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Review Article

A Review of the Effect of Drinking Water Contaminated with Arsenic on Liver Cancer

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Abstract
Arsenic (As) is a highly toxic and carcinogenic element. Drinking water and some foods (for example, rice, cereals, or fruit juices) are major sources of arsenic. Chronic arsenic poisoning, or arsenicosis, causes internal disorders, such as liver damage, as well as cancers. The purpose of this review study was to examine the epidemiological literature on the side effects of arsenic on liver cancer. Initially, 112 articles from January 1, 2000, to March 1, 2023, were found in the mentioned databases. Then, by removing duplicate items, 85 articles entered the stage of examining the title of the articles and removing irrelevant items based on the title of the article. After reviewing the full text of 38 articles, 14 articles were included in the study and used to investigate the effect of arsenic in drinking water on liver cancer. Many environmental pollutants, including arsenic, can cause many diseases in the human body. This metal can generally enter all body organs through the blood circulation system and affect them. The results of previous studies have shown that long-term exposure to arsenic causes disruption in normal liver function (hepatomegaly, sclerosis, fibrosis, and cirrhosis). Various mechanisms have been introduced for arsenic carcinogenesis. Among the important mechanisms that cause liver carcinogenesis by arsenic, the following can be mentioned: disturbance of the balance of liver enzymes, damage to the DNA wall, its destruction, inability to repair DNA, inappropriate function of estrogens, and liver apoptosis.
Keywords: Arsenic, Abnormal liver, Drinking water, Source of arsenic

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1. Introduction

Arsenic is one of the most toxic heavy metals, which is characterized by the symbol As in the periodic table and its atomic number is 33. This metal has many uses in industry (alloy making) and agriculture (as a pesticide). Arsenic is structurally very similar to phosphorus. Because of this similarity, it can be replaced with it in biochemical reactions, and hence it is toxic. When heated, it turns into arsenic oxide (1). Arsenic oxide is white and very dense, and it is extremely toxic. AsO3 was used in rodenticides (mouse death), but due to its high toxicity to humans and other mammals and environmental hazards, its use has been completely prohibited. Arsenic oxide smells like garlic. Arsenic and its compounds can also be converted to gas by heating (2). Arsenic is abundant in the earth's crust (1, 3). Drinking water and some foods (for example, rice, cereals, or fruit juices) are major sources of arsenic (4). Its presence in drinking water or food and its effects on people's health have become a major global problem. In Bangladesh, the consumption of drinking water and food contaminated with arsenic has put more than 80 million people in this country at risk (5). The current WHO standard for arsenic in drinking water is 10 μg/L (6). Previously, black foot disease (BFD) was believed to be caused by drinking arsenic contaminated water in Taiwan (7). BFD is a disease that causes gangrene of the lower extremities. In this country, water from artesian wells, which contained high levels of arsenic, was used for drinking and cooking, and later it was believed that BFD was caused by consuming water with high arsenic concentration. In other words, epidemiological studies have proven the association between drinking water contaminated with arsenic and its prevalence (8). Chronic arsenic poisoning, or arsenicosis, causes internal disorders, such as liver damage, as well as cancers. Inorganic arsenic (iAs) is widely found in groundwater. In most South American countries and some East Asian countries, high levels of arsenic have been observed in groundwater (9). The carcinogenic potential of arsenic is the most important concern. Excessive exposure to arsenic can cause many disorders in the body, which can appear as cancer in various organs of the body (10). Among the disorders caused by arsenic, liver cancer has not yet been proven and more epidemiological studies are needed. However, the effect of exposure to arsenic in causing skin, lung, and bladder cancers has been widely confirmed (11-16). IARC has classified arsenic as a group 1 carcinogen, which has the greatest role in causing liver cancer (1). Epidemiological studies show that exposure of mouse embryos to inorganic arsenic can cause malignant liver tumors in adulthood (17). Exposure to low levels of arsenic can also cause disorders. These disorders mostly affect the liver tissue and cause fibrosis, cirrhosis, sclerosis, and hepatomegaly. Laboratory and epidemiological studies showed that long-term exposure to inorganic arsenic plays a major role in the development of type 2 diabetes (18). The purpose of the present research is to investigate the level of arsenic in drinking water and the effects that contamination by arsenic has on the liver.

2. Materials and Methods

2.1. Search Strategy

The search was conducted to obtain all articles on the effect of arsenic in drinking water on liver cancer between 2000 and 2023. This review was conducted using databases including PubMed, Scopus, Web of Science, and Embase.

As can be seen in Fig. 1, initially 85 articles from January 1, 2000, to March 1, 2023, were found in the mentioned databases. Then, by removing duplicate items, 38 articles entered the stage of examining the title of the articles and removing irrelevant items based on the title of the article. After reviewing the full text of 21 articles, 14 articles were included in the study and used to investigate the effect of arsenic in drinking water on liver cancer (Fig. 1).

The keywords and MeSH terms used in the study were as follows: (As [Title/Abstract]) OR ("source"[Title/Abstract])) OR ("mechanism"[Title/Abstract])) AND ("liver cancer"[Title/Abstract])) AND (arsenic [Title/Abstract])

2.2. Study Selection

The primary evaluation of the retrieved articles was done based on (*a*) Title, (*b*) Abstract, and (*c*) Full text of the articles.

Articles that were not about the effect of arsenic in drinking water on liver cancer were removed. Related articles were downloaded after the abstract screening.

2.3. Inclusion Criteria

The criteria for screening the articles were as follows:

1. A descriptive study on drinking water contamination with arsenic

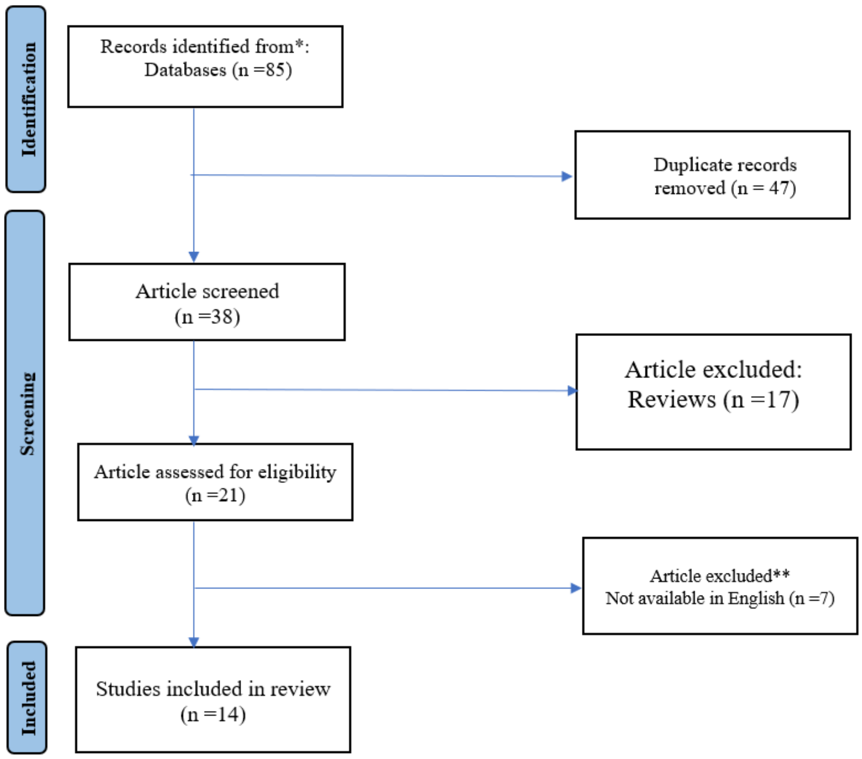

Fig. 1. Representation of the Search Strategy Based on PRISMA Flow Diagram

2. The availability of the full text
3. Original studies
4. The mechanism of the effect of arsenic on liver cancer.

2.4. Exclusion Criteria

1. Non-English articles
2. Books
3. Duplicate articles
4. Conference papers
5. Review articles
6. Systematic review articles

3. Results and Discussion

3.1. Source of Arsenic

Nature and various human activities have a great role in changing the global cycle of metalloids and heavy metals. Samples of toxic and heavy metals include arsenic, mercury, cadmium, chromium, and lead. These five heavy metals pollute water, air, food, and soil (19). Arsenic is a highly toxic substance that has a very complex metabolic pathway. It is an environmental contaminant that is toxic to both humans and plant and animal ecosystems (20). Arsenic is produced from natural sources and anthropogenic activities (industrial activities, cooking, and smoking) (21). The study done by Masaferi et al found that the level of arsenic in potable water in Ardabil varied between 6 and 61 µg/L, with a mean level of 39 ± 20 µg/L. The quantity of arsenic, a maximum of six times higher than the acceptable standards (10 µg/L), indicates the presence of arsenic bearing materials in the geological structure of the region (22). To determine the concentration of arsenic in the groundwater of Hamadan, Sobhanardakani et al conducted a study. The findings of the study indicated that the mean concentrations of arsenic in the samples of groundwater taken from different areas were 0.052, 0.007, 0.007, 0.006, and 0.004 mg/L. This study also demonstrated how the soil structure of the region caused arsenic to move into the groundwater (23) (Fig. 2).

Rice is a food that is widely consumed in Southeast Asia (especially in India and Bangladesh). In areas where rice cultivation is the main agricultural activity, we are faced with high concentrations of arsenic. Considering that rice is an important component of the diet in most parts of the world, the presence of arsenic in it is a big challenge. The lack of water in some countries has caused farmers not to care about the type of water they use to irrigate rice fields; for this reason, by irrigating paddy fields with polluted water, they increase the amount of arsenic in rice. Cereals like rice contain a lot of arsenic. The amount of arsenic accumulated in this product depends on the type of rice, agricultural soil, irrigation water, and chemical fertilizer. The WHO has declared the permissible amount of arsenic in rice to be 0.4 mg/kg (24).

Wheat is the second most important source of food in the world. The concentration of arsenic in wheat has been reported to be relatively lower than in rice because wheat is grown under aerobic conditions, and silica is less likely to accumulate in wheat grains (25). Legumes (legumes) are rich in protein. Legumes are consumed in Southeast Asia, especially by people on a vegetarian diet. The amount of arsenic in legumes is relatively low (26). Vegetables are another source of human food around the world. Numerous reports have evaluated the concentration of arsenic in a variety of vegetables and fungi. Potato (*Solanum tuberosum*) is one of the largest crops in the world (27-29). Studies in Bangladesh and several other countries have found that potatoes contain mineral arsenic and very little organic arsenic. Bhattacharya et al reported that the concentration of arsenic in potatoes is higher than in rice (30). Arsenic pollution in groundwater is caused by natural and human activities. Arsenic is present as a major element in many minerals (31, 32). The high concentration of arsenic in the groundwater of deltaic and alluvial plains is due to the excretion and dissolution of natural minerals and alluvial sediments (25). Arsenic is abundant in arsenopyrite (Feas). Arsenopyrite is found in stone-forming minerals such as sulfides, oxides, phosphates, carbonates, and silicate (9). In places where high concentrations of metal oxides (such as iron and hydrogen) or pyrite are present, arsenic concentration in sediments is also high. The deeper the sediment, the higher the concentration of arsenic (13, 33). Mostly, humans contaminate groundwater with arsenic through mining, burning, and toxin use. Coal burning can cause environmental arsenic pollution. Arsenic can be released into the environment by burning coal and eventually transferred to groundwater. The degree of groundwater contamination with arsenic by anthropogenic resources is much lower as compared to natural sources. However, they cannot be ignored (31, 34).

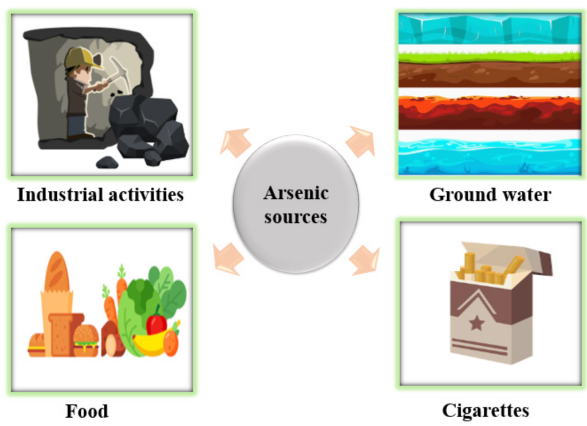

Fig. 2. Source of Arsenic

3.2. Effects of Arsenic on Human Health

This pseudo-metal exists everywhere on the earth's crust and humans are exposed to it mainly through the consumption of drinking water. The main sources of this toxic element entering drinking water are the output of some industries such as petrochemical, ceramic, and glass industries. Long-term consumption of water contaminated with arsenic causes skin complications and various types of cancers. WHO has announced that the maximum permissible arsenic concentration in drinking water is 10-50 ppm (35). Arsenic enters the body of living organisms in different ways. This element enters the human body through the digestive tract (contaminated food and drinking water), the respiratory tract (polluted air in industrial areas), and the skin (polluted soil in industrial areas) and accumulates in vital organs. Finally, the accumulation of arsenic in these organs disrupts their normal function (36). The symptoms of arsenic exposure are similar to those of most diseases. As a result, it is difficult to diagnose.

Air pollution attributed to arsenic is very high in industrial areas, as a result, inhalation is the main way of entering this element into the body of humans and living organisms. This toxic and dangerous pseudo-metal not only causes disease in living organisms but can also be a threat to the ecosystem and natural resources (37). As mentioned above, arsenic can enter the body in different ways and affect vital organs. Therefore, arsenic concentrations in urine, blood, and milk have been used as biomarkers of arsenic exposure (38).

3.2.1. Arsenic Toxicity (Carcinogenicity)

Arsenic is a highly toxic and carcinogenic substance that can cause cancer of the respiratory and gastrointestinal tracts. Epidemiological studies have shown through sufficient evidence that arsenic is a carcinogenic substance (39). As a result, these studies have confirmed the association between exposure to arsenic and carcinogenesis. The mineral compounds encompassing arsenic can be classified as carcinogenic (group 1) and potentially carcinogenic (group 2B). This classification is the result of animal, epidemiological, and international studies by IARC. Epidemiological studies have shown that consumption of drinking water containing high levels of arsenic (150 μg/L) is associated with cancer (40).

3.2.2. Non-carcinogenic Effects

Arsenic can accumulate in the body because it has the property of accumulating. Arsenic accumulation in childhood causes neurobehavioral disorders during adolescence and neurobehavioral changes in adulthood (41). Norite, which affects the sensory function of peripheral nerves, can be the most well-known effect of arsenic on the human body. Researchers in Mexico have found an association between arsenic exposure and verbal intelligence and long-term memory (42). While organic arsenic, mostly found in seafood like fish, oysters, prawns, mussels, and so on, does not cause significant health problems in humans, exposure to inorganic arsenic through the ingestion of contaminated food and water and inhalation of contaminated air does. Arsenicosis is a term used to describe a variety of health issues that result from prolonged exposure to low levels of arsenic (43). Skin lesions, circulatory problems, neurological problems, diabetes, respiratory problems, hepatic and renal dysfunction, and mortality from chronic diseases are among the negative consequences of low to moderate levels of arsenic exposure (10-300 μg/L) from drinking water (44). It is believed that approximately 100 million people worldwide are exposed to arsenic levels exceeding 50 μg/L through both industrial processes and drinking water (45).

3.3. Liver Cancer

Liver cancer is a chronic liver disease. Liver cancer is considered one of the most malignant and common cancers among men and women in the world. In general, the rate of this disease is higher in men than in women (almost 3 times). Environmental conditions are very effective in the spread of this disease; therefore, in high-risk countries, this disease occurs at a young age (20 years old), but in low-risk countries, it can occur at an older age (50 years old) (46). Epidemiological studies have shown that chronic arsenic exposure causes liver disorders and liver cancer.

3.3.1. Abnormal Liver Function

Gastrointestinal problems (such as indigestion and anorexia) and the increase in serum enzymes are symptoms of abnormal liver function, which are often due to exposure to arsenic in drinking water (47) or inhalation of arsenic by burning coal (48).

3.3.2. Hepatomegaly

In epidemiological studies conducted in West Bengal, the researchers found that there was a strong association between high arsenic levels in drinking water and hepatomegaly (more than 75%). In another study conducted in China, researchers found that the incidence of hepatomegaly due to exposure to smoke from burning coal is higher compared to drinking water contaminated with arsenic (47).

3.3.3. Hepatic Sclerosis (Non-cirrhotic Portal Hypertension)

Hepatic sclerosis is a rare disease that occurs after chronic exposure to arsenic. Researchers have found that in a hospital in India, patients with arsenicosis drank highly arsenic-contaminated water. Chronic poisoning with oral arsenic, through drinking water, traditional medicines, and so on, has been reported to cause liver sclerosis in Indian populations. Hepatic endothelial cell damage and parenchymal cell damage are the results of chronic arsenic exposure in animals (49).

3.3.4. Liver Fibrosis and Cirrhosis

Cirrhosis of the liver can be caused by high levels of hepatic arsenic. Patients who consume “home-brewed” prepared with highly arsenic-contaminated water are more likely to develop liver cirrhosis. Foods that are cooked by burning coal contain high amounts of arsenic, which can increase the risk of liver fibrosis. Cirrhosis of the liver was the leading cause of death from arsenic in China in 2002 (47).

3.3.5. Biodegradation of Liver and Arsenic

After ingestion, arsenic is absorbed from the gastrointestinal tract and reaches the liver. Arsenate is converted to Arsenite in the liver. The liver is the main site of arsenic detoxification due to its glutathione content. The main site of arsenic methylation is also the liver. However, in patients with liver disease, the methylation capacity of arsenic is compromised (50).

3.4 The Effect of Arsenic on Liver Cancer

Various potential mechanisms for arsenic carcinogenesis have been proposed, but the underlying mechanism is not completely understood (51). Scientists have introduced various mechanisms for arsenic carcinogenesis. Among the important mechanisms that cause liver carcinogenesis by arsenic, the following can be mentioned: damage to the DNA wall, its destruction, inability to restore damaged DNA, abnormal estrogen signaling, and hepatic apoptosis (Fig. 3) (3).

3.4.1. Oxidative DNA Damage

Arsenic causes hepatotoxicity and possibly carcinogenicity, producing oxidative stress (1). Acute high-dose exposure to arsenic can increase the number of genes associated with oxidative stress, such as co-oxygenase-1and metallothionein. However, in chronic exposure to low doses of arsenic, the expression of stress-related genes does not increase. Various adaptive mechanisms are created in the body that can reduce the acute toxicity of arsenic. These mechanisms are developed to protect the liver and other organs against arsenic-induced oxidative stress (51). Glutathione plays a very important protective role in the liver because it can transfer arsenic out of the liver and dispose of it (47).

3.4.2. Impaired DNA Repair

DNA repair mechanism can repair arsenic-induced oxidative DNA damage. However, it has been shown that arsenic may interfere with nucleotide cleavage and basal cleavage by interacting with zinc finger proteins. Zinc finger proteins play a key role in DNA binding and protein-protein interactions. Intracellular targets appear to be sensitive to arsenic. Arsenic is known to inhibit many enzymes, and exposure to it disrupts DNA repair (52).

3.4.3. Apoptotic Tolerance and Hyper Proliferation

If the damage is severe enough, arsenic-poisoned cells can be killed by apoptosis. However, during chronic exposure to arsenic, adaptation to the effects of arsenic, including apoptosis, occurs, and this often leads to general resistance to apoptosis. Arsenic can cause cell apoptotic resistance. Following the tolerance of apoptosis, which plays a key role in the occurrence of all types of cancers, cells multiply in large numbers; the same issue occurs in most cancers (including liver cancer). Acquired resistance to apoptosis occurs in cancers, including liver cancer. Resistance to apoptosis can be associated with increased cell proliferation (53).

3.4.4. Aberrant Estrogen Signaling

Researchers have found that exposure to arsenic can cause cancer in organs such as the liver, ovaries, adrenals, uterus, and fallopian tubes. The estrogen signaling system is a potential factor in inducing or promoting liver cancer after exposure to carcinogens such as arsenic. ER-α overexpression in liver tumors, uterine tumors, and bladder carcinoma can be observed in pregnant women after arsenic exposure (54).

3.5. Arsenic and Liver Cancer Worldwide

Numerous epidemiological studies have been performed around the world showing that arsenic is known to be a carcinogen that can cause cancer of the liver. Studies in various countries, including Mongolia, China, Bangladesh, and Japan, have shown that arsenic in drinking water is associated with liver cancer. A study in China also showed that environmental exposure to arsenic through the use of coal containing high arsenic content causes excessive mortality (due to liver cancer) (55). However, another Chinese article claimed that there was no association between liver cancer mortality and environmental arsenic exposure (2).

4. Conclusion

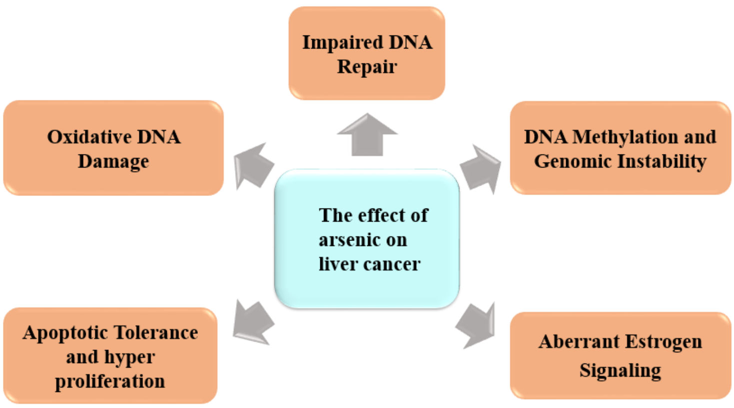

Fig. 3. The Effect of Arsenic on Liver Cancer

Arsenic is available from a variety of sources, including natural resources, groundwater, industrial activities, food, and tobacco. One of the elements that can cause problems for the environment and humans is arsenic. Humans are exposed to arsenic in a variety of ways. Researchers have shown that arsenic is transmitted to humans through drinking water, food, smoking, and cosmetics. Arsenic is highly toxic and carcinogenic to humans and dangerous to the environment. They are widely used in industry, medicine, and agriculture. The molecular mechanism of arsenic is not known; however, the process of arsenic transport and biological transformation is known. Human exposure to environmental toxins may affect their health and cause disease. Generally, after arsenic is absorbed by the digestive system, it enters the bloodstream and circulates throughout the body. Then, the liver cells absorb arsenate. Liver cancer is a chronic liver disease. Laboratory and epidemiological studies have shown that long-term exposure to arsenic causes disturbances in the normal function of the liver (hepatomegaly, sclerosis, fibrosis, and cirrhosis). There are various potential mechanisms for arsenic carcinogenesis including DNA dysfunction, acquired tolerance to apoptosis and excessive cell proliferation, DNA methylation changes, genomic instability, and abnormal estrogen signaling. Therefore, the association between environmental arsenic exposure and liver cancer has been demonstrated by several studies worldwide.

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Supervision: Majid Farhadi.
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Writing–original draft: Rohangiz Maleki, Ali Farhadi.
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Competing Interests
The authors declare that they have no competing interests.

Consent to Participate
Not applicable.

Data Availability Statement
Not applicable.

Ethical Approval
According to the national guidelines, studies such as this do not require individual consent.

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References
1. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, World Health Organization, International Agency for Research on Cancer. Some Drinking-Water Disinfectants and Contaminants, Including Arsenic. IARC; 2004.
2. Chen JG, Chen YG, Zhou YS, Lin GF, Li XJ, Jia CG, et al. A follow-up study of mortality among the arseniasis patients exposed to indoor combustion of high arsenic coal in Southwest Guizhou Autonomous Prefecture, China. Int Arch Occup Environ Health. 2007;81(1):9-17. doi: 10.1007/s00420-007-0187-y .
3. Sadaf N, Kumar N, Ali M, Ali V, Bimal S, Haque R. Arsenic trioxide induces apoptosis and inhibits the growth of human liver cancer cells. Life Sci. 2018;205:9-17. doi: 10.1016/j.lfs.2018.05.006.
4. Jackson BP, Taylor VF, Karagas MR, Punshon T, Cottingham KL. Arsenic, organic foods, and brown rice syrup. Environ Health Perspect. 2012;120(5):623-6. doi: 10.1289/ehp.1104619.
5. Hossain MF. Arsenic contamination in Bangladesh—an overview. Agric Ecosyst Environ. 2006;113(1):1-16. doi: 10.1016/j.agee.2005.08.034.
6. Fagbote EO, Olanipekun EO, Uyi HS. Water quality index of the ground water of bitumen deposit impacted farm settlements using entropy weighted method. Int J Environ Sci Technol. 2014;11(1):127-38. doi: 10.1007/s13762-012-0149-0.
7. United States Environmental Protection Agency. Arsenic and Clarifications to Compliance and New Source Monitoring Rule: A Quick Reference Guide. Washington, WA: EPA; 2001.
8. Tseng WP. Effects and dose--response relationships of skin cancer and blackfoot disease with arsenic. Environ Health Perspect. 1977;19:109-19. doi: 10.1289/ehp.7719109.
9. Smedley PL, Kinniburgh DG. A review of the source, behaviour and distribution of arsenic in natural waters. Appl Geochem. 2002;17(5):517-68. doi: 10.1016/s0883-2927(02)00018-5.
10. Saki H, Goudarzi G, Jalali S, Barzegar G, Farhadi M, Parseh I, et al. Study of relationship between nitrogen dioxide and chronic obstructive pulmonary disease in Bushehr, Iran. Clin Epidemiol Glob Health. 2020;8(2):446-9. doi: 10.1016/j.cegh.2019.10.006.
11. Liu J, Waalkes MP. Liver is a target of arsenic carcinogenesis. Toxicol Sci. 2008;105(1):24-32. doi: 10.1093/toxsci/kfn120.
12. Wang X, Jiang F, Mu J, Ye X, Si L, Ning S, et al. Arsenic trioxide attenuates the invasion potential of human liver cancer cells through the demethylation-activated microRNA-491. Toxicol Lett. 2014;227(2):75-83. doi: 10.1016/j.toxlet.2014.03.016.
13. Neisi A, Mohammadi MJ, Takdastan A, Babaei AA, Yari AR, Farhadi M. Assessment of tetracycline antibiotic removal from hospital wastewater by extended aeration activated sludge. Desalin Water Treat. 2017;80:380-6 .
14. Neisi A, Farhadi M, Takdastan A, Babaei AA, Yari AR, Mohammadi MJ, et al. Removal of oxytetracycline antibiotics from hospital wastewater. Fresenius Environ Bull. 2017;26(3):2422-9.
15. Farhadi M, Sicard P, De Marco A, Khoshgoftar M, Taiwo AM, Mohammadi MJ, et al. Hot spots of NOx emission from the cement factory main stacks. Fresenius Environ Bull. 2017;26(12A):8345-552.
16. Richards LA, Sültenfuß J, Ballentine CJ, Magnone D, van Dongen BE, Sovann C, et al. Tritium tracers of rapid surface water ingression into arsenic-bearing aquifers in the lower Mekong basin, Cambodia. Procedia Earth and Planetary Science. 2017;17:845-8. doi: 10.1016/j.proeps.2017.01.055.
17. Shen L, Zhang G, Lou Z, Xu G, Zhang G. Cryptotanshinone enhances the effect of arsenic trioxide in treating liver cancer cell by inducing apoptosis through downregulating phosphorylated- STAT3 in vitro and in vivo. BMC Complement Altern Med. 2017;17(1):106. doi: 10.1186/s12906-016-1548-

4.
18. Afra A, Mollaei Pardeh M, Saki H, Farhadi M, Geravandi S, Mehrabi P, et al. Anesthetic toxic isoflurane and health risk assessment in the operation room in Abadan, Iran during 2018. Clin Epidemiol Glob Health. 2020;8(1):251-6. doi: 10.1016/j.cegh.2019.08.008.
19. Balali-Mood M, Naseri K, Tahergorabi Z, Khazdair MR, Sadeghi M. Toxic mechanisms of five heavy metals: mercury, lead, chromium, cadmium, and arsenic. Front Pharmacol. 2021;12:643972. doi: 10.3389/fphar.2021.643972.
20. Ng JC. Environmental contamination of arsenic and its toxicological impact on humans. Environ Chem. 2005;2(3):146-60. doi: 10.1071/en05062.
21. Khosravi-Darani K, Rehman Y, Katsoyiannis IA, Kokkinos E, Zouboulis AI. Arsenic exposure via contaminated water and food sources. Water. 2022;14(12):1884. doi: 10.3390/w14121884.
22. Mosaferi M, Shakerkhatibi M, Dastgiri S, Asghari Jafarabadi M, Khataee A, Sheykholeslami S. Natural arsenic pollution and hydrochemistry of drinking water of an urban part of Iran. Avicenna J Environ Health Eng. 2014;1(1):7-16. doi: 10.5812/ajehe.164.
23. Sobhanardakani S. Health risk assessment of inorganic arsenic through groundwater drinking pathway in some agricultural districts of Hamedan, west of Iran. Avicenna J Environ Health Eng. 2018;5(2):73-7. doi: 10.15171/ajehe.2018.10.
24. Yuan YC, Bazarova N, Fulk J, Zhang Z-X. Recognition of expertise and perceived influence in intercultural collaboration: A study of mixed American and Chinese groups. Journal of Communication. 2013;63 (3), 476-497. doi:10.1111/jcom.12026.
25. Matschullat J. Arsenic in the geosphere--a review. Sci Total Environ. 2000;249(1-3):297-312. doi: 10.1016/s0048-9697(99)00524-0.
26. Williams PN, Islam MR, Adomako EE, Raab A, Hossain SA, Zhu YG, et al. Increase in rice grain arsenic for regions of Bangladesh irrigating paddies with elevated arsenic in groundwaters. Environ Sci Technol. 2006;40(16):4903-8. doi: 10.1021/es060222i.
27. Leff B, Ramankutty N, Foley JA. Geographic distribution of major crops across the world. Global Biogeochem Cycles. 2004;18(1):GB1009. doi: 10.1029/2003gb002108.
28. Neisi A, Farhadi M, Ahmadi Angali K, Sepahvand A. Health risk assessment for consuming rice, bread, and vegetables in Hoveyzeh city. Toxicol Rep. 2024;12:260-5. doi: 10.1016/j.toxrep.2024.02.003.
29. Neisi A, Farhadi M, Cheraghian B, Dargahi A, Ahmadi M, Takdastan A, et al. Consumption of foods contaminated with heavy metals and their association with cardiovascular disease (CVD) using GAM software (cohort study). Heliyon. 2024;10(2):e24517. doi: 10.1016/j.heliyon.2024.e24517.
30. Bhattacharya P, Samal AC, Majumdar J, Santra SC. Arsenic contamination in rice, wheat, pulses, and vegetables: a study in an arsenic affected area of West Bengal, India. Water Air Soil Pollut. 2010;213(1):3-13. doi: 10.1007/s11270-010-0361-9.
31. Bissen M, Frimmel FH. Arsenic—a review. Part I: occurrence, toxicity, speciation, mobility. Acta Hydrochim Hydrobiol. 2003;31(1):9-18. doi: 10.1002/aheh.200390025.
32. Afra A, Singh K, Mohammadi MJ, Salam Karim Y, Abed Jawad M, Baqir Al-Dhalimy AM, et al. The effect of arsenic on the prevalence of diabetes. Health Scope. 2023;12(2):e135108. doi: 10.5812/jhealthscope-135108.
33. Islam AM. Membrane Distillation Process for Pure Water and Removal of Arsenic [thesis]. Gothenburg, Sweden: Chalmers University of Technology; 2004.
34. Muda I, Mohammadi MJ, Sepahvad A, Farhadi A, Fadhel Obaid R, Taherian M, et al. Associated health risk assessment due to exposure to BTEX compounds in fuel station workers. Rev Environ Health. 2023. doi: 10.1515/reveh-2023-0012.
35. Argos M, Ahsan H, Graziano JH. Arsenic and human health: epidemiologic progress and public health implications. Rev Environ Health. 2012;27(4):191-5. doi: 10.1515/reveh-2012-0021.
36. Hopenhayn C. Arsenic in drinking water: impact on human health. Elements. 2006;2(2):103-7. doi: 10.2113/gselements.2.2.103.
37. Chung JY, Yu SD, Hong YS. Environmental source of arsenic exposure. J Prev Med Public Health. 2014;47(5):253-7. doi: 10.3961/jpmph.14.036.
38. Mandal P. An insight of environmental contamination of arsenic on animal health. Emerg Contam. 2017;3(1):17-22. doi: 10.1016/j.emcon.2017.01.004.
39. Stea F, Bianchi F, Cori L, Sicari R. Cardiovascular effects of arsenic: clinical and epidemiological findings. Environ Sci Pollut Res Int. 2014;21(1):244-51. doi: 10.1007/s11356-013-2113-z.
40. Kapaj S, Peterson H, Liber K, Bhattacharya P. Human health effects from chronic arsenic poisoning--a review. J Environ Sci Health A Tox Hazard Subst Environ Eng. 2006;41(10):2399-428. doi: 10.1080/10934520600873571.
41. Wasserman GA, Liu X, Parvez F, Ahsan H, Factor-Litvak P, van Geen A, et al. Water arsenic exposure and children's intellectual function in Araihazar, Bangladesh. Environ Health Perspect. 2004;112(13):1329-33. doi: 10.1289/ehp.6964.
42. Tsai SY, Chou HY, The HW, Chen CM, Chen CJ. The effects of chronic arsenic exposure from drinking water on the neurobehavioral development in adolescence. Neurotoxicology. 2003;24(4-5):747-53. doi: 10.1016/s0161-813x(03)00029-9.
43. Hong YS, Song KH, Chung JY. Health effects of chronic arsenic exposure. J Prev Med Public Health. 2014;47(5):245-52. doi: 10.3961/jpmph.14.035.
44. Chen Y, Parvez F, Gamble M, Islam T, Ahmed A, Argos M, et al. Arsenic exposure at low-to-moderate levels and skin lesions, arsenic metabolism, neurological functions, and biomarkers for respiratory and cardiovascular diseases: review of recent findings from the Health Effects of Arsenic Longitudinal Study (HEALS) in Bangladesh. Toxicol Appl Pharmacol. 2009;239(2):184-92. doi: 10.1016/j.taap.2009.01.010.
45. Moon K, Guallar E, Navas-Acien A. Arsenic exposure and cardiovascular disease: an updated systematic review. Curr Atheroscler Rep. 2012;14(6):542-55. doi: 10.1007/s11883-012-0280-x.
46. Bosch FX, Ribes J, Díaz M, Cléries R. Primary liver cancer: worldwide incidence and trends. Gastroenterology. 2004;127(5 Suppl 1):S5-16. doi: 10.1053/j.gastro.2004.09.011.
47. Mazumder DN. Effect of chronic intake of arsenic-contaminated water on liver. Toxicol Appl Pharmacol. 2005;206(2):169-75. doi: 10.1016/j.taap.2004.08.025.
48. Cui X, Li S, Shraim A, Kobayashi Y, Hayakawa T, Kanno S, et al. Subchronic exposure to arsenic through drinking water alters expression of cancer-related genes in rat liver. Toxicol Pathol. 2004;32(1):64-72. doi: 10.1080/01926230490261348.
49. Centeno JA, Mullick FG, Martinez L, Page NP, Gibb H, Longfellow D, et al. Pathology related to chronic arsenic exposure. Environ Health Perspect. 2002;110(Suppl 5):883-6. doi: 10.1289/ehp.02110s5883.
50. Thomas DJ. Molecular processes in cellular arsenic metabolism. Toxicol Appl Pharmacol. 2007;222(3):365-73. doi: 10.1016/j.taap.2007.02.007.
51. Hartwig A, Blessing H, Schwerdtle T, Walter I. Modulation of DNA repair processes by arsenic and selenium compounds. Toxicology. 2003;193(1-2):161-9. doi: 10.1016/j.tox.2003.08.004.
52. Rossman TG. Mechanism of arsenic carcinogenesis: an integrated approach. Mutat Res. 2003;533(1-2):37-65. doi:

10.1016/j.mrfmmm.2003.07.009.
53. Kinoshita A, Wanibuchi H, Wei M, Yunoki T, Fukushima S. Elevation of 8-hydroxydeoxyguanosine and cell proliferation via generation of oxidative stress by organic arsenicals contributes to their carcinogenicity in the rat liver and bladder. Toxicol Appl Pharmacol. 2007;221(3):295-305. doi: 10.1016/j.taap.2007.03.024.
54. Waalkes MP, Ward JM, Diwan BA. Induction of tumors of the liver, lung, ovary and adrenal in adult mice after brief maternal gestational exposure to inorganic arsenic: promotional effects of postnatal phorbol ester exposure on hepatic and pulmonary, but not dermal cancers. Carcinogenesis. 2004;25(1):133-41. doi: 10.1093/carcin/bgg181.
55. Zhou YS, Du H, Cheng ML, Liu J, Zhang XJ, Xu L. The investigation of death from diseases caused by coal-burning type of arsenic poisoning. Chin J Endemiol. 2002;21(6):484-6.