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Review

# **Arsenic Toxicological Importance in Air Pollution**

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Abstract: Air pollution is a global environmental concern that poses significant risks to human health. Among the various pollutants, arsenic (As) has gained considerable attention due to its widespread occurrence and severe toxicological effects. This review paper aims to provide a comprehensive overview of the sources, distribution, and toxicological importance of arsenic in the context of air pollution. Arsenic is a naturally occurring element and can be found in various forms, including inorganic and organic compounds. Industrial activities, combustion processes, mining, and agricultural practices are the major anthropogenic sources contributing to arsenic emissions in the atmosphere. Once released into the air, arsenic can undergo complex transformations and transport over long distances, leading to its widespread dispersion and potential exposure to human populations. The toxicological significance of arsenic lies in its ability to exert detrimental effects on multiple organ systems, including the respiratory, cardiovascular, immune, and nervous systems. Inhalation of arsenic-containing particulate matter can cause respiratory disorders such as asthma, bronchitis, and lung cancer. Moreover, chronic exposure to arsenic has been associated with an increased risk of cardiovascular diseases, neurodevelopmental disorders, and various types of cancer. In conclusion, this review paper underscores the toxicological significance of arsenic in the context of air pollution. Understanding the sources, fate, and toxic effects of arsenic is crucial for developing effective preventive and control measures. Further research is warranted to elucidate the complex mechanisms underlying arsenic toxicity and to devise strategies to mitigate its adverse health impacts on exposed populations.

**Keywords:** air quality; pollution; heavy metals; public health; arsenic.

## 1. Introduction

Air pollution is considered one of the biggest problems of the modern age because it is one of the main risk factors for the development of cardiovascular and respiratory diseases, and it is also considered a risk factor for the development of cancer [1–3]. They are in focus research on the effects of pollution on the occurrence and development of other diseases, including is also an examination of the impact of pollution on the mental health of the population or the impact on the weakening of the immune system, especially in children. Evaluates that seven million premature deaths a year are caused by exposure to polluted air, whether it is air pollution in open or closed spaces. Of that, in the Western Balkans region, annually there are 3000 premature deaths, but also 8000 cases of bronchitis in children and other chronic diseases in adults [4]. In addition to the effect on human health, air pollution can also harm the environment so it is associated with the occurrence of acid rain, climate change, and global warming [5,6]. In the end, all the mentioned effects condition the appearance of inevitable economic consequences. Sources of air pollution are divided into natural and anthropogenic sources [7]. They belong to natural ones volcanic eruptions and forest fires that release carbon dioxide (CO2), carbon monoxide (CO), sulfur and nitrogen oxides (SOx, NOx), and others [8]. Anthropogenic sources of pollution include the burning of fossil fuels, whether for household heating or thermal power plant operation, industrial activities (processing metal ore, iron

and steel production, chemical industry, etc.), inadequate disposal of industrial waste, incineration of garbage as well as emissions from traffic. During these activities, suspended solids are released into the environment particles, ozone, nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), CO, and metal(oids). Suspended particles are the most abundant and most studied contaminant of today's environment because it has been observed that they can cause the most serious and harmful health consequences for the human body [9,10]. It is assumed that the composition is responsible for the negative health effect of the size of these particles [11]. The composition of suspended particles depends on their sources, in urban areas are mostly composed of metal(oids), ions, and organic compounds such as persistent organic pollutants (POPs) and polycyclic aromatic hydrocarbons (PAHs). For air quality monitoring, from the aspect of PAH content control, the concentration of benzo[a]pyrene is measured as representative of this group of compounds [12,13].

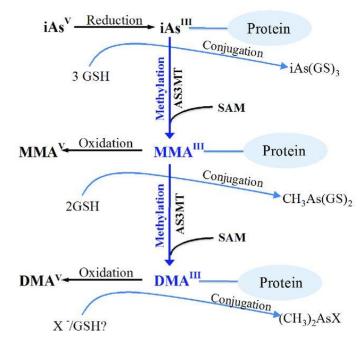
Metal(oids) are widely distributed elements in the environment, natural are constituents of the earth's crust, are found in many ores, and can be released during natural disasters such as volcanic eruptions and fires. At the beginning of the Industrial Revolution, in the second half of the 18th century, there was the expansion of the use of metal(oids) for various industrial activities. Metal(oids) are persistent in the environment and when once released, they cannot be destroyed. Therefore, they are significant from an aspect of professional toxicology but, more dominantly, as contaminants of life environment. Once in the environment, metal(oids) are deposited in suspended solids particles, which can then pass into the systemic circulation of a person and cause adverse health effects [14]. Among the metal(oids) that are toxic to human health include lead, cadmium, mercury, arsenic, nickel, chromium, and others [15].

## 2. Toxicological importance of arsenic

Arsenic is a naturally occurring element in the earth's crust and is the 20th most abundant element represented in it. It is found in water and sediment, so its natural source represents underground and surface water and geothermal sources, and it can go into the air due to volcanic eruptions [16]. It is chemically classified as metalloid which means it has properties of both metals and non-metals. They are present in nature and inorganic and organic arsenic compounds that are white or colorless, odorless, and taste [17]. It is precisely these organoleptic characteristics that it has in the past that made it suitable for use for criminal poisoning (in the Middle Ages it was known as "heirloom powder"). However, with the discovery of Marsh's test in 1836, criminal arsenic poisoning lost its importance because its presence could prove it in the corpse material, and therefore confirm that it was in the middle poisoning. Arsenic compounds were used as chemotherapeutics for the treatment of leukemia, psoriasis, syphilis, and other diseases. The first drug safe enough for human application to treat syphilis was salvation, whose discovery by Paul Ehrlich was awarded the Nobel Prize for Medicine in 1908. Today occupational poisonings are important because arsenic is widely used in industry: during the processing of ores containing arsenic, in the production of alloys, it is used in the synthesis of pesticides, herbicides, and insecticides, in the electronic industry (production of lasers, transistors, and conductors) and other industries [18]. Can also be found in tobacco smoke due to the absorption of arsenic from the soil by the plant *Nicotiana tabacum* or due to the application of arsenic-based insecticides on plantations tobacco. Also, arsenic is a frequent companion of copper and lead ores and thus is released into the environment during the mining and processing of these ores [19]. It can be in nature released from thermal power plants that use coal for their work as well as from incinerators. Because of all the above, arsenic is considered one of the main contaminants in today's environment, and increased concentrations in air, soil, and especially drinking water are an international problem. By its toxicological significance, the presence of elevated concentrations of arsenic in drinking water stands out, and countries with Bangladesh, Argentina, Chile, Mexico, Romania, Hungary, and others [20,21]. The Republic of Serbia is also facing this problem, and it is for this purpose safety of the citizens of Zrenjanin, water from the tap is prohibited for drinking and food preparation.

#### 3. Arsenic toxicokinetic and mechanisms of action

The most dominant routes of arsenic intake into the body are inhalation and ingestion. Arsenic is absorbed through the lungs or gastrointestinal tract using transport pathways for phosphate absorption [22]. One of the characteristics of metal poisons is not subject to biotransformation, however, arsenic is an exception and in the organism is subject to reduction and methylation that lead to the formation of mono- and dimethylated forms which are the dominant metabolites in the urine and are excreted this way [23,24] (Picture 1).



**Picture 1.** Arsenic metabolism pathway in the human body.

The mechanism of arsenic toxicity implies an effect on the respiratory chain mitochondria, where it inhibits complexes I, II, and IV, thereby inducing the formation of reactive forms of reactive oxygen species (ROS) and consequently, oxidative stress [25]. Another mechanism of toxicity involves binding to sulfhydryl groups protein [26]. Arsenic binds to the enzyme pyruvate dehydrogenase and thus inhibits it conversion of pyruvate to acetyl-CoA which inhibits the Krebs cycle [27]. Because of the inhibition of the Krebs cycle, the transition of cells to anaerobic occurs in metabolism and disturbances of the acid-base balance due to the occurrence of acidosis, which explains the rapid death due to acute poisoning. Arsenic is a non-genotoxic chemical carcinogen and the presumed mechanism by which it participates in the development of carcinoma is the generation of oxidative stress, occurrence of chromosomal aberrations, aneuploidy, DNA-protein cross-linking as well as repair modification DNA damage by inhibition of DNA ligase [28–30].

#### 4. Arsenic toxic effects

Acute poisonings most often occur after oral intake of arsenic and can end with a fatal outcome if the person was exposed to high arsenic concentrations (it was estimated that the lethal dose is about 0.6 mg/kg/day) [31]. A fatal outcome is preceded by diarrhea, kidney damage, redness and rash on the skin, excessive salivation, and toxic cardiomyopathy. When it comes to chronic poisoning, characteristic changes are observed on the skin: hyperpigmentation, hyperkeratosis, nail changes, and erythema [32]. Next to its effect on the skin, arsenic can lead to the development of disorders of the central function nervous system. Namely, due to induced apoptosis of microglial cells oxidative stress of the mitochondria in these cells leads to degeneration of neurons, damage to the integrity of the blood-brain barrier, and cognitive disorders such as loss of spatial memory. The results of certain studies indicate that children's IQ may decrease due to long-term exposure to

arsenic, and exposure to this element can begin during fetal development because arsenic passes the placenta. Except for not-carcinogenic effects, arsenic has the potential to contribute to the development of cancer lungs, mainly in workers who were exposed to arsenic in the working environment for a longer period (35 to 40 years), but also to the development of skin cancer that relates to population exposure via water [33]. Based on enough animal and human evidence, arsenic is classified as a group 1 carcinogen [34] (human carcinogen) by the International Agency for Research on Cancer (IARC). Metabolites of arsenic have long been considered non-toxic, however, new research indicates that metabolites, especially MMA-III and DMA-III can lead to DNA damage and mutation development. The workers who work in the previously mentioned are the most vulnerable industries but also the population living near those industry's plants and in areas with elevated arsenic concentrations in water.

For acute poisoning therapy, the chelating agent BAL is used as an antidote (dimercaptopropanol) which competes with arsenic for binding to sulfhydryl groups [35]. Due to the toxicity of BAL, other, more hydrosoluble ones were synthesized with less toxic compounds: dimercaptosuccinic acid (DMSA) and dimercaptopropanesulfonic acid (DMPS). Some studies have examined it application of DMPS in the case of chronic exposure to arsenic, in which he showed effectiveness in eliminating symptoms of neuropathy [36].

### 5. Human biomonitoring of arsenic

For human biomonitoring, if one wants to evaluate short-term exposure to arsenic, urine can be used as a biological sample the total amount of arsenic (inorganic and organic compounds) is measured [37]. If they are in arsenocholine and arsenobetaine present in the sample, may result in false positive positive results. Namely, these organic compounds of arsenic originate from fish and seafood and do not cause toxic effects because they do not succumb to metabolic changes, and the unchanged ones are eliminated in the urine [38]. Concentrations between 1.0 and 3.0 mg/kg are indicative of acute poisoning. On occasion assessments of long-term exposure to arsenic, hair, or nails. Concentrations indicative of chronic exposure are between 0.1 and 0.5 mg/kg in hair samples. When interpreting human biomonitoring results, it is necessary to collect information about when the arsenic exposure occurred and how long it lasted to predict the possibility more accurately and precisely manifestations of the toxic effects of arsenic. Atomic absorption spectrometry (AAS) with the hydride system is the most common method used to determine arsenic in biological samples as well as air samples, water, and food [39,40]. Arsenic from the sample is reduced to arsenic which is in a gaseous state and is introduced into the flame. This method can be used to determine inorganic arsenic, so it is the destruction of materials with nitric, sulfuric, or perchloric acid process preparation of material used to determine inorganic and organic arsenic or total arsenic. Apart from AAS, it is possible to analyze samples by atomic emission spectrometry with induced coupled plasma (ICP-AES) and mass by spectrometry with inductively-coupled plasma (ICP-MS) which has a lower detection limit than AAS so it can detect lower concentrations of arsenic in samples [41,42].

## 6. Conclusion

How is the awareness of the population about the effect of air pollution on human health increasing, risk assessment studies can guide regulatory authorities but also the general population in the direction of trying to reduce its pollution. Some proposals for these actions are: reducing and stopping the use of coal in thermal power plants, better control of the emission of toxic substances from industrial plants as well as a better air quality monitoring plan in responsible institutions. Except for change at the systemic level, the population can contribute to better quality air by reducing the use of coal and other solid fuels for heating households and switching to another type of firewood, as well as using public transport, instead of individual vehicles. Also, citizens can monitor the values concentration of contaminants in the atmosphere to plan activities in the open such as e.g. reduction of intense physical activities when concentrations of suspended particles in the air are high.

**Conflicts of Interest:** The authors declare no conflict of interest.

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