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Review Article

An Analysis of Arsenic Toxicity's Origins, Manifestations, and Remediation

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ABSTRACT

Arsenic (As) is a metalloid that comprises about 1.5 ppm of Earth's crust and is the 53rd most abundant element. It is found in groundwater and comes from soil and rock erosion, as well as from industrial and agricultural processes. Unacceptable levels of As are consumed by millions of individuals through their food and drinking water. If ingested, Arsenic acts as a toxicant and affects mostly each and every organ of the body. This review aims to discuss the reasons and causes of arsenic toxicity, focusing on the effects of arsenic toxicity in the environment and on biodiversity as a whole. The paper further elaborates on the effects of arsenic toxicity in the physiological and metabolic systems of our body, taking into consideration its neurotoxicity aspect. It also takes into account the effects of toxicity at the cellular and metabolic level, wherein studies have revealed that it also sometimes leads to cancer. The paper deliberates on the Arsenic trioxide having therapeutic value and concludes with various ways by which we can reduce Arsenic toxicity in our surroundings.

Keywords: Toxicity, Arsenic, Underground water, Neurotoxicity, Carcinogenicity

1. INTRODUCTION

Arsenic (As) is an element in Group 15 of the periodic table. Additionally, because it possesses both metal and non-metal qualities, it is chemically categorised as a metalloid. Since this metalloid has hazardous effects on people despite serving no physiological purpose, it is also categorised as a xenobiotic. It has a common co-occurrence with other metals and in numerous minerals found in the crust of the Earth. One of the most infamous toxins present on Earth since prehistoric times is Arsenic. Arsenic exposure in humans occurs mostly from ingesting water, air, food, work environments, and other environmental sources (Mandal & Suzuki, 2002; Roy & Saha, 2002; Tchounwou et al., 1999). Particularly, the majority of the arsenic found in seafood is in organic forms (such as arsenobetaine, arsenosugars, etc.), which are thought to be harmless or significantly less hazardous than inorganic arsenic (Duxbury et al., 2003; Meharg & Rahman, 2003; Sun et al., 2008).

The top As producers in recent years have been China, Russia, and Morocco (Sackett, 2016). Numerous As compounds were utilised as insecticides and herbicides up until recently (Rahman, 2004). Chromated copper arsenate was used to cure and preserve wood because of its antifungal properties. Due to their insecticidal effects, dimethyl arsenates and other arsenicals have also been widely employed to spray fruit plants up until recently. In fact, the most dangerous form of As, that is present in contaminated drinking water, may be found in many places of the world (e.g., arsenate and arsenite) (IARC, 2004; Zheng et al., 2004). In many countries like Argentina, Bangladesh, Chile, China, India, Mexico, and the United States of America, groundwater As concentrations are higher than 10 g/L. Arsenic in drinking

water has exposed tens of millions of people globally, including an estimated 50 million in Bangladesh, 30 million in India, 15 million in China, and tens of millions more in Europe, South and Central America, among other places (Ravenscroft, 2007). However, due to growing evidence of As toxicity, the usage of this molecule in consumer items was outlawed in the U.S.A. and the E.U. in 2004 (Mandal & Suzuki, 2002). On the Priority List of Hazardous Substances, As is number one (Substance Priority List, 2019). Arsenic (As) and inorganic arsenic (iAs) compounds are classified by the International Agency for Research on Cancer, (IARC) as Group 1 human carcinogens (IARC, 2004). The number of people exposed to As has rapidly increased since the world's population depends more and more on aquifers for their drinking water, and some aquifers are being poisoned by heavy metals (Singh et al., 2015). Human interaction with heavy metals has also increased as a result of the reliance on the excavation of deep strata for the extraction of rare metals. Heavy metals can also be released during volcanic eruptions. When combined, these factors significantly increase the likelihood of exposure to heavy metals in quantities well above those considered safe for human health. It has been found that a number of foods, including apple juice, frozen chicken, wine, beer, and rice etc. contain inorganic As (Wilson et al., 2012; Mori et al., 2016; Marshall, 2012; Nachman et al., 2013). The U.S. Food and Drug Administration (FDA) examined 193 brands of rice, rice infant meals, and rice cereals in 2012 and discovered As in almost every one of them (FDA, 2016).

Due to its high toxicity among heavy metals, As is receiving public attention. The situation of arsenic toxicity is frightening, and major health issues are recorded among the residents who rely on groundwater as a source of drinking water as a result of the worst As catastrophe that has developed in numerous parts of the world (NRC, 2001). New polluted regions are discovered every year. There are now more routes for arsenic exposure worldwide thanks to the use of groundwater for irrigation, the bioavailability of As to food crops, and the uptake by people and cattle in the food chain. According to projections, the As catastrophe will surpass that at Chernobyl, Ukraine in 1986, and Bhopal, India, in 1984 in terms of environmental disaster scale (Smith et al., 2000; Watanabe et al., 2001; Khan et al., 2003). Its harmful consequences include skin lesions, various kinds of cancers, cardiovascular, respiratory, and gastrointestinal disorders. It has been determined that this toxin affects almost every organ or tissue in the organism. This metalloid has been linked to neurodegeneration, encephalopathy, neurobehavioral changes, and peripheral neuropathies. Arsenic exposure over a long period of time is linked to a number of serious health problems such as dermatitis, cardiovascular diseases, diabetes mellitus, chronic bronchitis, immune disorders, peripheral neuropathy, liver damage, renal failure, unfavourable reproductive outcomes, hematological effects, and other illnesses (Mazumder et al., 1998; Wang et al., 2002; Mazumder, 2005; Tapio & Grosche, 2006; Meliker et al., 2007; Vahidnia et al., 2008; Ali et al., 2010; Argos et al., 2010). In actuality, As damages or dysfunctions all of the body's major organs.

Along with negative health effects, people living in As-affected nations often have social and economic problems. On the other hand, for over 3000 years, ancient China and Greece have employed arsenic trioxide (As_2O_3) as a medicine to treat a variety of illnesses (Swindell et al., 2013). Patients having acute promyelocytic leukemia (APL) have lately demonstrated As_2O_3's (Figure 1A) extraordinary therapeutic efficacy (Mathews et al., 2011). Although As_2O_3 has demonstrated remarkable efficacy for the treatment of APL, it was unable to control other solid tumours with adequate results when used alone (Subbarayan & Ardalan, 2014). Some organic As compounds have recently been discovered to have a potent anti-cancer impact against solid tumours. It would also be beneficial in clarifying the potential roles of various As species, such as inorganic As and its methylation metabolites, in relation to toxicities and arsenic's usefulness as a medication.

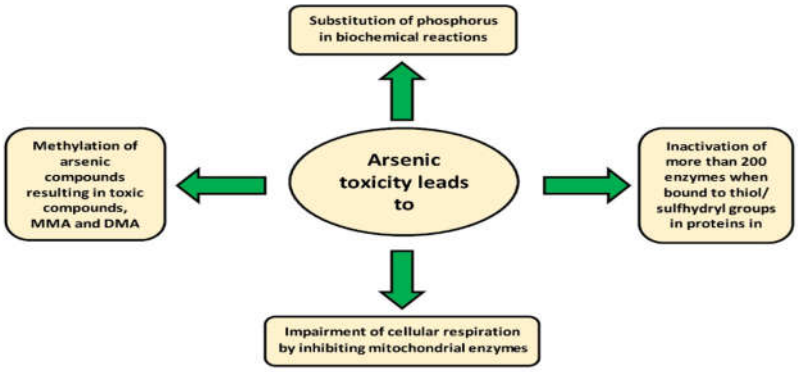

Figure 1: Different types of Arsenic Toxicity and their symptoms

2.1. Arsenic exposure from the environment

Arsenic contamination is both naturally occurring and also human induced. Arsenic contamination from various gold mining and refining operations affects the health and well-being of all the living organisms. Gold-bearing contains different quantities of sulphide and As compounds that interfere with effective gold extraction using current cyanidation technology (Simonato et al., 1994). Arsenic mainly occurs in the gold ore deposits as arsenopyrite (FeAsS), cobaltite (CoAsS), enargite (Cu_3AsS_4), niccolite (NiAs), orpiment (As_2S_3), realgar (AsS) and tennantite [$(Cu,Fe)_{12}As_4S_{13}$] (Azcue & Nriagu, 1995). In Myanmar, it was found that heavy metals are present in small scale gold mining sites (Tun et al., 2020). The concentrations of As reported in the soil of areas for gold mining in Ghana (8305 $mg.kg^{-1}$), (1752 $mg.kg^{-1}$), South Africa (79.40 $mg.kg^{-1}$), and Portugal (820 $mg.kg^{-1}$) were found to be higher than the desired limit (<3.6 mg/kg) (Ferreira da Silva et al., 2004; Ahmad & Carboo, 2000; Kofi Bempah et al., 2013; Kamunda et al., 2016; Shrivastava et al., 2015).

Arsenic can enter the environment from a lot of sources associated with gold mining, which includes waste soil and rocks, tailings, atmospheric emissions produced during ore roasting, and leaching. The waste is a rich source of As, tailings being the major contributor (Greer, 1993). People working at mines are twice more likely to die of lung cancer than the general population as lung cancer was strongly associated with exposure to soluble and insoluble forms of As (Simonato et al., 1994).

In mining-impacted lakes, As is commonly sequestered at the sediment–water interface through adsorption and/or co-precipitation with authigenic iron Fe-oxyhydroxides or sulphides (Miller et al., 2022). Arsenate [As(V)] is the predominant form of As and is less mobile and toxic than As(III) under soil oxidizing conditions, because it is strongly adsorbed to Fe hydroxides of soil (Álvarez-Robles et al., 2020). Effluents from runoffs, industrial discharge and natural sources release heavy metals in soil and food crops for animal and human intake (Srivastava et al., 2017). Due to the rise in industrial growth, the groundwater being supplied from the Ganga River Basin has also experienced the severity of As contamination (Chakraborti et al., 2018). Arsenic contamination in Indian states including those of northeast regions have been associated with the oxidation and reduction process of pyrite and iron oxide.

Another major anthropogenic source is power generation plants. Coal-fired power generation plants, which can contaminate water sources by aerial deposition of mercury emitted from boiler flues, is a significant non-point cause of As contamination. The business furthermore

produces a lot of ash, which itself contains heavy metals including As. Electronic waste is also identified as a major contributor of As.

2.2. Arsenic exposure from food

Arsenic can be ingested from contaminated groundwater, seafood, animal products, and crops irrigated with contaminated water. Arsenic contamination in food is a major public health problem. With the growth in population, the demand for food supplies has also increased. This has resulted in the use of a wide variety of chemicals, including heavy metals in soil and plants such as calcium, arsenite, and copper acetoarsenite (Paris green) as pesticides, and methylarsenic acid and dimethylarsenic acid as herbicides (Khan et al., 2022). The most common way by which As enters the human body is through contaminated groundwater as As is released from bedrock into the groundwater. As future climatic conditions are associated with increased accumulation of As in rice grains, exposure to As from rice consumption is of increasing concern. Rice grain is cultivated under flooded conditions which increases the chances of accumulation of As in it (Carrijo et al., 2022). Cases of As poisoning in infants were reported in Japan due to ingestion of contaminated milk powder, which led to the death of more than 100 infants (Yorifuji et al., 2010). In recent years, there have been concerns that infant formula sold in the United States contains heavy metals and semi-metals (metalloids) which can negatively affect the growth and development of children (Bair, 2022; Parker et al., 2022). No health risks associated with As have been identified from exposure to fruit or vegetable products (roots or legumes). Overall, the noncancer and cancer risks of As are determined by the presence of As in cereal products (Liu et al., 2022). It was found in the Netherland and Portugal that an increase in the levels of intake of seaweed increased the risk of exposure to As (Vellinga et al., 2021). Traditional Chinese medicine can be a source of As exposure which can lead to chronic As toxicity characterised by arsenical dermatitis (palmoplantar hyperkeratosis and hyperpigmentation), peripheral neuropathy, and peripheral vascular claudication (black foot disease) (Spilchuk & Thompson, 2019).

3. EFFECTS OF ARSENIC TOXICITY ON THE ENVIRONMENT

Arsenic is not only toxic to human beings and animals but it has been observed that it affects the environment too in a negative way (Moreno-Jiménez et al., 2012). The mass fraction of Cu in the aerial part of the plants that causes phytotoxicity was decreased in the presence of As in comparison to the values in the control samples, which can be considered to be a negative effect on the plants related to oxidative stress (Álvarez-Robles et al., 2022). The uptake of As by the plant causes a stress situation, provoking changes in both the primary and the secondary metabolism, as well as in the compounds that are involved in them. Although it has been reported that As is able to replace phosphorus in amino acid synthesis and protein synthesis which are essential for the plant, there are other compounds, such as pigments and enzymes that are affected as well (Martínez-Castillo et al., 2022). Phosphorus concentration in soil samples could increase the As accumulation in lentil roots, shoots and grains (Alam et al., 2019).

Besides plants, other animals are also affected negatively by the As toxicity, like fishes that might get exposed to contaminated environments. They are reported to have higher concentrations of various metals in their tissues. In the research conducted by Leite et al., it was shown how chronic consumption of canned sardines sold in Brazil is unsafe. Analysis was done on canned sardines from the Brazilian market for some elements, such as Aluminium, Arsenic, Barium, Cadmium, Cobalt, Chromium, Copper, Iron, Nickel, Lead, Selenium, and Zinc, including few toxic ones by using inductively coupled plasma optical spectrometry (ICP OES) in two species of sardines. It was evaluated on the basis of carcinogenic risk (*CR*), hazard index (*HI*), and hazard quotient (*HQ*). All samples had

unfavourable hazard quotient and hazard index, primarily due to arsenic content. The carcinogenic risk for As was found out to be above the proposed limit of 10^{-4} (Leite et al., 2022). A similar kind of study was also conducted for canned tuna fish groups where the carcinogenic risk values for As in groups were considerably unacceptable (≥10−4). Hazard quotients were >1 for As in all groups, while none of the sample was below 1 for HI (de Lima et al., 2021).

There have been numerous studies to report As contamination on the human health of an individual. As contamination in drinking water resources in developed countries exists as well. In the U.S.A., over 2 million people use drinking water from private wells with As concentrations exceeding the regulatory limit of 10 µg/L (Schreiber, 2021).

4. EFFECTS ON DIFFERENT PHYSIOLOGICAL AND METABOLISM SYSTEMS

Arsenic is absorbed by the human body mostly through the small intestine because of contaminated food and water, but it can also enter the human body through other routes like by inhalation or contact with the skin. The absorbed As is then distributed to the various tissues and organs of the body causing dysfunctions of numerous vital enzymes due to acute or chronic toxicity (Balali-Mood et al., 2021).

4.1. Acute toxicity

Gastroenteritis is one of the most common infections caused by acute As toxicity, when it is ingested in small quantities (under 5mg). The symptoms involved are vomiting, nausea, diarrhoea, and abdominal cramps seen after a few minutes or hours of ingestion. These symptoms generally resolve within 12 hours of exposure, but they might also persist for few days. Arsenic affects the gastrointestinal mucosa which results in the shedding of mucosal tissue and vasodilation that might eventually lead to damage of the vesicles of the mucosa (Montelescaut et al., 2014). Arsenic can have effects on our cardiovascular health resulting in hypotension, dehydration, and loss in volume. Inhalation of As can affect pulmonary health which might result in cough, chest pain, and dyspnea (Guo et al., 2022). Due to increased permeability non-cardiogenic pulmonary edema can also be seen. After getting exposed to As, cases of proteinuria, hematuria, and acute renal failure have also been reported (Kuivenhoven & Mason, 2022).

4.2. Chronic toxicity

Diffused or spotted hyperpigmentation, which has a "raindrop appearance" has been reported generally after six months to three years of exposure. Five percent of the patients also show the occurrence of Reynolds-Aldrich-Mees lines which are popularly known as Mees lines. These are 1 to 2mm wide transverse white bands across the fingernails seen after 4 to 6 weeks of exposure (Guo et al., 2022). Palmer-planter hyperkeratosis, eczema-like lesions, warts, alopecia are a few of the other dermatologic signs which is a chronic effect of As toxicity. Exposure to As can also lead to basal cell carcinoma and squamous cell carcinoma as a secondary symptom to hyperkeratosis (Guo et al., 2022). Lung and bladder cancer can be caused due to the exposure of inorganic As (Chen et al., 2019). Arsenic can have effects on the renal system as well by resulting in diseases like angiosarcoma, hepatomegaly, ascites, and non-specific abdominal pain (Khairul et al., 2017). Gangrene of the extremities which is also known as Blackfoot disease has been reported due to the consumption of water contaminated with As. Symptoms of toxicity observed due to arsine gas (which is the most toxic form of As) include garlic breath odour 1-12 hours after getting exposed, severe headache, acute chest pain, nausea and vomiting, diarrhea, and also loss of balance, tachycardia, fever, and kidney failure. Port wine-colored urine, reddish conjunctiva, and jaundice, referred to as "slate-bronze skin," have been reported 4-48 hours after exposure (Khairul et al., 2017). A physical examination has shown the tenderness of the liver and spleen. There may be

direct myocardial effects that may be related to conduction abnormalities, heart block, and asystole. Mees line are observable several weeks after exposure (Kuivenhoven & Mason, 2022). Few epidemiologic studies show exposure to arsenic can cause declined testosterone synthesis, apoptosis, and necrosis and as a result, induce gonad dysfunction, infertility, and low sperm quality, as well as erectile dysfunction in men (Kim & Kim, 2015).

4.3. Neurotoxicity

Drinking water contaminated with arsenic (as low as 10 to 50ppb) can cause peripheral neuropathy. The resulting impairment is observed primarily in sensory fibers and to a lesser extent in motor fibers. Sural nerve biopsies have shown a reduction in small myelinated and unmyelinated fibers occurring with peripheral nerve axonal degeneration. In children, impairment of the Central Nervous System may occur due to As exposure at a concentration of 50ppb or more but in the case of adults, the impairment is caused at higher concentrations (Mochizuki, 2019). Peripheral neuropathy from As exposure may be reversible in the long term, whereas CNS damage is less likely to be reversible. Neurotoxicity due to As is also associated with alterations in neurotransmitter metabolism resulting in changes in synaptic transmission. Experimental studies have shown that exposure to arsenic can induce inflammatory responses in the brain. Nitrosative stress can also be caused due to As due to the activation of the inducible NOS (iNOS) in the brain (Garza-Lombó et al., 2019).

5. EFFECT OF ARSENIC TOXICITY AT CELLULAR LEVEL

Toxicity caused by As in humans is usually caused by exposure to inorganic As, and it has also been observed that inorganic As(III), the trivalent form of arsenite is approximately 2-10 times more toxic than its pentavalent counterpart, As(V). The expected mechanism for arsenic's extensive effects on different organ systems, is by binding to thiol or sulfhydryl groups on proteins, the As(III) can inactivate more than 200 enzymes (Tchounwou et al., 2014). There are majorly two to three pathways by which As exerts its toxic effects at the cellular level of organisms (Figure 2).

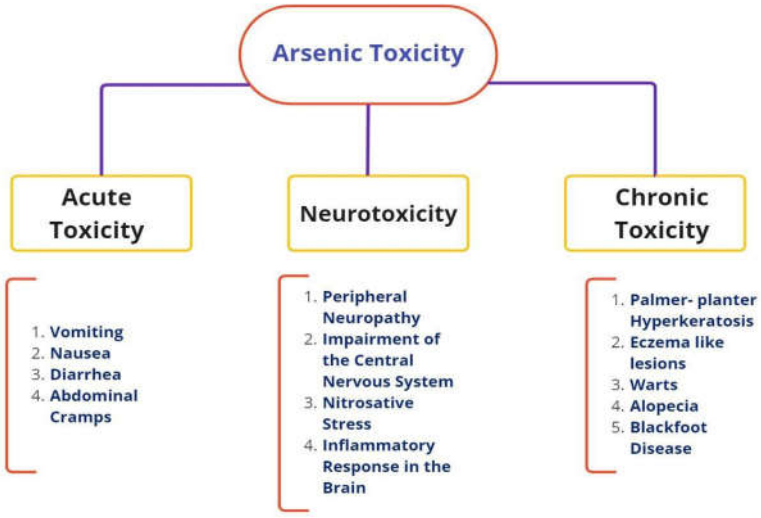

Figure 2: Consequences of Arsenic toxicity in organisms

One of them is by impairment of cellular respiration by the inhibition of several enzymes of the mitochondria. Usually, the pentavalent As interacts with sulfhydryl groups of enzymes

and proteins. It also has the ability to substitute the phosphorus in several important biochemical reactions resulting in As(V) toxicity (Tchounwou et al., 2014; Hughes, 2002). The other metabolic pathway used in it is methylation. The trioxides of inorganic As are methylated via a non-enzymatic process, resulting in a major metabolite, monomethylarsonic acid (MMA). This is enzymatically methylated to dimethyl arsenic acid (DMA), eventually getting excreted via urine. Earlier, this methylation process was thought of as a pathway of As detoxification. But newer studies have shown that methylation of trivalent As, sometimes may prove to be more toxic than As itself (Tchounwou et al., 2003; Tchounwou et al., 2014).

Arsenic interactions with proteins are also one of the mechanisms to understand its toxicity. Molecules of As(III) interact with various kinds of structures in proteins, including spatial clusters of individual cysteines, ZnF motifs and also RING finger domains. When As interacts with proteins, it affects the function of protein targets in human cells and also leads to inhibition or sometimes disruption of cellular pathways including DNA damage repair, DNA and histone's epigenetic modifications and ribosome associated protein quality control. Studies also show that these disruptive interactions are mechanisms associated with development of diseases associated with chronic As exposure (Vergara-Gerónimo et al., 2021).

6. CARCINOGENICITY

Epidemiological studies claim to prove association between exposure to As and development of malignant cells in different parts such as breast, pancreas, brain, stomach, prostate and pharynx (García-Esquinas et al., 2013). There are several hypotheses proposed, trying to elucidate As induced carcinogenesis' mechanism. Zhao et al. (1997) showed that As might behave as a carcinogen by bringing about DNA hypomethylation, aiding aberrant gene expression. Trouba at al. (2000) drew the inference that high levels of As exposed for a long time may make cells subject to alterations in mitogenic signalling proteins which in turn can promote carcinogenic action. It has also been observed that, the particular alteration in signalling pathways or the targets giving rise to the development of tumours was brought about by As.

Nine possible modes of action of As induced carcinogenesis have been discussed by Miller et al. (2002), which include: induced chromosomal aberrations, oxidative stress, alteration in DNA repair, alteration in DNA methylation patterns, alteration of growth factors, increased cell proliferation, progression, suppression of p53 expression and gene amplification. Out of these nine mechanisms, three mechanisms - chromosomal abnormality, oxidative stress and alteration of growth factors, have been proven by several researches, both in experimental setups and human systems (Miller et al., 2002).This shows that As might be acting as co-carcinogen, a promoter or a carcinogen progressor also.

Tumour protein p53, which is controlled by the p53 gene plays a key role in controlling cell division and cell death, also has a high impact on the mutation in tumours obtained from As exposure. The p53 gene has an active role in many cellular pathways, like that of cell cycle control, DNA repair, cell differentiation and programmed cell death. Many studies collectively conclude that several different forms of As have the ability to change the gene expressions and those alterations could substantially lead to the toxic and carcinogenic effects of As ingestion across human populations (Tchounwou et al., 2014). It is also evident that oxidative stress plays a key role in As induced cytotoxicity, a system modulated by antioxidants like ascorbic acid and n-acetyl cysteine (Yedjou et al., 2008).

Since As is a fundamental cause of DNA damage, or genotoxicity, tests have been conducted to find out other implications of this. It has been found out by several tests for

genotoxicity that As and its compounds instigate chromosomal abnormalities, sister chromatid exchange, and micronuclei formation in human cells in culture (Patlolla & Tchounwou, 2005; Hartmann & Speit, 1994; Jha et al., 1992).

7. ARSENIC IN THERAPEUTICS

Arsenic trioxide has therapeutic value in the treatment of acute promyelocytic leukaemia. In spite of all the negative effects of As, there have been clinical trials of As conducted recently. It has proved therapeutic value of As in the treatment of acute promyelocytic leukaemia, which is garnering interest among the scientist community for exploring its effectiveness in other cancers also (Tchounwou et al., 2014). The particular molecular pathway critical to the formation of cancerous cells in acute promyelocytic leukaemia is very well known. Research conducted by Puccetti et al. (2000) concluded that trioxide of arsenic is a tumour specific agent and has the ability to selectively induce apoptosis in acute promyelocytic leukaemia cells. Many newer researches have also proven that As has the capability to induce apoptosis via variations in other cell signalling pathways also (Seol et al., 1999).

Arsenic may also have therapeutic use for myeloma as reported in some research, but not much is available to prove this (Deaglio et al., 2001). Numerous cancer chemotherapy studies in cell cultures and in patients with acute promyelocytic leukaemia demonstrate that arsenic trioxide application may lead to cell-cycle arrest and apoptosis in malignant cells.

8. WAYS TO REDUCE ARSENIC TOXICITY

As is continuously being circulated in the environment and eventually entering our body in some or the other way (Figure 3). There are several ways by which we can try to reduce the amount of As toxicity from our environment. At a minor extent, As on the riverine system can be minimised by creating various pools along the water course to favour the deposition and precipitation of As-rich sediments. However, the deposited sediments in the pools will have to be periodically removed and treated or disposed of in a specific landfill (Lazzaroni et al., 2022).

8.1. Bioremediation

In many situations, microorganisms may mitigate the toxicity of As and influence its migration, which is a form of bioremediation (Sher & Rehman, 2019). Although As cannot be broken down, it can be detoxified or eliminated by altering its solubility by the effect of microorganisms (Rahman & Singh, 2020). One efficient approach of bioremediation of hazardous metals and metalloids is biosorption and bioaccumulation by bacteria. The energy-dependent biosorption of As by microorganisms involves chelation, ion exchange, and physical absorption through physicochemical interactions. As is bound to several functional groups to cause the biosporation (Sher & Rehman, 2019).

Arsenic can be converted from an inorganic form to a somewhat less toxic organoarsenic compound through the methylation of inorganic As, also known as biovolatilisation, which also results in the production of volatile trimethylarsine gases (Satyapal et al., 2018). Trimethylated As (TMA) is a methylated intermediate that is transitory and does not accumulate in cells. Trimethylarsine oxide (TMAO), one of the byproducts of methylation, is also considerably less hazardous than As(III). Anaerobic Archaea, *Methanosarcinaacetivorans* C2A, is known to methylate As anaerobically (Wang et al., 2014).

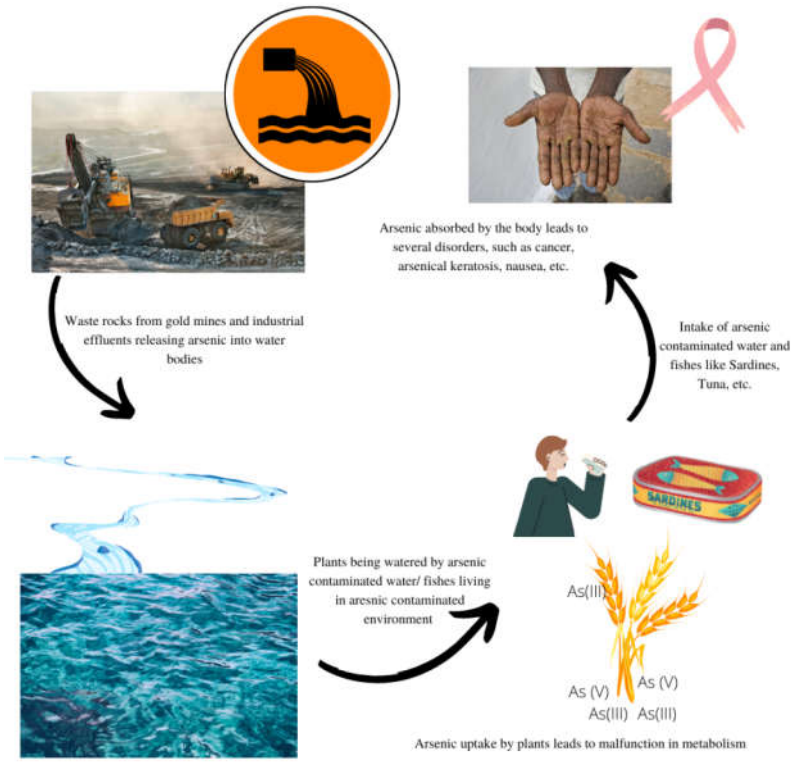

Figure 3: Flowchart showing the circulation of arsenic in the ecosystem (Photos source: www.flickr.com)

Arsenic-resistant bacteria (*Acidithiobacillus*, *Bacillus*, *Deinococcus*, *Desulfitobacterium,* and *Pseudomonas)* can play a notable role in reducing As from fertile soil as well as increasing plant growth. In a recent study conducted in the Terai region of Nepal, Arsenic-resistant *Bacillus* species were isolated and characterised from 36 different samples collected and were found to possess some astounding properties such as high As tolerance and the ability to transform toxic form of arsenic: As(V) to less toxic form As(III) (Magar et al., 2022). As(III) in comparison to As(V) is less toxic and is considered to be able to readily be removed by forming precipitates along with the oxides and hydroxides of aluminium and iron (Burton et al., 2014).

Arsenate reductase, first reported in *Staphylococcus aureus* plasmid pl258, is responsible for the reduction of arsenate. In *Escherichia coli,* five genes (arsA, arsB, arsC, arsD, arsR) were responsible for the As detoxification, compared to three genes (arsB, arsC, arsR) in *Staphylococcus* (Ji & Silver, 1992). Additionally, the express regulation of the ars genes, which is essential for As detoxification, is regulated by ArsR, an arsenite-responsive transcription regulator (Chen & Rosen, 2014; Kumar et al., 2021).

According to a study by Han et al. (2022), the BARI Mashur 1 and BARI Mashur 5, both lentil genotype had higher shoot length, root and shoot mass of lentil in 8 mg kg^{-1} and 45 mg kg^{-1} Arsenic concentrated*Arbuscular* mycorrhizal fungi (AMF) applied soils than non-AMF. It also reduced the uptake of As significantly in both of the treated lentil genotypes. Another study by Sharma et al., (2017) demonstrated that the plant colonised by *R. intraradices* or *G. etunicatum* showed reduction in Arsenic-induced oxidative damage in wheat plants by alleviating the potential of arbuscular mycorrhiza, much more with increase in severity of As stress. Dilution effect taking place due to increase in biomass, more favorable P:As ratio,

better antioxidative capacity, augmented glyoxalase system, and higher thiol metabolites to sequester arsenic results in higher Arsenic tolerance in mycorrhizal plants.

Studies on the protective effects of *Limosilactobacillus fermentum* GR-3 strain against As(III) toxicity in *Procambarusclarkii* revealed that strain GR-3 administration decreased As levels in crayfish tissues, enhanced oxidative stress and histomorphological injury while also maintaining the composition and function of intestinal flora which contributes to the defence system against pathogens and promotes individuals growth in crayfish. Strain GR-3 intervention of 30 days caused decrease in As(III) accumulation in the abdominal muscles (0.13 μg/g), and hepatopancreas (0.45 μg/g) (Han et al., 2022).

8.2. Phytoremediation

Biological techniques used for remediation strategies are less expensive and more effective than physical and chemical methods used. Phytoremediation and PGPB (Plant Growth Promoting Bacteria) remediation are some of the methods used under bioremediation for mitigation of As toxicity (Rojas-Solis et al., 2023). Mayda et al. (2014) conducted an experiment from October 2012 to April 2013 in the Department of Botany, Jahangirnagar University, Dhaka, Bangladesh. They studied the process in four non-edible ferns and four soil As concentrations. Using non edible plant material for mitigating As, they showed that these plants help by stopping As toxicity from entering the food chain (Mayda et al., 2014). Out of the four ferns observed, *Pteris vittate* L. was found as the As hyperaccumulating plant. *P. vittate* could survive in soil with a very high concentration of As and also accumulate up to 27829.7 ppm As when treated with 4000 ppm As soil concentration. They also observed that plant leaf biomass was maximum provided by *P. vittate* which also proved that it could survive well in the As-containing soil conditions. The group concluded that *P. vittata* is an excellent plant for phytoremediation of As and can help reduce As levels in soil (Mayda et al., 2014).

8.3. Genetic engineering and nanotechnology in Arsenic mitigation

To lessen As absorption by food crops, a variety of mitigation strategies, including agronomic practices, plant breeding, and genetic manipulation, may also be used (Zhao et al., 2010). The most often used approach to detoxify As is chelation treatment. However, this approach has negative consequences that might result in toxicities such hepatotoxicity, neurotoxicity, and other unfavourable outcomes. Native medicines made from plants have been found to effectively and gradually relieve the symptoms of arsenic-mediated poisoning without causing any negative side effects. Additionally, it has been shown that these phytochemicals help the biological system eliminate As; as a result, they may be more successful than traditional therapeutic treatments in reducing arsenic-mediated toxicity (Susan et al., 2019). Curcumin, quercetin, diallyl trisulfide, thymoquinone, and other phytoconstituents function through a number of different molecular pathways, mainly by reducing oxidative damage, membrane damage, DNA damage, and proteinopathies. If taken as a preventative measure and in combination with other chemotherapeutic drugs, these medications may offer an efficient method for treating As poisoning. In a few cases, such tactics as co-administration of phytochemicals with a well-known chelating agent have increased the extent of As removal from the body with less deleterious off-site consequences. This is achievable due to the fact that combination therapy ensures the employment of a phytochemical and a chelating agent at a lower dose without affecting treatment. As a result, these treatments are more useful than traditional therapeutic drugs in reducing arsenic-mediated toxicity (Khan et al., 2022).

ZnO nanoparticles (NPs) and potassium (K^+) were reported to reduce As toxicity in *Vicia faba* L. seedlings by increasing NO content in both normal and As-polluted soil. Because

zirconium dioxide (ZrO2) NPs have high porosity and adsorption capacity for As(III) and As(V), they may be used for As mitigation because they can bind both As(III) and As(V) and remove As through oxidation of As(III) (Sinha et al., 2023).

Computer-based technologies aid in making cost-effective decisions to use arsenic-free water. The modelling program (GMS 10.2), which aids in the prediction of both water flow and As transport, enables the assessment of potential As content in bodies of water as well as deep and shallow aquifers. By preventing polluted water use in drinking and irrigation, such modelling software, in conjunction with advanced numerical modelling, may aid in improved monitoring and health management (Sinha et al., 2023).

There are many other technological options available to mitigate the effect of As toxicity from ground water. The best technological solution is in-situ remediation of As from groundwater systems or aquifer decontamination but it is a very costly and tedious task because of the lack of complete knowledge. A short-term solution to supply potable, arsenic-free groundwater for residential use exclusively appears to be ex-situ remediation of tapped groundwater using appropriate removal technologies. Although it may seem logical to use surface water sources as a substitute for the supply of treated contaminated groundwater, doing so would necessitate the availability and supply of surface water flow as well as a well-organised water supply system to guarantee the supply of both drinking water and irrigation water. This method may prove to be a viable alternative to provide the drinkable water needed in places impacted by As where there is a dense population. Another obvious idea may be to draw water from other secure aquifers that are free of As. On a local level, this has also been investigated in numerous regions. This strategy would necessitate considerable research and analysis in order to map the availability of groundwater, identify freshwater reserves, and assess the spatial and temporal scales of arsenic mobilisation in the aquifer as a result of forcing disturbance.

9. CONCLUSION

Arsenic compounds can be found in a variety of places, including the workplace and the surroundings. Acutely hazardous exposure to different levels of long-term or lifetime exposure are all possible. High quantities of As are possibly found in food or drink. Chronic poisoning can occasionally occur by water or certain occupational situations, which may even result in cancer. People exposed to high or prolonged levels of radiation may experience acute, sub-acute, or characterised by skin lesions, cardiovascular conditions, and/or neurological symptoms, persistent poisoning signs and symptoms. Pentavalent natural form appears to be less hazardous than trivalent methylated and inorganic form as reported in marine animals.There are quite a few methods of mitigation of Arsenic toxicity, commonly by bioremediation or phytoremediation. Recently, genetic engineering methods and nanotechnological methods have also been adopted to reduce the Arsenic toxicity in our environment.

CONFLICT OF INTEREST

There is no conflict of interest among the authors.

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