

Chapter 11

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



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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 breathe 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 (III) > Arsenite (III) > 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 (*bio-accumulation*) 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. As⁷⁵ 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 protoplasmic poison because it affects the sulphhydryl 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 (Ratnaik 2003).

Arsenic has ionic characteristics, which make it complex than other heavy metals. Arsenic form compounds like cationic and anionic and also transform ion into neutral atoms. Many oxidation states of arsenic are found in the natural system, like 2III, 0, 1III, 1V, 3III, and 5V, which are the most prevalent arsenic states in nature.

The most commonly available valence states of arsenic are Arsenide (-3), elemental arsenic (0), arsenite ($+3$), and arsenate ($+5$). Arsenite (As_{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 ($50\text{--}200\text{ }^\circ\text{C}$) 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, tranquilizers, 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 ground-water 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 $\text{As}(\text{OH})_3$ 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 arsenic 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 $[\text{Cu}(\text{CH}_3\text{COO})_2 \cdot 3\text{Cu}(\text{AsO}_2)_2]$ increases the level of arsenic in groundwater and soil of urban areas of Calcutta, India. Pesticides such as lead arsenate (PbAsO_4), Paris green $[\text{Cu}(\text{CH}_3\text{COO})_2 \cdot 3\text{Cu}(\text{AsO}_2)_2]$, 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, bio-availability, 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 (Mehar 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 (Edvartoro 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/m³, while in urban areas this concentration exceeded up to 3–200 n³/m³. More than 1000 ng/m³ 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 products 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 $\text{HAs}(\text{CH}_3)_2$, AsO_2H_2 , and dimethylarsenic acid $(\text{CH}_3)_2\text{AsO}_2\text{H}$. 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 (III) > Arsenite (III) > 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. **Peroxi-dation** 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 EPA 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 $<1\text{--}3\text{ ngm}^{-3}$, while in urban areas the level is quite deviated and ranges from $20\text{--}30\text{ ngm}^{-3}$ (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 $>100\text{ gL}^{-1}$ (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 $1\text{--}5\text{ }\mu\text{g/L}$ and $0.01\text{--}0.1\mu\text{g/L}$. Arsenic accumulates in nails and hairs, and highest recorded level is from 0.1 to $1\mu\text{g As/g}$. 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 than 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 administered 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 α -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 prostate 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 decarboxylation 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 hydrolyses. 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(NH₂)) 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 (Kobyas 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)
Electrocoagulation	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)
	Iron and aluminum	Oxidation	100%	–	Well water	López-Guzmán et al. (2019)
	Iron electrodes	Oxidation	–	–	Drinking water	Baneji 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 ⁻ chemical process	–	–	Synthetic water	Ortega et al. (2017)	
	Fe ₃ O ₄ /halloysite nanocomposite		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	Bayelite 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	<i>Pteris vittata</i>	Absorption	≥95%	–	Groundwater	Yang et al. (2017)
	<i>Lemna valdiviana</i>	Absorption	82%	1190 mg/kg	Synthetic water	de Souza et al. (2019)
	<i>Vallisneria spiralis</i>	Oxidation, methylation, absorption	73.24%	–	Synthetic water	Li et al. (2018)
	<i>Echinodorus cordifolius</i> , <i>Arthrobaacter creatinolyticus</i>	–	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 electro dialysis** 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 Fe₃O₄/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 electro dialysis. 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 (Baudhdh 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 $200 \mu\text{g L}^{-1}$ to $<10 \mu\text{g L}^{-1}$. The maximum absorption of arsenic was $\geq 95\%$ (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 $0.0488 \text{ mmol L}^{-1}$ (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 ($\geq 95.65 \pm 0.10\%$). 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 $96 \pm 3\%$ (Prum et al. 2018).

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