ARSENIC: A HARMFUL AND DESECRATE COMPOUND FOR THE HUMANS

SURESH CHANDRA¹, ARYENDU KUMAR SAINTII*, AKASH KUMAR GUPTA²

¹Department of Pharmacy, Pranveer Singh Institute of Technology, Kanpur, Uttar Pradesh, India. ²Department of Pharmacy, Bhabha University, Bhopal, Madhya Pradesh, India. Email: aryendu77@gmail.com

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INTRODUCTION

Arsenic toxicity has become a burgeoning concern as several millions of people are exposed to this chemical through drinking water contamination by arsenic. Arsenic remains a major public health problem. Acute and chronic arsenic exposure through drinking water has been reported in many countries of the world, where a large proportion of drinking water is contaminated with high concentrations of arsenic. As contamination in groundwater has been found to be in more than 105 countries around the world, it has become the worldwide health problem as several millions of people are exposed to this toxicant. Inorganic arsenic contamination in the groundwater has been found to be in more countries like Bangladesh, Vietnam, Nepal, Thailand, and Chile. Arsenic is one of the most toxic metals that shares most of the properties of metals and originates from natural environment. The catastrophe is that the majority of human arsenic toxicity is from polluted drinking water rather than agricultural sources (fertilizers or pesticides). The different areas across the Gangetic plains in Nepal and India also recently reported being affected by the arsenic. The hippocampus is a part of the limbic system that is crucial to memory function and spatial navigation. Hippocampus lesions due to arsenic in humans produce devastating impairments in declarative memory, and similar results have been seen in non-human primates with hippocampus neurobehavioral disorders.

SOURCE OF ARSENIC EXPOSURE

Groundwater is a major source of drinking water in many parts of the world, especially the South-East Asia Region (SEAR) countries. Arsenic contamination of groundwater has been reported in many SEAR countries. The areas across the Gangetic plains in India and Nepal also recently reported as the area affected by it. The World Health Organization (WHO) estimates that >200 million persons worldwide might be chronically exposed to arsenic in drinking water at concentrations above the WHO safety standard of 10 µg/L [7]. In Bangladesh, more than 07–80 million people are at risk of drinking contaminated water. The arsenic levels in the drinking water were found to be ranged from non-detectable to 4700 µg/L. In Chile, it was very high and about 750–800 µg/L. In Argentina, the groundwater concentration of arsenic ranged from 100 to 2000 µg/L. In West Bengal (India), the concentration of arsenic in drinking water is found to be about 60–5700 µg/L and about 40 million people are affected by it [8,9]. In the middle Ganga plain, Bihar, 206 tube wells (95% of total) were analyzed for arsenic content and showed that 56.8% tube wells have exceeded the arsenic concentration of 50 µg/L and 19.9% have more than 300 µg/L. In China, arsenic concentration in well water was 50 µg/l–2000 µg/l in the affected areas and around 2 million people in the affected area use the drinking well water contained with arsenic more than the common standard. In New Hampshire, USA, morganic arsenic was present in about 95% sample of drinking water and the concentration was from 0.01 µg/l to 180 µg/l. Arsenic-contaminated drinking water; non-dermatological features of chronic arsenical poisoning by consuming were first reported in 1961 by Tseng et al., in Taiwan. The first report in world literature of chronic arsenical dermatosis from consuming arsenic...
contaminated tube well water is Saha's report. In Taiwan, the arsenic concentration in drinking water is about 10–1000 µg/L. Arsenic is also reported in groundwater of Australia, where the concentrations levels are well above the drinking water standard of 7 µg/L recommended by the National Health and Medical Research Council and the Natural Resource Management Ministerial Council of Australia [10]. Arsenic in groundwater has emerged as the largest environmental health disaster that has put a lot of people at the risk of cancer and other related disease. Recent studies have indicated the occurrence of arsenic in the Central Gangetic plains of Uttar Pradesh, Bihar, Jharkhand, and different regions of Madhya Pradesh and Chhattisgarh. Arsenic in groundwater is often associated with geologic sources, but in some locations, anthropogenic inputs can be extremely important. Ingestion of geogenic as from groundwater sources is manifested as chronic health disorders in most of the affected regions of the world. Arsenic is also found in widely scattered geographical areas in the United States and Canada as well as in many other countries of Latin America such as Mexico, Argentina, Bolivia, Brazil, and Nicaragua, where the sources are geogenic as well as the anthropogenic source. The contamination of groundwater by as has, therefore, received significant attention from researchers and policymakers worldwide during recent years. Nowadays, arsenic-contaminated drinking water issue in Pakistan is highly topical in news bulletin at national and international. In fact, the data regarding as groundwater contamination in Pakistan are relatively scarce and are not sufficient enough to be used for making decision and policies. Therefore, the existing problem of groundwater contamination by as in Pakistan needs to be monitored properly. Groundwater As contamination in Pakistan was unexplored until a joint project for as assessment in Pakistan in 2000 launched by the United Nations International Children's Emergency Fund and Pakistan Council of Research in Water Resources. After this project, several studies in different regions of Pakistan reported as contamination of groundwater to a varying extent (below detection limit to 3090 µg/L). Arsenic concentrations in Kamchatka, New Zealand, Japan, Alaska, California, and Wyoming are high in the thermal waters, where black shales are common, but they are low in thermal waters from Hawaii and Iceland [11-15], where most of the rocks are geologically young basalts. The water sources in Bangladesh have been contaminated with microorganisms that are responsible for the cause of morbidity [16].

**ARSENIC IN GROUNDWATER**

Arsenic is not found in high amount in the earth’s mainland outside it is less bottomless than a few of the “uncommon earth” components. Not at all like the uncommon earth components, be that as it may, arsenic is usually moved in sulfide-bearing mineral stores, particularly those related with gold mineralization, and it has a solid proclivity for pyrite, one of the more universal minerals in the earth’s covering. It is likewise packed in hydrous iron oxides. Arsenic can be effectively solubilized in groundwater relying on pH, redox conditions, temperature, and arrangement organization. Numerous geothermal waters contain high groupings of arsenic. Common arsenic in groundwater at fixations over the drinking water standard of 10 µg/l is not extraordinary [17-23]. Man-made wellsprings of arsenic, for example, mineral extraction and preparing squander, poultry and swine feed added substances, pesticides, and very solvent arsenic trioxide reserves are additionally related with gold mineralization, and it has a solid proclivity for pyrite, but as compared with mono-methylarsinic acid [35]. A small amount of dimethylarsinic acid is the dominant urinary metabolite (60–80%) of the absorbed arsenic undergoes hepatic biomethylation to form monomethylarsonic acid and dimethyl arsenic acid that are less toxic but not completely innocuous. It is estimated that around 50% of the ingested dose may be eliminated in the urine in 3–5 days. Dimethylarsonic acid is the dominant urinary metabolite (60–80%) as compared with mono-methylarsonic acid. A small amount of inorganic arsenic is also excreted unchanged. After acute poisoning, electrothermal atomic absorption spectrometry studies show that the highest concentration of arsenic is in the kidneys and liver [36]. If chronic arsenic ingestion occurs, then arsenic accumulates in the liver, heart, kidneys, lungs, muscles, spleen, and gastrointestinal tract. Most of the arsenic is cleared from these sites, residual amounts remain [37,38].

**ACUTE POISONING**

Neurological manifestations include peripheral neuropathy or encephalopathy. Most instances of intense arsenic harming happen from incidental ingestion of bug sprays or pesticides and less normally
from endeavored suicide. Little sums (<5 mg) bring about spewing; furthermore, loose bowels, however, resolve in 12 h and treatment is revealed not to be necessary. The deadly dosage of arsenic in intense harm ranges from 100 mg to 300 mg. The risk appraisal information system database expresses "the intense measurement of inorganic arsenic to people has been assessed to be around 0.6 mg/kg/day." A 23-year-old man ingested about 9 grams of arsenic and despite the nature of acute toxicity of arsenic and amount ingested, the patient survived for 8 days. An understudy who expended 30 g of arsenic looked for help following 15 h and survived 48 h, however, passed on in spite of gastric lavage and treatment with British hostile to lewisite (an arsenic remedy) and hemodialysis [32-40].

Hematological anomalies revealed are hemoglobinuria, intravascular coagulation, bone marrow despondency, serious pancytopenia, and normocytic normochromic sickness and haemolytic stippling. A real disappointment was accounted for in four of eight mariners presented to arsenic. Respiratory disappointment and pneumonic edema are basic highlights of intense poisoning. Echocardiopathy is a typical indication, what is more, the likelihood of arsenic harmfulness must be considered if the etiology of echocardiopathy is indeterminate. Echocardiopathy has happened after the intravenous organization of arsphenamines. The reason for the echocardiopathy is thought to be expected to hemorrhage. Metabolic changes with intense arsenic harming are detailed. Acidosis has happened in a solitary patient and hypoglycemia and hypocalcemia in cattle [41].

CHRONIC POISONING
Chronic arsenic exposure at high doses has neurologic, dermatologic, vascular, and carcinogenic effects. Exposure to arsenic from drinking water increases the risks of skin, lung, and bladder cancers. Chronic arsenic exposure has been implicated in several noncancerous conditions, in particular, skin disease, diabetes mellitus, hypertension, and cardiovascular disease, perturbed porphyrin metabolism, and irreversible noncirrhotic portal hypertension (1). It has been long known that arsenic exposure is associated with skin pathology, including hyperpigmentation, hyperkeratosis, and skin cancers. In the majority of cases, in which internal cancer has been ascribed to arsenic exposure [35], a dermatologic hallmark of arsenic poisoning was also identified. Bangladesh and India arsenic are related to skin, lung, liver, kidney, and bladder cancers. There is confirmed from different nations that arsenic presentation causes malignancies of the skin, lung, liver, kidney, and bladder. Data from Taiwan likewise archive malignancies of the bladder, kidney, skin, lung, nasal hole, bone, liver, larynx, colon, and stomach and in addition lymphoma.

The components, however not completely decided, are perhaps an antagonistic effect on DNA repair, methylation of DNA, and expanded free radical arrangement and enactment of the proto-oncogene c-myc. Arsenic may go about as a cocancer-causing agent, tumor promoter, or tumor progressor in specific situations.

Large amounts of arsenic are teratogenic in animals. Structural chromosome distortions were contemplated in a gathering of people who expended arsenic from well water in Finland.

There are numerous reports on the event of fringe neuropathy due to interminable presentation of arsenic through drinking water. Peripheral neuritis characterized by paresthesia (shivering, deadness, appendage shortcoming, and so forth) was available in 74 (47.4%) of 156 patients of incessant arsenicosis because [42,43] of arsenic defiled water (0.5–14.2 mg/l) in West Bengal, India.

Effect of arsenic on genitourinary system
The Millard County contemplate additionally detailed an expanded mortality from nephritis and prostate cancer. Guo et al., in 1997, examined growth registry information (1980–1987) of tumors of the bladder and kidney in Taiwan and announced that high arsenic levels in drinking water from wells were related with transitional cell carcinomas of the bladder, kidney, ueter, and every urethral disease in the two guys and females, and adeno carcinomas of the bladder in males. The creators propose that the cancer-causing nature of arsenic might be cell-type particular. An examination from Finland has found a relationship with bladder malignancy chance yet not kidney growth, notwithstanding low arsenic fixations in the bored wells [44].

More information is required to set up a firm causal connection between arsenic ingestion and unfavorable results amid pregnancy and on neonatal bleakness and mortality. In pregnant Andean ladies who expended water with arsenic centralizations of around 200 µg/L arsenic in-line blood (9 µg/l) was nearly as high as in maternal blood (11 µg/l). In a similar gathering, placental arsenic was 34 µg/l and only 7 µg/l in ladies unexposed to arsenic [45].

Skin
Various skin changes happen with long-haul exposure. Dermatological changes are a typical component and the underlying clinical determination is regularly in view of hyperpigmentation, palmar, and sun-based keratosis. The keratosis may show up as a uniform thickening or as discrete nodules. It is underscored that both palmar and sunlight-based keratosis are a critical demonstrative measure. Hyperpigmentation happens as diffuse dim darker spots, or less discrete diffuse obscuring of the skin, or has a trademark "raindrop" appearance [46]. Arsenic-related skin tumor, Bowen's ailment, is an extraordinary indication in Asians and might be due to the high skin melanin content and expanded presentation to bright radiation. Arsenic has been found to cause the basal cell carcinoma. The dormant period after presentation might be the length of 60 years and has been accounted for in patients treated with Fowler's answer, in sheep plunge laborers, in vineyard specialists utilizing arsenical pesticides, and from drinking sulfide wine. Another sign due to arsenic testimony in keratin-rich territories is conspicuous transverse white lines in the fingernails and toenails called Mees' lines [47].

Expansive populace-based investigations from West Bengal in India demonstrate a connection between an arsenic focus in tube well water, measurement per body weight, and hyperpigmentation and keratoses and that people with a poor wholesome status were more powerless. Anyway, the investigation by Smith et al. reports that arsenic instigated skin sores to happen among Atacamo individuals in Northern Chile, notwithstanding a decent wholesome status [12].

Toxicity related to lungs
The most common form of toxicity that has been found due to arsenic is lung cancer and is proved by the number of deaths from different studies. Those who were exposed to arsenic were associated with the higher incidence of lung cancer and this was seen in epidemiological studies. A high mortality rate was recently seen in the people of Japan due to lung cancer who consumed the high concentrated arsenic drinking water [48].

Toxicity related to nervous system
Arsenic, being a common environmental toxicant, is widely distributed around the world. Symmetrical peripheral neuropathy, more commonly affected, is the sensory nerves rather motor nerves [49]. Neurons with long axons are more affected than the neurons with short axons. Clinical symptoms include numbness and paresthesia of the peripheral extremities with legs that are more affected than arms. These signs and symptoms usually take the period of 2 h–2 years to develop with diarrhea or vomit, both occurring simultaneously and preceding with the onset of symptoms [50-54]. The main pathological changes that are responsible for these symptoms are demyelination following the arsenic exposure. The distal portion of nerves of patients exposed to arsenic has shown fragmentation, reduction, and complete degeneration of nerve’s axon. The results were in sync with the in vitro studies using
the cultures of dorsal root ganglia, in which they found that addition of 10 µmol arsenic to the culture medium inhibited neurite growth and myelination by 50% [55-59].

Toxicity related to endocrine system

In a study by Davey et al., at non-cytotoxic doses, that is, 1–50 µmol /kg arsenic was found to strongly suppress the estrogen-dependent gene transcription of 17-beta-estradiol, E2, vitellogenin II in chick embryo liver in vivo. In the culture of cells, non-cytotoxic level of arsenic (0.25–3 µmol) was seen to inhibited E2-induced gene activation of an estrogen-regulated reporter gene and the native estrogen-regulated reporter gene in human breast cancer MCF-7 cells [60].

Toxicity related to hematopoietic system

Exposure to arsenic through various sources such as drinking water and agricultural pesticide results in numerous disorders including disease related to the hematopoietic system. Hematopoiesis is a dynamic process, in which bone marrow stem cells produce a pool of functionally mature blood cells with constant support from the microenvironmental components [61]. In a study by Pereira et al., Swiss abino mice were exposed to 10 µg arsenic trioxide/g body weight through oral route and 5 µg arsenic trioxide/g body weight through intraperitoneally for a duration of 30 days, it was found that there was altered hemogram values in the peripheral blood that reflected the altered hematopoiesis that was next evident by reduced bone marrow cellularity and deviated bone marrow cell morphology that was observed by scanning electron microscopy. The stromal cells were not able to maintain a healthy matrix [62].

Toxicity of arsenic in the human brain

The health of workers with high occupational exposures, such as employees in the semiconductor manufacturing industry, was badly affected. Chronic arsenic exposure can result in multisystem diseases and the neurological system is a major target. The common quotient and long-term memory were decreased. In Swedish copper smelter workers, subclinical nerve injuries were detected. In arsenic exposed adult neural stem cells (NSC), it has been demonstrated that NSC can self-renew in mammals [63]. The subgranular zone of the hippocampus dentate gyrus and the subventricular zone of the lateral ventricles are two areas for NSGs existence [64]. In 1996, residents from the community immediately surrounding the plant were evaluated using various neurological and neurobehavioral measures. Peripheral neuropathy was present in 15% of the exposed subjects but in only 3% of the unexposed subjects. Several authors have reported encephalopathy, impairments of superior neurological functions such as learning, recent memory, and concentration, in patients with occupational exposure to arsenic compounds. The subtle central effects following low-level arsenic exposure have prompted neurobehavioral studies in animals, at exposure levels that do not produce symptoms of overt toxicity. Arsenic poisoning usually occurs in occupational, accidental, and environmental exposure. Arsenic toxicity has become a global health problem affecting millions of people and reported to cause diseases of neurological, while the clinical outcomes of arsenic poisoning are well documented, target structures or target cells responsible for the neurotoxic symptoms are not known and the toxicological mechanisms involved are not completely understood. The hippocampus is a part of the limbic system that is crucial to memory function and spatial navigation. Hippocampal lesions in humans produce devastating impairments in declarative memory, and similar results have been seen in non-human primates with hippocampal lesions [65-68]. Studies on the mechanisms of arsenic-induced toxicity have conferred that arsenic alters memory in different behavioral assays and shatter neurobiological processes. Cumulated arsenic exposure (ppm) was calculated as an arsenic concentration in well water neurobehavioral evaluation system, Taiwanese version, a computerized neurobehavioral test battery, which has been applied in many studies, was performed by each student. This hypothesis is that long-term cumulated arsenic exposure [69]. CAE might affect neurobehavioral development in adolescence. Four subtests, included continuous performance test, symbol digit, pattern memory, and switching attention, were applied in this study [70]. The problems that are caused by arsenic in different body parts are listed in Table 1.

Arsenic has been considered as poisonous to humans for a long time. Among all the problems that are exerted by the arsenic, carcinoma is the most common. From Table 1, it can be concluded that arsenic impacts almost all the organs of the body.

ECONOMIC COSTS

The financial noteworthiness of arsenic poisonous quality incorporates therapeutic costs, wage misfortune, and diminished harvest efficiency and quality due to soil and water sullying. The present well-being, financial, and nourishing issues would be enormously exacerbated when data with respect to arsenic defilement of the natural pecking order are better known and if horticultural items and animals are observed to be polluted. These issues are of genuine concern, especially in Bangladesh, where 97% of the country populace depends on groundwater for drinking [71,72].

CONTROL

Data are required to decide whether there is a limit for cancer-causing impacts to show and, furthermore, to characterize the measurements and length of exposure. Studies are required to connect lethal signs with conceivable hereditary polymorphism, age, sexual orientation, wholesome status, and the defensive part of vitamins, minerals, and [73]. In Bangladesh, there should be some steps to check and control the concentration of arsenic in the drinking water. This might be due to "moderate" or "quick" methylators of arsenic like patients with incendiary entral illness who are "moderate" or "quick" acetylators who consequently react distinctively to treatment with salicylate [74].

The arrangement of safe drinking water is a need. An assortment of techniques for differing multifaceted nature is accessible to expel arsenic from drinking water. The philosophy, particularly in creating nations, that is critically required ought to be reasonable, practical by the populace, and financially savvy [75]. Among the techniques accessible for expelling arsenic from water are procedures of precipitation or particle trade [76]. Filtration of arsenic from tube wells has generated a scope of channels of shifting advancement and cost and issues of moderateness, effectiveness, and support are connected with their utilization. Significantly, the procedure and cost of arranging the arsenic sequestered after filtration need cautious thought. Promising examinations are accounted for utilizing iron regarded normal materials, for example, the press treated initiated carbon, the press treated gel dots, and iron oxide covered sand, and of these iron oxides covered, sand was the best compound. The Stevens innovation for arsenic evacuation is modest and includes blending a little bundle of powder containing iron sulfate and calcium hypochlorite in a substantial pail of water [77,78].

Table 1: Arsenic affecting different organ systems with associated problems

| Organ system affected       | Problems                                      |
|-----------------------------|-----------------------------------------------|
| Digestive system            | Hepatomegaly, cirrhosis, jaundice, and non-cirrhotic portal hypertension |
| Respiratory system          | Lung cancer                                   |
| Nervous system              | Peripheral neuropathy                         |
| Hematopoietic system        | Megaloblastosis                                |
| Endocrine system            | Diabetes mellitus and goiter                   |
| Cardiovascular system       | Acrocyanosis and Raynaut’s phenomenon          |
| Integumentary system        | Melanosis, depigmentation, squamous cell carcinoma |

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No treatment of demonstrated advantage is right now accessible to treat ceaseless arsenic poisonous quality. Treatment alternatives pushed are vitamin and mineral supplements and cancer prevention agent treatment. The advantages of these treatment measures should be proven based to get underwriting and more extensive application.

At a cell level, in perspective of the apoptotic system of activity of arsenic, the impacts, particularly of cell reinforcements, are hypothetical of significant worth [79,80]. Although there is sufficient knowledge regarding the effect of arsenic on the human body but researches anticipate a lot more in this aspect should be done [81].

CONCLUSION
Arsenic is a characteristic metallicloid substance that might be available in groundwater. Ingestion just stances medical issues if a risky measure of arsenic enters the body. At that point, it can prompt tumor, liver infection, trance state, and passing. Treatment includes enteral water system, pharmaceutical, and cheletion treatment. It is uncommon to discover hazardous measures of arsenic in the regular habitat. Zones with unsafe arsenic levels are typically notable and arrangements exist to avert and handle the danger of harming. Any individual who suspects there might be high arsenic levels in their neighborhood condition should contact their nearby experts for more advise.

AUTHORS' CONTRIBUTIONS
The second and third author did the conception and data acquisition for the article. The first author revised the article for its intellectual content.

CONFLICTS OF INTEREST
No.

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