Research Article

Protective Effect of Selenium Against Arsenic-Induced Hematological, Biochemical Alteration, and Organ Development Anomalies in Adult Female Mice

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Abstract | A major environmental health concern across the world is chronic arsenic exposure from contaminated water, which is linked to hematological, biochemical, and many other significant systemic illnesses. The current study on adult female mice assessed the protective effects of Na-selenite against arsenic-mediated hematological, biochemical, and organ development toxicities. In this study, adult female mice (Swiss Albino) were categorized into four groups namely control, $NaAsO_2$, $NaAsO_2$+Na_2SeO_3, and Na_2SeO_3 (10 µm $NaAsO_2$ and 10 µm Na_2SeO_3, respectively) were orally administrated via drinking water up to 60 days of the treatment period. Then the hematological, biochemical parameters, organ-to-body weight ratio, and morphology of the Liver and Lung were assessed. Na-arsenite exposure caused significant ($p<0.05$, respectively) increases in WBC count, RBC count, platelet count, hemoglobin, ESR, TCE, and RDW SD. The result also showed that serum RBS, ALT (SGPT), Alkaline phosphatase, Total cholesterol, Triglyceride, and Uric acid levels were significantly ($p<0.01$) higher in the $NaAsO_2$ exposed group. Arsenic exposure also led to a significant ($p<0.02$) decrease in the organ-to-body weight ratio in the spleen and slight discoloration and consistency of the liver and lung than the control group. It's interesting to note that co-administration of sodium selenite markedly mitigated all the changes caused by arsenic-induced alteration of hematological parameters, serum biochemical parameters, organ to body weight ratio ($p<0.05$, $p<0.01$, $p<0.05$, respectively). The current study provides compelling evidence for the protective effectiveness of the co-administration of Na-selenite against hematotoxicity, biochemical change, and organ toxicity in adult female mice carried on by exposure to Na-arsenite.

Keywords | Sodium arsenite, Sodium selenite, Mice, Hematological and serum biochemical parameters, Lung, Liver

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INTRODUCTION

Arsenic is widely distributed in the environment and is emitted by both natural and man-made activities (Rahman *et al.*, 2018). Due to the drinking of tainted groundwater, a significant amount of people in Bangladesh and other countries are under threat of arsenic exposure (Barai *et al.*, 2017; Paul, 2006). It is well acknowledged that

arsenic poisoning is a serious worldwide health concern. The World Health Organization (WHO) states that the acceptable arsenic level in drinking water has lowered from 50 micro g/l to 10 micro g/l. However, the amount of arsenic and arsenic-induced toxicity is gradually rising, and pollution from natural sources in various geographically remote parts of the world can reach hundreds of micrograms per liter. Arsenic's rising environmental toxicity is concerning and poses a serious risk to the general public's health worldwide. Eating and drinking, inhalation, and cutaneous absorption are the most frequent sources of arsenic exposure (Halder *et al*., 2013; Palma-Lara *et al*., 2020; Sun *et al*., 2014). In addition to the increased risk of several cancers (Liu *et al*., 2013), long-term arsenic exposure has also been linked to non-cancerous health risks such as diabetes, skin conditions, cardiovascular disease, neurological toxicity, and toxic effects on the liver, lung, kidney, spleen, and heart (Basher *et al*., 2023; Karagas *et al*., 2015; Khatun *et al*., 2020; Mao *et al*., 2016; States *et al*., 2009). Arsenic poisoning is thought to occur through several different pathways, such as the creation of oxidative stress, the inhibition of enzymes, and alterations in mitochondrial function (Flora *et al*., 2007).

Arsenic poisoning has been shown to alter the concentration of liver enzymes, according to experimental research on the liver, which is the organ most susceptible to arsenic damage. Specifically, oxidative stress and ROS generation are linked to liver damage (Das *et al*., 2012). The liver is the primary organ involved in metabolism inside the body and is most affected by arsenic intoxication. Chronic exposure to arsenic leads to symptoms such as liver enlargement (hepatomegaly), cirrhosis, and impaired liver enzyme activity in affected individuals (Liu and Waalkes, 2008). Analyses of biochemistry, hematology, and histopathology may be used to assess the toxicant's mode of action since they can assist predict important sub-lethal effects. Hematological and biochemical examinations of blood parameters are crucial for determining the structural and functional condition of a person exposed to a toxin (Al-Forkan *et al*., 2016).

Arsenic-induced oxidative stress is the most common and widely accepted method of arsenic intoxication. Reactive oxygen species are created because of oxidative stress by interacting with sulfhydryl groups which leads to the inhibition of numerous enzymes like DNA repair enzymes and antioxidant-related enzymes (thioredoxin reductase and glutathione peroxidase) (Ganyc *et al*., 2007; Pi *et al*., 2002; Ruiz-Ramos *et al*., 2009). These arsenic-generated reactive species cause oxidative stress to rise in cells, which in turn causes oxidative DNA damage and apoptosis (Yedjou *et al*., 2010). Many studies have shown that this oxidative stress is capable of interfering with several cellular signaling pathways that may be crucial in the manifestation of an arsenic-mediated illness (Druwe and Vaillancourt, 2010; Sumi *et al*., 2010). Despite arsenic poisoning being recognized as a hazard to worldwide public health, most of its effective, trustworthy, and safe treatments are still unknown. Recent research has shown that antioxidants may have a role in the management or prevention of arsenic poisoning (Rahman *et al*., 2018; Shathy *et al*., 2020; Yu *et al*., 2016).

Selenium is a crucial antioxidant with possible cancer-prevention and chemoprotective properties (Patrick, 2004). Mammals have been examined for the antioxidant functions of selenium at low concentrations (Sun *et al*., 2001). It is a part of several selenoproteins, including those with crucial biological activities such as glutathione peroxidases and thioredoxin reductases. The antioxidant and detoxifying properties of these selenoproteins are well established. Numerous hypothesized mechanisms for selenium's chemoprotective properties have been put forth, including oxidant defense, altered carcinogen metabolism, improved immune surveillance, apoptosis modulation, and angiogenesis suppression (Letavayová *et al*., 2008; Zeng *et al*., 2005). Selenium has been shown to have protective and advantageous effects on mammals (Xue *et al*., 2010). The following cellular levels have shown that selenium has protective effects against arsenic toxicity: cultured human leukemia HI-I-60 cells (Zeng, 2001; Zwolak, 2020), human hepatocytes (Walton *et al*., 2003), and the A375 cell line (Wang and Guo, 2011).

Due to unavoidable exposure to arsenic, the mitigation of its toxicity is now a significant global research challenge. There is a great deal of understanding about selenium's antioxidant and protective abilities, but nothing is known about how it could lessen the toxicity caused by arsenic. There are notably few studies on the protective effects of selenium against arsenic-caused hematological, biochemical, and organ development issues in both people and animals. It is crucial to investigate how sodium selenite protects against sodium arsenite-induced anomalies given the biological relevance of selenium and arsenic coexisting in the environment as well as their prevalence in anthropogenic discharges. The complicated interaction between arsenic and selenium can have both antagonistic and synergistic effects when taken together. Through altering cytotoxicity, genotoxicity, and oxidative stress, selenium can reduce arsenic toxicity in both vivo and vitro (Chitta *et al*., 2013; Jamwal and Niyogi, 2017; Ponomarenko *et al*., 2017; Sah *et al*., 2013; Selvaraj *et al*., 2012). Therefore, this study hypothesizes that co-exposure to selenium may mitigate the hematological, biochemical, and organ development abnormalities caused by arsenic in adult female mice. As a result, the goal of this study for the first time was to investigate the protective potential of sodium selenite on hematological, biochemical, and organ

development anomalies in sodium arsenite-exposed adult female mice.

MATERIALS AND METHODS

Selection and maintenance of the lab animals

Swiss albino female mice, aged 4-5 weeks, were procured from the International Center for Diarrheal Disease Research, Bangladesh (icddr, b). Four mice per cage were randomly selected and placed in plastic cages with wood-cob bedding. and were reared at 23±2°C, maintaining 12 hours of a light-dark cycle in a well-ventilated, humidified room with proper feed and water supply at the laboratory animal facilities of the Department of Genetics and Animal Breeding at Hajee Mohammad Danesh Science and Technology University. Every other day, drinking water was changed to avoid arsenic oxidation. All the procedures and animal experiments using mice were commenced after prior approval and following the rules and regulations set by the laboratory animal ethics committee of the Institute of Research and Training (IRT), Hajee Mohammad Danesh Science and Technology University, Dinajpur-5200, Bangladesh.

Ethical approval statement

This research project has been approved by the animal ethics committee of the Department of Genetics and Animal Breeding at Hajee Mohammad Danesh Science and Technology University in Bangladesh at meeting resolution number 09, which was held on July 12, 2022, because the experimental design of the study was not objectionable or subversive to animal ethics.

Design of the experiment

For this experiment, 24 mice were selected at random and categorized into four groups (6 mice in each group), namely Group-I (control), Group-II (sodium arsenite-$NaAsO_2$), Group-III (sodium arsenite-$NaAsO_2$ plus sodium selenite-Na_2SeO_3), and Group-IV (sodium selenite-Na_2SeO_3). From the age of 8–9 weeks, treatment started accordingly and immediately. Mice from Group I were given only normal drinking water. Group (II) and Group (IV) mice were given 10 micromolar of sodium arsenite ($NaAsO_2$; Sigma-Aldrich, USA) and 10 micromolar Sodium selenite (Na_2SeO_3; Sigma-Aldrich, USA) (Cho *et al*., 2023; Jeong *et al*., 2023; Shi *et al*., 2013) dissolved in deionized distilled water (ddH_2O), and a combination of 10 micromolar of sodium arsenite and sodium selenite was given to the mice of Group (III) mice through drinking water for 60 days.

Collection and processing of samples

After 60 days of the treatment period, adult female mice were euthanized using light diethyl ether (W509043, Sigma-Aldrich, St. Louis, MI, USA) anaesthesia after overnight fasting. By the heart puncher, blood was quickly collected for a significant volume in a collecting tube for hematological and biochemical analysis. Different organs, namely the liver, lungs, kidney, spleen, heart, and uterus, were carefully removed for the analysis of organ morphology and organ-to-body weight ratio.

Hematological assessment

Lithium heparinized tubes (BD 36666; Thermo Fisher, Waltham, Massachusetts, USA) was used to collect the blood samples, and a complete blood count (CBC) was performed for these samples to determine the hematological parameters such as the estimation of red blood cells, white blood cells, platelets, hemoglobin, packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), differential leukocyte count (DLC), and others by using an automatic whole blood analyzer (BC-20; Mindray, Shenzhen, P.R. China). Hematological parameters were evaluated among different treatment groups.

Biochemical analysis

Clot activator tubes were used to collect blood samples for biochemical evaluation. After clotting, the blood samples were properly centrifuged (for 10 minutes at 6000 rpm) for the collection of serum (using a pipette). To analyze random blood sugar (RBS), alkaline transaminase (ALT), alkaline phosphatase (ALP), triglyceride, total cholesterol, and uric acid, a biochemical analyzer (18200; HUMAN, Wiesbaden, Germany) and commercially available reagent (RANDOX, Crumlin, County Antrim, United Kingdom) according to the manufacturer's protocol were used. Biochemical parameters were evaluated among different treatment groups.

Body weight and organ weight measurements of mice

Every day, an analytical balance was used to weigh and record each mouse in each group. The abdomen was surgically exposed by a ventral incision after 8 weeks of maintenance. The liver, lung, heart, kidney, spleen, and uterus were meticulously removed, thoroughly cleansed of all fat and connective tissue, and weighed. The organ-to-body weight ratio was then calculated by the following formula: (organ weight/body weight) ×100% and compared among different groups.

Gross morphology of vital organs

The visualization of different vital organs like the liver, lungs, spleen, heart, kidney, and uterus was evaluated according to size, shape, color, and consistency to understand the adverse effect of arsenic and the protective properties of selenium on organ development. A centimeter scale was used to determine the size of the organs and to take a clear photo

on color paper for easy differentiation and comparison among the four groups.

Statistical analysis

A minimum of three repetitions were run through each experiment. As a ratio to each control, the results are shown as mean ± SEM. The statistical differences were examined using a single-factor analysis of variance (ANOVA). Analysis of Variance, or ANOVA, is a statistical test that examines how the means of more than two groups differ from one another. One independent variable is used in a one-way ANOVA, with significance set at $p<0.05$. The student-Newman-Keuls test was additionally utilized to compare the two groups, this test is step-by-step multiple comparison technique to determine which sample means differ significantly from one another. When differences reached a p-value of 0.05, they were deemed significant. Differences were considered significant at the level of $p<0.05$.

RESULTS AND DISCUSSION

Potential role of sodium selenite in recovering Hematological aberrations induced by sodium arsenite

Hematological alterations were found due to sodium arsenite exposure. The current study evaluates the ameliorative effect of selenium on hematological status. The values of hematological parameters are presented in Table 1. The results revealed that sodium arsenite caused a significant ($p<0.05$, respectively) increase in total WBC (white blood cell) count, RBC (Red blood cell) count, platelet count, Hb (hemoglobin concentration), ESR, TCE, PCV%, and RDW SD (red blood cell dimension width-standard deviation) compared to the control (Table 1). But interestingly, when the sodium arsenite ($NaAsO_2$) was exposed, adult female mice were supplemented with sodium selenite (Na_2SeO_3) at the same concentration in the $NaAsO_2$+Na_2SeO_3 group, significantly ($p<0.05$, respectively) reduced than the Na-arsenite ($NaAsO_2$) group of mice (Table 1). A similar trend is found among the groups for neutrophils, eosinophils, lymphocytes, and monocytes (Table 1).

Na-selenite (Na_2SeO_3) improves Na-arsenite ($NaAsO_2$) induced biochemical abnormalities

The impact of arsenic exposure on the serum biochemical levels in mice is depicted in (Table 2). The liver is regarded as one of the most crucial organs in the body because of its capacity to metabolize nutrients, cleanse dangerous chemicals, and carry out a variety of other essential tasks. ALP and ALT levels were tested since it is known that higher activity of these enzymes is associated with

Table 1: Hematological parameters of Mice with different treatment group.

Parameters	Treatments			
	Control	$NaAsO_2$	$NaAsO_2$+Na_2SeO_3	Na_2SeO_3
TC of WBC (/cmm)	4400±84.11	7000±115.47a	4223.33±14.52*	4800±43.30b**$
Neutrophils (%)	3±0.11	5±0.15a	7±0.05b*	5±0.1c$
Lymphocytes (%)	90±1.52	86±0.57	85±0.57a	87±0.57
EosinoPhils (%)	3±0.11	4±0.1a	3±0.05*	3±0.05**
Monocytes (%)	4±0.11	5±0.05a	5±0.05b	5±0.05c
HB (g/dl)	11.4±0.30	14.1±0.1a	13.5±0.05b*	13.8±0.05c$
ESR (mm in 1st hour)	6±0.57	4±0.05a	4±0.05b	3±0.05c*$
TCE (/cmm)	132±0.57	280±6.42a	126±0.57b*	144±0.57c**$
Platelet count (/cmm)	653000±1000	1133000.33±1157.88a	579000±563.47b*	758000±556.77c**$
RBC count (million/cmm)	7.05±0.07	9.11±0.00a	8.63±0.01b*	9.56±0.03c**$
PCV (%)	38±0.57	47±0.57a	45±0.28b*	46±0.52c
MCV (fl)	47.4±0.55	49.1±0.60	48.2±0.15	47.1±0.20*$
MCH (Pg)	16.1±0.20	16.4±0.26	16.3±0.02	15.3±0.18a*$
MCHC (g/dl)	34±0.5	33.5±0.15	33.9±0.1	32.5±0.26a*$
RDW SD (fl)	34.6±0.2	35.8±0.05a	33.1±0.05b*	35.1±0.1**$
RDW CV (%)	17.2±0.20	17.2±0.15	16.2±0.15a	17.6±0.11c*$

Among the Control, $NaAsO_2$, $NaAsO_2$+Na_2SeO_3, and Na_2SeO_3 exposed group of mouse hematological parameters are evaluated and compared. Values are presented as mean ± SEM (n=3). TC: total count; WBC: White blood cell; Hb: Hemoglobin; TCE: Trichloroethylene; RBC: Red blood cell; PCV: Packed cell volume; MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW-SD: red blood cell dimension width-standard deviation; RDW-CV: Red cell distribution width-coefficient of variation. a, b, and c indicate a significant difference from the control. *, ** indicates the significant (p=<0.05) difference from $NaAsO_2$. $ indicates the significant difference (p=<0.05) from ($NaAsO_2$+Na_2SeO_3).

Table 2: Biochemical Parameters of different treatment groups of mice.

Parameters	Treatments			
	Control	$NaAsO_2$	$NaAsO_2$+Na_2SeO_3	Na_2SeO_3
RBS (mmol/L)	3.2±0.05	5.4±0.11a	3.1±0.05*	4.3±0.05b**$
ALT (SGPT) (U/L)	12±0.57	17±0.57a	8±0.28b*	14±0.57c$
Alkaline phosphatage (U/L)	109±0.57	192±2.30a	128±4.72b*	97±1.52c**$
Total Cholesterol (mg/dl)	134±0.57	274±2a	174±3.05b*	196±2.08c**$
Triglyceride (mg/dl)	209±2.08	285±2.88a	252±1.52b*	244±3.05c**
Uric acid (mg/dl)	1.6±0.05	3.7±0.05a	2±0.05b*	2.1±0.05c**

Serum biochemical assessment and comparison among control and $NaAsO_2$, $NaAsO_2$+Na_2SeO_3, and Na2SeO3 exposed adult female mice. Data are presented as mean ± SEM (n=3). RBS: Random blood sugar; ALT: Alanine transaminase; SGPT: Serum glutamic pyruvic transaminase. a, b, c indicates the significant difference from the control. *, ** indicates the statistically significant (p<0.01, respectively) difference from $NaAsO_2$. $ indicates the statistically significant (p<0.01, respectively) difference from ($NaAsO_2$+Na_2SeO_3). Serum RBS, ALT (SGPT), Alkaline phosphatase, Total cholesterol, Triglyceride and Uric acid levels in the Na-arsenite group were 5.4±0.11, 17±0.57, 192±2.3, 274±2, 285±2.88 and 3.7±0.05 respectively which are significantly (P<0.01, respectively) higher than that of the control group measuring at 3.2±0.05, 12±0.57, 109±0.57, 134±0.57, 209±2.08 and 1.6±0.05 respectively (**Table 2**). With the ameliorative effect of the selenium, however, the Na-arsenite+Na-selenite group registered a significant (p<0.01, respectively) reduction of biochemical parameters than the Na-arsenite treated group.

Table 3: The organ-to-body weight ratio of different treatments groups.

Treatments	Organ to body weight					
	Liver	Lung	Kidney	Heart	Spleen	Uterus
Control	6.95±0.59	1.37±2.85	1.73±0.39	0.45±0.06	0.59±0.05	0.98±0.39
$NaAsO_2$	6.02±0.42	0.84±0.09	1.06±0.10	0.37±0.00	0.35±0.04*	0.37±0.06
$NaAsO_2$+Na_2SeO_3	6.11±0.41	1.11±0.05	1.29±0.16	0.47±0.07	0.37±0.06**	0.68±0.14
Na_2SeO_3	6.11±0.76	1.03±0.09	1.59±0.23	0.46±0.04	0.57±0.11	0.88±0.24

The organ-to-body weight ratio was assessed and compared among the control, $NaAsO_2$, $NaAsO_2$+Na_2SeO_3, and Na_2SeO_3 exposed adult female mice. Values are presented as mean ± SEM (n=3). *Indicates statistical significance (p<0.02) between control and sodium arsenite exposed group. **Indicates statistical significance(p<0.05) between control and $NaAsO_2$+Na_2SeO_3 exposed group of mice.

liver dysfunction as well as with other organ problems. The results showed that the abnormalities in various biochemical parameters posed by the Na-arsenite treatment among the Swiss albino female mice were successfully ameliorated by the Na-selenite treatment as shown in the Na-arsenite+Na-selenite group (Table 2). Serum RBS, ALT (SGPT), Alkaline phosphatase, Total cholesterol, Triglyceride and Uric acid levels in the Na-arsenite group were 5.4±0.11, 17±0.57, 192±2.3, 274±2, 285±2.88 and 3.7±0.05 respectively which are significantly (P<0.01, respectively) higher than that of the control group measuring at 3.2±0.05, 12±0.57, 109±0.57, 134±0.57, 209±2.08 and 1.6±0.05 respectively (Table 2). With the ameliorative effect of the selenium, however, the Na-arsenite+Na-selenite group registered a significant (p<0.01, respectively) reduction of biochemical parameters than the Na-arsenite treated group. In this group, Serum RBS, ALT (SGPT), Alkaline phosphatase, Total cholesterol, Triglyceride and Uric acid levels were 3.1±0.05, 8±0.28, 128±4.72, 174±3.05, 252±1.5, 2±0.05 respectively (Table 2).

Organ to body weight ratio assessment

We measured body weight and the ratio of organ-to-body weight to assess the rescue effect of selenium on arsenic-induced toxicity. The organ-to-body weight analysis of various vital organs like the liver, lungs, kidney, heart, spleen, and uterus revealed that only the spleen registered the ameliorative effect of the arsenic and selenium (combined) treatment group (Table 3). According to the results, spleen weight in the Na-arsenite exposed group was 0.35±0.04 significant (p<0.02) reduction from the control group which stands for 0.59±0.05 (Table 3). This detrimental effect of Na-arsenite exposure was significantly (p<0.05) higher by the Na-selenite treatment as shown in the Na-arsenite+Na-selenite group with a value of 0.37±0.06 (Table 3).

The rescue effect of selenium on arsenic-induced toxicity of organ morphology

The impact of Na-arsenite on different organs was assessed in adult female mice, and their amelioration with the supplementation of sodium selenite (Figure 1) was compared among different treatment groups. Visual observation of the morphological characteristics of different organs showed slight discoloration and abnormal consistency of the liver (Figure 1A, B) and lung (Figure 1B,

E, F), which were substantially affected in the NaAsO2-exposed group compared to a non-treated control group. Interestingly, the liver (Figure 1C) and the lung (Figure 1G) in the NaAsO2+Na2SeO3-treated group comparatively improved compared to the sodium arsenite-exposed group.

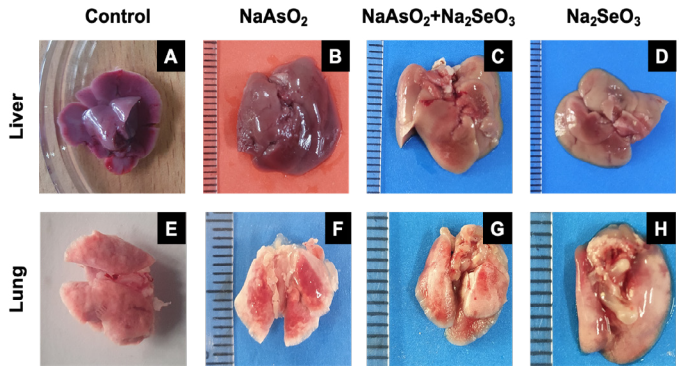

Figure 1: Ameliorative effect of selenium on arsenic-induced morphological alteration of the liver and lung. After the sacrifice of the mice the internal organ namely the liver (A, B, C and D) and lung (E, F, G and H) were collected and photographed and compared among control, $NaAsO_2$, $NaAsO_2$+Na_2SeO_3, and Na_2SeO_3 exposed group of adult female mice.

Arsenic and selenium are comparable to one another in terms of their chemical composition and metabolic fates (Zeng *et al*., 2005). To a certain extent of exposure, both also exhibit cytotoxicity and anticancer action; however, selenium exhibits lower levels of cytotoxicity, genotoxicity, and oxidative toxicity than arsenic. Combination therapy is gaining popularity in the medical community recently for the treatment of diseases like cancer, neurological disorders, and others to ensure beneficial effects on the target objects (Hsueh *et al*., 2017; Wang *et al*., 2015). Selenium is regarded as a key regulator of this protein's production and function, which strengthens cellular defenses both *in vivo* and *in vitro* (Schnabel *et al*., 2008). From this vantage point, we conducted this study to determine the protective effects of selenium on arsenic-induced hematological, biochemical, and defective organ development in adult female mice. The analysis of hematological and serum biochemical parameters yields crucial knowledge about the changes that take place in the physiology of the blood in the presence of sickness or hazardous pollution (Ola-Davies and Akinrinde, 2016). The study demonstrated a significant increase in total WBC count and platelet count in arsenic-exposed groups due to leukocytosis and thrombocytosis (Ola-Davies and Akinrinde, 2016). The impact was noticeably reversed when the mice were supplied with a Na-selenite and Na-arsenite combination, which significantly reduced the parameters. The results also showed that RBC count, Hb, and PCV significantly increased in the arsenic-treated group, which is comparable with the study of an increase or reduction in the number of red blood cells that can be caused by arsenic depending on the quantity and method of delivery, according to prior research (Yi *et al*., 2020). Hypoxia, or low oxygen partial pressure, causes the release of erythropoietin (EPO), which increases the formation of red blood cells (Wojan *et al*., 2021). The present study demonstrated that the co-supplementation of Na-selenite with arsenic rescued the hepatotoxicity by a significant reduction of the parameters. As an important antioxidant, selenium affects a variety of tissues and cells by increasing the amount of selenoproteins such GPx. Its principal role is to protect against oxidative damage by removing reactive oxygen species (ROS), especially hydroperoxides (Zhang *et al*., 2023). The liver is one of the most crucial and active organs for the retention, distribution, and detoxification of toxins (Akan *et al*., 2012) and to assess the liver, there are several tests available. Typically, the levels of ALT and ALP are evaluated to detect problems with the bones, gallbladder, kidney, and liver cells. ALP is found in a range of tissues, including the liver, bones, intestines, kidneys, and other organs, whereas ALT is believed to be largely concentrated inside liver cells. Most cases of liver damage or inflammation result in some elevation in ALP and ALT values (Barai *et al*., 2017). On the other hand, one of the major issues in cases of arsenic poisoning is oxidative damage. One of the most crucial methods to stop harm to this hazardous metal is to increase the antioxidant potential of arsenic pollutants. In the current study, we demonstrated that mice exposed to arsenic compared to control animals had considerably higher serum levels of ALP and ALT. According to prior research, elevated levels of these enzymes suggested liver damage in exposed animals (Barai *et al*., 2017; Mazumder, 2005; Zhang *et al*., 2014). However, ALT and ALP levels were lower in the animals exposed to both arsenic and sodium selenite supplementation than they were in the arsenic-alone exposure group, demonstrating that selenium has a significant ameliorative impact on the toxicity caused by arsenic. Previous studies demonstrated that selenium possesses a protective role against arsenic-induced hepatic damage by reducing lipid peroxidation and restoring glutathione peroxidase (GPx) activity in the liver (Xu *et al*., 2013). Due to perfusion and a rise in expelled chemical concentration in renal tubular cells, the kidney is more susceptible to injury (Messarah *et al*., 2013). Renal function is determined by urea levels in the serum. Only after parenchyma tissue damage does the urea levels start to rise (Messarah *et al*., 2013). In this study serum urea level was significantly higher in the arsenic-exposed group compared to the control which is comparable with the earlier studies (Messarah *et al*., 2013; Raeeszadeh *et al*., 2022; Singh *et al*., 2015). But interestingly the remarkable restoration of blood urea level after selenium treatment with arsenic showed that the kidney was protected against arsenic poisoning. Selenite treatment has been demonstrated to reduce

arsenite's harmful effects on antioxidant enzymes including catalase (CAT) and superoxide dismutase (SOD) and to decrease renal lipid peroxidation. Furthermore, selenite therapy shields renal tissue against the histopathological alterations caused by arsenite (Jalaludeen *et al*., 2015). As per the literature, this hyperlipidemic condition imposed by arsenic is an outcome of oxidative stress (Sinha *et al*., 2010). The antioxidant properties of selenium effectively protect such oxidative imbalance evidenced by the observed values of lipid profile. In this study, we also found that serum RBS, total cholesterol and triglyceride levels were significantly higher in an arsenic-treated group than the control which is similar to the previous studies (Raeeszadeh *et al*., 2022; Yousef *et al*., 2008). The pancreatic islet cells are damaged by increased oxidative stress brought on by arsenic exposure, which raises blood glucose levels and disrupts lipid metabolism. Decreased fatty acid oxidation inside the mitochondria may be the result of increased oxidative stress brought on by mitochondrial damage within the hepatocytes However, supplementing with selenium and arsenic significantly decreased levels of RBS, total cholesterol, and triglycerides. The outcomes of the present work showed that supplementation of sodium selenite alone surprisingly had a toxic effect. Because of its enduring potential for adverse effects, arsenic buildup in cells and tissues is a serious issue. When consumed by humans or animals, arsenic is known to accumulate in several organs, including the liver, kidneys, heart, lungs, muscles, and spleen (Barai *et al*., 2017; Dua *et al*., 2015; Sayed *et al*., 2015). In this study, Na-arsenite-exposed mice showed a substantial decrease in spleen weight compared to the control group. Our results are in line with other studies that showed that increasing MDA and H_2O_2 levels cause the spleen to generate an oxidative imbalance that severely disrupts the function of the antioxidant enzymes CAT and GSH-Px, confirming oxidative damage to immunological organs (Duan *et al*., 2017). But the antioxidant properties of selenium with the supplementation of arsenic were able to significantly reduction of organ damage by improving the spleen weight (Table 3) and organ morphology (Figure 1) whereas sodium selenite alone was firmly contradictory. Throughout many life science fields, histopathology is a fundamental subject that provides a primary method for examining the microscopic features of tissues and making a wide range of illness diagnoses. However, in the context of this study, histopathological analysis of various organs poses a significant limitation in determining organ-specific alterations.

CONCLUSIONS AND RECOMMENDATIONS

The current study has demonstrated the mitigating effect of Na_2SeO_3 on hematological and serum biochemical parameters and the development of internal organs altered by sodium arsenite exposure in adult female mice. Oxidative stress has been identified as one of the main processes of arsenic toxicity. By this concept, sodium selenite's capacity to reduce oxidative stress may protect against the toxicity caused by arsenic. Numerous selenoproteins with antioxidant and detoxifying capabilities may have aided overall safety from the negative consequences. Sodium selenite has tremendous potential to reduce the negative effects of arsenic. These outcomes could potentially emphasize the role of selenium in reducing arsenic-induced toxicity in both people and animals. although its precise function in this process is yet unclear. Further experimentation is needed to clarify the effect of selenium against arsenic toxicity at the molecular level of observations and formulate an amelioration strategy. Therefore, it's critical to conduct additional research on the physiological, cellular, and molecular mechanisms of selenium against arsenic-induced toxicity. Such research initiatives may lead to the creation of a therapeutic drug based on selenium that is intended to lessen the negative consequences that result from human exposure to arsenic. These outcomes could potentially emphasize the role of selenium in reducing arsenic-induced toxicity in both people and animals, although its precise function in this process is yet unclear.

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NOVELTY STATEMENT

The novelty of this study is that it provides preliminary information on the ameliorative effects of selenium against arsenic-induced hematological and biochemical alteration and organ development anomalies in female mice and these findings may lead to the creation of a therapeutic drug based on selenium that is intended to lessen the negative consequences that result from human exposure to arsenic.

AUTHOR'S CONTRIBUTION

Conceptualization and design of the research, M.R.I.; methodology, M.R.I.; experimental investigation, M.K.B.,

S.S., M.S.H., and S.S.; sample resources, M.R.I.; writing-original draft preparation M.K.B., S.S., and M.R.I.; writing-review and editing, M.K.B., S.S., M.S.H., S.S., and M.R.I; supervision, M.R.I.; project administration, M.R.I. All authors have read and agreed to the published version of the manuscript.

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Compliance with ethical standards

This article does not contain any studies with human participants performed by any of the authors.

Conflict of interest

The authors have declared no conflict of interest.

REFERENCES

Akan J, Salwa M, Yikala B, Chellube Z (2012). Study on the distribution of heavy metals in different tissues of fishes from River Benue in Vinikilang, Adamawa State, Nigeria. Br. J. Appl. Sci. Technol., 2(4): 311-333. https://doi.org/10.9734/BJAST/2012/1716

Al-Forkan M, Islam S, Akter R, Shameen AS, Khaleda L, Rahman Z, Salma CD (2016). A sub-chronic exposure study of arsenic on hematological parameters, liver enzyme activities, histological studies and accumulation pattern of arsenic in organs of Wistar albino rats. J. Cytol. Histol. S, 5(2).

Barai M, Ahsan N, Paul N, Hossain K, Rashid MA, Kato M, Ohgami N, Akhand AA (2017). Amelioration of arsenic-induced toxic effects in mice by dietary supplementation of Syzygium cumini leaf extract. Nagoya J. Med. Sci., 79(2): 167.

Basher MK, Sarkar S, Mobarak MH, Islam MR (2023). Inorganic arsenic exposure during pregnancy affects post-natal growth, blood parameters, and organ development of mice offspring. J. Adv. Biotechnol. Exp. Ther. 6(2): 445-457.

Chitta KR, Landero Figueroa JA, Caruso JA, Merino EJ (2013). Selenium mediated arsenic toxicity modifies cytotoxicity, reactive oxygen species and phosphorylated proteins. Metallomics, 5(6): 673-685. https://doi.org/10.1039/c3mt20213e

Cho YJ, Park SH, Ryu KY (2023). Mild oxidative stress induced by sodium arsenite reduces lipocalin-2 expression levels in cortical glial cells. Int. J. Mol. Sci., 24(21): 15864. https://doi.org/10.3390/ijms242115864

Das N, Paul S, Chatterjee D, Banerjee N, Majumder NS, Sarma N, Sau TJ, Basu S, Banerjee S, Majumder P (2012). Arsenic exposure through drinking water increases the risk of liver and cardiovascular diseases in the population of West Bengal, India. BMC Publ. Health, 12(1): 1-9. https://doi.org/10.1186/1471-2458-12-639

Druwe IL, Vaillancourt RR (2010). Influence of arsenate and arsenite on signal transduction pathways: An update. Arch. Toxicol., 84: 585-596. https://doi.org/10.1007/s00204-010-0554-4

Dua TK, Dewanjee S, Gangopadhyay M, Khanra R, Zia-Ul-Haq M, De Feo V (2015). Ameliorative effect of water spinach, Ipomea aquatica (Convolvulaceae), against experimentally induced arsenic toxicity. J. Trans. Med., 13(1): 1-17. https://doi.org/10.1186/s12967-015-0430-3

Duan X, Gao S, Li J, Wu L, Zhang Y, Li W, Zhao L, Chen J, Yang S, Sun G (2017). Acute arsenic exposure induces inflammatory responses and CD4+ T cell subpopulations differentiation in spleen and thymus with the involvement of MAPK, NF-kB, and Nrf2. Mol. Immunol., 81: 160-172. https://doi.org/10.1016/j.molimm.2016.12.005

Flora S, Bhadauria S, Kannan G, Singh N (2007). Arsenic induced oxidative stress and the role of antioxidant supplementation during chelation: A review. J. Environ. Biol., 28(2): 333.

Ganyc D, Talbot S, Konate F, Jackson S, Schanen B, Cullen W, Self WT (2007). Impact of trivalent arsenicals on selenoprotein synthesis. Environ. Health Perspect., 115(3): 346-353. https://doi.org/10.1289/ehp.9440

Halder D, Bhowmick S, Biswas A, Chatterjee D, Nriagu J, Guha MDN, Šlejkovec Z, Jacks G, Bhattacharya P (2013). Risk of arsenic exposure from drinking water and dietary components: implications for risk management in rural Bengal. Environ. Sci. Technol., 47(2): 1120-1127. https://doi.org/10.1021/es303522s

Hsueh YM, Su CT, Shiue HS, Chen WJ, Pu, YS, Lin YC, Tsai CS, Huang CY (2017). Levels of plasma selenium and urinary total arsenic interact to affect the risk for prostate cancer. Food Chem. Toxicol., 107: 167-175. https://doi.org/10.1016/j.fct.2017.06.031

Jalaludeen AM, Lee WY, Kim JH, Jeong HY, Ki KS, Kwon EG, Song H (2015). Therapeutic efficacy of biochanin A against arsenic-induced renal and cardiac damage in rats. Environ. Toxicol. Pharmacol., 39(3): 1221-1231. https://doi.org/10.1016/j.etap.2015.04.020

Jamwal A, Niyogi S (2017). Dose and chemical species-specific effects of selenium against arsenite toxicity in cultured hepatocytes of rainbow trout (*Oncorhynchus mykiss*). Metallomics, 9(6): 744-756. https://doi.org/10.1039/C7MT00006E

Jeong S, Ahn C, Kwon JS, Kim K, Jeung EB (2023). Effects of sodium arsenite on the myocardial differentiation in mouse embryonic bodies. Toxics, 11(2): 142. https://doi.org/10.3390/toxics11020142

Karagas MR, Gossai A, Pierce B, Ahsan H (2015). Drinking water arsenic contamination, skin lesions, and malignancies: A systematic review of the global evidence. Curr. Environ. Health Rep., 2: 52-68. https://doi.org/10.1007/s40572-014-0040-x

Khatun MF, Hasan MM, Islam R, Sarkar S, Haque MA (2020). Effect of spirulina (*Spirulina platensis*) and vitamin E on arsenic induced toxicity in Quail. Asian J. Med. Biol. Res., 6(1): 93-98. https://doi.org/10.3329/ajmbr.v6i1.46483

Letavayová L, Vlasáková D, Spallholz JE, Brozmanová J, Chovanec M (2008). Toxicity and mutagenicity of selenium compounds in Saccharomyces cerevisiae. Mutat. Res. Fundament. Mol. Mech. Mutagen., 638(1-2): 1-10. https://doi.org/10.1016/j.mrfmmm.2007.08.009

Liu FF, Wang JP, Zheng YJ, Ng JC (2013). Biomarkers for the evaluation of population health status 16 years after the intervention of arsenic-contaminated groundwater in Xinjiang, China. J. Hazard. Mater., 262: 1159-1166. https://

doi.org/10.1016/j.jhazmat.2013.03.058

Liu J, Waalkes MP (2008). Liver is a target of arsenic carcinogenesis. Toxicol. Sci., 105(1): 24-32. https://doi.org/10.1093/toxsci/kfn120

Mao J, Yang J, Zhang Y, Li T, Wang C, Xu L, Hu Q, Wang X, Jiang S, Nie X (2016). Arsenic trioxide mediates HAPI microglia inflammatory response and subsequent neuron apoptosis through p38/JNK MAPK/STAT3 pathway. Toxicol. Appl. Pharmacol., 303: 79-89. https://doi.org/10.1016/j.taap.2016.05.003

Mazumder DG (2005). Effect of chronic intake of arsenic-contaminated water on liver. Toxicol. Appl. Pharmacol., 206(2):169-175.https://doi.org/10.1016/j.taap.2004.08.025

Messarah M, Saoudi M, Boumendjel A, Kadeche L, Boulakoud MS, Feki AE (2013). Green tea extract alleviates arsenic-induced biochemical toxicity and lipid peroxidation in rats. Toxicol. Ind. Health, 29(4): 349-359. https://doi.org/10.1177/0748233711433934

Ola-Davies, O. E., and Akinrinde, A. S. (2016). Acute sodium Arsenite-induced hematological and biochemical changes in wistar rats: Protective effects of ethanol extract of Ageratum conyzoides. Pharmacogn. Res., 8(Suppl 1): S26. https://doi.org/10.4103/0974-8490.178645

Palma-Lara I, Martínez-Castillo M, Quintana-Pérez J, Arellano-Mendoza M, Tamay-Cach F, Valenzuela-Limón O, García-Montalvo E, Hernández-Zavala A (2020). Arsenic exposure: A public health problem leading to several cancers. Regul. Toxicol. Pharmacol., 110: 104539. https://doi.org/10.1016/j.yrtph.2019.104539

Patrick L (2004). Selenium biochemistry and cancer: A review of the literature. Altern. Med. Rev., 9(3).

Paul K (2006). Groundwater arsenic contamination and human sufferings in West Bengal, India and Bangladesh: A review. Abstracts Pap. Am. Chem. Soc.,

Pi,J, Yamauchi H, Kumagai Y, Sun G, Yoshida T, Aikawa H, Hopenhayn-Rich C, Shimojo N (2002). Evidence for induction of oxidative stress caused by chronic exposure of Chinese residents to arsenic contained in drinking water. Environ. Health Persp., 110(4): 331-336. https://doi.org/10.1289/ehp.02110331

Ponomarenko O, La Porte PF, Singh SP, Langan G, Fleming DE, Spallholz JE, Alauddin M, Ahsan H, Ahmed S, Gailer J (2017). Selenium-mediated arsenic excretion in mammals: A synchrotron-based study of whole-body distribution and tissue-specific chemistry. Metallomics, 9(11): 1585-1595. https://doi.org/10.1039/C7MT00201G

Raeeszadeh M, Karimi P, Khademi N, Mortazavi P (2022). The effect of broccoli extract in arsenic-induced experimental poisoning on the hematological, biochemical, and electrophoretic parameters of the liver and kidney of rats. Evid. Based Complement. Altern. Med., https://doi.org/10.1155/2022/3509706

Rahman MM, Uson-Lopez RA, Sikder MT, Tan G, Hosokawa T, Saito T, Kurasaki M (2018). Ameliorative effects of selenium on arsenic-induced cytotoxicity in PC12 cells via modulating autophagy/apoptosis. Chemosphere, 196: 453-466. https://doi.org/10.1016/j.chemosphere.2017.12.149

Ruiz-Ramos R, Lopez-Carrillo L, Rios-Perez AD, De Vizcaya-Ruíz A, Cebrian ME (2009). Sodium arsenite induces ROS generation, DNA oxidative damage, HO-1 and c-Myc proteins, NF-κB activation and cell proliferation in human breast cancer MCF-7 cells. Mutat. Res. Genet. Toxicol. Environ. Mutagen., 674(1-2): 109-115. https://doi.org/10.1016/j.mrgentox.2008.09.021

Sah S, Vandenberg A, Smits J (2013). Treating chronic arsenic toxicity with high selenium lentil diets. Toxicol. Appl. Pharmacol., 272(1): 256-262. https://doi.org/10.1016/j.taap.2013.06.008

Sayed S, Ahsan N, Kato M, Ohgami N, Rashid A, Akhand AA (2015). Protective effects of *Phyllanthus emblica* leaf extract on sodium arsenite-mediated adverse effects in mice. Nagoya J. Med. Sci., 77(1-2): 145.

Schnabel R, Lubos E, Messow CM, Sinning CR, Zeller T, Wild PS, Peetz D, Handy DE, Munzel T, Loscalzo J (2008). Selenium supplementation improves antioxidant capacity *in vitro* and *in vivo* in patients with coronary artery disease: The selenium therapy in coronary artery disease patients (SETCAP) study. Am. Heart J., 156(6): 1201. e1201-1201. e1211. https://doi.org/10.1016/j.ahj.2008.09.004

Selvaraj V, Yeager-Armstead M, Murray E (2012). Protective and antioxidant role of selenium on arsenic trioxide–induced oxidative stress and genotoxicity in the fish hepatoma cell line PLHC-1. Environ. Toxicol. Chem., 31(12): 2861-2869. https://doi.org/10.1002/etc.2022

Shathy MA, Hasan MM, Aziz FB, Islam R, Sarkar S (2020). Prevention of arsenic toxicity in quail by using spirulina and garlic. Int. J. Nat. Soc. Sci., 7: 26-31.

Shi K, Jiang Q, Li Z, Shan L, Li F, An J, Yang Y, Xu C (2013). Sodium selenite alters microtubule assembly and induces apoptosis *in vitro* and *in vivo*. J. Hematol. Oncol., 6(1): 1-9. https://doi.org/10.1186/1756-8722-6-7

Singh MK, Yadav SS, Yadav RS, Chauhan A, Katiyar D, Khattri S (2015). Protective effect of Emblica-officinalis in arsenic induced biochemical alteration and inflammation in mice. Springerplus, 4(1): 1-8. https://doi.org/10.1186/s40064-015-1227-9

Sinha D, Roy S, Roy M (2010). Antioxidant potential of tea reduces arsenite induced oxidative stress in Swiss albino mice. Food Chem. Toxicol., 48(4): 1032-1039. https://doi.org/10.1016/j.fct.2010.01.016

States JC, Srivastava S, Chen Y, Barchowsky A (2009). Arsenic and cardiovascular disease. Toxicol. Sci., 107(2): 312-323. https://doi.org/10.1093/toxsci/kfn236

Sumi D, Shinkai Y, Kumagai Y (2010). Signal transduction pathways and transcription factors triggered by arsenic trioxide in leukemia cells. Toxicol. Appl. Pharmacol., 244(3): 385-392. https://doi.org/10.1016/j.taap.2010.02.012

Sun HJ, Rathinasabapathi B, Wu B, Luo J, Pu LP, Ma LQ (2014). Arsenic and selenium toxicity and their interactive effects in humans. Environ. Int., 69: 148-158. https://doi.org/10.1016/j.envint.2014.04.019

Sun Y, Butler J, Whanger P (2001). Glutathione peroxidase activity and selenoprotein W levels in different brain regions of selenium-depleted rats. J. Nutr. Biochem., 12(2): 88-94. https://doi.org/10.1016/S0955-2863(00)00130-3

Walton FS, Waters SB, Jolley SL, LeCluyse EL, Thomas DJ, Styblo M (2003). Selenium compounds modulate the activity of recombinant rat AsIII-methyltransferase and the methylation of arsenite by rat and human hepatocytes. Chem. Res. Toxicol., 16(3): 261-265. https://doi.org/10.1021/tx025649r

Wang S, Geng Z, Shi N, Li X, Wang Z (2015). Dose-dependent effects of selenite (Se4+) on arsenite (As3+)-induced apoptosis and differentiation in acute promyelocytic leukemia cells. Cell Death Dis., 6(1): e1596-e1596. https://doi.org/10.1038/cddis.2014.563

Wang ZF, Guo X (2011). Arsenite-induced apoptosis is prevented by selenite in A375 cell line. Biol. Trace Element Res., 140: 7-17. https://doi.org/10.1007/s12011-010-8674-5

Wojan F, Stray-Gundersen S, Nagel MJ, Lalande S (2021). Short exposure to intermittent hypoxia increases erythropoietin levels in healthy individuals. J. Appl. Physiol., 130(6): 1955-1960. https://doi.org/10.1152/japplphysiol.00941.2020

Xu Z, Wang Z, Li JJ, Chen C, Zhang PC, Dong L, Chen JH, Chen Q, Zhang XT, Wang ZL (2013). Protective effects of selenium on oxidative damage and oxidative stress related gene expression in rat liver under chronic poisoning of arsenic. Food Chem. Toxicol., 58: 1-7. https://doi.org/10.1016/j.fct.2013.03.048

Xue W, Wang Z, Chen Q, Chen J, Yang H, Xue S (2010). High selenium status in individuals exposed to arsenic through coal-burning in Shaanxi (PR of China) modulates antioxidant enzymes, heme oxygenase-1 and DNA damage. Clin. Chim. Acta, 411(17-18): 1312-1318. https://doi.org/10.1016/j.cca.2010.05.018

Yedjou C, Tchounwou P, Jenkins J, McMurray R (2010). Basic mechanisms of arsenic trioxide (ATO)-induced apoptosis in human leukemia (HL-60) cells. J. Hematol. Oncol., 3(1): 1-9. https://doi.org/10.1186/1756-8722-3-28

Yi Y, Gao S, Xia J, Li C, Zhao Y, Zhang Y, Liang A, Ji S (2020). Study of the accumulation and distribution of arsenic species and association with arsenic toxicity in rats after 30 days of oral realgar administration. J. Ethnopharmacol., 247: 111576. https://doi.org/10.1016/j.jep.2018.10.037

Yousef MI, El-Demerdash FM, Radwan FM (2008). Sodium arsenite induced biochemical perturbations in rats: ameliorating effect of curcumin. Food Chem. Toxicol., 46(11): 3506-3511. https://doi.org/10.1016/j.fct.2008.08.031

Yu H, Liu S, Li M, Wu B (2016). Influence of diet, vitamin, tea, trace elements and exogenous antioxidants on arsenic metabolism and toxicity. Environ. Geochem. Health, 38: 339-351. https://doi.org/10.1007/s10653-015-9742-8

Zeng H (2001). Arsenic suppresses necrosis induced by selenite in human leukemia HL-60 cells. Biol. Trace Element. Res., 83: 1-15. https://doi.org/10.1385/BTER:83:1:01

Zeng H, Uthus EO, Combs Jr GF (2005). Mechanistic aspects of the interaction between selenium and arsenic. J. Inorgan. Biochem., 99(6): 1269-1274. https://doi.org/10.1016/j.jinorgbio.2005.03.006

Zhang F, Li X, Wei Y (2023). Selenium and selenoproteins in health. Biomolecules, 13(5): 799. https://doi.org/10.3390/biom13050799

Zhang Z, Gao L, Cheng Y, Jiang J, Chen Y, Jiang H, Yu H, Shan A, Cheng B (2014). Resveratrol, a natural antioxidant, has a protective effect on liver injury induced by inorganic arsenic exposure. BioMed. Res. Int., https://doi.org/10.1155/2014/617202

Zwolak I (2020). The role of selenium in arsenic and cadmium toxicity: an updated review of scientific literature. Biol. Trace Element Res., 193(1): 44-63. https://doi.org/10.1007/s12011-019-01691-w