1 Class, mode, and fate of PCPs

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Personal care products (PCPs)	Fragrances and synthetic musks	Direct disposal of industrial effluents and shower waste	Terrestrial runoff freshwater, wastewater treatment plants, estuaries, and sediments	Musk ketone, galaxolide, polycyclic and macrocyclic musks, tonalide	Ellis (2006) and Verlicchi et al. (2010)
	Antiseptics			Chlorophene Triclosan	
	Stimulants			Caffeine	
	UV filters			Methylbenzylidene camphor, Benzophenone	
	Antihypertensive			Diltiazem	
	Insect repellents			N,N-diethyltoluamide	

15.3.2 Agriculture (Table 15.2)

Table 15.2 Class, mode, and fate of agriculture

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Agriculture	Pesticides	Agricultural waste	Water and soil	DDT, chlordane, aldrin	Ellis (2006) and Verlicchi et al. (2010)
	Herbicides			Terbuthylazine, diuron, mecoprop	

15.3.3 Detergents and Perfluorinated Compounds (PFCs) (Table 15.3)

Table 15.3 Class, mode, and fate of PFCs

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Detergents and perfluorinated compounds (PFCs)	Perfluorooctanoic acid	Households, pesticides, industries, laundries, agricultural applications in dispersants and pesticides	Sewage treatment plants	Alkylphenol carboxylates, alkylphenols (octylphenol and nonylphenol)	Ellis (2006) and Verlicchi et al. (2010)
	Perfluorooctane sulfonate				

15.3.4 Additives (Table 15.4)

Table 15.4 Class, mode, and fate of additives

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Additives	Gasoline	Disposal of exhausted engine oil and mobile exhaust	Water, soil, and air	Methyl t-butyl ether, dialkyl ethers	Ellis (2006) and Verlicchi et al. (2010)
	Industrial	Municipal waste and food resources		Aromatic sulfonates, chelating agents (EDTA)	

15.3.5 Flame Retardants (Table 15.5)

Table 15.5 Class, mode and fate of flame retardants

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Flame retardants		Industries and household stuff (electronics, baby products, furniture, appliances)	Dry and wet disposition on sediment and soil that leads to bioaccumulation in the food chain	Hexabromocyclododecane, diphenyl ethers, tetrabromobisphenol A tris(2-chloroethhyl) phosphate, C10–C13 chloroalkanes, polybrominated	Ellis (2006) and Verlicchi et al. (2010)

15.3.6 New Class (Table 15.6)

Table 15.6 Class, mode, and fate of new class pollutants

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
New class	Antibiotic resistance genes	Genetic adaptation and mutations	Transfer of horizontal gene in microorganisms	tet (O), tet (W), sul (I), sul (II)	Ellis (2006) and Verlicchi et al. (2010)
	Nanomaterials	Research institutes	Water		

15.3.7 Human Pharmaceuticals and Veterinary Drugs (Table 15.7)

Table 15.7 Class, mode, and fate of pharmaceuticals and veterinary drugs

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Human pharmaceuticals and veterinary drugs	Antibiotics	Hospital disposal/ discharges, farmland waste, accidental spills	Groundwater, streams, river and wastewater treatment plants	Cefazolin, ciprofloxacin, erythromycin, lincomycin, amoxicillin, chlortetracycline, norfloxacin, doxycycline, penicillin	Ellis (2006) and Verlicchi et al. (2010)
	Antidiabetics			Glibenclamide	
	Analgesics			Acetylsalicylic acid, diclofenac, ibuprofen, indomethacin, acetaminophen, codeine, dipyrone, ketoprofen, paracetamol, mefenamic acid naproxen	
	Blood lipid regulators			Bezafibrate, etofibrate, fenofibric acid, atorvastatin, clofibric acid, pravastatin, gemfibrozil	
	Cardiovascular drugs (β-blocker)			Metoprolol, sotalol, atenolol, propranolol, timolol	
	Psychiatric drugs			Gabapentin, salbutamol, phenytoin, primidone, carbamazepine, diazepam	
	Veterinary drugs			Flunixin	
	X-ray contrast agent			Diatrizoate, iopromide, iopamidol	
	Drugs of abuse			Cocaine, tetrahydrocannabinol, amphetamine	

15.3.8 Endocrine Disruptive Chemicals (EDCs) (Table 15.8)

MPs are commonly found in water bodies at very low concentrations, ranging from a few mg/L to more than a few μg/L. The "minimum concentration" and the vast variety of MPs are not only difficult to detect by the associated analysis procedure but also generate challenges for wastewater and drinking water treatment processes. Wastewater treatment plants (WWTPs) nowadays are not designed specifically to eliminate MPs. Consequently, the majority of these MPs are able to pass through the treatment methods used for wastewater because of their continuous introduction and significance of persistency. Furthermore, monitoring actions and precautions for MPs have been fully implemented in majority of the wastewater treatment plants (WWTPs) (Bolong et al. 2009). So, as a result, the fate of most of these MPs lies within the aquatic environment, where they pose great threats to the biological ecosystem and also create mass trouble for the drinking water plants. The occurrence of MPs in the marine environment has been most commonly associated with a large number of harmful effects which consist of long-term and short-term toxicity and microorganisms resistant to antibiotic and disrupting effects of endocrine (Fent et al. 2006; Pruden et al. 2006).

Currently, for most of the micro-pollutants, standard protocols and discharge guidelines do not exist. In order to set proper guidelines and standard permissible limits for significant MPs, further advanced research on the biotic responses to these pollutants (including long-term and short-term toxic effects) is of utmost importance. Furthermore, the regulatory and scientific communities should provide insight into the impact of each of the MP and also their antagonistic and synergistic effects. Throughout the globe many research articles have been published regarding the occurrence of emerging MPs in different aquatic environments and water bodies such as groundwater (Deblonde et al. 2011) and wastewater (Lapworth et al. 2012) as well as effective treatment methods for the removal of MPs (Bolong et al. 2009). Additionally, researchers reviewed the removal of pharmaceutical and its efficiency by the conventional activated sludge systems by analyzing the municipal wastewater (Verlicchi et al. 2010). Similarly, Ze-Hua et al. (2009) studied the significant biological, chemical, and physical removal of endocrine-disrupting compounds. Moreover, no data have been recorded yet concerning the comprehensive summary of the occurrence of such miscellaneous MPs in the aquatic environment and also the removal of significant MPs in advanced treatment processes.

Table 15.8 Class, mode, and fate of EDCs

Micro pollutant	Class	Mode of entry	Fate	Examples	Author
Endocrine disruptive chemicals (EDCs)	Steroids and hormones		Groundwater and soil	Estriol, diethylstilbestrol, estradiol, androstenedione, ethinylestradiol, estrone, testosterone, progesterone	Ellis (2006) and Verlicchi et al. (2010)

15.4 Environmental Effects

Environmental risks and effects posed by MPs mainly depend on their chemical and physical speciation and affinity for water and solid matter, which can cause a significant change and impact on their bioavailability. Moreover, the danger of such MPs for the biotic entities is also dependent on the mobility and their ability to accumulate and end up in the food chain. In recent studies, it has been revealed that contaminants get accumulated in the tissues of marine organisms mainly by suspended matter or ingesting water. Results however concluded that the concentration level of MPs in the tissue of marine organisms may be recorded at a level comparable with the concentration level found in the marine environment or even more. The vast variation in the ecological conditions in different aqueous regions can also influence the bioavailability. Conditions such as temperature, pH changes, salinity, and turbidity can be illustrated. Additionally, the physicochemical parameters along with the species sensitivity can change the ability to bioaccumulate the malicious pollutant. The majority of different MPs have different potential levels to bioaccumulate, even when they are being exposed to the same concentration level of a specific pollutant. Similarly, individuals of one species belonging to a specific group when exposed to an equal concentration of contaminants during the same period of time cannot possibly accumulate the contaminant at the same rate. It is associated with many factors such as individual size, age, sex, and other physiological condition of the organism (Garnaga 2012).

The current data recorded for the concentration of MPs in the treated effluents are quite low in order to assess the risk posed to the marine ecosystem. Target and nontarget compounds after being chemically analyzed provided only a little information about the significant danger associated with MPs to the human life and the surrounding environment. Furthermore, the analysis and detection of nontarget elements posed difficulties for a research analyst. Despite the fact that in treated sewage effluents a complex mixture of MPs is present along with transformation and degradation of MPs is also occurring, therefore it is difficult to foresee the hazard associated with this type of approach, which is entirely based on the criteria for each of the chemical substance (Fang et al. 2017). Most of the MPs in the treated wastewater that are present exhibit toxic properties. Therefore, the major detrimental consequence of MPs is basically attributed to the potential sublethal and acute toxicity effects on the marine biota. Several studies on ecotoxological provided the desirable results and seem to be an effective and suitable tool for assessing the negative impacts arising from the treated wastewater flooded with MPs. In certain marine ecosystems, the occurring results reflecting from the ecotest are posing the actual threat to the organisms. They are performed in less time, and the need of specialized analytical tools and analyst is excluded. Ecotoxicity experiments are carried out on a biological sample, that is, a population of a specific species of organism, exposed to certain modifications, that is, a particular contaminant for a period of time. Advance studies associated with the ecotoxicological studies are based on marine organisms, that is, bacteria, macrophytes, mollusks, crustacean, algae, and fish.

Furthermore, it is highly recommended to perform experiments incorporating different species that represent several trophic levels (Tran et al. 2018).

Research studies made in decade back revealed that many of the MPs identified have a great potential to interrupt the endocrine processes in many organisms. These chemicals are termed as endocrine-disrupting chemicals (EDCs). Basically, EDCs are occurring naturally as well as anthropogenically in the environment. The definition adopted by the World Health Organization (WHO) is that EDCs are exogenous and a mixture of EDCs compounds have the ability to disrupt the function of the entire endocrine system which will consequently show negative responses in an individual organism or affect their offsprings or in the entire subpopulation. The EDCs belong to different families and are being able to disturb the natural hormonal system by counteracting or mimicking as a natural hormone in the organisms that are exposed to such chemicals (Huerta et al. 2016). At present estimation, there are about a hundred thousand of emerging compounds among which thousand are EDCs (Gore et al. 2014). Those chemicals may include bisphenol, phthalates, brominated flame retardants, polychlorinated biphenyls (PCBs), organic tin compounds, and some pesticides (Kima et al. 2015). Standard protocols for the biological treatment of waste effluents incorporated in a typical WWTPs result only to remove a certain fraction of compounds from the entire group of EDCs, comprising mainly of polar nature (Välitalo et al. 2016). The presence of EDCs is detected in samples taken from the surface water as well as in the groundwater. This observable fact is alarming due to EDCs, when released into the water bodies are more likely to affect the biotic entities, even when they are present at very low concentration (Kima et al. 2015). Ample of literature reported that even at very low concentrations EDCs can cause a very adverse effect on the marine environment. One study reported that zebrafish were susceptible to estradiol at a concentration very low, that is, 0.2 ng/L (Westerlund et al. 2000).

15.5 Treatment Technologies for Micro-pollutant Removal

For the complete elimination of MP groups, there is no specific technique and is quite difficult and somewhat impossible because of their distinctive characteristics. The treatment methods cannot remove both MPs and bulk compounds with a maximum efficiency rate. The most applicable treatment technique used for MPs is activated carbon absorption (GAC and PAC), coagulation-flocculation, advance oxidation process (AOPs) and ozonation, membrane bioreactor (MBR), and membrane processes.

15.5.1 Coagulation-Flocculation

Coagulation-flocculation treatment process is generally used to eliminate most of the dissolved particulate matter and colloids. Table 15.9 represents the removal efficiencies of some of the significant MPs processed by the coagulation-flocculation process.

Commonly, the coagulation-flocculation treatment procedures are ineffective for the removal of most of the MPs. A study is conducted by Matamoros and Salvadó (2013) to evaluate the elimination efficiency of MPs in a coagulation-flocculation. Similarly, a maximum elimination efficiency recorded was 50% in treated hospital wastewater by the process of coagulation-flocculation, and a significant reduction was recorded up to 80% of compounds such as musk, that is, tonalide and galaxolide. Similarly, other elimination efficiencies were 23%, 42%, and 46% for ibuprofen, naproxen, and diclofenac, respectively. Another similar study was done by Asakura and Matsuto (2009) which concluded that by the treatment technique of coagulation, the removal of bisphenol A was not very effective for the treated landfill effluents, but comparatively results for MPs such as nonylphenol (90%) and DEHP (70%) were quite impressive.

Taking into account, all the techniques and process of coagulation-flocculation provided a minimum elimination efficiency for majority of MPs except for some significant pharmaceuticals and musk, that is, nonylphenol and diclofenac. This procedure also showed poor results for the pesticides. Moreover, neither the temperature factor nor the dose of coagulant effect of the removal of pesticide substantially was recorded in various studies (Thuy et al. 2008). The chemical composition of wastewater, when treated by the coagulation-flocculation processes, influences the elimination rates of MPs either positively or negatively. However, the waste effluents have a huge content of fats that enable to remove large amounts of

Table 15.9 Eliminations of some MPs during coagulation-flocculation progression

Coagulant	pH and dosage	Compounds	Removal efficiency (%)	Author
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Diclofenac	21.6 ± 19.4	Surez et al. (2009)
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Carbamazepine	6.3 ± 15.9	
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Tonalide	83.4 ± 14.3	
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Ibuprofen	12.0 ± 4.8	
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Naproxen	31.8 ± 10.2	
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Sulfamethoxazole	6.0 ± 9.5	
$Al_2(SO_4)_3$/ $FeCl_3$	7 and 25, 50 ppm	Galaxolide	79.2 ± 9.9	

hydrophobic compounds (Surez et al. 2009). However, due to the fact that the dissolved humic acid maximizes the elimination rates of common pharmaceutical compounds such as ibuprofen, diclofenac and bezafibrate (Vieno et al. 2006). On the other hand, the suspended organic matter in the waste effluents may block the elimination of MPs (Choi et al. 2008). Factors like pH, temperature, alkalinity, and mixing conditions also affect the efficiency of coagulation-flocculation (Alexander et al. 2012).

15.5.2 Activated Carbon Adsorption

Basically, the treatment technique of activated carbon adsorption (ACA) is used to control odor and taste in treated water, especially in drinking water. ACA techniques provide better removal of more specifically the secondary waste effluents for treatment. ACA procedure when compared to coagulation-flocculation is more efficient in the elimination of MPs from the treated wastewater (Choi et al. 2008). Furthermore, granular activated carbon (GAC) and powdered activated carbon (PAC) have been widely applied for the adsorption purposes. The efficient elimination of MPs is dependent on the properties and type of adsorbate and also the adsorbent used (Kovalova et al. 2013).

15.5.3 Powdered Activated Carbon (PAC)

Removal of biodegradable organic compounds and resistant compounds when treated with powdered activated carbon (PAC) is considered an exclusive and effective adsorbent. One of the main advantages of using PAC is that they supply continuously fresh carbon, and that in turn can be utilized in certain prevailing circumstances, that is, when the level of contaminant rise in water (Snyder et al. 2007). One research was conducted by Kovalova et al. (2013) in which PAC procedure was applied to evaluate the elimination efficiency of MPs in the treated effluents taken from the MBR hospital wastewater. In the conducted study, PAC dosages were chosen as 8 mg/L, 23 mg/L, and 43 mg/L, and the time selected for retention was about 2 days. Results for the study revealed that PAC adsorbent provided substantial elimination efficiency, especially for metabolites, industrial chemicals, and pharmaceuticals. The removal rate of total load was recorded as 86%. In another study batch tests were conducted and concluded that the high removal rate was >94 % for bisphenol, personal care products, and nonylphenol (Hernandez-Leal et al. 2011).

The removal efficiency of PAC reactors for many MPs also depends on many factors like contact time, physical properties of targeted contaminants, PAC concentration/dosage, and water composition (Snyder et al. 2006; Boehler et al. 2012). Similarly, a research study is conducted by Westerhoff et al. (2005), and they observed in their experiments that at the higher dosage of PAC (i.e., 20 mg/L), the elimination efficiencies of MPs were quite impressive regardless of their initial MP concentration. So it was concluded from the study that the addition of PAC in the wastewater treatment plants seems to be an efficient way for the elimination of majority of micro-pollutants in unit time (Bolong et al. 2009).

15.5.4 Granular Activated Carbon (GAC)

Rossner et al. (2009) assessed that the dose of about <10 mg/L of granular active carbon (GAC) was used in order to control the taste and odor of drinking water. The dose used was sufficient enough for the treatment of lake water and the majority of compounds were removed, providing an elimination efficiency of about 99%. Elimination efficiencies of pharmaceuticals and steroidal estrogen were evaluated and found to be in a full-scale GAC plant for the treatment of wastewater. Maximum removal rates were recorded for steroidal estrogens, but the removal rates recorded for pharmaceuticals were found to be very low. More specifically, the elimination efficiencies of indomethacin, diclofenac, and mebeverine ranged from 84% to 99%. However, the elimination efficiencies of propranolol and carbamazepine ranged from 17% to 23% (Grover et al. 2011). Evaluating PAC the contact time of GAC also influenced the efficiency rates. The minimum contact time of GAC reactor decreased its adsorption performance. More specifically, the removal of contaminants depends upon the association between contaminant and particle and pore blocking (Bolong et al. 2009). So treating high contaminated waste effluent with GAC provides very poor results. Overall study results showed that PAC and GAC processes can be considered as efficient techniques for the removal of MPs from the treated wastewater. Moreover, maximum elimination rates of MPs can be achieved by some significant factors such as shape of contaminant, its high compliance of pore size, and its nonpolar characteristics (Rossner et al. 2009; Verlicchi et al. 2010). However, the blocking of pores is basically due to the existing organic matter (OM) that minimizes the efficiency of active carbon (Table 15.10).

15.5.5 Ozonation and Advanced Oxidation Processes

Conventional biochemical and physicochemical actions are not effective for the elimination of major MPs due to their determined structure. In such type of cases, advanced oxidation process and ozonation are the solution considered. Having more degradation rates, the stated technology is not selective to remove contaminants. Besides this, these procedures have an effect of disinfection for water to reuse (Hernandez-Leal et al. 2011). Ozone destroys the pollutants directly or indirectly, but most of the time by producing the hydroxyl (OH), which is strong enough and less choosy for the emerging compounds. The nature of most of the MPs are very

Table 15.10 Elimination of MPs during the process of adsorption

Adsorbent	Dosage mg/L	Contaminants	Removal efficiency (%)	Author
PAC	8, 23, and 43	Sulfamethoxazole	2, 33, 62	Grover et al. (2011) and Kovalova et al. (2013)
PAC	8, 23, and 43	Diclofenac	96, 98, 99	
PAC	8, 23, and 43	Carbamazepine	98, 99, 100	
PAC	8, 23, and 43	Propranolol	>91, >94	
GAC	Full scale	Carbamazepine	23	
GAC	Full scale	Diclofenac	>98	
GAC	Full scale	Estrone	64	
GAC	Full scale	Proponolol	17	
GAC	Full scale	17α-Ethinylestradiol	>43	
GAC	Full scale	17β-Estradiol	>43	

sensitive towards advanced oxidation processes (AOPs) and ozone such as naproxen but some of the MPs are only sensitive to (OH) radicals like atrazine. However, some MPs like TCEP and TCPP have resistance to both forms of oxidation and ozonation (Gerrity et al. 2011). The presence of ultraviolet, Fenton reagent, and H_2O_2 are responsible for the production of hydroxyl radicals (OH).

Ozonation is an effective method of removing tiny pollutants in a full-scale WWTPs (Hollender et al. 2009). Hernandez-Leal et al. (2011) examined the rate of elimination of MPs in the biological way of treatment gray water by ozonation by ozone dose of 5 mg/L. In a wide range, all MPs are selected and treated under substantial levels. Under the same environment with the only change in ozone dose of 5 mg/L, it showed higher removal percentage for most of MPs (Sui et al. 2010). The elimination rates of most significant MPs such as diclofenac, carbamazepine, sulpiride, trimethoprim, and indomethacin exceeds more than 95%. However, the rate for bezafibrate removal was evaluated, which resulted in 14% only because of the stable molecular structure of bezafibrate (Kim et al. 2009) compared the elimination efficiencies of compounds like pharmaceutical compound using UV. The results show us that the UV process alone acquires high rates of removal (>90%) for diclofenac, antipyrine, and ketoprofen, but the rate of elimination for macrolides ranged from 24% to 34%. Another study confirmed that H_2O_2 and UV together achieved much higher rate of efficiencies for most micro-pollutants. However, under the same situation when UV is applied to the Fenton process, the total rate of removal is increased. In addition, the presence of such dissolved organic material in wastewater enhances the removal rate of MPs. The oxidation process is not able to provide the complete mineralization of such emerging compounds and produce byproducts. Also, metabolite arises from such reactions (Hollender et al. 2009; Reungoat et al. 2011). Sand filtration or activated carbon filtration may be applied to eliminate these unwanted compounds (Table 15.11).

Table 15.11 Removals of some MPs during ozonation and AOPs

Treatment (Dose)	Compounds	Removal efficiency (%)	Author
O_3 (5 mg/L)	Metoprolol	80–90	Luo et al. (2014)
O_3 (5 mg/L)	Trimethoprim	>90	
O_3 (5 mg/L)	Bezafibrate	0–50	
O_3 (5 mg/L)	Carbamazepine	>90	
O_3 (5 mg/L)	Ibuprofen	83	
O_3 (5 mg/L)	DEET	50–80	
O_3 (5 mg/L)	Diclofenac	>90	

15.5.6 *Membrane Processes*

Usually, the removal of micro-pollutants by the process of membrane is acquired by adsorption process onto charge repulsion, membrane and size of pores. The removal percentage of membrane processes mostly depends upon the membrane process type, blocking of membrane pores, operating condition, properties of selected tiny pollutants, and characteristics of membrane (Schäfer et al. 2011). Ultrafiltration (UF) and microfiltration (MF) are more effective in eliminating process for turbidity, and such type of processes are inadequate for eliminating micro-pollutants because of the molecular sizes of significant MPs. Contaminants, however, can be eliminated via contact with the natural organic matter (NOM), or it can be eliminated through adsorption onto the polymers of membrane. Jermann et al. (2009) examined the efficiency removal of estradiol and ibuprofen by ultrafiltration without the existing natural organic matter. In hydrophilic ultrafiltration membrane, removal rates of estradiol and ibuprofen were found nearly 8% and negligible, respectively. In hydrophobic membrane, eliminating efficiencies of estradiol and ibuprofen are generally increased to 80% and 25%, respectively. However, UF and MF processes worked alone in removing of MPs due to their poor performance. So these processes have to combine with other methods of treatment, like reverse osmosis (RO) or nanofiltration (NF). Garcia et al. (2013) combined the RO and MF processes for the reuse of domestic wastewater and for the removal of micro-pollutants. For example, up 50% DEHP was removed with the microfiltration treatment technique only. However, the combined system of RO and MF improved the rate of elimination of micro-pollutants. Removal efficiencies of such MPs lied between 65% and 90% excluding nonylphenol and ibuprofen. A study presented that the combined system of RO and MF has significant removal efficiencies greater than 95% for most MPs, except caffeine and mefenamic acid (Sui et al. 2010) (Table 15.12).

Reverse osmosis (RO) has such a great effect for the complete removal of almost all the persistent micro-pollutants (Yangali-Quintanilla et al. 2011). Comparatively, the performance rate of reverse osmosis treatment is more effective than nanofiltration for pesticides, endocrine disruptors and pharmaceuticals. The removal rate of micro-pollutants obtained by RO was very similar to NF's result. Removal efficiencies for ionic contaminants and neutral contaminants treated by the NF were estimated as 97% and 82%, respectively. Removal efficiencies of same pollutants treated by reverse osmosis were found as 99% and 85%, respectively.

Table 15.12 Elimination of some MPs by membrane processes

Membrane	Water type	Membrane type	Compounds	Removal efficiency (%)	Author
UF	Synthetic water	RC4 flat-sheet	Estradiol	Up to 80	Yangali-Quintanilla et al. (2011)
UF	Synthetic water	PES flat-sheet	Ibuprofen	Negligible	
UF	Synthetic water	PES flat-sheet	Ibuprofen	7	
UF	Synthetic water	RC4 flat-sheet	Estradiol	Up to 25	
RO	Secondary effluent	Filmtec TW30	Sulfonamides	>93	
RO	Secondary effluent	Filmtec TW30	Ibuprofen	>99	
RO	Secondary effluent	Filmtec TW30	Bisphenol A	>99	
RO	Secondary effluent	Filmtec TW30	Macrolides	>99	

15.5.7 Membrane Bioreactor (MBR)

Membrane bioreactor is a process that combines the treatment of membrane filtration and stimulated sludge biological treatment. There are so many benefits of this technology (MBR) associated with conventional WWTPs. Such benefits involve the higher effluent quality, precise control of the SRTs, higher biomass concentration, less requirement of space, minimum increasing of the sludge problem, and converting the flexibility of current WWTPs to MBR system. Membrane bioreactor has a great ability to eliminate a very wide range of MPs that include the emerging compounds resistant to stimulated sludge process (Radjenovic et al. 2009). The removal of MPs through the MBR process most of the time depends upon the SRT, content of water, concentration, conductivity, operating temperature, and pH (Kovalova et al. 2012).

Trinh et al. (2012) investigated that the MBR process eliminates the micro-pollutants on a full scale. Higher rates of elimination were found for most of the micro-pollutants. However, the removal efficiencies of carbamazepine, diclofenac, amitriptyline, diazepam, sulfamethoxazole, fluoxetine, omeprazole, trimethoprim, and gemfibrozil ranged in between 24a% and 68%, and such compounds are said to be the indicators due to their less rate of removal in MBR treatment. The main source of drugs is waste effluents that arise from hospitals (Verlicchi et al. 2010). Kovalova et al. (2012) examined the fate of such MPs in the membrane bioreactor process treating hospital waste. Hence, the wastewater is mainly composed of iodinated contrast mean, and total eliminating rates of metabolites and pharmaceuticals were found at only 22%. Total reduction would be around 90% in case if such content were ignored. Beier et al. (2011) suggested that the waste of hospitals could be efficiently treated if we maintain the age of sludge very high (>100 days) in a membrane bioreactor system designed especially for treating the hospital effluent.

MBR technology and conventional activated sludge process usually linked with each other in the sense of removing the MPs. Radjenovic et al. (2007) compared the performance of treatment of laboratory-scale conventional activated sludge and MBR process in terms of removing the pharmaceuticals. Both systems are treated with ibuprofen, naproxen, hydrochlorothiazide, paroxetine, and acetaminophen in high level. However, results showed that membrane bioreactor system was comparatively stable for removing several contaminants, and some MPs were treated somewhat more than the process of conventional activated sludge.

Like other technologies of treatment, MBR processes were also influenced by numerous factors such as HRT, operating temperature, and SRT. MBR systems functioned at greater sludge age offer greater eliminating efficiency for such pollutants due to diverse MPs present in wastewater (Roh et al. 2009) (Table 15.13).

15.6 Conclusion

In the present time, MPs are frequently detected in significant drinking water reservoirs and sources like rivers, lakes, and groundwater. Presences of the MPs in high amount in different aqueous bodies in various parts of the world pose a threat to the aquatic as well as human ecosystem severely. However, the typical WWTPs cannot provide the expected results for the elimination of the majority of MPs. In order to achieve the desired results, it is important to apply appropriate treatment technologies to minimize the ecotoxicological effects of MPs in the surrounding environment. Many of the existing conventional WWTP elimination performances of MPs are futile because of the presence of low amount of MPs in the waste effluents and also because of the vast MP physicochemical properties. MPs especially having the biodegradable nature and polar molecular structure pass during the WWTPs to the water bodies receiving such treated water without being sufficiently treated. However, with little effort, upgrading and optimizing the current process in the WWTPs is all set to crucially decrease the loading rates of MPs. Besides all the conventional procedures and processes, coagulation-flocculation, advance oxidation processes (AOPs), activated carbon adsorption (granular activated carbon and powdered activated carbon), membrane bioreactor, and membrane processes are also applied for the removal of MPs. Within the persistent treatment procedures, membrane system and advanced oxidation processes come to forefront. However, these treatment techniques are very effective in eliminating the MPs, but they also have some disadvantages such as causing to produce new byproducts and metabolites at a very high operating cost. In the removal of micro-pollutant and inhibiting the production byproducts and metabolites and other pollutants, a combined treatment should be preferred to achieve the better results.

Table 15.13 Elimination of some MPs by MBR

Water type	Membrane type	Contaminants	Removal efficiency (%)	Author
Raw wastewater	Full-scale hollow fiber	Carbamazepine	24	Radjenovic et al. (2007)
Raw wastewater	Full-scale hollow fiber	Estriol	~100	
Raw wastewater	Full-scale hollow fiber	Ibuprofen	~100	
Raw wastewater	Full-scale hollow fiber	Estrone	~100	
Raw wastewater	Full-scale hollow fiber	Bisphenol A	~100	
Raw wastewater	Full-scale hollow fiber	Diclofenac	43	
Raw wastewater	Full-scale hollow fiber	Trimethoprim	30	
Raw wastewater	Full-scale hollow fiber	Sulfamethoxazole	60	
Hospital effluent	Full-scale flat sheet	Ibuprofen	>80	
Hospital effluent	Full-scale flat sheet	Diclofenac	<20	
Hospital effluent	Full-scale flat sheet	Carbamazepine	<20	

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T. Ahmed, M. Z. Hashmi (eds.), *Hazardous Environmental Micro-pollutants, Health Impacts and Allied Treatment Technologies*, Emerging Contaminants and Associated Treatment Technologies, https://doi.org/10.1007/978-3-030-96523-5