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**Evaluation of human exposure to Arsenic:
A Review**

Undergraduate research project

*Submitted to the Department of Chemistry in Partial Fulfillment of the
Requirement for the completion of the degree of Bachelor of Science in
Chemistry*

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First Semester, Dec.2016

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Title:

Evaluation of human exposure to Arsenic: Review

Abstract:

This review describes the various routes of human exposure to arsenic, the toxicity effects of arsenic on human and evaluation of drinking water, food and other environmental compartments to their contents of arsenic. Particular interest is focused on children's food because at the age of below 1 year the children immune system is not fully developed.

Keywords: Arsenic, Speciation, Toxicity, Food, Drinking water

Introduction:

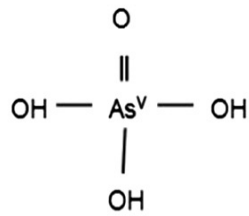
Arsenic (As) is a metalloid with a ubiquitous presence in the environment; it occurs in different forms (organic and inorganic) in rock, soil, water, air and living organisms.

(Mandal & Suzuki, 2002). Arsenic is the 20th most abundant element of the Earth's crust and over 245 arsenic bearing minerals are known (Mandal & Suzuki, 2002). The major natural source of As entering the soil is weathering of rocks containing As, while the anthropogenic sources include combustion of coal (contains 9 mg/kg or higher) (Yudovich and Ketris, 2005), industrial activities like smelting of base metal ores (metallic pyrites contain 10% arsenic) (Bowel et al. 2014), application of As-based pesticides, chromated copper arsenate (CCA) for wood preservation and mining activities (Smedley and Kinniburgh, 2002). High-purity arsenic is used in the electronics industry to manufacture semi-conductors, solar cells, and specially coated optical materials [USGS]. The main sources of human exposure to As are water and certain food matrices, such as rice, wheat, seaweed, mushrooms and some fishery products [EFSA, WHO, 2010]. It has been evidently reported that As consumption from drinking water has affected about 150 million people worldwide (mainly in Bangladesh, India, China, Hungary, Pakistan, Argentina, Chile, Mexico, Taiwan, Vietnam and many parts of USA (Smedley et al., 2002)).

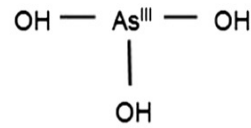
Arsenic can be present as inorganic (i-As), the most prevailing toxic compound found in water and food, and organic compounds (o-As), which originate from the metabolism of i-As in living organisms. The forms of most common species of arsenic are presented in Figure 1.

This review summarizes the methods of human exposure to arsenic through water and food and the toxicity effects of arsenic species and the impact on human health.

Inorganic Arsenic

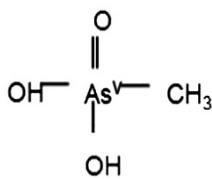


Arsenic Acid

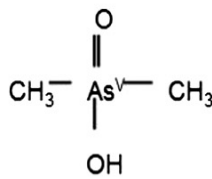


Arsenous acid

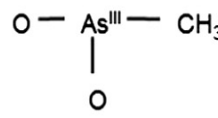
Organic Arsenic



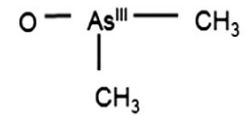
Monomethylarsonic acid
(MMA(V))



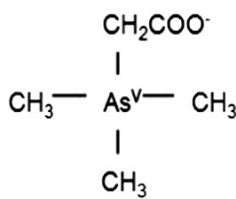
Dimethylarsinic acid
(DMA(V))



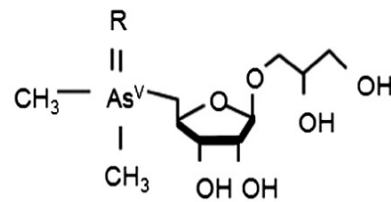
Monomethylarsonous acid
(MMA(III))



Dimethylarsinous acid
(DMA(III))

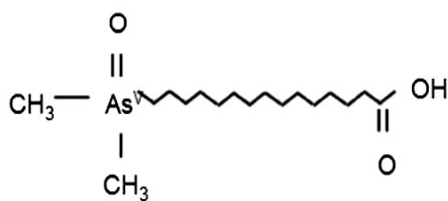


Arsenobetaine

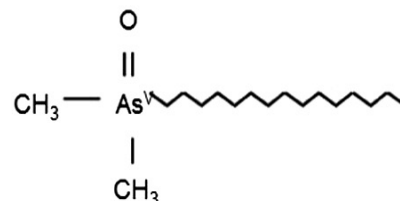


R = O Oxo-arsenosugar
R = S Thio-arsenosugar

Arsenosugars



Arsenolipids (longchain fatty acids)



Arsenolipids (hydrocarbons)

Figure 1: Most common species of arsenic compounds

2- Arsenic in the environment

Arsenic occurs in the environment as due to natural (leaching from soil matrices, volcanic activity, erosion and sedimentation events, and seasonal flooding) and anthropogenic sources (industrial, agricultural and mining activities (Mandal and Suzuki, 2002)). Arsenic exposure routes for humans are via ingestion (food, beverages, drinking water and soil), inhalation (air and dust respiration), and dermal contact (soil and pathing). (Al-Rmalli et al., 2011; Arain et al., 2009).

2-1: Arsenic in water

The occurrence, distribution, and speciation of arsenic in aquatic systems are particularly important in determining its bioaccumulation and trophic transfer through the food chain. Although inorganic arsenic species (AsV and AsIII) are the major species, methylated and complex organic species have also been found in marine and fresh waters. Arsenic species found in natural waters are shown in Table 1.

Table 1: Arsenic species found in aquatic environment

	Name	Formula	Abbreviation
1	Arsenous acid or arsenite	H_3AsO_3	As(III)
2	Arsenic acid or arsenate	H_3AsO_4	As(V)
3	Monomethylarsonous acid	$CH_3As(OH)_2$	MMA(III)
4	Monomethylarsonic acid	$CH_3AsO(OH)_2$	MMA(V)
5	Dimethylarsinous acid	$(CH_3)_2As(OH)$	DMA(III)
6	Dimethylarsinic acid	$(CH_3)_2AsO(OH)$	DMA(V)
7	Trimethylarsine	$(CH_3)_3As$	TMA
8	Trimethylarsine oxide	$(CH_3)_3AsO$	TMAO
9	Arsenocholine	$(CH_3)_3As^+CH_2CH_2OH$	AsC
10	Arsenobetaine	$(CH_3)_3As^+CH_2CO_2^-$	AsB
11	Arsenosugars	$(CH_3)_2AsOCH_2C_4H_4O-R^a$	AsS
12	Arsenic glutathione complex	$(GS)_3As(III)^b$	$(GS)_3As(III)$

^a R can be an alcohol, phosphate, sulfate, sulfite, carboxylic acid or a heterocycle.

^b GS represents the glutathione anion.

Concentrations of arsenic in surface freshwater systems (rivers and lakes) vary widely with baseline concentrations in waters of various contaminated rivers range between 0.1 and 2.1 mg / L. However high concentrations of naturally occurring arsenic have been reported in the Ron Phibun river, Thailand (average 218 and range 4.8–583 µg/L, [Williams et al 1996](#)). The mining and processing of arsenopyrite ores lead to very high level of arsenic in Mole River, Australia 110–600 (up to 13900 µg/L)([Ashley and Lottermoser](#) (1999).

Arsenic concentration with an average of 1.5 µg/L tends to be less variable in marine waters than those of freshwaters, for example the arsenic concentration in deep Pacific and Atlantic waters is between 1.0–1.8 µg/L ([Cullen and Reimer, 1989](#)), and 1.1-1.6 µg/L in coastal waters of southern Australia([Maher, 1985a](#)) .

In drinking and ground water the maximum concentration limit set by WHO is 10µg/L. However an estimation of about 100 million populations all around the world are exposed to arsenic levels more than 50µg/L (Moon et al., 2012) via drinking water especially in some Asiatic countries such as India, Taiwan, Nepal, Pakistan, Vietnam, Cambodia, China and Bangladesh due to natural leaching of arsenic from soil and rock to ground water ([Ravenscroft et al., 2013](#)). Uncontaminated drinking water contains very low level of arsenic, for example , in Italy the Tap water contain an average of 0.6µg/L with a range of 0.2-1.1µg/L while the Bottled water contain an average of 2.1µg/L with a range of 1.2-3.5µg/L([Cubadda, F. et. Al. 2016](#))

2-2 Arsenic in soil

The major natural source of As entering the soil is weathering of rocks containing As, the average concentration of arsenic in igneous and sedimentary rocks is 2 mg kg⁻¹ and in most rocks it ranges from 0.5 to 2.5 mg kg⁻¹ ([Kabata-Pendias, H. Pendias](#)), while the anthropogenic sources include various human activities such as smelting of base metal ores, mining and application of As-based pesticides, chromated copper arsenate (CCA) for wood preservation ([Smedley and Kinniburgh, 2002](#)). It is also observed that continuous irrigation with As-contaminated groundwater may lead to a build-up of arsenic in soils, which in turn may prompt its entry into the food chain in harmful

concentrations. Indeed, the level of Arsenic uptake and accumulation in crops is strongly influenced by the concentrations of As in soils and irrigated water (Smith et al., 2006) The level of arsenic in the soils varies considerably among geographic regions as shown in table 2.

Table 2: Variations of soil arsenic content in different geographic locations

Country	Range mg/kg	Mean mg/kg	Reference
Greece (contaminated)	16-1200	210	E.K.Evdokia and E.E Economou 2017
India, Bihar	3.528 – 14.690 mg/kg.	---	Manjo et. al. 2016
Chili	2.7-202	----	De Gregori et. al. 2003
Colorado	3-14	----	Colorado Department of Public Health and Environment
Central india	9-390	----	Vicky-Singh et al., 2010

The most common forms of arsenic species found in soil are pentavalent and trivalent (As(v) and As(iii)), the arsenate species are predominant in oxidizing environment while the in reducing condition the arsenite or arsenic sulfide are most common (Liying Xua et al. 2016).

2-3 Arsenic in air

Arsenic can be released from soils into the atmosphere due to microbial metabolism, in addition to volcanoes, low temperature volatilization, wind erosion, forest fires and sea spray. Arsenic species that has been identified in atmospheric samples are mainly As(III) and Av(V), and to a minor extend monomethyl arsenic acid (MMA) and dimethylarsinic acid DMA, these species are associated with the particulate materials (adsorbed)

whereas arsines (AsH_3) and methylated arsines such as mono, di and trimethyl arsines (MeAsH_2 , Me_2AsH , Me_3As) correspond to the gaseous phase.

The mean worldwide concentration of arsenic in ambient air was estimated in 1978 as 2.8 ng/m^3 [2]. However, due to increased industrial activities and smelting of metals the previous estimated value should be dealt with wariness (Chilvers, et al. 1987).

For instance, a mean value of 51 ng/m^3 was reported in for main cities in China (Duan& Tan , 2013). In 2010, Alberta province in Canada set a permission value of 10 ng/m^3 .

The first regulation concerning As in ambient air was established by the EU in 2005 with a target value of $6 \text{ ng Arsenic/ m}^3$ in PM10 (particulate material with 10 um). In 2010, Alberta province in Canada set a permission value of 10 ng/m^3 (Alberta Environment). Particulate matter (PM), also referred as aerosol, represents the solid or liquid suspended particles present in the atmosphere. Expressed in microns (e.g. PM10 and PM2.5, usually designed as “coarse” and “fine” particles). The smaller the diameter of the particles, the higher their capacity to penetrate into the respiratory system: PM10 particles can reach the larynx, PM2.5 the bronchi, and PM1 the alveoli (EPA, 2004).

The different arsenic species along with their concentrations and in which size of particulate materials found in various countries are presented in table 3.

Table 3: Concentrations of arsenic specie in particulate materials of air in different regions

Country	Arsenic species	Concentration ng/m ³	Reference
Japan	MMA	0-485 TSP	Mukai and Ambe(1987)
	DMA	3-53 TSP	
	TMA	6-604 TSP	
Greece	As(V)	3.2 TSP	Tsopelas, et al. 2008
	As(V)	1.7 PM2.5	
	As(V)	1 PM 10	
California, USA	As(iii)	0.14-1.51 TSP	Solomon, et . al. 1993
	As(V)	0.17- 6.54 TSP	
Beijing, China	As(iii)	0.73-20 TSP	Yang, et al. 2012
	As(V)	14-250 TSP	
Huelva, Spain	As(iii)	0.01-2.7 PM2.5	Sanchez de la Campa et al 2008
	As(V)	0.01-56.2 PM2.5	

TSP: total suspended particulate, PM 10: particulate materials with 10 µm, PM2.5 with 2.5 µm

3-Toxicity of arsenic species

The toxic properties of arsenic were known hundreds of years ago, where the **realgar** (arsenic sulfide with crystal of -red-orange color) kills horses and cattle when put into water. The Chinese are credited with using arsenic sulfides as an insecticide as early as 900 AD. Exposure to inorganic arsenic through consumption of water and food and occupational exposure to air leads to serious effects on human health. Low doses and

long term exposures of arsenic leads to a range of medical complications termed as “Arsenicosis” (McCarty et al., 2011).

Toxicity of arsenic to human depends on many chemical and biological factors, such as chemical forms and oxidation states (speciation of arsenic), level of exposure (amount or concentration), exposure pathway, duration of exposure, nutritional status, the rate of absorption and elimination, the particle size (in case of inhalation), bioavailability and presence of co-carcinogenic factors like exposure to sunlight or cigarette smoking.

The inorganic arsenic compounds [As(III) and As(V)], including arsenic trioxide, arsenite, and arsenate are classified as carcinogenic to humans by the International Agency for Research in Cancer (Group I), with extensive evidence of lung, bladder and skin cancer, and positive association with kidney, liver and prostate cancer (IARC, 2016). The benchmark dose lower bound BMDL for inorganic arsenic is set to be 3 µg/kg bw/day and the estimated half life of inorganic arsenic in plasma is 3-4 hours (ASTDR, 2007). The three most commonly employed biomarkers used to identify or quantify arsenic exposure are total arsenic in hair or nails, blood arsenic, and total or speciated metabolites of arsenic in urine

The inorganic As species arsenite (As(III)) and arsenate (As(V)) are predominantly detected in water, over 75% of inorganic arsenic is absorbed through the human gastrointestinal tract, and excretion occurs mainly via urine as methylated arsenic (Spayd et al., 2012). Low to moderate levels of arsenic exposure (10–300 µg/L) through drinking water has adverse effects such as skin lesions, circulatory disorders, neurological complications, diabetes, respiratory complications, hepatic and renal dysfunction including mortality (death) due to chronic diseases (Chen et al., 2009). However, the acute toxicity of high dose of inorganic arsenic leads to death.

After ingestion of inorganic arsenic the metabolism is characterized by reduction of As(V) to As(III) followed by oxidative biological methylation of As(III) to form methylated products, where primarily MMA(V) and DMA(V) are readily excreted in urine.

It is well known that inorganic species of arsenic are more toxic than the organic forms of arsenic and the As(III) is more toxic than As(V). However, recent findings show the following order of acute toxicity:

MMA(III) > As(III) > As(V) > DMA(V) > MMA(V),

Knowing that MMA(III) has not been detected in food or water (EFSA, 2009).

4-Arsenic in food

Air, soil, food, and water exist as transfer pathways of arsenic to the human body, the continuous use of contaminated water with arsenic in irrigation usually lead to increase the arsenic concentration in soil and as a consequence the bio transfer of arsenic to plant and food.

Food is the second important source of human exposure to arsenic after drinking water, The As(v) species (such as phenylarsonic acids and 3-nitro-4-hydroxy- phenylarsonic acid) have been used as feed additives for disease control and for improvement of weight gain in swine and poultry. These compounds are known to be rapidly excreted within 5 days

The form or species of arsenic present in food depend on the type of food, for this reason we will disuses the arsenic content in important categories of human food.

4-1: arsenic in terrestrial plants

Some plants have potential for phytoremediation, which is the property of absorbing elements present in soil. This property is an advantage if the plant uses it to absorb essential elements. However, the presence of toxic elements such as arsenic may lead to dangerous health issue if the plant were ingested by human.

Rice seems to contain higher levels of arsenic compounds than many other terrestrial plants or crops (Meharg et al., 2009; Williams et al., 2007). It accumulates significantly higher levels of inorganic arsenic from soil and water than other crops due to anaerobic paddy soil culture, which renders inorganic arsenic highly available for plant uptake, leading to 10-fold higher concentrations in grain compared to aerobically grown grains such as wheat or barley (Meharg & Zhao, 2012; William et al., 2007; Xu,).

The concentration of total arsenic in rice and other selected terrestrial plants are presented in table 4.

Table 4: Total arsenic content of some selected plant food

Plant	Total arsenic $\mu\text{g}/\text{kg}$	Reference
Maize	152	Diaz et al. 2004
Beans	22	Diaz et al. 2004
Apple	3-81	Heather et al. 2014
Spinach	121	Diaz et al. 2004
Rice	3-1800	Heather et al. 2014
Rice	192-899	Norton et al. (2012)

It has been shown that most of arsenic in rice present in the inorganic form ([Heather et al. 2014](#)); the most toxic species of arsenic.

4-1-1: Effect of cooking on arsenic content of rice

The European Food Safety Authority (EFSA) stated that an intake ranging from 0.3 to $8\mu\text{g kg}^{-1}$ body weight (b.w.) per day should be used as a reference for characterizing As risk (European Food Safety Authority, 2014a,b, Rice as a traditional food worldwide it's content of arsenic should be evaluated after cooking, this is important in calculating the exposure to arsenic through by this way and to determine the health risk associated with consumption of cooked rice. A recent study conducted by Jitaru et. al ([2016](#)) showed that the cooking procedures have the potential to reduce the level of As in rice, particularly by rinsing and discarding the boiling water, However, in real world the rice is boiled in water until complete absorption.

4-2: arsenic in seafood

Phytoplankton is the most common primary producer in marine food chains and the arsenic in phytoplankton will transfer to other higher species in the food chain, and may

biomagnified to higher concentrations. Arsenic concentration and speciation vary greatly in phytoplankton. In algae the arsenic content also vary upon the species of algae, brown algae contain much higher levels of total arsenic (up to 230 mg g⁻¹ dwt) than green (up to 23.3 mg g⁻¹ dwt) and red (up to 39 mg g⁻¹ dwt)(Molin et al 2015). Although fish and seafood are the food groups with the high arsenic content as shown in [table 5](#) (Heather et al. 2014), these food groups are generally low in inorganic arsenic (usually less than 50%)(EFSA.2009, Uneyama et. al. , 2007) . The most or predominant species of arsenic found in seafood is the non toxic compound arsenobetaine (figure 1) which is known as fish arsenic. Perhaps a few exceptions exist, e.g. some marine algae contains vary high percentage of inorganic arsenic (EFSA.2009)

Table 5: Total and inorganic arsenic content of marine food

Type/ species	ti As	tAs µg/kg
Fish	0.001-0.600 (0.045)	0.0022 -75 (5)
Seaweed/algae	0.014-120.(11)	0.031-150 (39)
Seafood(various)	0.29-1700(0.13)	0.0071-100 (10)

ti As: Total inorganic arsenic, tAs: total arsenic

4-3: arsenic in rice-based infant formula

Infant rice cereals, often the first solid food an infant receives at the ages 4-6 months, because of the good ability of infant stomach to digest rice compared to other solid food. Due to the high dependence of infants on rice foods during their first year, and because of the weak immune system of infants, several studies (Burlo, et al 2012, Ljung et al 2011, Carbonell et al. 2012) have quantified both total As and inorganic As contents in baby rice. The varied concentrations of arsenic species in rice-based infant formulas are presented in [table 6](#). A recent study (Courtney et Al. 2016) estimated the infant exposure to arsenic based on data adapted from US Food and Drug Administration for the arsenic

content of rice formula as(median :total arsenic: 0.20 µg/g; inorganic arsenic: 0.12 µg/g) and the maximum (total arsenic: 0.37 µg/g; inorganic arsenic 0.25 µg/g) . The study revealed that that rice cereal can markedly increase arsenic exposure among US infants relative to breast milk and formula

Table 6: Total and inorganic arsenic in infant rice and infant food

Country	Food	tAs µg/kg	iAs µg/kg	Reference
Spain	Infant rice	126 ± 26	69 ± 8	Carbonell, et al. 2012
	Infant cereals	33 ± 6	26 ± 5	
UK	Infant rice	---	60-160	Meharg et al.2008
China	Infant rice	148 ± 16	114 ± 15	Carbonell, et al. 2012
USA		260 ± 66	125 ± 14	Carbonell, et al. 2012
Sweden	Infant rice	30	---	Ljung, et al. 2011

The above table show that both total As and inorganic As contents are significantly high in baby rice as a main food for infants.

5-Analysis of arsenic species

First of all, representative samples from the environment (food, soil, air or water) l must be collected very carefully, the tools of collection must be clean, (free of metals especially arsenic) and a blank procedure must be followed in the field and in lab to be sure that the arsenic content of representative samples is not of external source other than the sample itself. To have a good estimation of arsenic content of various environmental samples, multi samples must be collected (at least 3 sample replicates) to represent only single reading. Certified reference materials (CRM) also must be analyzed along with the actual samples to validate the method of analysis.

5-1: Total arsenic analysis:

For the determination of total arsenic content, a sample size of less than 0.5 g is digested with 16% HNO₃ and 30% H₂O₂ using microwave, these condition leads to digest the samples with conversion of all As(iii) and organic arsenic to As(v), and the prepared sample can be analyzed by ICP-MS or hydride generation –AAS.

5-2: Speciation of arsenic:

If the above procedure is performed with lower strength of the oxidizing condition (very mild condition) less than 0.2% HNO₃ and 1% H₂O₂, in this case the inorganic As(iii) will be oxidized to the As(v) however the organic form will not be affected and the sample can be analyzed by ion chromatography–ICPMS. In this case MA and DMA and other organic arsenic species can be quantified.

A selective solid phase extraction sorbent were used to adsorb As(v) but not As(iii) for example the adsorbent 3-(2- amino ethyl amino) propyl trimethoxy silane (AAPTS) modified ordered meso porous silica(Li-Chen, et al. 2014)

For water samples the various arsenic species can be analyzed directly using HPLC (Chen et al., 2013)

6-Arsenic removal

It is important to remove arsenic form well(underground) and drinking water as an important source of arsenic exposure, several arsenic treatment technologies are now available, and most of them can effectively reduce the arsenic concentration in drinking water to a level below the US EPA regulated maximum contaminant level (MCL) of 10 µg/L (parts per billion, or ppb). Most of these methods depend

- The adsorption of arsenic species on various types of a solid phase
- Anion exchange resins require regular regeneration on-site because of low arsenic selectivity
- Reverse osmosis (generate a reject waste stream)
- Oxidation/filtration processes.

Conclusion and recommendations

The major routes of human exposure to arsenic are drinking water and the consumption of food. The continuous exposure to low doses of arsenic species leads to what called Arsenicosis (disease). However, the exposure to high doses of arsenic may lead to death. The toxic effect of arsenic depends largely on the form of arsenic, the inorganic arsenic compounds are more toxic than the organics, and As(iii) species are more toxic than As(v). In food commodities other than fish and seafood the inorganic As content vary typically from 50% to 100% of the total As content.

For the protection of human health from the potential carcinogenic effects due to exposure of arsenic through drinking water or contaminated food, the drinking and ground water should not exceed the WHO level of 10 µg/L.

Special attention must be paid for children's food especially the rice cereals for infant

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