invited review

Sources and impact of arsenic on livestock in India and its amelioration through dietary strategy

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Abstract: Arsenic is one of the major toxic minerals that is naturally present in the environment and have significant adverse effect on animal health. Inorganic arsenic present in ground water enters the food chain through irrigation and ultimately affects the animal and human health. The presence of arsenic in groundwater in India is the most serious health hazard. Lower Gangetic region which includes West Bengal, Jharkhand, Bihar, Uttar Pradesh are in serious threat to arsenic contamination because of its geographic location. Ground water is the major source of arsenic toxicity, though arsenic also enters the animal body through feeds and fodder. Arsenic toxicity is a serious health hazard because of its oxidative damage capacity. Apart from that, it has the properties of carcinogenicity, neurotoxicity, hepatotoxicity and nephrotoxicity. Chronic arsenic toxicity in animals is more commonly seen than that of acute toxicity. Arsenic toxicity can be avoided by removing arsenic from ground water which is a very tough task. However, Government of India has taken some serious steps to reduce the arsenic load from ground water. Effects of arsenic toxicity, specifically oxidative damage can be reduced in the animals by various dietary treatments such as Vitamin E, vitamin C, probiotics, minerals like Se, Zn, herbal drugs like turmeric, ginger etc. However, these treatments are reported to have very less effect on removing arsenic from body. Therefore, significant and continuous efforts are needed to develop new technologies to reduce the arsenic load from ground water as well as from animals.

Keywords: Arsenic, Animal health, Oxidative damage, Toxicity, Water

Introduction

Arsenic is a crystalline “metalloid”, a natural element with features intermediate between metals and non-metals. It occurs naturally as an element, ranks as the 20th most occurring trace element in the earth’s crust, 14th in seawater, and 12th in the human body (Mandal and Suzuki, 2002). 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 (Martinez et al., 2011). Arsenic exists mainly in four oxidation states—arsenate (As$^{5+}$), arsenite (As$^{3+}$), arsenic (As), and arsine (As$^{3-}$) and its solubility depends on the pH and ionic environment. Among them, the As$^{5+}$ is the most stable form (Gupta et al., 2011). As$^{5+}$ is thermodynamically stable state in aerobic water, while As$^{3+}$ is predominant in reduced redox environment. In general, inorganic arsenicals are more toxic than organic ones (Meharg and Hartley-Whitaker, 2002). As$^{3+}$ is usually more toxic than As$^{5+}$ (Schat et al., 2002). The World Health Organization (WHO) and the U.S. Environmental Protection Agency (US 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 (Basu et al., 2014). South Punjab and Sindh regions in Pakistan are reported to have higher arsenic content in water and fodder samples than normal level (Zubair et al., 2018).

Ground water, soil, feeds and fodders grown on these contaminated soils and air act as source of contamination to animals and human beings. The presence of arsenic in groundwater in India is the most serious health hazard. According to the latest data of the ministry of drinking water and sanitation a population of 1.47 crore across almost 17,000 areas in the country faces a major health hazard due to arsenic contaminated
drinking water, Arsenic is present in drinking water above the permissible limits in 16,889 areas while 12,029 areas have high levels of fluoride and 2384 habitations have heavy metal contamination. Iron is also present in 23613 areas and around 14069 areas have high levels of salinity. Nitrates have also been found in 1809 areas (The Hindustan Times, 2018). Lower Gangetic region which includes West Bengal, Jharkhand, Bihar, Uttar Pradesh are in serious threat to arsenic contamination because of its geographic location. Assam and Manipur in flood plain of Brahmaputra and Impal rivers, and Rajnandgaon village in Chhattisgarh state have so far been exposed to drinking arsenic contaminated hand tube-wells water. According to some researchers (Rajaganapathy et al., 2011; Singh and Ghosh, 2012) feeds and fodders of this region which are irrigated with contaminated water found to contain arsenic in higher concentration than normal.

Arsenic has been reported to be responsible for defective cell mediated immunity and decreased percentage of T helper cells in the body. Arsenic may produce ROS which may damage DNA or arsenic may directly damage the sulphydryl group of DNA which stands as a factor of carcinogenicity (Zhang et al., 2015). Oxidative damage which is a pronounced effect of arsenic toxicity can be treated by various nutritional anti-oxidants treatments such as vitamin E (Mohanta et al., 2014), vitamin C (Singh et al., 2010); herbal treatments like turmeric (Hazarakia et al., 2015), ginger root (Biswa et al., 2016); minerals such as zinc (Ganger et al., 2016) and selenium. Saccharomyces cerevisiae have property of binding with arsenic in acidic medium in water which can protect it from being absorbed in body.

**Sources of arsenic**

The primary source of arsenic in the environment (hydrosphere, pedosphere, biosphere and atmosphere) is the release of arsenic from arsenic-enriched soil or rocks. The sources of Arsenic includes both natural and anthropogenic. Natural sources include contamination of As compounds adsorbed onto pyrite ores and subsequently into the water by geochemical factors. Anthropogenic sources include use of insecticides, herbicides and phosphate fertilizers, semi-conductor industries, mining and smelting, industrial processes, coal combustion, timber preservatives etc.

**Fly ash**

One of the major routes of arsenic contamination to ecosystem is through fly ash from fuel gas of thermal power plant and coal pyrite. Arsenic comes to the ecosystem in the form of arsenic trioxide and dispersed to soil, water and air. Arsenic concentration in fly ash generally ranges from 4 to 440mg/kg; however, depending on the quality of coal the concentration may reach up to 1000 mg/kg (Jambhulkar et al., 2018).

**Ground water**

According to the WHO guidelines, the recommended limit of arsenic in drinking water is 0.01ppm. The levels of As in unpolluted surface water and ground water vary typically from 1–10 ppb. Ground water concentrations of As is reported to be very large range from less than 0.5 to 5000 ppm covering natural As contamination found in more than 70 countries (Ravenscroft et al., 2009). Consumption of contaminated water is the primary reason of arsenic toxicity in south-eastern Asia which is a life threatening problem for many lives. Leaching of geological materials, inputs from geothermal sources, mining wastes are major sources of As in groundwater as well as in surface water (Korte & Fernando, 1991).

**Surface Water**

Arsenic is mainly transported in the environment by water. In oxygenated water, arsenic usually occurs as arsenate, but under reducing conditions, for instance, in deep well-waters, arsenites predominate. In water, the methylation of inorganic arsenic to methyl- and dimethyl arsenic acids is associated with biological activity. Some marine organisms have been shown to transform inorganic arsenic into more complex organic compounds, such as arsenobetaine, arsenocholine and arsonium phospholipids. Uncontrolled anthropogenic activities such as smelting of metal ores, use of arsenical pesticides and wood preservative agents may release arsenic directly to the environment (Bhattacharya et al., 1995). Occurrence of arsenic in natural water depends on the local geology, hydrology and geochemical characteristics of the aquifer materials. Several studies have suggested that high concentration of arsenic in summer season as compared to that of winter season in lake water (Hasegawa et al., 2009). The geothermal inputs, evaporation and groundwater contamination are the main cause of high concentrations of As in rivers. Mining activity can also contribute in the occurrence of high As concentrations in river waters.

**Marine water**

In sea water, the As concentration is usually less than 2 ppb. Mining and industrial activities are one of the causes for the marine water contamination with arsenic in coastal areas. But marine water contamination is of less importance because of very less consumption and use in agriculture (Smedley and Kinniburgh, 2002).

**Soil**

The major sources of its contamination in soil are identified to include many man-made activities e.g. the use of insecticides, herbicides and phosphate fertilizers, semi-conductor industries, mining and smelting industrial processes, coal combustion, timber preservatives etc. (Bundschuh et al., 2011). The concentration of arsenic in soil varies according to the source of contamination. In oxygenated soil, inorganic arsenic is present in the pentavalent form. Under reducing conditions, it is in the trivalent form.
Leaching of arsenate is slow because of binding to hydrous oxides of iron and aluminium. Arsenic concentrations in uncontaminated soil are generally in the range 0.2–40 mg/kg (WHO, 1981).

**Feeds and fodder**

Because of the contaminated water and soil, arsenic deposition takes place in feeds and fodder. Arsenic can enter into food chain causing wide spread distribution throughout the plant and animal kingdoms (Kile et al., 2007). Contaminated fodder and water are also considered to be the source of accumulation and source of toxicity in milch animals, and subsequently pose a threat to

**Table 1** States, districts and blocks of India considered as arsenic contaminated (Government of India report)

| States             | District (example) | Blocks where high Arsenic is observed in observation wells of Central Ground Water Board (CGWB) |
|--------------------|-------------------|-------------------------------------------------------------------------------------------------|
| Assam              | Dhemaji           | Dhemaji, Bodordi, Sisiborgaon                                                                 |
| Bihar              | Bhojpur           | Barhara, Shahpur, Koilwar, Arrah, Bihia, Udawant nagar                                         |
| Bhagalpur         | Jagdishpur        | Sultanganj, Nathnagar                                                                          |
| Begusarai         | Mathani, Begusarai| Barauni, Balia, Sabhpur, Kamal, Bachwara                                                       |
| Buxar             | Brahmpur          | Semary, Chakki, Buxar                                                                           |
| Darbhanga         | Biraul            |                                                                                                 |
| Khagaria          | Khagaria, mansi   | Gogri, Barbatia                                                                                 |
| Kishanganj        | Kishanganj        | Bahadurganj                                                                                     |
| Katihar           | Mansahi, Kursela, | Sameli, Barari, Manihari                                                                        |
| Lakhisera         | Piparia, Lakhisera|                                                                                                 |
| Munger            | Jamalpur, Dharhara| Bariarpur, Munger                                                                               |
| Patna             | Maner, Danapur,   | Bakhtiarpur, Barh                                                                               |
| Purnea            | Purnea East, Kasba|                                                                                                 |
| Saran             | Dighwara, Chapra, | Revelganj, Sonpur                                                                               |
| Samastipur        | Mohinuddin Nagar, | Mohanpur, Patori, Vidyapati Nagar                                                                 |
| Chattishgar       | Vaishali          | Raghopur, Hajipur, Bidupur, Desri, Sahdei Bujurg                                                  |
| Rajnandgaon       | Ambagarh Chouki   |                                                                                                 |
| West Bengal       |                  |                                                                                                 |
| Bardham           | Purbasthali I & II| Katwa I & II and Kala II                                                                         |
| Haora             | Uluberia I and    | Shampur II                                                                                      |
| Hugli             | Balagarh          |                                                                                                 |
| Malda             | English Bazar,    | Manikchak, Kaliachak I, II & III Ratua I & II                                                    |
| Murshidabad       | Raninagar I & II, | Domkal, Nowda, Jalangi, Hariharpura, Suti I & II Bhagwangola I & II, Beldanga I & II Berhampur, Raghunathganj I & II, Farakka, Lalgor, Murjigang, Sambhorgunj, Sandeshkhali I & II, Sandeshkhali I & II, | |
| Nadia             | Karimpur I & II, | Tehatta I & II, Kaliganj, Nawadwip, Haringhata, Chakda, Santipur, Naksipara, Hanshali, Krishnanagaj, Chapra, Ranaghat I & II, Krishnanagaj I & II, Habra I & II, Barasat I & II, Rajarhat, Deganga, Beduria, Gaighata, Amdanga, Parganas | Bagda, Boangaon, Haroa, Hasnabad, Basirhat I & II, Swarupnagar, Barackpur I & II, | |
| North 24          | Habra I & II,     | Barasat I & II, Rajarhat, Deganga, Beduria, Gaighata, Amdanga, Parganas | Baruiupur, Sonarpur, Bhangar I & II, Joynagar I, Bishnupur I & II, Mograhat II, | |
| Parganas          |                  |                                                                                                 |
| South 24          |                  |                                                                                                 |
| Uttar Pradesh     | Agra              | Agra, Etmadpur, Fatehabad, Khairagarh                                                          |
| Agra              | Jawan Sikandarpur |                                                                                                 |
| Balrampur         | Belhari, Bari,    | Muralichapra, Reoti, Siar                                                                      |
| Ballia            | Gaindas bujurg,   | Gainsari, Harraiyabazar, Pachparwa, Sridatganj, Tulsipur                                        |
| Gonda             | Bhelsar, Colonelganj, Haldarmau, Katrabazar, Nawabganj, Pandari Kripal, Tarabgan, Wazirganj, Gorakhpur, | |
| Gorakhpur         |                  |                                                                                                 |
| Lakhimpur Kheri   | Daurahra, Ishanagar, Nighasan, Pallia, Ramia Vihar                                              |
| Mathura           |                  | Mathura                                                                                         |
| Moradabad         |                  | Moradabad                                                                                        |
Humans through the ingestion of meat and milk from these animals (Brahman et al., 2016). Food may contribute up to 30-50% of the total dietary intake of arsenic when feed is generated from arsenic contaminated sources (Naidu et al., 2006) because feeds and fodder can accumulate higher amount of arsenic, for example: tuberous vegetables accumulate higher amount of arsenic than leafy vegetables, while major oilseeds and pulses have also been reported to contain high levels of arsenic. Apart from that, high yielding rice varieties have more arsenic accumulation than the local varieties which may cause arsenic toxicity to animals (Bhattacharya, 2017).

Arsenic is an approved animal dietary supplement and is found in specifically approved drugs added to poultry and other animal feeds. Researchers from the National Institutes of Health and the USDA's Food Safety Inspection Service reported alarmingly high levels of arsenic contamination in the broiler flesh because of use of roxarsone, a feed additive. It is assumed that arsenic ingested through chicken pose potential risks to human health. Roy et al. (2008) reported that arsenic content of different feeds and fodder in Haryana were found to be much less than the maximum permissible limit (Singh et al., 2005) ranging between 0.38 ppm in cotton seed cake to 0.44ppm in pellets of concentrate diet of ruminants. The maximum content of arsenic in complete feed has been set by the European Union at 2 mg/kg feed (with 12% moisture) for all animal species and 10 mg/kg for fish and fur animals (European commission, 2002). The US NRC reported that in cattle the maximum tolerable dose of arsenic is 50 and 100 mg/kg diet for inorganic and organic arsenic compounds (NRC, 2005), respectively, and in goats is 30 mg/kg diet (NRC, 2007).

Impact of arsenic in the environment and eco-system

The most common source of elevated levels of As in the environment is attributable to both natural process and anthropogenic activities. In natural process weathering of rocks acts as the predominant reactions for As cycle. Like soil, in aquatic environment As concentration alters due to natural process and anthropogenic activities. In hydrosphere, As occurs as the predominant reactions for As cycle.

Enhanced air concentration of arsenic is mainly due to metal smelting and refining of gold, silver, copper etc; coal burning, combustion of fossil fuels like gasoline, burning of vegetation treated with arsenical pesticides; careless or extensive use of arsenical herbicides, pesticides, and defoliants in plants like potato. Atmospheric deposition of arsenic can steadily increase and could be estimated through sedimentary evidences (Smith et al., 1987). Elevated concentration of Arsenic in water bodies is observed near mining operation, mineral springs, dumping of land wastes and sewage sludge, use of detergents, run off agricultural pesticides containing arsenic compounds, and sinking of drinking-water wells into naturally arseniferous rock (NRCC, 1978; US EPA, 1980). Arsenic is being continuously recycled in the environment through oxidation, reduction, or otherwise metabolization through organisms and chemical processes. In soil, insoluble or slightly soluble arsenic compounds are being resolubilized, presented for plant uptake or reduced by the act of microorganisms. The overall arsenic cycle is similar to that of phosphate cycle; however, regeneration time is much slower (NAS, 1977). In soil ecosystem oxidation, reduction, adsorption, dissolution, precipitation, and volatilization of As are the predominant reactions for As cycle.

Like soil, in aquatic environment As concentration alters due to natural and anthropogenic processes. In hydrosphere, As occurs

### Table 2 State-wise number of habitations affected by Arsenic contamination (As per Ministry of Drinking Water & Sanitation, Government of India) as on August, 2016

| S. No. | State                | Population | Sl. No. | State                | Population |
|-------|----------------------|------------|---------|----------------------|------------|
| 1.    | Andhra Pradesh       |            | 13.     | Madhya Pradesh       | 401        |
| 2.    | Arunachal Pradesh    | 334        | 14.     | Maharashtra          | 1          |
| 3.    | Assam                | 3498       | 15.     | Meghalaya            | 1          |
| 4.    | Bihar                | 1049       | 16.     | Odhisa               | 2          |
| 5.    | Chattisgarh          |            | 17.     | Punjab               | 491        |
| 6.    | Gujarat              |            | 18.     | Rajasthan            |            |
| 7.    | Haryana              | 45         | 19.     | Telengana            |            |
| 8.    | Himachal Pradesh     | 150        | 20.     | Tripura              | 1          |
| 9.    | Jammu & Kashmir      | 2          | 21.     | Uttar Pradesh        | 154        |
| 10.   | Jharkhand            | 123        | 22.     | West Bengal          | 6,733      |
| 11.   | Karnatak             | 12         |         | TOTAL                | 13,000     |
| 12.   | Kerala               | 3          |         |                      | 7,651      |
as a mixture of arsenate and arsenite, with arsenate being the predominant form. Higher concentration of As influences the aquatic ecosystem. Fish is usually considered as an ideal model for biomonitoring of pollution of aquatic environment. It affects various physiological systems such as growth, reproduction, ion regulation, gene expression, immune function, enzyme activities, biochemical profiles and histopathology of fish and other aquatic animals (Kumari et al. 2016). In aquatic environments, several species of microorganisms make As biologically available to other organisms (Duker et al. 2005). Thus As gets entry into phytoplanktons, fish, other eatable aquatic species and finally reach to the food chain of higher vertebrates including wildlife and human.

**Status of arsenic in India**

More than 30 countries, including India, have been reported to have quite high levels of arsenic in groundwater, soil, plants and/or animal tissues (Pandey et al., 2011). Arsenic has received significant attention in the last three decades due to its serious health effects on millions of people and has been termed “the biggest Arsenic calamity in the world” (Smith et al., 2001). Apart from West Bengal, Arsenic contamination in ground water has been found in the states of Bihar, Chhatisgarh, Uttar Pradesh and Assam. Arsenic in ground water has been reported in 15 districts in Bihar, 9 districts in U.P and one district each in Chhatisgarh and Assam states. The occurrence of Arsenic in the states of Bihar, West Bengal and Uttar Pradesh is in Alluvium formation but in the state of Chhatisgarh, it is in the volcanic rocks exclusively confined to Dongarga-Krhotri ancient rift zone. In Ludhiana district of Punjab, arsenic content of drinking water was higher than the WHO specified limits which reflected higher blood arsenic content of buffaloes of that region, however, buffalo milk had arsenic content below the FSSAI regulations (Yeotikar et al., 2018). In central plain and sub-mountainous regions of Punjab, arsenic content of rice straw was 2-fold higher than the rice grain which was correlated with the higher arsenic concentration of water and soil. These arsenic concentrations of straw and grain were below the standard i.e 1ppm. However, livestock population was under the threat to arsenic toxicity as they consume more paddy straw and green fodder, as compared to that of grains (Sidhu et al., 2012).

Information of As particularly in animal feeds and fodders are scanty. Most of the reports are limited to water resources. In India, Singh et al. (2005) and Rajaganapathy et al. (2011) reported the presence of arsenic in feeds and fodder. Singh and Ghosh (2012) indicated that there is a very high health risk in the arsenic contaminated Maner blocks of the Patna district. In that area, an average of 142 μg/l of arsenic was detected with the highest value of 498 μg/l of As measured in the Haldichapra Panchayat of Maner block, Patna. However, the highest level of 2182 μg/l of arsenic was reported in the Buxar district of Bihar (SOES, 2012). Other arsenic affected areas of Bihar, where the level of arsenic in drinking water exceeded 100 μg/l are Bhojpur, Patna, Samastipur, and Bhagalpur districts. In West Bengal, 79 blocks in 8 districts have Arsenic beyond the permissible limit of 0.05 mg/L. The most affected districts are on the eastern side of Bhagirathi river in the districts of Malda, Murshidabad, Nadia, North 24 Parganas and South 24 Parganas and western side of the districts of Howrah, Hugli and Bardhaman. The occurrence of Arsenic in ground water is mainly in the intermediate aquifers up to the depth of 100m. The North Eastern Regional Institute of Water and Land Management (NERIWM) report (Chakraborty, 2007) indicated that arsenic levels in Assam, Manipur, Tripura and Arunachal pradesh were above 300 parts per billion (ppb).

**Chronic and acute arsenic toxicity**

| S. No. | Botanical Name | Part of the plant used | Experimental model | Organ/tissue of importance |
|-------|----------------|------------------------|--------------------|---------------------------|
| 1     | Zea mays       | Grain                  | Rats               | Liver, kidney, spleen, lungs, skin |
| 2     | Azadirachta indica | Leaf                  | Rat                | Liver                      |
| 3     | Emblica oficinalis | Fruit                 | Mice               | Thymocyte                  |
| 4     | Carica papaya  | Fruit                  | Mice               | Testes                     |
| 5     | Camellia sinensis | Green tea             | Rats               | Liver                      |
| 6     | Chlorophytm borivilianum | Root       | Mice               | Testes                     |
| 7     | Moringa oleifera | Leaf                  | Mice               | Liver, Heart, Kidney       |
| 8     | Irvingia gabonensis | Leaf                  | Rats               | Liver                      |
| 9     | Tephrosia purpurea | Aerial parts         | Rats               | Liver                      |
| 10    | Ipomea aquatica | Aerial parts           | Mice               | Liver, kidney, heart, brainand testes |
| 11    | Phyllanthus emblica | Leaf                  | Mice               | Liver, kidney and spleen   |
| 12    | Withania somnifera | Root                  | Rats               | Testes, liver, kidney      |
| 13    | Triticum aestivum | Leaf                  | Rats               | Liver, kidney              |

(Bhattacharya, 2017a)
Arsenic toxicity is a medical condition that occurs due to elevated levels of arsenic in the body. If exposure occurs over a brief period of time, symptoms may include vomiting, abdominal pain, encephalopathy, and watery diarrhea that contains blood. Symptoms of arsenic poisoning vary with the type and concentration of the poison. Long term exposure can result in thickening of the skin, darker skin, abdominal pain, diarrhea, heart disease, numbness and cancer. Inorganic arsenic may cause abdominal pains, destruction of red blood cells (hemolysis), shock, and death quickly. Lower concentrations of inorganic arsenic and organic arsenic may cause less severe symptoms. There may be some degree of skin absorption of trivalent arsenic oxide since it is more lipid-soluble than the pentavalent form. Organic arsenic may be non-toxic or far less toxic to many biologic systems than inorganic arsenic.

**Acute toxicity**

Symptoms of acute intoxication usually occur within 30 minutes of ingestion but may be delayed if arsenic is taken with the food. Early clinical symptoms at acute arsenic intoxication may be muscular pain, weakness with flusking skin. Severe nausea and vomiting, colicky abdominal pain, and profuse diarrhoea with rice-water stools abruptly ensure. Capillary damage leads to generalized vasodilatation, transudation of plasma, and vasagenic shock. Arsenic’s effect on the mucosal vascular supply, not a direct corrosive action, leads to transudation of fluid in the bowel lumen, mucosal vesical formation, and sloughing of tissue fragments. Cardiac manifestations include acute cardiomyopathy, subendocardial haemorrhages, and electrocardiographic changes. The most common changes on an electrocardiogram are prolonged QT intervals and non-specific ST-segment changes (Glazener et al., 1968).

**Chronic toxicity**

Chronic arsenic poisoning is much more insidious in nature. In case of ruminants, continuous intake of arsenic either through contaminated water or through contaminated feeds and fodder may lead chronic arsenic toxicity. Signs and symptoms of chronic toxicity include peripheral and central nervous system changes, such as sensory changes, numbness, tingling and muscle tenderness. Burning sensation in feet and hands are also felt some time. Neuropathy (inflammation and wasting of nerves) is usually gradual and occurs over several years of exposure. Hyperpigmentation in the area that are not exposed to sunlight, excessive formation of skin on the palms and soles (hyperkeratosis), or white bands of arsenic deposits across the bed of the fingernails (usually 4-6 weeks after exposure). Birth defects, liver injury and malignancy are also possible. The skin pigmentation is patchy and has been given the poetic description of “raindrops on a dusty road”. The hyperkeratosis is frequently punctuated and occurs on the distal extremities. A diffuse desquamation of the palms and soles is also seen. Long-term cutaneous complications include the development of multicentric basal cell and squamous cell carcinomas (Pershagen et al., 1981).

**Arsenic toxicity mechanism and effects**

**Absorption and distribution of Arsenic**

Arsenicals are readily absorbed from GIT and skin. After absorption, As is distributed throughout body but tends to reach higher concentration in liver, kidneys, heart and lungs. The lower amount of arsenic is observed in muscles and neuronal tissues (Klaassen, 1996). High concentration of arsenic is detected in hair and nails. In animals, As is partly methylated in liver and rapidly excreted in the urine. Arsenate is reduced to arsenite by glutathione which is further methylated to form monomethyl arsenite and then dimethylarsenite which is readily eliminated from body. As crosses placental barrier in significant amount but its passage to CNS through blood brain barrier is limited.

**Mechanism of toxicity**

Arsenite inhibits not only the formation of Acetyl-CoA but also the enzyme succinic dehydrogenase. Arsenate can replace phosphate in many reactions. It is able to form Glu-6-Arsenate *in vitro*; therefore, it has been argued that hexokinase could be inhibited (eventually this may be a mechanism leading to muscle weakness in chronic arsenic poisoning). In the glyceraldehyde-3-P-dehydrogenase reaction arsenate attacks the enzyme bound thioester. The formed 1-arsen-3-phosphoglycerate is unstable and hydrolyzes spontaneously. Thus, ATP formation in glycolysis is inhibited while bypassing the phosphoglycerate kinase reaction. Thus, by a variety of mechanisms arsenate leads to an impairment of cell respiration and subsequently diminished ATP formation. Depletion in ATP may lead to various tissue damage, depressed organ function and depressed immunity. Arsenicals have the potential for both genetic and epigenetic changes, meaning it can have mutagenic effects at the DNA sequence level. Short-term exposure is connected to the increased production of reactive oxygen species (ROS) which may lead to oxidative damage to the body (Zhang et al., 2015).

**Carcinogenicity**

Sulphydryl groups are frequently found in DNA-binding proteins, transcription factors, and DNA-repair proteins. As may attack on these molecules and may alter the functionality of DNA. Arsenic produces a dose-dependent decrease of DNA ligase activity. But DNA repair enzymes are not inhibited by arsenic poisoning. This might indicate that inhibition of DNA repair is an indirect effect due to changes in cellular redox levels or altered signal transduction and consequent gene expression. So, elevated DNA damage may be seen during arsenic toxicity. Tumors that develop after inhalation of arsenic are observed primarily in the lung (Lee-Feldstein, 1986); whereas, they are initially observed in the skin after oral exposure to arsenic in
human beings (Cebrian et al., 1983). However, additional studies indicate that cancer of internal organs occurs in individuals who chronically consume arsenic-contaminated drinking water. Tumor sites include bladder, liver, and kidney.

**Oxidative stress**

Decreased level of antioxidants, increased levels of oxidation products in blood were reported in human population exposed to arsenic (Wu et al., 2001). Various studies reported that arsenic could participate in the cellular oxidation–reduction reactions resulting with the formation of excess ROS such as superoxide anion (O2•−) and hydroxyl radical (OH•) via a chain reaction (Garcia-Shavez et al., 2006). The potential role of oxidative stress in the injury associated with arsenic poisoning suggests that antioxidants may enhance the efficacy of treatment protocols designed to mitigate arsenic induced toxicity. Moreover, arsenic could cause oxidative stress by depleting the cell’s antioxidants, especially the ones containing thiol groups. The accumulation of ROS like hydroxyl radicals, superoxide radicals and hydrogen peroxides causes aberrant gene expression at low concentrations and lesions of lipids, proteins and DNA in higher concentrations which eventually lead to cellular death.

**Arsenic-induced cardiovascular dysfunction**

Long-term exposure to inorganic arsenic may cause various cardiovascular disorders such as atherosclerosis, hypertension, ischemic heart diseases, and ventricular arrhythmias. Arsenite stimulates nicotinamide adenine dinucleotide phosphate (NADPH) oxidase present in the plasma membrane of vascular endothelial cells and vascular smooth muscle cells (VSMC) to increase the generation of reactive oxygen species (ROS) such as superoxides and hydrogen peroxide (Smith et al., 2001). ROS generated during arsenite exposure increases the expression of atherosclerosis related genes such as heme oxygenase-1 (HO-1), monocyte chemo-attractant protein (MCP-1), and interleukin-6 (IL-6) and thus its exposure promotes the attachment, penetration, and migration of monocytes in VSMC (Lee et al., 2005).

**Neurotoxicity**

Brain is a soft target for arsenic toxicity as it freely crosses blood-brain barrier (Yadav et al., 2010). Arsenic exposure is associated with wide range of neurological complications in humans such as impaired memory, poor concentration, Parkinson’s disease, Guillain-Barre like neuropathy, verbal comprehension, encephalopathy, and peripheral neuropathy. The mechanism postulated for arsenic-induced neurotoxicity majorly involve oxidative stress with increased reactive oxygen species, lipid peroxides along with decrease in superoxide dismutase and reduced glutathione levels. Arsenic exposure has been reported to alter metabolism of various neurotransmitters such as monoamines, acetylcholine, gamma amino butyric acid, and glutamate (Dwivedi et al., 2011). Arsenite-mediated neurotoxicity involves induction of apoptosis in the cerebral neurons by activating p38 mitogen-activated protein kinase (p38MAPK) and JNK3 pathways (Namgung et al., 2001).

**Hepatotoxicity and nephrotoxicity**

The key enzyme of biomethylation of arsenic is present in liver and kidneys which are the major route of arsenic excretion but arsenic as a toxicant is linked to hepatic damage and damage in the kidney including capillaries, tubules, and glomeruli leading to kidney dysfunction after chronic exposure. Chronic exposure of arsenic in case of sheep may cause renal and hepatic toxicity by diminishing the excretion of arsenic by urine and faeces and lead to more accumulation of arsenic in wool. (Maji et al., 2016). Acute renal dysfunction due to arsenic exposure is characterized by acute tubular necrosis and cast formation with increase in blood urea nitrogen and creatinine levels. This arsenic-induced renal toxicity can be attenuated by Curcuma aromatica and Curcuma aromatica (Das et al., 2010).

**Government’s schemes for arsenic problem mitigation**

Ministry of Drinking Water and Sanitation, Government of India launched (22-March, 2017) National Water Quality Sub Mission on Arsenic and Fluoride. The main aim of this mission is to provide safe drinking water to about 28,000 affected habitations in the country by March 2021 with an outlay of Rs. 25,000 crores in 4 years. In West Bengal presence of arsenic is the major problem; whereas, Rajasthan suffers from presence of fluoride in drinking water with serious health hazards. There are about 17 lakh 14 thousand rural habitations in India, of which about 77 percent have been provided with safe drinking water of more than 40 liters per person per day under the National Rural Drinking Water Programme (NRDWP). About 4 percent of the habitations are suffering from problems of water quality, designated as “water-quality affected habitations”—meaning those with contaminated water in the rural areas. Among 170 million plus rural households only 54 % have access to tap water and around 70,000 rural habitations are suffering from problems of water quality. The Ministry of Drinking Water and Sanitation has prepared a strategic plan to cover 90 % rural household through surface pipeline supply of safe drinking water by the year 2022 as a sustainable long term solution, subject to availability of funds. Moreover, Government is planning to provide tap water on a sustained basis in every household by 2030 as per the United Nations Sustainable Development Goals for which Rs. 23,000 crores of central fund will be required annually till the target is achieved.

**Arsenic removal from ground water**

One of the common methods that is adopted in West Bengal for removal of arsenic from tube well water is removal by alum coagulation, sedimentation and filtration. The treatment process involves attachment of a removal plant with the principle of
addition of sodium hypochloride (Cl₂) and aluminum alum in diluted form, mixing, flocculation, sedimentation and up flow filtration in a compact unit. This unit has been found effective in removing 90 percent arsenic from tube well water having initial arsenic concentration of 300mg/L (Ahmed, 2001). Along with that arsenic can be removed from ground water by several biological processes such as using biological oxidizing agent which oxidize the As³⁺ to As⁵⁺, which can be removed by conventional method, bioaccumulation of arsenic by some microbial biomass, phytoremediation with some aquatic plants such as Azolla and Spirodella (Spirodela polyrhiza, Wolffia globosa, Lemma gibba, L. minor, Azolla caroliniana, Azolla filiculoides, Azolla pinnata, Ceratophyllum demersum and Pistia stratiotes) (Barznji, 2015). Algae species Cladophora sp. and water hyacinth (Eichhornia crassipes) can also be helpful in removing arsenic from natural water bodies (Jasrotia et al., 2017).

**Mitigation of arsenic toxicity through dietary treatment**

**Vitamin E and C**

Vitamin E (α-tocopherol) is a fat-soluble vitamin known to be one of the most potent endogenous antioxidants. Vitamin C (Ascorbic acid) is a water-soluble antioxidant occurring in the organism as an ascorbic anion. It also acts as a scavenger of free radicals and plays an important role in regeneration of α-tocopherol. Ascorbate can both chelate and reduce transition metal ions and the reduced metal ions in turn can reduce oxygen or H₂O₂ to superoxide and hydroxyl radicals, respectively. Therefore, ascorbic acid forms the first line of antioxidant defense. Experimentally, it was observed that L-ascorbic acid can be used for mitigation of toxic effects of arsenic in rodents. Therefore, it is assumed that it can also be used for human therapeutics (Singh and Rana, 2007).

Arsenic exposure didn’t affect the production performance of goats but arsenic content of milk was increased significantly. Treatment with Vit E @100IU or 150IU reduced arsenic excretion non-significantly. So specific protection of α-tocopherol may be helpful to combat arsenic retention in animal. As exposure adversely affected the retention of zinc, cell mediated immunity and humoral immune responses, which were largely ameliorated by vitamin E supplementation in goats (Mohanta et al., 2014).

**Probiotics**

Specific probiotic strains have capability of binding with heavy metals like As, Cd, Pb. The positive zeta potential of native and methylated Lactic Acid bacteria (LAB) at certain pHs indicate the existence of positively charged surface groups. Therefore, it is expected that native LABs should have cationic binding sites for the removal of anionic As (V) (Halttunen, 2007). The rapid removal of arsenic (V) by L. casei indicates that the binding occurs at the bacterial surface. The highest removal is achieved at pH 7. This removal probably results from the formation of anionic species such as, H₂AsO₃ and H₂AsO₄ (Zoghi et al., 2014). *Saccharomyces cerevisiae* removed 82.2%, 87.8% and 90.46% of arsenic from water containing 200ppb, 300ppb and 400ppb arsenic respectively and it is highly effective method for the As (III) removal from the contaminated water (Roy et al., 2013). When yeast cell cultures were incorporated with silver particles they obtained a higher capacity to remove arsenic than that of normal carbonized yeast culture (Selvakumar et al., 2011).

**Minerals**

Some minerals such as zinc, selenium, copper act as oxidizing agent or reduce the oxidative stress that can be helpful in ameliorating the arsenic toxicity. Zinc induces the metallothioneine and increases its concentration thus helps in the amelioration of arsenic toxicity (Ganger et al., 2016). Selenium along with vitamin E improves the immunity of animals and reduces the oxidative damage. Selenium alone or along with vitamin E can be beneficial in reducing the arsenic related oxidative stress in chicks (Mashkoor et al., 2013) and rats (Messarah et al., 2012). Organic or inorganic copper supplementation helps in increase in the superoxide dismutase concentration in dairy cows (Cortinhas et al., 2010); therefore, it might be beneficial in ameliorating the arsenic toxicity. However, not much data is available on this aspect, which can be explored by future researches.

**Herbal drug**

In Ayurveda, several herbs like *Haridra* (turmeric), *Shanthy* (dried ginger root) and others are used for the management of arsenic poisoning. Turmeric and ginger given at the rate of 10mg/kg BW can be helpful in the therapy of chronic arsenic toxicity in calves. It eliminates the Arsenic from body through faeces thus reducing their amount in hair and plasma (Biswas et al., 2017). Turmeric is a potent source of curcumin, essential oils, fibers and vitamins. Aqueous extract of turmeric contains some protein which prevents depletion of –SH group during lipid peroxidation of brain tissue by protecting the –SH group of enzyme thus act as scavenger against ROS. It also inhibits arsenic induced cell damage by blocking the c-Jun amino-terminal kinase (JNK) pathway. Hazarika et al. (2015) reported that treatment with turmeric powder alone or turmeric and *Amaranthus spinosus* or turmeric and *Eclipta alba* resulted in reduced arsenic deposition in body of cattle by increasing the excretion, even its encapsulated form was found to be more effective (Sankar et al., 2015) . Ginger contains many flavonoids and phenol compounds. It shows significant antioxidant activities due to presence of phenolic contents and flavonoids (Shirin and Prakash, 2010).

Supplementation of *Tephrosia purpurea*, *Psidium guajava* leaves extract had protective action against induced arsenic toxicity in Wister rats (Roy and Roy, 2011; Gora et al., 2013). Similar effects were observed by supplementation of *Syzygium cumini* leaf extractin mice (Barai et al., 2017).
Conclusions

Arsenic in Water-Food-Feed chain is the major concern as potential health hazard in some parts of India; especially in Indo-Gangetic plain. Food (milk, meat, egg, milk products, fish) form animal/fish/poultry origin are also contaminated in the As affected areas. Contaminated water is the major route of exposure of As to the animals and through irrigated contaminated water arsenic enters the food chain and ultimately attack the human population. The conventional methods of mitigation of arsenic toxicity from different sources of environment are costly as well as have limited efficacy. Treatment of arsenic toxicity in animals has been specifically done by anti-oxidants. Several dietary sources like vitamin E, vitamin C, Se along with probiotics and herbal drugs are used for arsenic toxicity mitigation; however, they are found to have variable action. A long-term environmental planning and sincere research is essential to develop novel, effective and economical technologies to reduce the arsenic load from natural environment as well as new safe drugs is to be developed to mitigate of arsenic toxicity in India.

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