ARSENIC AND ITS SPECIFICATION

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ABSTRACT
Arsenic is a naturally occurring poison that contaminates food, water, soil and air. Arsenic is present in both inorganic and organic form but in both of them the inorganic form of arsenic is very dangerous for human. Arsenic is a homicidal and suicidal agent due to its use and involvement in many high profile murders. Arsenic is referred as “poison of king” because of its potency and discreetness. Arsenic is basically present in trivalent and pentavalent states metabolism of arsenic is carried out by trivalent state followed by arsenic methyl transferase. It is a sequential process of reduction from pentavalent to trivalent stage. The following review covers complete description related to arsenic, its source, uses, acute and chronic toxicity, arsenic poisoning and its treatment.

KEYWORDS: Arsenicosis, arsenic toxicity, pentavalent and trivalent stage.

INTRODUCTION
Arsenic is a heavy metal, natural pollutant and toxic in nature. It is naturally present in rocks of earth metals. According to WHO the safe level of arsenic is less than 1 ppb. Arsenic is present in various forms in environment for eg. H₃AsO₃, H₂AsO₃, HAsO₃, H₃AsO₄, H₂AsO₄ and HAsO₄.¹ Acute arsenic poisoning is associated with nausea, vomiting, abdominal pain and diarrhoea. Chronic arsenic poisoning results in multi system disease. Arsenic exerts its toxicity due to inactivating upto 200 enzymes specially those involved in cellular pathway and DNA synthesis and DNA repair. Arsenic may cause arsenicosis due to the presence of arsenic in the water.
Sources of arsenic to human exposure

- **Arsenic in industry**
  In industry scale the main product that is contaminated from arsenic is dried milk. In dried milk di sodium phosphate is basically used as a stabilizer to preserve the acidity. The di sodium phosphate used in industry is of low purity and contains five to eight percent of arsenic.\(^2\)

- **Arsenic in drinking water**
  It is concluded from various analysis that about 100 million peoples are exposed to arsenic from drinking water. Drinking water contains arsenic more than a limit in certain country. Mainly 20 countries are most affected due to drinking water. This problem is most serious in Bangladesh and West Bengal (India). Arsenic in drinking water causes arsenicosis.\(^3\)

- **Arsenic in food**
  Food is also the source of arsenic. Fish, shellfish, meat, poultry, dairy products and cereals are the main sources of dietary intake. However, the arsenic content of fish and shellfish contains organic compounds that are of low toxicity.

- **Smoking**
  Tobacco contains a small amount of inorganic arsenic. Exposure of smokers to tobacco may ingest the amount of arsenic. The content of arsenic is increased when the tobacco plant is treated with lead arsenate insecticide. Smelter workers, who have an elevated risk of developing lung cancer due to arsenic exposure, further increase their risk by smoking.\(^4\)

**Arsenic toxicity**
Arsenic is one of the most toxic element present in the environment. It can produce acute and chronic effects both these condition requires immediate treatment.

**Acute toxicity**
The Acute Arsenic poisoning is most commonly occur due to ingestion of Insecticides or Pesticides. Small amounts of arsenic ingestion can be removed during twelve hours of ingestion provide complete treatment. Amount of arsenic between 100 to 300 mg is called a lethal dose. The common symptoms of Acute arsenic poisoning are nausea, vomiting, colicky abdominal pain, profuse watery diarrhoea, excessive salivation, Acute psychosis, a diffuse
skin rash, toxic cardiomyopathy, seizures, Haematological abnormalities, renal failure, respiratory failure, and pulmonary oedema are common.

**Chronic toxicity**
Long term exposure of Arsenic may cause serious Problems. Chronic arsenic poisoning mostly affects all body organs. Arsenic absorbed from the body is accumulated in the Kidney, Heart, Liver and Lungs. Chronic Arsenic poisoning may leads to Peripheral vascular disease, respiratory disease, diabetes mellitus, and neutropenia. Arsenic is deposited in the keratin reach tissue such as nails, hair and skin. Dermatological changes are most common such as hyperpigmentation and Keratosi.[5] Chronic exposure to As is associated with adverse effects on human health such as cancers, cardiovascular diseases, neurological diseases and the rate of morbidity and mortality in populations exposed is alarming.[6]

**Kinetics of Arsenic in the body**

**Absorption**
The absorption of arsenic is mainly depends on the solubility and particle size. Arsenic that reaches to the lungs is well absorbed. Arsenic in both pentavalent and trivalent form are rapidly and extensively absorbed from the GIT due to their high solubility. The insoluble form of arsenic like arsenic disulphide are poorly absorbed. inorganic arsenic react with sulphydril group of cellular protein and inhibit enzyme synthesis.

**Metabolism**
Metabolism of arsenic is take place by two pathways such as
(1)Reduction reaction-It converts pentavalent form in trivalent form.
(2)Oxidative methylation-In this type of pathway trivalent form of arsenic is methylated to form mono-, di- and trimethylated products using S-adenosyl methionine as the methyl donor and glutathione as an essential co-factor.

The metabolism and Disposition of arsenic is mainly affected by valence.

**Excretion**
Methylated products formed during metabolism are readily excreted in urine. Trivalent form of arsenic is extensively methylated results in long term excretion. Concentration of arsenic in blood, hair, nail and urine is mainly used as a biomarker for arsenic detection. The excretion of arsenic is mainly via the kidney.[7]
Ground water treatment

It is concluded that the main source of arsenic exposure to the body is ground water and it may cause a large number of abnormalities. Several methods are developed for removal of arsenic from the ground water and for neutralizes toxicity.

Determination of arsenic in ground water.

There are mainly two methods for determination of arsenic in ground water.

A. On the site testing

(1) On-Site Field Testing kit-colorimetric principle is used for onsite field testing method. It provide rapid result and not require a large cost investment in the laboratories. This method reduces arsenite to arsine gas under acidic condition with the addition of Zinc powder. The intensity of colour can be determined after a few hours.

(2) Electroanalysis-The method has low cost than the colorimetric testing kit and has low testing limits. It is also based on the reduction and oxidation of arsenic to measure concentration of different arsenic species.

B. Laboratory scale testing

It is a time consuming process and require special techniques & instrument for measurement of arsenic level. It is very time consuming, slow expensive but most accurate method.

Treatment

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<tr>
<th>S.NO.</th>
<th>NAME OF THE TECHNIQUE</th>
<th>PRINCIPLE AND WORKING</th>
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<tr>
<td>1.</td>
<td>Co-precipitation, Coagulation and Filteration</td>
<td>Activated hypochlorite is introduced in the aeration tank in water treatment process. Results in oxidation of As(III) to As(V) and then to lower arsenic concentrations below the standard level (&lt;0.05 mg/L)</td>
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<td>2.</td>
<td>Adsorption Based Technologies</td>
<td>Adsorption is the most common process for ground water treatment. Adsorbents like activated carbon, activated alumina, natural/modified clays and Zeolites are used for treatment.</td>
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<td>3.</td>
<td>Precipitation and Filteration at Household scale</td>
<td>It is based on the formation of co-precipitate of arsenic by adding ferric and hypochlorite salt followed by filtration of water through a bucket and filter.</td>
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4. Electrocoagulation

Electrocoagulation is an alternative method to using chemical coagulant for arsenic removal. And it is better to use the electricity then the chemical for formation of a coagulant. This technique based on the electrolytic oxidation of an anode material followed by in situ generation of coagulants. When a current is applied Fe$^{+2}$ and Al$^{+3}$ are released by oxidation. Fe$^{+2}$ is then oxidized.$^{8,9,10}$

**Diagnosis of Arsenic poisoning**

Acute Arsenic poisoning can be diagnosed by determining the concentration of arsenic in urine. The As level more than 50µg /l or 100µg in 24 hours shows acute arsenic toxicity. The urine should be collected in metal free container. Other biological samples like Blood, nail, and Hair samples are collected for chronic arsenic toxicity in laboratory scale.$^{[11]}$ The identification of arsenicosis is difficult. On small exposure the arsenicosis can be determined by Changes in skin colour and the thickening of skin on the palms and soles while on large contaminated areas internal symptoms are appeared rather than external symptoms. Biopsy is required for tissue and tumour examination.$^{[12]}$

**Medicinal property of arsenic**

Arsenic is known as poison of king but apart from this arsenic have a number of pharmaceutical and medicinal active property. Hippocrates (father of medicine) used arsenic sulphide to treat ulcers and abscesses Several Indian herbal Ayurvedic medicine contains arsenic. some of the medical and pharmaceutical property of arsenic are mentioned below.

(1) **Arsenic in Trypanosomiasis**

Arsenic and its derivative have a potent effect against sleeping sickness or trypanosomiasis. In 19th century atoxyl(arsenic derivative) was developed to treat trypanosomiasis, but after a few time it was withdrawl due to neurotoxicity. Arsenoxides which is very effective and very toxic, Arsenobenzene which is less effective and less toxic are developed.. Tryparsamide, a phenylglycinamide arsonate derivative of Atoxyl and melarsen, a melamine derivative of Atoxyl are mainly used in the middle of the 19th century. Suramin and Melarsoprol are the arsenic derivatives that are combined with arsenic antidote (BAL) to minimize the toxicity due to lewisite gas.
(2) Arsenic in Leukaemia

US FDA approved arsenic trioxide for the treatment of acute promyelocytic leukaemia (APL) in 2000. It is found by researchers from the American Universities that arsenic trioxide is very much effective in the treatment of end-stage high-risk multiple myeloma. Currently arsenic trioxide is used for the treatment of relapsed and refractory APL.

(3) Arsenic in Syphilis

Syphilis is also known as great pox. It is found from various studies that arsenic and its derivative like mapharside have a potent antisyphilis activity. Arsenic usually combined with either of barium and mercury for the treatment of syphilis during last several decades. It is most effective treatment for syphilis until the advent of penicillin.

(4) Other medicinal uses

In ancient time women used arsenic for whiten the face and kill the vermin from the hair and scalp. arsenic produces beauty and freshness on application on the skin. arsenic is commonly used as a cosmetic and this is the main source of arsenic poisoning. Arsenicals also have antimalarial and antitubercular activity. Stovarsol, and sodium acetarsone are the main marketed product for Tuberculosis.\(^{[13]}\)

(5) Arsenic in Industry

Arsenic is used industrially and commercially as alloying agent in the manufacture of Transistors, lasers, semiconductors, glass, pigments, textiles, paper, metal adhesives, wood preservatives. arsenic is also used as pesticides, feed additives and pharmaceuticals.\(^{[14]}\)

Prevention of Arsenic poisoning

WHO declares that the arsenic contamination problem as one of the world's primary environmental changes problem. The most important region is contaminated drinking water ingestion, It can only prevented by arsenic mitigation programme. It should be started by central government of the country where the arsenic problem is very dangerous like in west Bengal and Bangladesh. Arsenic mitigation programme should be followed with following objectives.

- To create Awareness by Public health programme.
- To find out all the cases related to arsenicosis and Proper study is carried out on each and every case and reports accordingly.
To use the suitable and non-hazardous chemicals and techniques for drinking water treatment.

To find out the source of arsenic exposure by the government and started different programmes for prevention and treatment of arsenic poisoning.

To make the treatment easily available and possible for each and every class of patient.

To aware the public for suitable drinking water treatment techniques like Precipitation and filtration, Electrocoagulation etc.\textsuperscript{[15]}

**Treatment & Management of Arsenic poisoning**

Gut decontamination and Haemodynamic stabilisation are the key factors for management of arsenic poisoning. Fluid and electrolyte replacement therapy are basically provided for acute toxicity. The following steps should be followed for acute and chronic arsenic poisoning.

- Intravenous fluid replacement therapy is more beneficial for chronic toxicity of arsenic.
- Gastric lavage is more beneficial in case of Acute arsenic toxicity. Polyethylene glycol is most commonly used for prevention of further absorption of arsenic from the GI tract.
- Activated charcoal with Cathartic is frequently recommended to remove arsenic from the body.
- Haemodialysis is most effective for the patient suffering from renal failure.
- In most of the cases Chelation therapy is used. Chelate forms a complex with arsenic and play a major role in removal of arsenic from the body.
- Nutrients and Vitamins (Basically Vitamin E) are given. Studies shows that Antioxidant (vitamin C & Vitamin E) promotes Methylation of arsenic which increase the excretion of arsenic from the body.\textsuperscript{[16]}

**Chelation therapy in Arsenic poisoning**

The chelation therapy is most effective in case of arsenic poisoning. Chelation therapy is most effective in controlling systemic clinical manifestations and reduction of arsenic stores in the body, reducing subsequent cancer risk.\textsuperscript{[17]} A number of chelating agents are used for the treatment of arsenic poisoning.

1) **Dimercaptol (BAL)**

First line agents for treating arsenic poisoning. It is mixed with Peanut oil and then administered Intramuscularly. BAL is the drug of choice in USA for arsenic poisoning. BAL is lipophilic in nature so it is distributed in both Intracellular and Extracellular sites. BAL is
most commonly used for serious ill patients. Dosing is 3-5 mg/kg every 4-6 hours. It have some limitations include hypertension, haemolysis, fever, sterile abcesses development. Dimercaptol increases the arsenic level in brain.

2) **Succimer (DMSA)**

Succimer is an oral analog of BAL that may be used in sub acute or chronic arsenic exposure. It is approved by FDA for used in children lead poisoning. It is used worldwide in arsenic intoxication. The major advantages of Succimer that it is less toxic, and not affect any other body organ.

3) **Dimerval (DMPS)**

It is accepted internationally for treating heavy metal poisoning. It is available in both oral and Parenteral form.[18,19,20]

**Combinational therapy**

New trends are introduced that more than one chelating agents are used for treatment of arsenic poisoning. It is a new and Novel therapy. Combination of n-acetyl cysteine with Succimer increases the mobilization of arsenic. Vitamins, Essential Amino acids and antioxidants are basically combined with the chelating agent and increases mobility of the metal in the body followed by excretion. Antioxidants used in arsenic may enhance the efficacy of the treatment protocol designed to mitigate arsenic poisoning.[21]

**Selenium in Arsenic toxicity**

It is concluded from various analysis that selenium is an Arsenic antagonist. Selenium Increases Biliary and Urinary excretion of arsenic. It reduces the Arsenic load in the body by counteracting Cellular toxicity, Chromosomal damage. Selenium forms complex with arsenic and form a methylated product that can be easily excreted from the body. It is observed in Bangladesh that persons that take low selenium dietary intake are most commonly suffered from the arsenic, and In high selenium Dietary intake areas the problem of arsenicosis is minor.[22]

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