TECHNIQUES FOR ARSENIC ANALYSIS, REMOVAL AND ITS BIOMEDICAL APPLICATIONS

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Abstract

In the realm of the environment, a great deal of research has been done on the poisonous and damaging impacts of heavy metals including arsenic, mercury, and others. Due to environmental pollution and the bioaccumulation of certain heavy metals in the food chain, they adversely impact human health despite their presence in low concentrations (10 ppm). Recent research studies suggest that exposure to arsenic during various life stages leads to gut microbial dysbiosis and is linked to immune dysfunction, altered lipid metabolism, and neurobehavioral damage. Therefore, it is important to detect, analyze and remove it from the environment to reduce its direct effect on human health.

Keywords: heavy metals, neurobehavioral damage, immune dysfunction, bioaccumulation

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1. TECHNIQUES FOR ARSENIC ANALYSIS

In current scenario various analytical techniques such as hydride generation atomic fluorescence spectrometry (HG-ASF), Inductively coupled plasma atomic emission spectroscopy (ICP-AES), inductively coupled plasma-mass-spectrometry (ICP-MS), hydride generation atomic absorption spectroscopy (HGAAS), graphite furnace atomic absorption spectroscopy (AAS), and fluorescence spectrometry have been used for the detection of heavy metals including As (Le et al., 2000). These instruments can detect low levels of arsenic, however, highly expensive and sophisticated instrumentation with a well-established laboratory set up is required for effective determination. They are also time consuming, not easily accessible, and are not suitable for on-site analysis. Moreover, with these methods, the cost of analyses can be as high as 8−10 USD per sample (Hu et al., 2012). Now-a-days the focus of researchers is on development of simple, portable and economical sensors with rapid and reliable Arsenite detection/analysis in environmental samples, especially in developing countries and in areas with insufficient infrastructure and technical facilities.

Electrochemical methods are advantageous as they are cost-effective, timely, and easy to implement. Various electroanalytical tools such as cyclic voltammetry (CV), linear sweep voltammetry (LSV), Anodic stripping voltammetry (ASV), differential pulse voltammetry (DPV) and square wave ASV (SWASV) can be employed to detect low concentrations of As with good sensitivity and reliability (Shen et al., 2017). Furthermore, stripping voltammetry techniques are adaptable for successful and rapid field screening, high accuracy, and enhanced sensitivity and demonstrate a very low detection limit (Cavicchioli et al., 2004). Employing the highly sensitive stripping voltammetry technique, researchers have detected As to a low detection limit and significant sensitivity using various electrode materials under optimized experimental conditions (Forsberg et al., 1975; Rahman et al., 2010; Yang et al., 2016).

Arsenic detection by electrochemical methods is investigated using mercury electrodes (Wang et al., 2013) such as hanging mercury drop electrodes (HMDE) because they provide a wider potential window for redox reaction of various metals and regeneration of a clean surface is quite easier via simply creating a new mercury drop. However, because of obvious toxicity considerations from mercury, it is very difficult to discard the used mercury and clean the whole electrochemical setup after each measurement (Kwang-Seok Yun et al., n.d.). Furthermore, various metals such as gold (Au), silver (Ag), and Hg could not be potentially detected on HMDE. Therefore, they have been significantly replaced by a number of solid electrodes such as platinum (Forsberg et al., 1975) silver, boron-doped diamond electrode (A. O. Simm et al., 2005), gold microwire electrode (Liu et al., 2014), gold microdisk (Simm et al., 2004) and iridium oxide-modified boron-doped diamond electrodes (Salimi et al., 2004).

Recently, researchers investigated the platinum NP-modified glassy carbon electrode for electrochemical sensing of arsenic in 1 M aqueous $HClO_4$ electrolyte solution. After optimization, a lower detection limit (LOD) of 2.1 ppb was obtained (Dai and Compton, 2006). Further, an iridium-modified boron-doped diamond electrode was generated by ion implantation method and exploited directly for electrochemical detection of arsenic to an LOD of 1.5 ppb. The aforementioned sensor was favorably able to selectively sense increased arsenic in tap water containing a substantial amount of various other elements as well (Ivandini et al., 2006). However, these materials are expensive, thus making AsIII detection not feasible for long-term applications.

The successful large-scale implication of the electrochemical sensors mainly depends on careful designing and fabrication of desired materials, which can facilitate adequate accumulation and subsequent oxidation of the analyte from its surface under optimized electrochemical conditions. Among many other solid electrode-based sensors, gold (Au)-centered materials have demonstrated enhanced electrochemical activity because of their advanced characteristic features in the field of catalysis, electroanalysis, and nanoscale devices (A. Simm et al., 2005). They have excellent electronic, optical, and electrical characteristics, which merely depend on the surface morphology and size of Au particles (Feeney and Kounaves, 2000). Therefore, microstructured/nanostructured Au electrodes have been exploited largely for applications in the detection of arsenic in water. They are superior to the commercially available metal electrodes because of the presence of more electroactive sites, much enhanced electron-transfer rate and favorable electrochemical kinetics (Welch et al., 2004).

Gold-based nanoscale materials can be fabricated by chemical synthesis, ultraviolet light or electron beam irradiation and electrochemical methods (Tan et al., 2002). Electrochemical methods are much facile and easy to use relative to other methods (Fukushima et al., 2003). Gold nanoparticles can be electrodeposited on the electrode using 0.1 mM $HAuCl_4$ solution, which show good As sensing at parts per billion levels (Dai et al., 2004) Gold nanoelectrodes also enable simultaneous detection of As, Hg, and Cu (Joya and de Groot, 2016). Furthermore, gold NP-modified indium tin oxide (ITO)-coated glass electrodes were prepared by direct electrodeposition method from 0.5 M H_2SO_4 solution containing $HAuCl_4$ solution. The Au-based films were nanostructured and detected As to an LOD of 5.0 ppb using the LSV technique (Babar et al., 2019).

However, it is a tedious method, and during deposition, subsequent accumulation of Au ions on cathodic sites also poses a challenge. To address this issue, separators are employed, which make the system more complex and thereby increase the cost for analyses (Joya and de Groot, 2016). The gold nanotextured electrode (Au/GNE) assemblage is exceedingly stable with promising reproducibility maintaining highly active nanoscale surface features by repeating the analyses several times and allows for very reliable, selective, and highly sensitive detection of arsenic using CV and SWASV. This method is also successfully employed in real water samples for arsenic analysis. In the complex system containing Cu^{2+}, Ni^{2+}, Fe^{2+}, Pb^{2+}, Hg^{2+} and other ions, Au/GNE is amazingly applicable for highly selective and sensitive detection of As in water. Next, the experiments are under process to scale up the Au/GNE-based electrochemical sensors for real-time applications owing to their simple fabrication and assembly, high reproducibility and robustness, and electro analytical performance for arsenic sensing (Babar et al., 2019).

2. REMOVAL OF ARSENIC FROM WATER

Removal of arsenic is very important and is the focus of several researchers, industries, environmental groups (Alka et al., 2021). The removal of arsenic from water can be achieved through different mechanisms, methods, technologies including adsorption, chemical precipitation, ion exchange, phytoremediation, electro kinetic techniques and membrane technology. Recent research focuses on different traditional and emerging technologies for the improvement of complex resources active in the elimination of arsenic and other substantial metals. Recently, the number of studies on arsenic removal techniques have been continuously increasing.

A. Nanomaterials as adsorbents

Adsorption has been a commonly used technique for water treatment as early as 4000 BCE. Cutting-edge Egypt, adsorption was used for the coloring of silk fibers, cotton fibers and some plant and animal fibers, in addition to decoloration of beverages and diet. Adsorption finds several applications in day-to-day life. In adsorption, the materials existing in a fluid stage are collected or adsorbed on the solid stage by physical/chemical adsorption, followed by their subsequent removal from the liquid, as a mass transfer. Arsenic removal by adsorption is economically feasible and very efficient, moreover, it does not require use of chemical additives. It is easy to use and applicable in areas lacking skilled manpower, moreover it does not require consistent electricity supply. The quantitative removal efficiencies reported for arsenate and arsenate remediation have been as high as >95% (M. Kumar et al., 2019; R. Kumar et al., 2019; Ratna Kumar et al., 2004).

Nanomaterials show significant benefits in the adsorption of arsenic from water because of grater superficial adsorption movement and great reactivity. The adsorbent nanomaterials showing excellent removal efficiency and less maintenance cost, particularly for removal of low concentration of heavy metals, highlight the use of adsorption as an encouraging method in arsenic removal from water. Presently, nanomaterial including carbon materials, metal oxides, metal-organic framework and chitosan have been used for removing arsenic from water (Alka et al., 2021; Liu et al., 2015, 2018). The unique hollow structure of carbon nanotubes, their large specific surface area, high porosity, and rapid transport of water make them ideal candidates as adsorbents for As elimination from water (Addo Ntim and Mitra, 2011; Dehghani et al., 2015). Vadahanambi et al. designed 3D graphene carbon nanotube-iron oxide for the elimination of arsenic from water. Iron-oxide nanoparticles shows significant adsorption of arsenic from water (Vadahanambi et al., 2013). Andjelkovic et al. also fabricated 3D graphene-iron oxide nanoparticle aerogel for elimination of arsenic from water (Andjelkovic et al., 2015). Iron-oxide covered carbon nanotubes for elimination of arsenic from water (Ma et al., 2018) but the nanotubes failed to show effective adsorption because of hydrophobic shells, unfortunate dispensability, and absence of functional groups.

B. Ion-exchange technology

Ion-exchange is a physicochemical process employed for the elimination of arsenic from the environment. In this technique, the ions were retained electrostatically on the solid surface and exchanged from the solution with ions having similar charge (Katsoyiannis and Zouboulis, 2006). Ion exchange is an effective method for adsorption and is mainly applied to decrease water hardness. It is also employed for excerpt pollutants like nitrate, arsenate, chromate and selenite ions from water (Al-jubouri and Holmes, 2020). The United States Environmental Protection Agency (EPA) has suggested definite ion-exchange materials, particularly chloride form, aimed to arsenic elimination (Jadhav et al., 2015). The ion-exchange resins remove the arsenic via mechanism describes ion-exchange resins that are filled by chloride ions in an conversation spot wherever water contaminated (Shankar et al., 2014). A study described the elimination of arsenic from water through ion-exchange resins. Hence these ion exchanges resins can be used for the elimination of toxic arsenic from water. Some factors that affect the removal of arsenic include the entire liquefied items, arsenic concentration, kind of resin used for removal and competing ions (Karakurt et al., 2019; Sarkar and Paul, 2016). Rivero et al. also demonstrated the removal of arsenic from water by using resin in a hybrid ion electrodialysis process.

C. Membrane technology

The membrane is an extensively recognized technology for the filtration of water and is one of the highest well-organized effective methods of arsenic removal with a potential to remove 96% of contaminated As from portable and groundwater. The technique is more effective for removing pollutants and cost-effective at the same time as the process requirements are minimal. Another advantage of this method is that it does not involve any chemical usage (Gonzalez et al., 2019; Ungureanu et al., 2015). Recent reports suggest that several forms of membranes are employed in the elimination of arsenic from water systems with their applications in technologies such as nanofiltration, microfiltration, ultra-filtration, and reverse osmosis (Gonzalez et al., 2019; Pramod et al., 2020). However, Pramod et al. used the combination of microfiltration and heterogeneous Fenton method for the elimination of arsenic from water (Pramod et al., 2020).

D. Chemical precipitation

Chemical precipitation is a method which usages sulfides, ferric salts, calcium and magnesium salts and other chemicals for the elimination of As from water. The chemicals assist in eliminating arsenic by changing dissolved form to its lesser soluble form. Precipitation by ferric arsenate and calcium arsenate is the most useful method for removal of arsenic in wastewater (Long et al., 2019). Chemical precipitation has been also used to treat arsenic and calcium from gold mining waste using two-stage nanofiltration (Sarankumar et al., 2020). Di Iorio et al. developed magnetite nanoparticles for the removal of arsenic from wastewater (Di Iorio et al., 2019).

E. Phytoremediation

Phytoremediation is a widely recognized technique which uses plants for the removal of contaminants. The major advantage of this technique is limited nutrient requirement, lesser maintenance and its role in ecological sustainability (Manoj et al., 2020). Phytoremediation is performed using plants by wide root system, great acceptance of toxicants and fast growing rate.

3. BIOMEDICAL APPLICATIONS OF ARSENIC

Being considered as one of the oldest poisons, arsenic is too recognized to consume a miracle effect for management several illnesses such as cancer, ulcers, malaria and bubonic plague (Zhao et al., 2021). Around 2,000 years ago, Chinese and Greek healers used arsenic for the treatment of major diseases from syphilis to cancer. From the 20th century, the discovery of chemotherapy and antibiotics led to the abandonment of arsenic based treatments (Zhu et al., 2002). Literature review suggests that these materials have been used as chemotherapeutics in leukemia and cancers due to their anti-proliferative and pro-apoptotic properties (Dilda and Hogg, 2007; Ettlinger et al., 2019; Kim et al., 2017; Tian et al., 2020; Yoon et al., 2016; Yu et al., 2020; Zhang et al., 2016). The therapeutic success further encouraged researchers to explore arsenic as a potential future solution for other types of cancers. For example, In a study the effectiveness of a combination of arsenic trioxide and L-buthionine-sulfoximine against advanced solid tumors was assessed. More detailed results of the tumor in figure 1 indicate the difference between the treatment and control group. The As_2O_3 (arsenite) shows cytotoxic effect by the generation of reactive oxygen species (ROS) followed by inhibition of radical scavenging that would enhance the therapeutic efficacy (Maeda et al., 2004). Multiple nanotechnology-based therapies are under development for the effective delivery of As. However, Zhang et al. developed core-shell nanoparticulate arsenic trioxide for effective treatment of solid tumors through the facile route (Zhang et al., 2016). pH-sensitive (zeolitic imidazolate framework-8 based) nanoparticles were developed for effective delivery of arsenic trioxide (Zhang et al., 2016). The anti-tumor activity of sodium meta-arsenite in glioblastoma through advanced Akt activities was assessed. Briefly, to estimate the anti-tumor activity of sodium meta-arsenite (dose 2 mg/kg and 5 mg/kg), the tumor was evaluated for 21 days in mice injected with U87-MG orthotopic xenograft tumor. The results showed a important decrease in growth of tumor with reduced Akt stimulation as shown in figure 2. The effective amounts of sodium meta-arsenite employed in this case have remained described to be non-toxic (Lee et al., 2020). Arsenic trioxide is used as an anticancer agent traditionally; it demonstrations a important healing outcome against severe promyelocytic leukemia (Zhu et al., 2002). Recently, the U.S. FDA approved arsenic trioxide as the first-line management against acute promyelocytic leukemia. The mechanism of arsenic trioxide triggering both apoptosis and differentiation of leukemic cells, in a way similar to that of retinoic acid (Antman, 2001; Leu and Mohassel, 2009; Mathews et al., 2001). The result of arsenic trioxide on cervical cancer and reported an increased apoptosis by 3-fold related to control group was observed (L. Zhang et al., 2020).

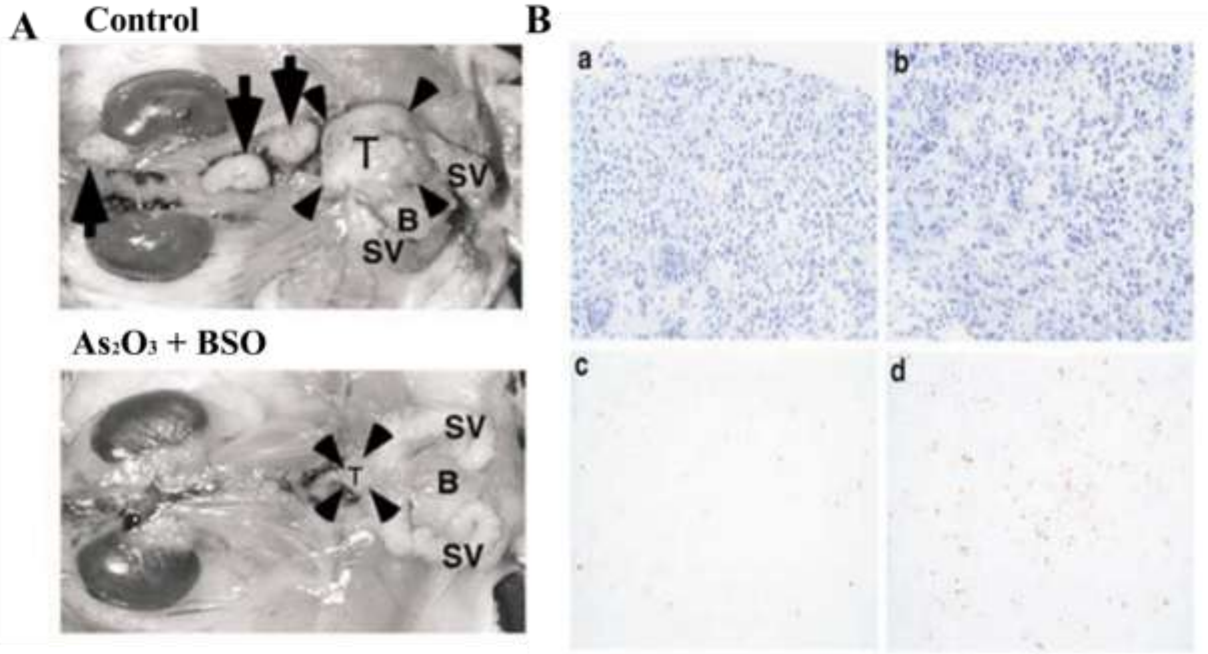

Fig 1: In vivo tumor growth inhibition and survival rates in the orthotopic mouse model of androgen-independent prostate cancer treated with As_2O_3 (Arsenic trioxide) and BSO (Buthionine-sulfoximine). (A) Representative cases 7 weeks after orthotopic inoculation of PC-3 cells. Seminal vesicles (SV) and the bladder (B) Representative histology of an orthotopic tumor formed by PC-3 cells after treatment. Hematoxylin and eosin staining (a, b) and in situ TUNEL (TdT-mediated dUTP Nick End Labeling) assay for detection of apoptosis (c, d) were performed in the saline-treated group (a, c) and the group treated with 2 mg/kg As_2O_3 plus BSO (b, d). Growth inhibition is clear both in the orthotopic tumor (black arrow-heads) and retroperitoneal lymph node metastases (black arrows) in the mouse treated with 2 mg/kg As2O3 plus BSO. (Modified from Maeda H, Hori S, Ohizumi H, Segawa T, Kakehi Y, Ogawa O, et al. Effective treatment of advanced solid tumors by the combination of arsenic trioxide and L-buthionine-sulfoximine. Cell Death Differ 2004; 11:737–46. https://doi.org/10.1038/sj.cdd.4401389) (Maeda et al., 2004).

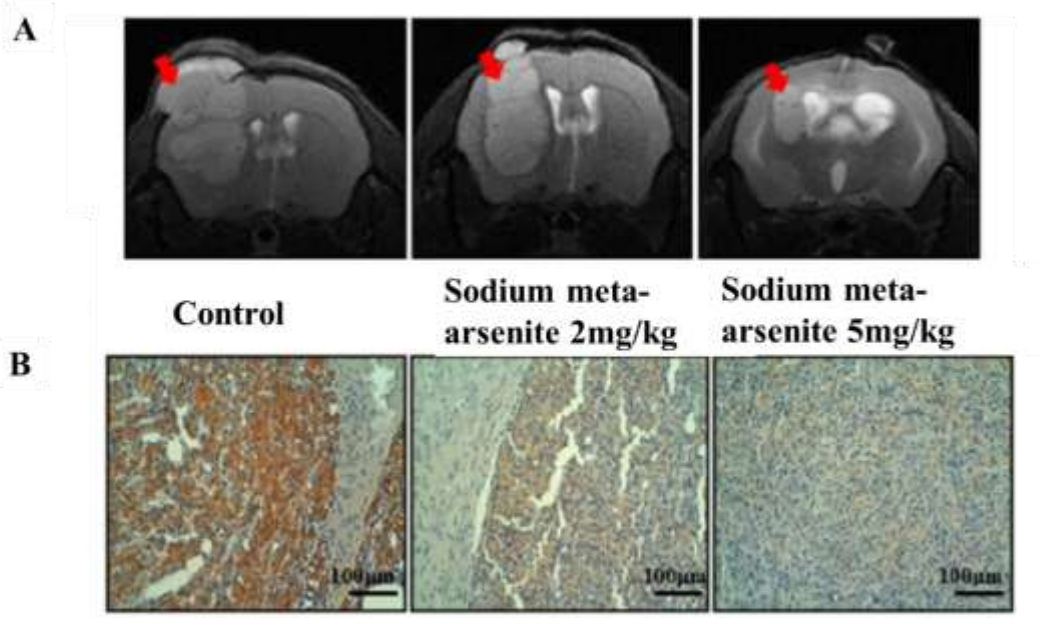

Fig 2: Anti-tumor effects of sodium meta-arsenite in orthotopic xenograft models. (A) Brain MRI images on day 21 of mice (control, and subjected to 2 mg/kg and 5 mg/kg of sodium meta-arsenite). Representative pictures indicate mouse brain regions of the corpus callosum and its surrounding structures. (B) Tumor tissues were fixed and stained with anti-pAkt antibodies. Scale bars = 100 µm. White arrows indicate tumors. (Adapted from Lee EJ, Sung JY, Koo KH, Park JB, Kim DH, Shim J, et al. Anti-tumor effects of sodium meta-arsenite in glioblastoma cells with higher akt activities. Int J Mol Sci 2020;21:1–19. https://doi.org/10.3390/ijms21238982.) (Lee et al., 2020)

Several radioisotopes of arsenic and their traces are used in medical, biomedical and environmental applications. Arsenic is versatile and is incorporated into several chemical structures that permit the synthesis of radiopharmaceuticals through possible usefulness in treatment and identification of numerous illness (Emran and Phillips, 1991).

A photosensitizer is used in combination with chemotherapy toward kill cells by ROS generation in the occurrence of oxygen and light radiation (Agostinis et al., 2011; Cheng et al., 2019; Dhas et al., 2021a; Zhang et al., 2018; Zhou et al., 2016). The arsenical-based chemotherapy might not only encourage cell apoptosis, but also control cancer microenvironments to progress the photodynamic therapy against hypoxic tumors. A photodynamic therapy based on chemotherapy sensitization in contradiction of hypoxic tumors and demonstrated the effective drug filling of phenyl arsine oxide in the porphyrinic metal-organic structure along with surface modification of hyaluronic acid. The results demonstrated an improvement in biocompatibility and improved the special tumor buildup and exact cellular uptake of the surface-modified formulation (Yuan et al., 2020). Potassium arsenite (Fowler's solution) has been used for the management of malaria and syphilis in the late 1700s (Bjorklund et al., 2020; Drobna et al., 2009b). Numerous clinical applications for Fowler's solutions have been studied and applied over the years, but toxicities have limited their usefulness (Ho and Lowenstein, n.d.). The therapeutic effects of As included limitations of serious adverse reactions, unsatisfactory therapeutic effect and toxicity at a high level of dose (Ettlinger et al., 2019; Zhang et al., 2016).

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