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Review

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Arsenic: A Review of the Element's Toxicity, Plant Interactions, and Potential Methods of Remediation

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ABSTRACT: Arsenic is a naturally occurring element with a long history of toxicity. Sites of contamination are found worldwide as a result of both natural processes and anthropogenic activities. The broad scope of arsenic toxicity to humans and its unique interaction with the environment have led to extensive research into its physicochemical properties and toxic behavior in biological systems. The purpose of this review is to compile the results of recent studies concerning the metalloid and consider the chemical and physical properties of arsenic in the broad context of human toxicity and phytoremediation. Areas of focus include arsenic's mechanisms of human toxicity, interaction with plant systems, potential methods of remediation, and protocols for the determination of metals in experimentation. This assessment of the literature indicates that controlling contamination of water sources and plants through effective remediation and management is essential to successfully addressing the problems of arsenic toxicity and contamination.

KEYWORDS: *arsenic mechanism, arsenic toxicity, human health, plant interaction, phytoremediation, environmental contamination, metal determination protocols, remediation*

INTRODUCTION

Overview of Arsenic Contamination Worldwide. Arsenic has been studied for centuries and is an important topic in both mainstream media and the scientific literature. The element is classified by the International Agency of Research on Cancer (IARC) as a class I carcinogen that exhibits acute and chronic toxicity depending on the type of exposure.[1] All instances of arsenic contamination are treated with care and consideration. The World Health Organization (WHO) and the U.S. Environmental Protection Agency (EPA) list a threshold of 10 μg/L of arsenic in drinking water. Unfortunately, water sources in Bangladesh, India, China, Argentina, Ghana, Chile, Vietnam, Canada, Laos, Mexico, the United States, and several other countries have been reported to contain the toxicant in levels that exceed this threshold.[2] Arsenic contamination in water across the United States can be seen in Figure 1.

The worldwide epidemic of arsenic contamination is due to both anthropogenic and natural sources of the element. Arsenic shares properties with both metals and nonmetals and is thus best classified as a metalloid. The desorption of arsenic-containing minerals is a major natural source of the toxicant, whereas human industrial activities such as mining and fossil fuel combustion also contribute to the problem.[3] This contamination has led to serious toxicological consequences in the West Bengal region of India as well as Bangladesh. The naturally high concentration of arsenic present in alluvial sediments in the area affects millions of people living in the area.[2] Studies in other affected areas have been conducted in locations such as Poland, Pakistan, Serbia, Hungary, Iran, and Basque Country in Spain.[4−9] Due to the continued exposure of people to arsenic, further investigation into exposure routes is appropriate. The Agency for Toxic Substances and Disease Registry's (ATSDR) toxicological profile[10] acts as the gold standard for information about arsenic toxicity. However, new studies from around the world continually reveal more about the toxic properties and behavior of arsenic.

Factors of Biological Response to Arsenic. Biological response to arsenic exposure is complicated and can lead to many possible effects. Factors such as chronic exposure versus acute exposure[11] and developmental state of the organism[12] can influence which cells are targeted and the magnitude of the effect. Concentration is the most important factor in considering arsenic exposure. According to the ATSDR, the minimum risk level (MRL) of acute oral exposure to inorganic arsenic is 5 μg/kg/day for up to 14 days. Acute toxicity can produce effects such as vomiting and diarrhea. Nearly every organ in the body is potentially at risk, but the lungs and skin are particularly vulnerable.[10] Although high concentrations of arsenic are readily coordinated to various health effects, determining if lower concentrations cause significant deleterious effects has been more problematic.[13] The ATSDR has determined that the MRL for chronic exposure is 0.3 μg/kg/day for a year or more. This type of exposure has been experimentally demonstrated to lead to cardiovascular, respiratory, gastrointestinal, and neurological issues as well as cancer.[10]

Another factor that cannot be ignored in arsenic behavior is speciation. The element can be present in both organic and inorganic forms. Organic methylated arsenic species such as monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) are toxic in low concentrations, but their inorganic counterparts arsenate (AsO_4^{3-}/H_3AsO_4) and arsenite ($AsO_3^{3-}/$

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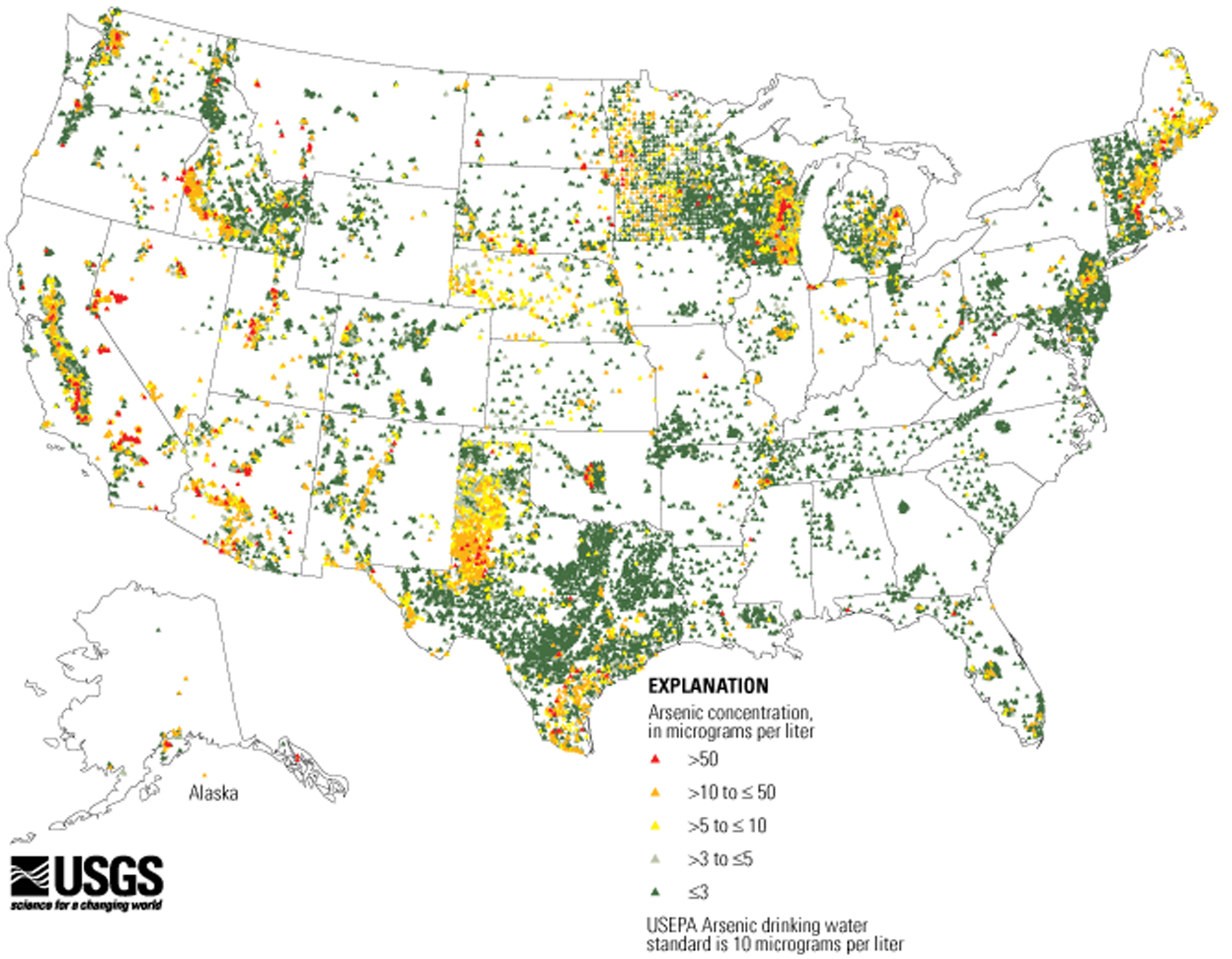

Figure 1. Arsenic levels in groundwater in the United States (data found by U.S. Geological Survey; chart source http://water.usgs.gov/nawqa/trace/arsenic/).

H_3AsO_3) are even more toxic.[4,14] Distinguishing between species is important due to the differences in properties and mechanisms of toxicity.[15] An example of a property that influences arsenic stability differently for separate species is pH. One study employed the agricultural residue rice polish to sorb inorganic arsenic. Rice polish is a byproduct of the milling process composed of a starchy material and inner coating of the rice hull, and this study found that the maximum sorption for AsO_4^{3-}/H_3AsO_4 on rice polish occurs at neutral pH, whereas AsO_3^{3-}/H_3AsO_3 has maximum sorption at a pH of 4.[2,16] The relatively higher stability of AsO_4^{3-}/H_3AsO_4 at neutral pH makes it more readily removed than AsO_3^{3-}/H_3AsO_3.

A third factor to consider in toxicity is the route of exposure. According to the WHO, most human diseases can be attributed to water pollution.[17] Uptake through drinking water is the most important source of arsenic in humans.[18] Inhalation is another relevant mode of exposure and is known to contribute to respiratory system problems including lung cancer.[10] Another route known for causing deleterious effects in humans is dermal exposure. The susceptibility of the skin to arsenic can lead to lesions and aggressive, non-melanoma skin cancers.[19] Another less direct route that has come to public attention in recent years is the uptake of arsenic via contaminated fruits and vegetables.

Arsenic Interaction in Plants and Soil. Clearly, arsenic contamination is not limited to water sources. The contamination of soil has emerged as a serious environmental hazard, especially in agricultural areas of the world.[20] The health of the soil can be compromised by chemical contaminants including arsenic.[21] Arsenic can cause problems with microbial activities in the soil, which in turn affects the microbes' interaction with other life.[22] Soil can act as a sink for arsenic and other hazardous metals with the capacity to transfer these pollutants to plant roots.[23] High concentrations of arsenic can cause deleterious effects to the plant including cell necrosis, chlorosis, inhibition of growth, and even death.[24] Human consumption of arsenic-contaminated food products may also provide a hazardous amount of the element. Food chain transport of arsenic and trace metals is thus a threat to human health.[23] Because research has yielded inconclusive evidence on the health effects of consuming contaminated crops,[5] more studies are needed in this area. It is worth noting that different species of plants have unique methods of reaction to arsenic exposure.[25] For example, data suggest that tomatoes do not efficiently accumulate arsenic,[9] yet rice is so efficient an accumulator that millions of tons of grain are rendered unsafe for consumption on a yearly basis.[26] The behavior of each plant in response to chemical contamination is important both in

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terms of consumption and for the plant's ability to take up and tolerate contaminants.

With regard to the health risks of consuming contaminated plants, it is helpful to consider the capacity of plants for remediation. Phytoremediation is the process of plants extracting arsenic and other contaminants from soil via their roots.[27] Although there is ongoing experimental research concerning direct remediation of water,[28] phytoremediation has emerged as the most promising potential technique for reducing arsenic and heavy metals from contaminated areas due to its eco-friendly methods. However, the process has a few important drawbacks. One problem is that phytoremediation tends to be time-consuming. Another is that if the remediating crops are not properly disposed of or treated, these contaminants can still enter the food chain through fodder or other means of animal consumption.[18] A recent study has investigated the possibility of effluxing arsenic from plants,[29] but the efficiency of these experimental technologies needs further study. Although phytoremediation is not yet an ideal solution to the problem of arsenic contamination, it is a promising technology that could evolve over time into the most effective method of arsenic cleanup. An improved understanding of this technique will pave the way for greater insight into the worldwide problem of contaminated crops.

Purpose of Review. The purpose of this review is to consider the chemical and physical properties of arsenic in the broad context of human toxicity and phytoremediation. The behavior of arsenic is key to its interaction with plants and humans. Therefore, attention will be brought to the results of recent studies concerning arsenic and its mechanisms of toxicity and transport. The connection of arsenic to human health will be evaluated in relation to its toxicological properties. Although some ailments such as cancer have been attributed to arsenic exposure for many years, new studies are being conducted to determine other deleterious effects for which arsenic may be responsible. Effects of exposure proposed by recent experimentation will also be evaluated and compared.

Another area of interest to be addressed will be the interaction of plants with arsenic and other contaminants such as heavy metals. This review will cover mechanisms and interactions commonly seen between plants and metals including arsenic. Details of specific plants that are well-suited for remediation will be noted, as will a few species that are resistant to the process. This process will be covered in depth with an emphasis on arsenic cleanup. Finally, the commonly employed methods of arsenic determination, alongside a few newly proposed techniques, will be described. It is important to understand the potential health risks posed by arsenic and heavy-metal accumulation as well as the possible environmental utility of phytoremediation. Compiling this research will create a greater understanding of arsenic toxicity and provide insight on where further research may be needed.

PHYSICOCHEMICAL AND MECHANISTIC PROPERTIES OF ARSENIC AND IMPLICATIONS ON HUMAN HEALTH

Origin and Behavior. Arsenic is an important element because it is ubiquitous in the environment.[30] It is a naturally occurring element in rock formations containing copper and lead. The metalloid is known to persist in soil, water, and air as well as their rock structures of origin.[31] Arsenic in groundwater ranges from 0.5 to 5000 μg/L in more than 70 countries worldwide.[32] It makes up only 0.0001% of the Earth's crust and is far from the earth's most abundant element.[33] Water and soil near arsenic-enriched formations tend to have high concentrations of the element.[1] Areas with soils of high organic carbon content are generally more susceptible to accumulating arsenic than sandy soils.[34] Arsenic is a member of group 15 on the periodic table of elements and is classified as a heavy metalloid.[35] It has been compared to other elements including phosphorus, antimony, chromium, and selenium[22,36,37] to help assess its physicochemical properties and toxicity. These comparisons are particularly helpful when arsenic accumulation in plants is evaluated.

The inorganic arsenic-containing compounds are considered a much more important threat to environmental health than the organic forms. AsO_4^{3-}/H_3AsO_4 and AsO_3^{3-}/H_3AsO_3 are often separated and speciated because they have different mechanistic properties and interact differently with biological systems.[38] In aerobic environments of moderate, near-neutral pH, most AsO_4^{3-}/H_3AsO_4 is present as anions $H_2AsO_4^-$ and $HAsO_4^{-2}$. In anoxic settings, AsO_3^{3-}/H_3AsO_3 occurs as H_3AsO_3.[33] Studies of the different species of arsenic show trivalent species are generally more toxic than pentavalent ones,[3] although one review suggests that the species' potencies are ultimately dependent on the biological system in question.[18] Research has determined that different species may target different parts of biological systems. One study suggests that AsO_3^{3-}/H_3AsO_3 targets human prostate stem cells and gives them an aggressive, malignant phenotype, whereas other research has revealed that AsO_4^{3-}/H_3AsO_4 is an analogue for inorganic phosphate that can potentially replace the phosphate nutrient in essential reactions and disrupt normal processes.[18,39] The subtle differences in the species of arsenic are key to defining the mechanisms of remediation.

Common Effects on Human Health. The effects of arsenic on human health are well-known, and both chronic and acute toxicities have been connected with exposure to the metalloid. Symptoms widely attributed to the element such as skin lesions, liver fibrosis, and cancer have been reported in more than 30 countries worldwide.[40] Cases of "black-foot" disease have been reported in areas of extreme contamination such as Bangladesh.[1] Black-foot is a peripheral vascular disease that can result in severe pain in the extremities and eventually the mummification and falling off of affected areas.[41] More common lesions caused by arsenic on the skin are less debilitating, but are unique from other dermal damage such as that caused by UV light because they can affect multiple sites.[19] Damage to skin by the toxicant can result in hyperpigmentation and hyperkeratosis, which can act as a precursor to cancer.[42] Chronic exposure to arsenic is connected to non-cirrhotic portal fibrosis (NCPF).[43] This disease can manifest even at an early age. One study found a statistical correlation between arsenic-affected areas and NCPF in children in Kolkata, India.[44]

The skin, lungs, and bladder are considered to be the main target areas of arsenic carcinogenesis.[42] Arsenic-related skin lesions can progress to malignancies including squamous cell carcinoma, Bowen's disease, and basal-cell carcinoma. This process may be potentiated by other carcinogens such as those in tobacco products.[1] There is a higher risk of developing lung cancer as a result of arsenic exposure. Studies show that the element is both cytotoxic and genotoxic to human lung cells.[45] Although it is primarily connected to contaminated drinking water,[1] there is research speculating that arsenic inhalation also plays a significant role in inducing lung cancer.[46] In the bladder, cytokines can be inflamed by the metalloid, leading to potential

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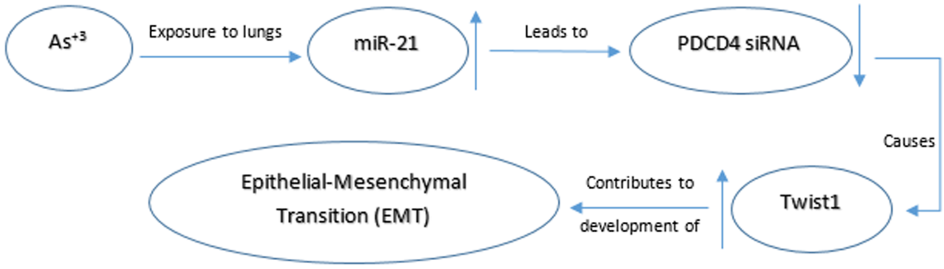

Figure 2. Flowchart of the development mechanism of EMT as a result of arsenite toxicity. Mechanism proposed in ref 62.

malignancies.[47] Bladder cancer follows mechanisms of carcinogenesis similar to those of lung cancer.[48] Evidence suggests a synergistic relationship of the toxicant with tobacco.[1] This may promote cancer development in both organs for smokers.[49] The study of these common forms of cancer resulting from arsenic exposure will be instrumental in determining future cancer treatment options as well as understanding the nature of the element and its role in carcinogenesis.

Other Target Organs and Cancer. Although arsenic is most commonly associated with malignancies in the skin, bladder, and lungs, there is evidence that strongly suggests that the toxicant may contribute to cancer development in other organs as well. Organs that have been experimentally associated with arsenic carcinogenesis include the kidneys, liver, and prostate.[42] Although these may not be as prevalent as cancers of the skin and lungs, there has been research to strongly suggest the connection. One study in Bangladesh reported that the statistical relationship between arsenic concentration and renal cancer cells indicates that it is a causal factor even in nonsmokers.[50] Because the liver is the body's primary organ for detoxification, it is expected that the liver would be a target of this toxic element. A previous thorough review of the literature found that chronic exposure from drinking water increases liver cancer mortality.[51] Another study suggests that the metalloid causes androgen independence of the prostate, promoting cancer progression.[52] Even though it is not yet widely connected to the toxicant, one study suggests a tie between arsenic methylation and breast cancer.[14] The broad spectrum of target sites for arsenic carcinogenesis illustrates the versatility of the metalloid and its threat to human health.

Cancer has historically been the focus of worldwide study of chronic arsenic exposure. However, new studies have reported that the metalloid may be responsible for other deleterious effects as well.[13] An interesting characteristic of arsenic is its ability to adversely affect entire multiorgan body systems via chronic toxicity called arsenicosis.[40] This effect has been linked to the element's mutagenic and carcinogenic potential.[53] Arsenicosis is pronounced during periods of development, where the toxicant can potentially leave the patient immunocompromised and at higher risk for other diseases.[12] Thus, the toxicant can affect almost the entire body in some way. Experimental studies have revealed potential links to a variety of problems. Patients experiencing arsenicosis have shown cognitive impairment and other neuropathic issues.[40] Some evidence suggests that children are especially vulnerable to these cognitive effects due to their continuing development.[54] One study determined a connection between arsenic exposure and the dilation of the pulmonary artery in response to chronic lung disease.[55] Another study reported low levels of chronic arsenic exposure might contribute to the development of diabetes.[56] Cardiovascular diseases such as ischemic heart disease have also been found to be related to inorganic arsenic exposure.[40] Toxicant accumulation of heavy metals and arsenic is largely individualized and can be influenced by genetics and environmental surroundings.[57] This list of potential effects is therefore not complete or universally applicable. Nevertheless, it is clear that the scope of arsenic toxicity is broad, and research will almost certainly discover new disease connections in the future.

Possible Mechanisms of Action. The scientific understanding of the arsenic mechanism of action in biological systems is far from complete. Unlike some xenobiotics, arsenic can affect several biological mechanisms and result in a wide range of effects.[12] It has the potential for both genetic and epigenetic changes, meaning it can have mutagenic effects at the DNA sequence level.[58] Short-term exposure is connected to the increased production of reactive oxygen species (ROS),[59] which are apoptosis-inducing agents that are capable of disrupting a number of key processes.[59] One human mechanism ROS may interrupt is mRNA deadenylation. In this case, AsO_3^{3-}/H_3AsO_3 selectively induces proteolytic degradation of two enzymes, Tob and Pan3, which results in disruptive oxidative stress.[60] Oxidative stress has also been connected with cancer as well as other benign diseases.[61]

Research suggests that one of the most sensitive sites for arsenic exposure is the lungs.[55] The methylation of arsenic species to organic acids is considered to be connected to cancer in the lungs and the bladder.[48] This sensitivity may also be in part because of the miRNA-21 molecules in the lungs. One study has indicated that AsO_3^{3-}/H_3AsO_3 up-regulates miR-21, which in turn represses the expression of the PDCD4 siRNA. The up-regulation of the oncogene Twist1 caused by a decrease in the neoplastic transformation inhibitor programmed cell death 4 (PDCD4) small interfering RNA (siRNA) contributes to epithelial−mesenchymal transition (EMT).[62] This effect is more clearly illustrated in the flowchart in Figure 2.

Human prostate epithelial cells are another target of arsenic and ROS. One study showed that the expression of DNA repair genes ERCC6, XPC, and OGG1 are influenced by arsenic.[63] The study concluded that chronic exposure causes DNA damage while increasing cell survivability, promoting the possibility of neoplastic transformation. The sensitivity of the skin to the toxicant may be partially due to the inhibition of SIRT1 activity.[19] The number of potential targets for arsenic is daunting, but it means that there are many proteins that can be used to detect the effects of arsenic exposure. A study on urinary tract epithelial cells identified one example where three cytokines were found that can potentially be monitored as arsenic biomarkers.[47] Establishing these biomarkers and analyzing the related mechanisms are among the most promising leads available in controlling and eliminating arsenic-related ailments as a worldwide threat.

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Therapeutic Applications. Whereas arsenic has long been associated with cancer and other health problems, it has also been shown to have therapeutic effects in blood and solid cancers.[64] Arsenic trioxide is a chemotherapeutic that has been adopted for the treatment of leukemia.[65] Studies demonstrate that it can be an effective countermeasure for cancers such as mesothelioma, breast cancer, and cervical cancer.[64,66,67] This is possible because of arsenic's capacity to induce apoptosis. Arsenic trioxide is specifically used due to its ability to cause autophagic cell death.[68] It induces the mitochondrial pathway via oxidative stress, DNA damage, change of mitochondrial membrane potential, and translocation/up-regulation of apoptotic protein.[65] Experiments with arsenic sulfide have shown promise that it could be an effective anticancer drug.[69] This new compound has not yet been as widely adapted as arsenic trioxide. Despite its success in combating cancer, the use of arsenic and autophagy is still somewhat controversial.[68] This is due to the bidirectional nature of the element and its capacity to harm as well as help.[61]

Worldwide Exposure and Study. Arsenic contamination worldwide is a problem of epidemic proportions. This is particularly true in terms of polluted water sources. Surveys from organizations such as the EPA and the British Geological Survey predict that millions of people have been exposed to arsenic via contaminated drinking water.[70] Recent research has investigated the role of accumulation in edible plants as a potential source of heavy metals and arsenic. Studies in places such as (Sargohda) Pakistan, (Delhi) India, Bangladesh, and the Xinjiang province in China are all in agreement that metal and arsenic contamination in produce poses a threat to human health.[5,20,71,72] There is research in (San Luis Potosi) Mexico, (Gejiu) China, and the Bengal Delta Plain[5,24,26,73] that has focused on the effects of arsenic contamination on the plants themselves as well as in soil biota. All of these studies have contributed to a better understanding of the interaction of plants with arsenic and heavy metals.

INTERACTIONS OF PLANTS WITH ARSENIC AND HEAVY METALS

Plants and Arsenic Uptake. There are several key factors to consider in the interaction of plants with arsenic and other pollutants. A very thorough review of arsenic's interaction and metabolism in plants was conducted in Meharg and Hartley-Whitaker's paper.[74] Due to the broader scope of the present review, these processes will be only summarized and expanded for subsequent experimental evidence. The most important thing to note is the nature of the mechanisms activated within plants in response to the contamination. Plants grown in areas of high arsenic contamination have been shown to exhibit slightly reduced biomass,[25] but the problem of contamination is broader than just the size of the plant. Most of the arsenic and heavy metals present in plants come from the cultivation soil,[9] which in most cases is initially contaminated via irrigation water and tainted fertilizers.[73]

Hazards and Risks of Accumulation. The safety of consuming produce irrigated by arsenic- or metal-contaminated water is a worldwide health concern. Even plants that contain only trace levels of a contaminant can still contribute to the total risk of exposure.[71] Some research states that vegetables with higher water retention accumulate more arsenic.[20] This has led to studies of plants such as lettuce, which showed a high concentration of arsenic in the roots.[7] Produce that has shown potential for dangerous arsenic accumulation include maize, tobacco, lotus roots, spinach, bitter gourd, Chinese jujubes, arum, radish, and most grains.[3,13,19,21,70−73] One grain of particular interest in the research community is rice. This plant is an inherently efficient accumulator of arsenic and constitutes a major exposure route for arsenic's inorganic species.[75] The high sensitivity of rice to contamination is attributed to its nodulin 26-like intrinsic aquaporin channels, which allow arsenic to interfere with amino acid mechanisms and compromise the nutritional value of the grain.[76] This makes growing rice problematic worldwide. It becomes especially difficult in flooded paddy fields, which facilitates the mobilization of AsO_3^{3-}/H_3AsO_3 and enhances its bioavailability in the soil.[73] Although research states that brown rice tends to accumulate more arsenic than white rice,[75] all types of rice are potentially significant sources of contamination. Rice is so efficient an accumulator that one study even incorporated rice in experimental phytoremediation techniques.[25]

Whereas many studies have been conducted on phytoremediation of polluted areas, other research has sought to identify plants naturally resistant to contamination. One such plant that has shown promise is the tomato. Analysis of tomato roots grown in contaminated soil showed a high concentration of arsenic uptake,[20] but another study found very little accumulation of arsenic or any metals in the fruit portion of the plant.[9] This means that tomato roots serve as an effective protection mechanism and might make it an effective crop for areas where contamination is a concern. Extreme arsenic concentrations have still been found to decrease root length and fruit size in tomatoes.[31] The prevalent emphasis of research is therefore still on phytoremediation of the soil.

Environmental Effects and Interactions. Arsenic and heavy metals in soil can present problems for soil biota as well as plants and animals. Research suggests that polluted soil, particularly sites that suffer repeated contamination, suffers a decrease in enzyme activity, bacterial life, and fungal growth.[77] Because of the major role the biota play in soil function, the resulting environmental stress can have far-reaching effects.[22] Xenobiotics enter the plants alongside other nutrients in the rhizosphere through the roots and enter the shoots. These parts have a unique relationship of translocation, which varies from plant to plant.[78] Generally, metal accumulation is higher in the roots than in the shoots, forming a natural barrier to protect the sensitive fruits from potential toxicity.[20] There are several plants that are exceptions to this general rule, however, and accumulate metals in their shoots.[79] Studies suggest that this protective mechanism has various degrees of success depending on the contaminant.[6] For example, one study reported that arsenic is more bioaccessible for edible parts of plants than the similar group 15 element antimony.[36] Vegetables are also capable of absorbing metals out of the air in their exposed parts,[5] although this is not the most efficient mechanism.

Effects of Arsenic Speciation on Plant. Another important factor in the interaction between plants and arsenic is speciation. Research has determined that the species of arsenic present makes a noticeable impact on uptake and translocation.[30] AsO_4^{3-}/H_3AsO_4 is generally more easily absorbed through roots than other inorganic species.[76] This property, along with the affinity of AsO_4^{3-}/H_3AsO_4 to replace phosphate in reactions, has translated into the use of phosphate fertilizers to prevent arsenic accumulation in crops such as tobacco.[80] Once it is inside the plant it has been determined that AsO_4^{3-}/H_3AsO_4 is readily reduced to AsO_3^{3-}/H_3AsO_3.[18] The concentrations of AsO_4^{3-}/H_3AsO_4 and AsO_3^{3-}/H_3AsO_3

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tend to fluctuate in plant systems but maintain a stable ratio over time.[15]

Areas of Potential Further Study. The unique interactions of arsenic with each plant system make it an area in need of further research. A more complete understanding of these relationships will be vital in the effort to better control human exposure. It may also provide new insight into the safe removal of arsenic from contaminated areas. The natural accumulation of nutrients and contaminants by plants has already given rise to phytoremediation and similar bioremediation methods as highly promising mechanisms of cost-effective environmental cleanup.[35] These methods have already been the topic of thorough research, and studies are ongoing to improve worldwide practices of remediation.

TECHNIQUES FOR THE REMEDIATION OF ARSENIC AND OTHER METALS FROM WATER AND SOIL

Commonly Accepted Methods of Remediation. Remediation techniques are broad in scale and scope. They are often large-scale undertakings that are both laborious and costly.[34] Remediation can be used to remove metals such as arsenic and organic contaminants such as pesticides from water and soil, both of which employ unique methods. Water remediation methods have been the topic of particularly intense study. Two well-established methods include oxidation and forward osmosis.[32] Experimental methods also continue to be developed for the removal of arsenic from water. One such method is electrocoagulation, which aims to remove the toxicant using iron electrolysis with locally available materials.[81] Titanium dioxide-based technology is another method that uses granular columns to adsorb AsO_3^{3-}/H_3AsO_3 and cadmium from highly concentrated areas such as smelting wastewater.[82] There are also hybrid technologies that combine different methods to create a potentiating effect.[28] Improved water remediation could have widespread effects on biological systems. Improving soil conditions is equally important for plant life. There are fewer techniques used to remediate contaminants in soil. Two that are commonly used include thermal treatment to volatize molecules or simple soil washing to try to pull away soluble ions.[83] These methods are useful for removing arsenic, but can also be used effectively for mercury.

Experimental Methods and Appropriate Application. Experimental work in remediation has yielded potential techniques such as nanoscale iron particles, which react with particles in soil or water when injected.[84] Another study investigated biosurfactants that use anionic agents to mobilize contaminants including arsenic.[85] A third process focused on phosphate fixation, which transforms many contaminants including arsenic into insoluble or barely soluble species and can be used in extremely cold environments.[86] Chemical coagulation is a particularly effective method for removing arsenic from water but can potentially leave undesired anions behind and is therefore not very environmentally efficient.[81]

Remediation techniques vary based on conditions, and the most efficient application method for remediation is highly situational based on chemical circumstances.[87] Therefore, the most experimentally proven bioremediation techniques such as phytoremediation are widely used due to their environmental consciousness and versatility.[34] Bioremediation is the use of microorganisms and plants for the purpose of remediating soil.[88] These methods are unique from older methods of environmental cleanup in that they exploit natural biological processes to help certain microorganisms better remediate soil and groundwater.[32] They are particularly effective when it comes to the treatment of heavy metals. Two examples of this are the use of bacteria such as hay bacillus (*Bacillus subtilis*), which employs chemical reduction of Cr(VI) to the less toxic Cr(III), and the organic material biochar, which is charcoal used to improve soil productability, to raise soil pH to make hazardous metals less bioavailable for plant uptake.[88] In terms of arsenic, both AsO_3^{3-}/H_3AsO_3 and AsO_4^{3-}/H_3AsO_4 can be treated with bacteria for remediation, although AsO_3^{3-}/H_3AsO_3 can also be aerobically oxidized via arsenite oxidase enzymes.[33] One microbial agent that is particularly adept at detoxifying AsO_4^{3-}/H_3AsO_4 is *Chrysiogenes arsenatis*, which uses nitrate and nitrite as electron acceptors.[33]

Some research has attempted to develop new, advanced techniques to improve remediation efforts. Biosorbents such as iron oxide-coated biomass (IOCB) have increased in popularity due to their eco-friendly nature. The capacity of IOCB to remove aqueous arsenic makes it an effective alternative to more conventional treatments.[2] A recent study developed an in situ method involving the injection of iron-containing reagents into an aquifer, causing the arsenic to participate in the iron oxidation process and be trapped in crystalline structures. A simulation of this technique involving added arsenic yielded promising results, with all of the aqueous arsenic being removed.[89] Another approach to establishing new techniques is to combine bioremediation techniques with phytoremediation to reduce the level of a target contaminant. Called phytobial remediation, these hybrid methods are designed to utilize both types of technique in a way that they complement each other's limitations.[35] Although they are not yet widely adopted over more traditional approaches such as phytoremediation, these advanced methods could represent the future of environmental arsenic cleanup.

Phytoremediation and Environmental Fate. Phytoremediation of contaminants such as arsenic can occur through at least five mechanisms, including phytoextraction, phytostabilization, phytovolatization, phytofiltration, and phytostimulation.[35] The downside to this technique is that regardless of the mechanism, contaminants can potentially interfere with growth and essential metabolic processes.[18] Some evidence suggests that contaminants accumulate more readily in the roots of plants than in their shoots. This may be a mechanism to protect the plant's other more susceptible parts.[7] This effect is dependent on the plant. For arsenic, speciation is key to how the contaminant interacts with plant uptake and translocation.[30] For example, AsO_4^{3-}/H_3AsO_4 is reportedly more prone to being absorbed by roots than AsO_3^{3-}/H_3AsO_3.[76] Once inside the plant, however, AsO_4^{3-}/H_3AsO_4 is readily reduced to AsO_3^{3-}/H_3AsO_3.[18] AsO_3^{3-}/H_3AsO_3 is considered in most cases to have more deleterious effects on plants, such as shorter root systems and decreased fruit size, than AsO_4^{3-}/H_3AsO_4. This may be because it inhibits enzymes that need free sulfhydryl groups to function properly or because AsO_3^{3-}/H_3AsO_3 is the more soluble of the two inorganic species.[31]

Although speciation of contaminants is important, bioaccumulation, bioavailability, and bioaccessibility are the most important properties of phytoremediation and environmental fate.[87] Whether one is considering metal uptake in edible plants or environmental restoration, the capacity of each metal's bioaccumulation, bioavailability, and bioaccessibility must not be overlooked. These properties are closely related, but each serves a different purpose in the phytoremediation process. Studies in toxicology and human health are particularly

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Instrumentation	Detection Limit	Strengths	Weaknesses
GFAAS Thermo Elemental AAS, GFAAS, ICP or ICP-MS? Which technique should I use? 2001	Sub-ppb range	• Small sample size • Compact • Few spectral interferences	• Slower • Chemical interferences • 1 – 6 elements / determination • No screening ability • Limited range
ICP-OES Thermo Elemental AAS, GFAAS, ICP or ICP-MS? Which technique should I use? 2001	1 – 10 ppb range	• Multi-element (73) • High productivity • Few chemical interferences • Robust • Excellent screening abilities • High total dissolved solids • Solid or organic samples	• Moderate to low detection limits • Spectral interferences • Some element limitations
ICP-MS Thermo Elemental AAS, GFAAS, ICP or ICP-MS? Which technique should I use? 2001	ppt range	• Multi-element (82) • High productivity • Wide dynamic range • Isotopic measurements • Fast semi-quant screening • Hybrid techniques (LA, LC) • Easily interpreted data	• Method development skill required • Higher initial capital cost • Some spectral interferences (well defined) • <0.2% dissolved solids
XRF http://serc.carleton.edu/research_education/geochemsheets/techniques/XRF.html	Ppm range	• Well-suited for bulk analysis in rock/sediment • Field applications (FPXRF)	• Not as precise or accurate with elements Z<11 • Cannot distinguish isotopes • Large sample sizes
Mercury CVAA http://www.labcompare.com/10-Featured-Articles/133134-Mercury-Analyzers-in-the-Laboratory/	ppt range	• Short analysis time (1-3 min)	• Only analyzes for mercury

Figure 3. Strengths and weaknesses of several common techniques of analysis. Inductively coupled plasma optical emission spectrometry (ICP-OES) is also called inductively coupled plasma atomic emission spectroscopy (ICP-AES). Graphite furnace atomic absorption spectrometry (GFAAS), inductively coupled plasma mass spectrometry (ICP-MS), and ICP-OES are all useful for determining arsenic concentration. Sources: Labcompare, Thermo Scientific, and Science Education Resource Center at Carleton College.

interested in bioaccumulation. Bioaccumulation is the process of contaminants moving up the food chain, and it is important to take into account intake, biotransformation, and elimination of each species on the food chain, which all affect the ultimate human toxicity of the contaminant.[90]

The difference in bioaccessibility and bioavailability is that the former refers to the total amount of a contaminant in an environment, whereas the latter is only the amount that can enter living beings.[87] Bioaccessibility can be affected by environmental conditions. Thiols can cause an increase of bioaccessible arsenic in the form of methylarsenicals including monomethyl monothio arsenic acid ($MMMTA^{5+}$) and dimethyl monothio arsenic acid ($DMMTA^{5+}$).[91] Bioavailability has been reported to be the most vital of the three when it comes to remediation.[87] One environmental assessment states that this is due to the fact that bioavailability is closely tied to risk characterization.[92] Determining the phytoremediation abilities of individual plants provides more information not only about how to clean up environmental contaminants but also which consumable crops pose a risk to human health.

Hyperaccumulators. Phytoremediation is based on a group of plants called hyperaccumulators. In these plants arsenic is naturally stored in the shoots instead of in the roots, as is the case in most plants.[34] In hyperaccumulators, organic acids serve as chelating agents, which allow the plant to store more metals and arsenic than other plants without suffering deleterious effects to their growth and metabolism.[93] This removal of contaminants from the soil system can help make the system safer for future crops. One study recommends multiple phytoremediation cycles to further optimize the soil.[27]

The first plant established as a hyperaccumulator was the Chinese brake fern (*Pteris vitatta*), and today the species is used for its tolerance of up to 1500 ppm of arsenic in soil.[94] The fern can increase arsenic bioavailability by exuding dissolved organic carbon to change rhizospheric pH.[30] Other plants considered to be hyperaccumulators of arsenic include barnyard grass, curly endives, and most other ferns.[25,31,73] It is important to note that different plant species hyperaccumulate different contaminants. For example, fire phoenix (*Festuca arundinacea*) and alfalfa (*Medicago sativa*) are highly efficient in extracting polycyclic aromatic hydrocarbons (PAHs),[95] whereas Alpine penny-cress (*Noccaea caerulescens*) can tolerate large amounts of zinc and cadmium.[93] Choosing the proper phytoremediation technique and hyperaccumulating species is essential to effective environmental remediation. Understanding the properties of individual plants has important implications for human consumption and health.

Controlling the Contamination Problem. Although phytoremediation and other techniques have helped improve conditions in arsenic-contaminated areas, the effects of arsenic toxicity are still spread throughout the world, although the removal of environmental arsenic is extremely important, understanding the nature of its toxicity is key to minimizing its influence on society. This is especially true in places where exposure has reached epidemic proportions such as Bangladesh and India.[20,23] Determining all possible targets of arsenic toxicity will greatly support future efforts to fight the symptoms

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and even identify methods of early detection. To further aid in the understanding of arsenic, research is constantly being conducted on better ways to analyze contaminants. One such experiment combined traditional methods to help better track its inorganic species in water.[38] The continued study of these new methods will lead to better phytoremediation in the future.

METHODS OF ARSENIC AND METAL QUANTIFICATION

Commonly Accepted Methods of Metal Determination. There are several accepted methods used to determine metal concentrations. Figure 3 contains brief descriptions of a few commonly used techniques. The appropriate technique is dependent on factors such as sample size and necessary detection limit. One method that is commonly employed due to its capacity to test for multiple metal concentrations is inductively coupled plasma mass spectroscopy (ICP-MS).[57] Some experiments have conducted arsenic speciation using high-performance liquid chromatography (HPLC).[30] One method uses HPLC to separate different species of arsenic in blood plasma and then find the concentration of each using ICP-MS with a detection limit of 2.5 ppb.[10] When a study is primarily interested in the total concentration, atomic absorption spectrometry can assess a digested solution via graphite furnace (GFAAS).[27] This technique can employ digestion of soft tissue samples from a plant to determine the total arsenic present with a detection limit of 200 ppb.[10] It is useful for assessing accumulation and has been used experimentally to evaluate vegetable uptake.[72] Other analytical methods that are proficient for finding even low arsenic concentrations include hydride generation atomic fluorescence spectrometry (HG-AFS), which has arsenic detection limits as low as 100 ppb, and inductively coupled plasma optical emission spectroscopy (ICP-OES), which can detect as little as 8 ppb in an acid solution.[7,10,38,96]

Emerging and Experimental Methods. Several emerging studies propose that developing hybrid techniques, such as coupling HPLC and HG-AFS, may result in simple, reliable methods for routine laboratory procedures.[97] One study aims to find a viable method of direct water determination by combining dispersive liquid−liquid microextraction with solid-phase extraction to prepare samples for the graphite furnace.[38] Another method sometimes used for its uniquely non-destructive testing is magnetic resonance imaging (MRI) alongside high-resolution magic angle spinning nuclear magnetic resonance (HR-MAS NMR) to observe changes in metabolites of polluted samples.[98] All established and experimental methods should be considered in future studies and could serve a role in solving the problem of arsenic worldwide.

DISCUSSION

On the basis of this assessment of the literature, arsenic toxicity is clearly a topic of widespread importance. Even with the foundation of knowledge established by years of research, the scientific understanding of the metalloid is continuously evolving. Arsenic has unique physical and chemical properties that facilitate dozens of interactions with biological systems, and each year more mechanisms in various plants and animals are proposed through new studies. Some of these involve human health, and the effects of the element on different organs and systems in the body can be dangerous and even fatal. Continuing to study the interactions between arsenic and human systems is important, as it will help guide not only options of toxicity treatment but also methods of safe cleanup and exposure prevention all the way down to the trophic level of plants.

Accumulation of the toxicant in plants has ramifications across the entire food chain. Several methods of remediation have been investigated for the cleanup of this contaminant. However, the most important problem at present is the tainting of food crops for millions of people in over a dozen countries. Although there is some ongoing research into human arsenic uptake via consumable plants, more is needed to assess the risk of eating specific products. More studies would yield new information concerning which plants are resistant to arsenic accumulation, which ones to avoid planting in contaminated areas, and which are contributing a significant amount of arsenic to the human diet. This research would be instrumental in controlling arsenic exposure and make major progress in permanently solving the problem on a worldwide scale.

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Notes

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ABBREVIATIONS USED

WHO: World Health Organization
IARC: International Agency of Research on Cancer
ATSDR: Agency for Toxic Substances and Disease Registry
MRL: minimum risk level
EPA: U.S. Environmental Protection Agency
MMA: monomethylarsonic acid
DMA: dimethylarsinic acid
AsO_4^{3-}/H_3AsO_4: arsenate
AsO_3^{3-}/H_3AsO_3: arsenite
As-GAC: granular activated carbon-based, iron-containing adsorbents
NCPF: noncirrhotic portal fibrosis
ROS: reactive oxygen species
PDCD4: programmed cell death 4
EMT: epithelial−mesenchymal transition
$MMMTA^{5+}$: monomethyl monothio arsenic acid
$DMMTA^{5+}$: dimethyl monothio arsenic acid
IOCB: iron oxide-coated biomass
PAH: polycyclic aromatic hydrocarbons
ICP-MS: inductively coupled plasma mass spectroscopy
HPLC: high-performance liquid chromatography
GFAAS: graphite furnace atomic absorption spectrometry
MRI: magnetic resonance imaging
HR-MAS NMR: high-resolution magic angle spinning nuclear magnetic resonance
HG-AFS: hydride generation atomic fluorescence spectrometry
ICP-OES: inductively coupled plasma atomic emission spectroscopy

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