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# Sodium Selenite Ameliorates the Effects of Sodium Arsenite on Some Biomolecules and Enzymes of Energy Metabolism in the Testes of Albino Rats

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**Abstract:**
Heavy metal exposure is becoming more common in our contemporary society as a result of its widespread availability and use. Arsenic is a well-known example of a heavy metal that can harm live creatures' reproductive systems and biochemical pathways. Twenty-four male Albino rats were randomly divided into four groups (n = 6) and exposed to sodium arsenite (SA) and sodium selenite (SS) for 5 weeks to investigate the ameliorative role of sodium selenite on sodium arsenite-induced testicular toxicity on some biomolecules and enzymes of energy metabolism. Group I (control) received just distilled water, whereas groups II and III were given 40 ppm SA in drinking water *ad libitum*; additionally, group III received 0.25 mg/kg bwt SS orally, while group IV received 0.25 mg/kg bwt SS orally only. Significant increases ($p < 0.05$) in xanthine oxidase, aldolase, lactate dehydrogenase, and aspartate aminotransferase activities, and nitric oxide and hydrogen sulphide levels were observed in the SA-exposed group (group II), while hexokinase and $\alpha$-ketoglutarate dehydrogenase activities decreased significantly. Sodium selenite treatment ameliorated the apparent effects of SA exposure, as seen in groups III and IV. This study supports the use of SS as a safe therapy for SA-induced testicular toxicity.

**Keywords:** *heavy metal exposure, selenium, reproductive organs, biomolecules, energy metabolism*

## 1 Introduction

Heavy metal exposure is becoming more common in our contemporary society as a result of its widespread availability and use. Arsenic is a well-known example of a heavy metal that can harm live creatures' reproductive systems and biochemical pathways. Arsenic exists in both inorganic and organic forms (Matschullat, 2000) and with varying oxidation numbers in nature (Afolabi et al., 2015). The inorganic forms are predominantly present in water, food, soil, and air. There are reports of arsenic contamination of water bodies in both urban and rural settings around the world (Ahoule et al., 2015). Acute and chronic exposures to inorganic arsenic compounds result in multi-organ damages and perturbations in biological pathways (Gwaltney-Brant, 2013).

Selenium is an essential micro-element that affects numerous physiological activities in both animals and plants. In trace amounts, it is a good antioxidant with anticancer and anti-mutagenic properties and improves reproductive system and developmental activities (Hariharan & Dharmaraj, 2020; Mojapelo & Lehloenya, 2019). Selenium exists in two forms: organic and inorganic. One of the most common inorganic forms is sodium selenite (SS), used for its dietary potential as a food supplement (Arshad et al., 2021). Selenium has been reported to alter the toxic potential of heavy metals by interacting with them at

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their primary sites of action, and it can alter the way the body responds to noxious substances by altering their metabolism and transport (Rahman et al., 2019).

In order to find a safer treatment for arsenic-induced testicular toxicity, SS was employed due to its antioxidant and chemo-protective properties. This current study aims to investigate the ameliorative roles of SS on sodium arsenite-induced testicular damage in male Albino rats.

# 2 Materials and Methods

## 2.1 Chemicals

Sodium arsenite (a source of arsenic, SA) and sodium selenite (a source of selenium, SS) were products of Sigma-Aldrich, Missouri, USA. All other chemicals and reagents used are of analytical grade.

## 2.2 Experimental Animal and Design

A total of 24 adult male albino rats (weight: 211 g ± 23) were randomly selected into four groups. These were housed in plastic cages with good ventilation and fed *ad libitum* with rat chow. The protocols of this study were approved by the Animal Ethical Committee of the Department of Biochemistry, College of Biosciences, Federal University of Agriculture, Abeokuta, Ogun State. After initial acclimatization of the animals for two weeks, the animals were exposed to SA and treated with SS. Group I (control) received distilled water; groups II and III were given 40 ppm SA in drinking water *ad libitum*; additionally, group III received 0.25 mg/kg bwt SS orally, while group IV received 0.25 mg/kg bwt SS orally only. The SS dose utilized in this study was previously published by Aslanturk et al. (2014). The experiment lasted five weeks.

## 2.3 Animal Sacrifice

The animals were sacrificed a day after the treatment had ended, following an overnight fast. All materials were stored at a temperature of around 4°C. The rats were anesthetized with phenobarbital, and the testes were excised using a dissecting kit. The organs were transferred into a chilled saline solution. The rinsed organs were mopped with filter paper and weighed with an analytical balance. A 10% homogenate solution of the organ was prepared with Sucrose-Tris-EDTA buffer (containing 0.25 M, 10 mM Tris, and 0.05 mM EDTA, pH 7.4). The mitochondrial fraction (pellet) of the homogenate was obtained after centrifugation at 12,000 rpm for 3 minutes at 4°C. The supernatant was decanted, and the pellet was reconstituted with 1 ml of the buffer (Mela & Seitz, 1979). This was used for the biochemical assay.

## 2.4 Biochemical Assays

### 2.4.1 Estimation of Testicular Hydrogen Sulphide and Nitric Oxide Levels

Hydrogen sulphide was assayed according to the protocol of Zhu et al. (2007), while nitric oxide levels were assayed according to the protocol of Tsikas (2005).

### 2.4.2 Determination of Testicular Xanthine Oxidase Activity

The assay for xanthine oxidase activity followed the protocol of Bergmeyer et al. (1974).

### 2.4.3 Determination of Testicular Aldolase Activity

The assay for aldolase activity followed the protocol of Jagannathan et al. (1956).

### 2.4.4 Determination of Testicular Lactate Dehydrogenase Activity

The assay for lactate dehydrogenase (LDH) activity followed the protocol of Borgmann et al. (1974).

### 2.4.5 Determination of Testicular Aspartate Amino Transferase Activity

Aspartate amino transferase activity was assayed according to the protocol of Reitman and Frankel (1957).

### 2.4.6 Determination of Testicular $\alpha$-Ketoglutarate Dehydrogenase and Glutamate Dehydrogenase Activities

Testicular $\alpha$-ketoglutarate dehydrogenase and glutamate dehydrogenase (GLDH) activities were assayed according to the protocols of Reed and Mukherjee (1969), and Srasketa et al. (2014) respectively.

### 2.4.7 Protein Determination in the Testes

The protein concentration was determined using the Biuret method. This was used to determine the specific enzyme activity.

## 2.5 Statistical Analysis

The results are shown as the mean ± standard error of mean (SEM). To assess group homogeneity, one-

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way analysis of variance (ANOVA) was used. If there was heterogeneity, the Duncan test was used to divide the groups. A p-value of $p < 0.05$ indicated statistical significance. All analyses were carried out using the Statistical Package for Social Sciences version 24.

## 3 Results and Discussion

Table 1 shows the total amount of arsenic intake by each rat in the SA-exposed groups. The weekly average of arsenic intake ranged from 7.37 to 7.94 mg, culminating in 36.85 and 39.74 mg of arsenic ingested by groups III and IV, respectively (Babayemi et al., 2022). One of the major sources of arsenic exposure is through the consumption of contaminated water due to its ubiquitous nature (Matschullat, 2000). The ingested arsenite is absorbed into the circulatory system via the gastrointestinal tract and distributed across organs (including testes), causing imbalances in biomolecule levels and enzyme activities, resulting in metabolic disorders and organ pathologies (Babayemi et al., 2022).

Table 1: Weekly, total, and average arsenic ingested by each rat.

| Week | Group II (mg) | Group III (mg) |
|---|---|---|
| 1 | 9.24 | 7.38 |
| 2 | 9.67 | 9.51 |
| 3 | 7.06 | 5.82 |
| 4 | 6.74 | 6.78 |
| 5 | 7.00 | 7.36 |
| **Total** | **39.74** | **36.85** |
| **Arsenic per week per rat** | **7.94** | **7.37** |

Figure 1 shows the relative organ weights of the rats. There were no significant ($p < 0.05$) differences in the relative organ weights of the groups when compared to the control. Groups II, III, and IV were 15%, 4%, and 13% lower than the control group, respectively. The highest decrease was seen in Group II, where arsenic exposure resulted in organ injury due to oxidative damage from the overwhelming presence of free radical species (Babayemi et al., 2022; Souza et al., 2019). This reduction becomes more prominent over time if SA exposure is not checked.

Table 2 depicts the levels of signaling biomolecules (NO and $H_2S$) and xanthine oxidase (XO) activities in the testes. Compared to the control group, there was a 30% and 32% increase in testicular levels of mitochondrial NO and $H_2S$ in group II, respectively, but these signaling biomolecules were restored to

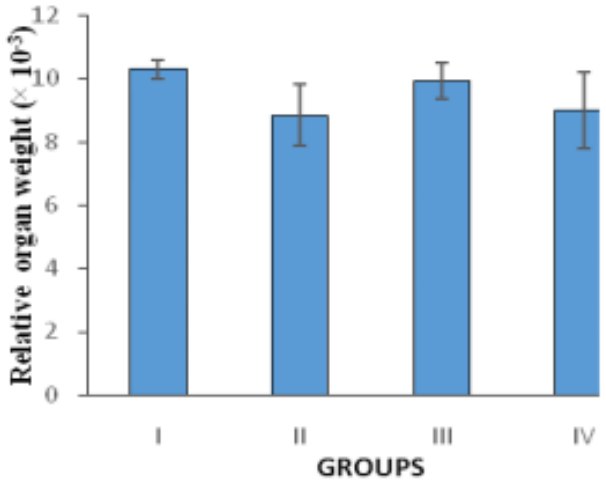


Figure 1: Relative organ weights of the rats. Values are means ± SEM.

normal levels in groups III and IV. Elevated levels of these gasotransmitters may result in imbalances and perturbations in the performance of the sperm cells (Dutta et al., 2024). There was a significant increase ($p < 0.05$) in XO activity due to arsenic exposure, with a 111% increase in group II, which was reversed to 39% in group III with selenium treatment. XO is a major contributor to reactive oxygen species, causing oxidative damage to cell membranes and enzymes, disrupting their functions (Darbandi et al., 2018). Sodium selenite was able to reduce the oxidative damage by inhibiting XO activity and reducing the oxidative power of reactive oxygen species due to its antioxidant capacity (Pisoschi et al., 2015).

The activities of some glycolytic enzymes in the testes are shown in Table 3. Exposure to sodium arsenite resulted in a 48% inhibition of hexokinase activity in group II compared to the control group, but this was reduced to 18% in group III with selenium treatment. The aldolase activity in group II was fifteen times that of group I, while in group III, it was significantly ($p < 0.05$) reduced with selenium treatment to the control level. The pattern of LDH activity in the testes was the reverse of that of hexokinase activity. When compared to the control group, LDH activity increased in the arsenic-exposed group (II) by 466%, but this was reduced to 150% and 26% with selenium administration in groups III and IV, respectively. The significant roles of testes in spermatogenesis and hormone synthesis

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Table 2: Effects of sodium selenite on signaling biomolecule levels and xanthine oxidase activities in the testes of arsenic-exposed rats.

| **Groups** | **NO levels** ($\mu$M/mg protein) | **$H_2S$ levels** ($\mu$M/mg protein) | **XO activity** (U/mg protein) |
|---|---|---|---|
| I | 349.47 ± 6.73$^{a}$ | 1096.55 ± 59.51$^{a}$ | 0.46 ± 0.18$^{a}$ |
| II | 454.78 ± 19.14$^{b}$ | 1455.74 ± 33.07$^{b}$ | 0.97 ± 0.09$^{b}$ |
| III | 318.88 ± 40.85$^{a}$ | 1125.94 ± 130.20$^{a}$ | 0.64 ± 0.10$^{ab}$ |
| IV | 285.92 ± 18.48$^{a}$ | 920.00 ± 65.68$^{a}$ | 0.40 ± 0.11$^{a}$ |

All values are expressed as mean ± SEM. Values with different superscripts indicate significant differences ($p < 0.05$) down the column.

Table 3: Effects of sodium selenite on glycolytic enzyme activities in the testes of arsenic-exposed rats.

| **Groups** | **Hexokinase** (U/mg protein) | **Aldolase** (U/mg protein) | **Lactate dehydrogenase** (U/mg protein) |
|---|---|---|---|
| I | 51.70 ± 0.64$^{c}$ | 0.98 ± 0.25$^{a}$ | 0.41 ± 0.02$^{a}$ |
| II | 21.20 ± 2.00$^{a}$ | 14.12 ± 0.96$^{b}$ | 2.32 ± 0.02$^{d}$ |
| III | 42.60 ± 1.98$^{b}$ | 1.45 ± 0.22$^{a}$ | 1.02 ± 0.03$^{c}$ |
| IV | 44.44 ± 2.68$^{b}$ | 1.10 ± 0.10$^{a}$ | 0.52 ± 0.02$^{b}$ |

All values are expressed as mean ± SEM. Values with different superscripts indicate significant differences ($p < 0.05$) down the column.

in reproduction require the availability of energy. The energy metabolic process is a target of arsenic toxicity (Chen et al., 2020). Glycolysis serves the purpose of providing quick ATP and high-energy compounds from glucose breakdown; hexokinase is one of the regulatory enzymes of this pathway. Arsenic species form complexes with hexokinase and glucose due to their structural resemblance to phosphate, inhibiting the phosphorylation of glucose and slowing down glycolysis (Machado et al., 2023). During this deprived energy condition, the cells source their energy needs using alternate pathways and enzymes. The activities of aldolase and LDH increase as alternate sources of energy production. Aldolase also participates in the pathways of glucose synthesis and fructose metabolism, and LDH provides less energy through lactate production, a toxic metabolite (Fukushi et al., 2022). These effects were reversed with SS supplementation due to its competitive capacity for active sites of enzymes with arsenic (Zwolak et al., 2020).

Table 4 shows the activities of some enzymes involved in Krebs' cycle and protein metabolism in the testes. Testicular $\alpha$-KGDH activity (one of the regulatory enzymes of the Krebs' cycle) was inhibited by arsenic exposure in group II by 84% when compared to the control group, but this was reduced to 30% by SS supplementation in groups III and IV. This agrees with the finding of Machado-Neves (2023), in which arsenic-induced toxicity inhibits the $\alpha$-KGDH activity, thereby decreasing the amount of reducing equivalents produced for the electron transport chain for ATP production which may result in energy starvation. Due to its antioxidant capacity, SS was able to reverse oxidative damage to the enzyme (Saikiran et al., 2020).

Compared to group I (control), there was a significant ($p < 0.05$) increase in testicular AST activity in group II by 29% and 135% in group III, but a 51% decrease was observed in group IV with SS supplementation. The activity of GLDH in group IV (with SS supplementation only) was reduced by 37% but increased by 41% and 22% in groups II and III, respectively, when compared to group I. AST and GLDH enzymes play a role in ammonia and energy homeostasis. Elevated enzyme activity may indicate tissue damage or disease (Giffen et al., 2002).

As a result of decreased energy metabolism, the tissue activates protein breakdown mechanisms to produce glucose from non-carbohydrate sources. This is the body's attempt to compensate for the energy loss, as indicated by an increase in AST and GLDH activity in arsenic-exposed groups. The ameliorative actions of SS on the effects of arsenic-induced testicular toxicity could apparently be based on certain possibilities. The possibility of the formation

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Table 4: Effects of sodium selenite on some enzymes of TCA cycle and protein metabolism in testes of arsenic-exposed rats.

| **Groups** | $\alpha$-**KGDH** (U/mg protein) | **AST** (U/mg protein) | **GLDH** (U/mg protein) |
|---|---|---|---|
| I | $70.95 \pm 2.71^{c}$ | $1507.44 \pm 141.13^{b}$ | $0.36 \pm 0.06^{ab}$ |
| II | $11.52 \pm 2.17^{a}$ | $1955.01 \pm 79.31^{c}$ | $0.51 \pm 0.10^{b}$ |
| III | $49.76 \pm 6.02^{b}$ | $3556.45 \pm 44.99^{d}$ | $0.44 \pm 0.04^{b}$ |
| IV | $49.00 \pm 2.36^{b}$ | $733.94 \pm 115.03^{a}$ | $0.23 \pm 0.03^{a}$ |

All values are expressed as mean ± SEM. Values with different superscripts indicate significant differences ($p < 0.05$) down the column.

of inactive complexes of As-Se, Se antioxidant bolstering ability, and fast excretion of methylated As species (Zwolak, 2020).

## 4 Conclusion

In summary, this research corroborates the use of SS against SA-induced testicular toxicity by ameliorating the effects of SA on the activities of XO, hexokinase, aldolase, LDH, $\alpha$-KGDH, AST, and GLDH, as well as the testicular levels of NO and $H_2S$. This research supports the use of SS as a safe remedy for the treatment of SA-induced testicular toxicity.

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