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Review Article

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Arsenic Toxicity

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ABSTRACT

Arsenic (As) is ubiquitously prevalent in organic and inorganic forms in the environment. Inorganic arsenic is classified as Group I carcinogen to both humans and animals. It is causing contamination of water, air, and soil, which has led to chronic arsenicos is as a newly-emerging public-health issue. Acute or chronic exposure of arsenic through groundwater endangers the health of more than 100 million people worldwide specially the residents of the densely populated Indo-Bangladesh Gangetic delta. Microbial reduction of iron oxyhydroxide(FeOOH) that causes major arsenic pollution in the plains of Ganges-Meghna-Brahmaputra Rivers has also been discussed. Long–term exposure to arsenic can cause skin lesions, cancer, pulmonary diseases, cardiovascular diseases, neurotoxicity, and memory loss. Several experimental studies performed in Zimapan, Mexico have shown high concentration of inorganic As in BECs, which can be used as a marker for cancer. With more stringent regulations, arsenic content requires to be reduced to a few parts per billion. Various techniques are being developed to provide arsenic-free drinking water like membranes, coagulation, anion exchange, disposable iron media, softening etc. Several natural methods like bioremediation and phytoremediation are also being widely used.

Keywords: Arsenic, drinking water, arsenicosis, urinary bladder epithelial cells, iron oxyhydroxides

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INTRODUCTION

Arsenic, a naturally occurring toxic metalloid is ubiquitously found in the environment. It is the 20th most abundant metal in the Earth's crust and is one of the major constituent of more than 200 minerals like sulphides, arsenates, arsenites and oxides [1].It can be derived from natural as well as man-made activities [2].

In nature it spreads through the weathering of arsenic containing rocks and ores, volcanic eruptions and certain biological activities. The permissible concentration of arsenic in soil is 0.2-40 µg/g, in urban air is 0.02ng/m^3 and in natural water is 1-2 µg/L^2. In addition to this, anthropogenic activities like metal extraction, smelting, burning of fossil fuels, processing wastes, poultry and swine feed additives and use of arsenical herbicides or pesticides are also a source of arsenic contamination [3].

Over the centuries arsenic has been used for manufacturing herbicides, pesticides and wood preservatives [4].Today, Gallium Arsenide is a fundamental compound used in semiconductor, light emitting diodes, transistor technology, and detection of X-rays [5]. It is a well-known poison and is used to make rat poison. Arsenicum album (white arsenic), prepared from arsenic trioxide powder isused as a homeopathic remedy [6]. Despite being a potential toxic, arsenic is an essential element needed for our physiology. A level of about 0.00001% is needed for our growth and a healthy nervous system. WHO has set guideline value of 0.01 mg/L (10 ppb) for As in drinking water [7].

It occurs in the environment in two forms- inorganic and organic arsenic. Organic arsenic is found in some food like fish and shellfish. On the other hand, inorganic arsenic is prevalent in nature in various oxidation states (-3,0,+3,+5) but is mostly found as trivalent arsenite(iAs^{III}) or pentavalent arsenate (iAs^{V}) [8]. It is usually found in industries, building products and arsenic contaminated water. Arsenic is extremely toxic in its inorganic form and is also

regarded as number one toxin in the United States Environmental Protection Agency(UNEPA) list of pollutants and as Group I carcinogen by International Agency for Research on Cancer(IARC) [9], [10].

Arsenic contamination in water is a global problem, majorly affecting the people of countries like Argentina, Chile, Mexico, China, USA, Hungary and South and East Asia [11]. The most affected region is the Indo-Bangladesh Gangetic delta, with an estimated 25 million people in Bangladesh in over 42 districts and over 20% of the population of West Bengal being exposed to contamination. Hence, Arsenic exposure is a major environmental concern [12].

2. MECHANISM OF ARSENIC EXPOSURE

Ingestion and/or inhalation are the two routes of As exposure. Trivalent arsenic oxide, being more lipid-soluble, is easily absorbed by the skin as compared to the pentavalent form. The exact mechanism for the metabolism of arsenic is still not known, but a few hypotheses have been put forward.

Arsenic metabolism is a chain of reduction and oxidation reactions[16]. As show in figure 1, the gastrointestinal tract absorbs iAsIII and iAsV and the methylation of As by the enzyme methyltransferase takes place in the liver. Inside the cell, AsV is converted to AsIII, in the presence of S-adenosylmethionine (SAM), a methyl donor and co-factor glutathione (GSH). It is then methylated to monomethylated (e.g., MMAIII, MMAV) and dimethylated arsenic metabolites (e.g., DMAIII, DMAV) [13], [14], [16]. It has been proposed that methylation can activate the toxic and carcinogenic properties of arsenic, since it has been shown that mono/dimethylated As species can affect gene transcription, and are more formidable enzyme inhibitors and cytotoxins than non-methylated arsenical species. Cellular damage by biotransformation of As can occur through reactive oxygen species (ROS), and also through epigenetic mechanisms like changes in DNA methylation patterns, altered expression of microRNAs and histone modification [15], [16].

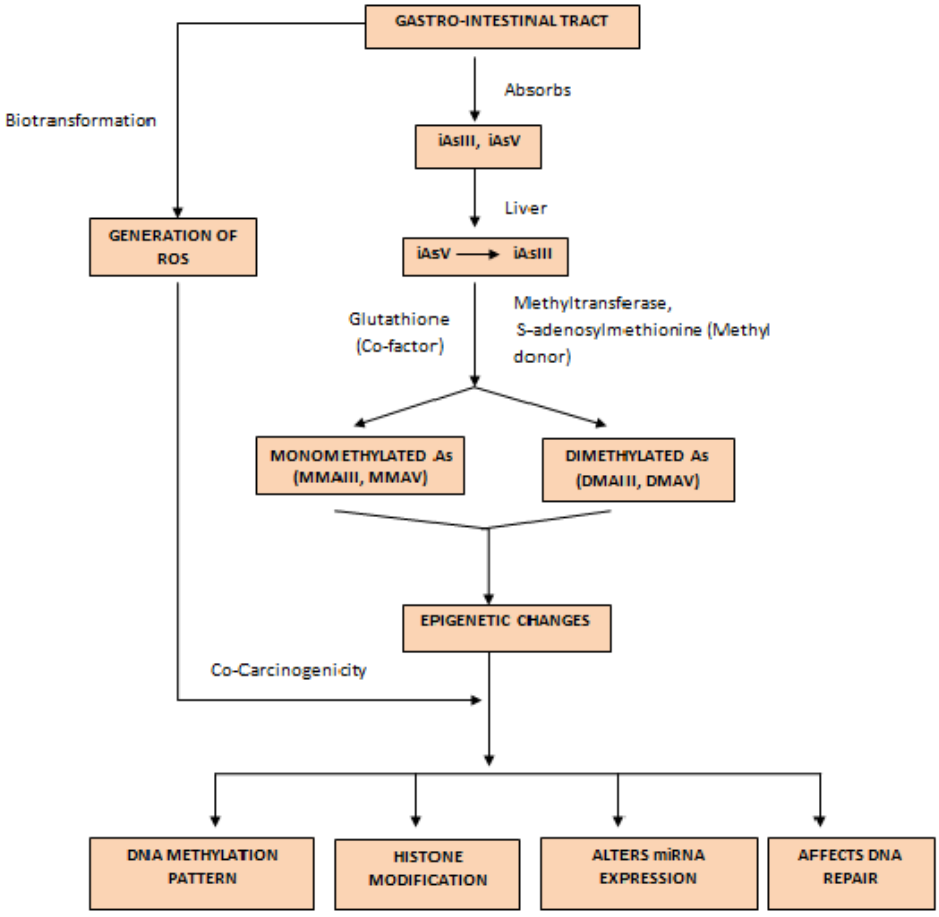

Figure 1: Schematic representation of proposed arsenic-induced carcinogenic mechanisms [1], [16]

2.2 STAGES OF ARSENIC POISONING

There are two types of Arsenic Poisoning:

Acute Poisoning: Acute arsenic poisoning occurs due to accidental ingestion of pesticides or insecticides and sometimes from attempted suicide. Doses less than 5mg result in vomiting and diarrhoea but are resolved within 12 hours without treatment. Lethal doses for acute poisoning varies from 100mg to 300mg and depending on the amount consumed, death occurs in 24 hours to 4 days [17].Some clinical features observed are nausea, vomiting, abdominal pain, acute psychosis, skin rash and seizures. Haematological abnormalities, respiratory failure, pulmonary oedema, frequent neurological manifestations like peripheral neuropathy and metabolic changes are also reported. Best indicator of recent ingestion (1-2 days) is urinary arsenic concentration [18].

Chronic Poisoning: Long term exposure to arsenic leads to arsenic poisoning or arsenicosis. The absorbed arsenic accumulates in liver, lungs, kidney, muscles, nervous system, spleen and heart with smaller amounts depositing in keratin rich tissues like hair, skin and nails even at low exposure. This leads to multiple organ failure and hence malignancy. General clinical features include skin lesions with hyperpigmentation, depigmentation, and hyperkeratosis, arsenic-related malignancies of the skin, lung, kidney and liver, vascular diseases such as peripheral and cardiovascular diseases, arteriosclerosis, Blackfoot disease, and Hypertension. Non-specific symptoms include abdominalgia, diarrhoea, dyspepsia and mental slowing or loss of memory[19].

3. CHRONIC ARSENICOSIS IN CATTLE WITH SPECIAL REFERENCE TO ITS METABOLISM IN ARSENIC ENDEMIC VILLAGE OF NADIA DISTRICT WEST BENGAL INDIA.

More than 60 million people are at high risk of arsenic exposure in Asia alone, out of which maximum people are from West Bengal, India. According to the reports, in spite of being supplied with arsenic free water for 12 years, people still suffer from arsenicosis. It was found that this was mainly due the consumption of milk and milk products being obtained from cattle that consumed As in drinking water[20]. Bakul K. Dattaet al. (2010) performedan experiment using the cattle faecal matter, hair,etc to find out whether the ingested arsenic in cattle was present in the milk that was consumed by the people directly or indirectly by milk product [21]. Thirty milch cattle were selected randomly from both Ghetugachi village, Chakda block of district Nadia, West Bengal, India (experimental village) and Akna village of district Hooghly, West Bengal, India (control village). Hair, faeces and milk samples were collected from the cattle. Drinking water, straw samples andIndian cottage cheese (chena) from sweet shopswere also collected. Speciation of arsenic in milk and faeces of experimental and control village was done**.** Arsenic content was observed in all the samples using atomic absorption spectrometer.It was found that thetotal arsenic content in the samples of milk, milk products, water, straw, hair and faecal matter were high in the cattle of the experimental village in comparison to the control village. As shown in Figure 2, speciation study demonstrates that the mean arsenite concentration was 77.29%,while the mean arsenate concentration was14.49% and organoarsenic compounds concentration was 8.21% in the milk samples. Whereas the concentration of organoarsenic compounds in faeces was 90.93%.

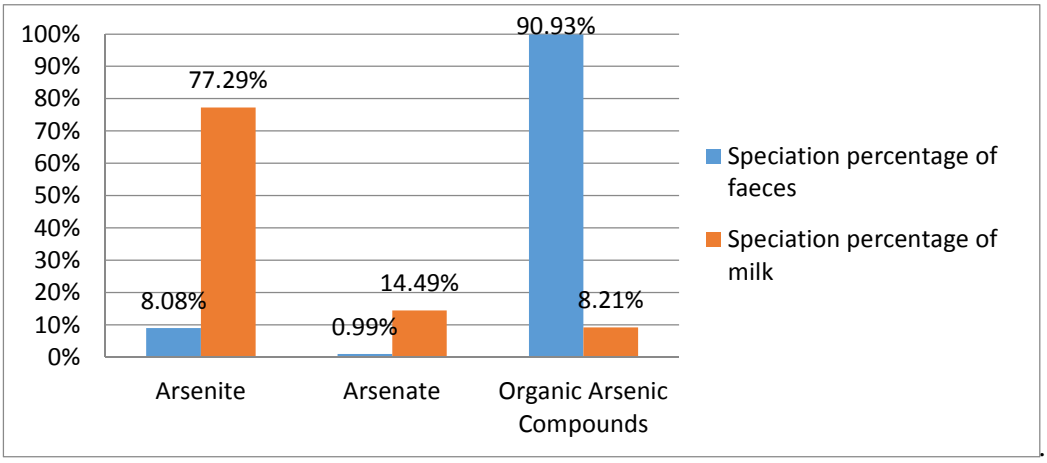

Figure 2- Graphical representation of speciation percentage in faeces and milk [21]

4. SPECIATION OF ARSENIC IN EXFOLIATED URINARY BLADDER EPITHELIAL CELLS FROM INDIVIDUALS EXPOSED TO ARSENIC IN DRINKING WATER

In human being, inorganic arsenic is methylated to methyl- As (MAs) and dimethyl-As (DMAs) species. Dimethylthioarsinic acid (DMTA) has recently been detected in urine samples of the people in the arsenic affected areas [22]. Studies have shown that arsenic concentration in urine can be used as a marker in order to mark inorganic

arsenic. Series of experiments were performed where twenty-one individuals (2 males and 19 females between 14–64 years of age) were randomly selected from Zimapan, Mexico, where the people were exposed to high concentration of arsenic in drinking water**.** The urine samples as well as bladder epithelial cells (BECs) were collected from these people. BECs were centrifugated at 300 × g for 10 minutes at 4°C in order to isolate them and the cells were transferred into a 1.5-mL eppendorf. Washing was done using phosphate-buffer saline (PBS), and centrifugation was again performed at 300 ×g for 5 minutes at 4°C. The cells were again washed with PBS and centrifuged. The pellets were packed and stored in dry ice at –80°C for a few days. The urine samples were stored at –75°C. Lysis of BECs pellets and urine samples was done using 1.25 mL of 0.5% solution of Triton X-100 (Sigma-Aldrich) in deionized water. The BEC lysates were treated with 2% L-cysteine hydrochloride at room temperature for 70 minutes, which reduced pentavalent arsenic species into trivalent species. Then it was treated with Sodium borohydride ($NaBH_4$) in a Tris-HCl(Sigma- Aldrich) buffer (pH 6.0) for generating hydrides. Analysis of As species in urine and BECs samples was done using hydride-generation atomic absorption spectrometry using cryotrapping (HG- CT-AAS).

Arsenic concentration in the urine samples was found to range from 4.8 to 1,947 ng As/mL.69% of arsenic metabolites were found to be DMAs [8]. In BECs, the arsenic concentration ranged from 0.18 to 11.4 ng As/mg protein out of which 43% were DMAs. 42% of inorganic arsenic was present in BECs as compared to 17% in urine. MAs were present in lesser concentration in BECs as well as in urine samples. The As metabolites in human urine have been used as markers for a person's capacity to methylate inorganic arsenic. This study shows no important connections between the concentration of As species in urine and BECs [9].The test on urinary samples shows that Asspecies have shown only a recent exposure to inorganic As. However, As species concentration in BECs reflect the integrated exposure over a time of about 200 days. Thus, Arsenic species in BECs provide a more appropriate tool for risk assessment of cancer of urinary bladder and other diseases which are associated with chronic exposure [12].

5. TESTING POLLUTION MECHANISMS FOR SEDIMENTARY AQUIFERS IN BANGLADESH

Aquifers, 100m-300m deep provides Bangladesh and West Bengal with more than 90% of its drinking water. The groundwater contains more than 50 µg/L of arsenic in up to 1,000,000 water wells placing the health of 20 million people at a risk. In aquifers beneath the Holocene floodplains, in the alluvial and deltaic plains of the Ganges, Meghna and Brahmaputra Rivers, the concentration of arsenic commonly exceeds the Bangladesh drinking water standards (50 µg/L) [23]. Data was collected for water samples from the wells of Faridpur and Lakshmipur districts of Bangladesh and compared with the literature data to test three mechanisms proposed to explain the release of As in groundwater –

1. Anoxic conditions permit reduction of iron oxyhydroxides (FeOOH) and release of sorbed arsenic to solution
2. Arsenic is released by oxidation of arsenical pyrite in the alluvial sediments as aquifer drawdown permits atmospheric oxygen to invade the aquifer
3. Arsenic anions sorbed to aquifer minerals are displaced into solution by competitive exchange of phosphate anions derived from overutilization of fertilizer to soil surface.

It was inferred that the mechanism of arsenic pollution by the oxidation of arsenical pyrite is acceptable only for oxic environments, typically surface waters. When the arsenic pollution occurs in subsurface and anoxic environments, the pyrite oxidation model is not applicable, and a different model is necessary. Therefore, the reduction of FeOOH is a suitable model that would be applicable in most of the situations as it is generic and not site specific. In the deltaic plain of the Ganges-Meghna-Brahmaputra Rivers, concentrations of arsenic in groundwater commonly go beyond the regulatory limits because FeOOH is microbially reduced and releases its sorbed load of arsenic into the groundwater. The pyrite oxidation method and competitive exchange with fertilizer phosphate method do not contribute to arsenic pollution. Microbial degradation of buried deposits of peat causes severe pollution. Reduction of FeOOH and release of sorbed arsenic serve as a generic model for arsenic contamination of aquifers where the water is anoxic, especially where the organic matter is abundant (e.g.- in deltaic areas that support peatland during climatic optimum conditions).

6. ARSENIC REMOVAL FROM WATER

As contamination in groundwater is a problem of catastrophic proportion because arsenic at high concentrations in drinking water causes severe health effects. Moreover, the epidemiological evidence indicates that arsenic concentration exceeding 50µg/L is not safe for public health [24].Arsenic removal technologies have become increasingly important. The current regulation of drinking water standard is becoming more stringent and requires arsenic content to be reduced to a few parts per billion. Conventionally, there are several methods for arsenic removal like coagulation and flocculation, precipitation, membrane filtration, adsorption and ion exchange[25], [27].

Alternative methods like ozone oxidation, bioremediation, phytoremediation and electrochemical treatments are also used in the removal of arsenic.

In the process of arsenic removal, coagulation and flocculation are among the most common methods employed. Electrocoagulation (EC) is a favourable electrochemical treatment technique that does not require the addition of chemicals or regeneration. Ion exchange resin and IOCS method are both capable of removing organic species of arsenic from drinking water. The technique of precipitation, generally using Fe (III) or lime softening is suited for removal of higher concentrations of arsenic [26], [28]. Membrane technology, especially nanofiltration is used to meet the regulations for low arsenic concentrations in drinking water. Table-1 shows some of the main arsenic removal technologies along with their advantages, disadvantages and percentage of arsenic removed by them.

Table-1: A review of some of the main arsenic removal technologies [27]

Technologies	Advantages	Disadvantages	Removal (%)
Reverse osmosis	No toxic solid waste is produced.	High tech operation and maintenance required	96
Electrodialysis	Capable of removing other contaminants.	Toxic wastewater is produced	95
Iron coagulation	Common chemicals are available.	Sedimentation and filtration are needed	94.5
Iron oxide coated sand	No regeneration is required. Expected to be cheap.	Produces toxic solid waste. Yet to be standardized.	93
Ion exchange resin	Well-defined medium and capacity. The process is less dependent on pH of water. Exclusive ion specific resin to remove Arsenic.	High cost medium. Requires high-tech operation and maintenance. Regeneration creates a sludge disposal problem.	87
Membrane techniques(Nanofiltration)	Well-defined and high-removal efficiency.	Very high-capital cost. High water rejection.	95
Oxidation/precipitation (Chemical oxidation)	Oxidizes other impurities and kills microbes. Relatively simple and rapid process.	Efficient control of the pH and oxidation step is needed.	90

The advantage of these technologies is that they efficiently remove contaminants but have certain drawbacks like toxic waste production in solid, liquid or sludge form, requirement of high tech operations and maintenance and high purchasing costs. As shown in Table-1, reverse osmosis and nanofiltration techniques are comparable in their high arsenic removal capacity with no toxic waste production. But the cost and maintenance requirements are high in case of nanofiltration.

We also observed that adsorption and membrane filtration techniques are more efficient than other chemical based technologies. Furthermore, Iron Oxide Coated Sand (IOCS) filtration technique based on adsorption of As by iron oxide coated sand, is widely used due to its capability to remove arsenic to a value of less than 5 µg/L, simplicity, ease of operation and applicability to small scale treatment systems. Environment friendly biological methods like bioremediation and phytoremediation that involve removal of arsenic from water by microorganisms and plants respectively are also economical.

CONCLUSION

Contamination of drinking water by arsenic remains a serious public health problem, affecting hundreds of millions individuals worldwide. It affects multiple biological systems, sometimes even years after exposure. Moreover, although a number of mechanisms have been proposed, the exact etiology of arsenicos is is still not known. Arsenic contamination causes health related issues in both human beings and animals. It mostly enters the body of the cattle through straw and drinking water that they consume. Human beings maybe affected by the consumption of As contaminated milk and milk products, in addition to drinking water. The inorganic arsenic gets stored in the skin, nails, hair and epithelial cells of the urinary bladder leading to cancer in the urinary bladder and other diseases. Hence detection as well as removal of arsenic is important from the environment in order to protect humans and animals from its hazardous effects. Removal methods like coagulation and flocculation, precipitation, adsorption and ion exchange, membrane filtration are some of the methods employed for the removal of arsenic in addition environment friendly methods like bioremediation and phytoremediation.

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