**American Journal of BioScience**
2016; 4(3-1): 1-4
Published online February 23, 2016 (http://www.sciencepublishinggroup.com/j/ajbio)
doi: 10.11648/j.ajbio.s.2016040301.11
ISSN: 2330-0159 (Print); ISSN: 2330-0167 (Online)

# Nephrotoxic Effects of Arsenic in Albino Mice

**Suman Sharma[1], Anjali Singh Gill[1], Zorawar Singh[2, *], Charanjit Kaur[1], P. Vijaya[1]**

[1]Department of Zoology & Environmental Sciences, Punjabi University, Patiala, India
[2]Department of Zoology, Khalsa College, Amritsar, Punjab, India

**Email address:**
zorawarsinghs@rediffmail.com (Z. Singh), drsumansharma.15@rediffmail.com (S. Sharma), gillanjali3@gmail.com (A. S. Gill), sanghacharanjit@ymail.com (C. Kaur), pvijaya193@gmail.com (P. Vijaya)

**To cite this article:**
Suman Sharma, Anjali Singh Gill, Zorawar Singh, Charanjit Kaur, P. Vijaya. Nephrotoxic Effects of Arsenic in Albino Mice. *American Journal of BioScience.* Special Issue: Recent Trends in Experimental Toxicology. Vol. 4, No. 3-1, 2016, pp. 1-4.
doi: 10.11648/j.ajbio.s.2016040301.11

**Abstract:** Arsenic is an ubiquitous element in the environment. In the present study we investigated the effects of arsenic trioxide (AsIII) on lipid peroxidation and on the activity of antioxidant enzymes in the kidney of albino mice. Albino mice were divided into three groups. Group I were kept as control. Group II were administrated an oral dose of arsenic trioxide (3mg/kg b.w.). Group III were given an oral dose of arsenic trioxide (6mg/kg b.w.). They were acclimatized for 15 days before administration of arsenic trioxide. The autopsies were done from all the groups at 15 days post-treatment. Malondialdehyde (MDA) and activities of Superoxide dismutase (SOD) and Catalase (CAT) were analyzed in kidney of albino mice. The results showed a significant increase in concentration of MDA ($p<0.05$). Activities of SOD and CAT were found to decrease significantly ($p<0.05$). The results indicated that arsenic induced oxidative stress in albino mice by producing free radicals and lipid peroxidation where antioxidant enzymes were used as biomarkers.

**Keywords:** Arsenic, Malondialdehyde, Lipid Peroxidation, Oxidative Stress, CAT, SOD

## 1. Introduction

Arsenic occurs in both organic and inorganic forms in nature but inorganic species of arsenic [As(III) and As(V)] represent a potential threat to the environment, human and animal health due to their carcinogenic and other effects [1]. Humans and animals are generally exposed to arsenic by consumption of contaminated ground water or through food chain [2]. Arsenic has an affinity toward the SH group of proteins [3] that leads to inhibition of cellular respiration, impaired glycolysis and oxidative process [4] and finally death of cells. Though almost all the systems are being affected, liver and kidneys are most susceptible to arsenic toxicity [5].

The exact mechanism by which arsenic induces cancer still remains poorly understood. Many different mechanisms of action have been proposed and some potential mechanisms include genotoxicity, cell proliferation, altered DNA repair and DNA methylated oxidative stress, co-carcinogenesis, and tumor promotion [6]. Among them, the oxidative damage is considered to play an important role in arsenic carcinogenesis.

Arsenic initiates cytotoxicity by introducing oxidative damage [7]. Oxidative stress arises when reactive oxygen species (ROS) such as free radicals, lipid hydroperoxides, aldehydes, hydrogen peroxides are generated, which can react with cellular constituents such as thiols and lipids and alter the antioxidant defense systems [8-10]. During a metabolic process arsenic gets methylated in liver by arsenic methyltransferase to form organo-arsenics that are excreted by kidney through urine. Continuous exposure to arsenic damages the kidney through generation of excessive free radicals inside the nephrons. This study was undertaken to assess the impact of arsenic exposure on the antioxidant defense system in kidney of albino mice.

## 2. Materials and Methods

### *2.1. Test Animals*

Albino mice were procured from Central Research Institute, Kasauli. They were kept and acclimatized to the laboratory conditions for 15 days under optimal conditions of light and temperature and *ad libitum* access to distilled water. The animals were handled with humane care in accordance with the guidelines of the Institutional Animal Ethical Committee.

### *2.2. Chemicals*

Arsenic trioxide was obtained from Qualikems fine Chemical Pvt. Ltd., New Delhi. The dose was prepared by preparing stock solution and administered orally to mice.

### *2.3. Experimental Design*

The mice were divided into three groups. Group I – Animals were given distilled water and kept as control. Group II – Mice were administered a single oral dose of 3mg/kg body weight of arsenic. Group III – Mice were given a single oral dose of 6 mg/kg body weight of arsenic. Mice were autopsied 15 days post treatment. Kidneys were removed and blotted dry.


***Figure 1.*** *Division of Albino mice into different groups under experimental setup. Group I represents control mice. Group II and III represent exposed mice to different arsenic concentrations.*

### *2.4. Biochemical Studies*

Kidney homogenates were prepared with the help of tissue homogenizer in 3 ml of phosphate buffer and used for estimation of SOD, CAT and Malondialdehyde.

### *2.5. Statistical Analysis*

Significance of the results between control and experimental data was compared using Student's *t*-test. All the statistical analyses were performed using windows statistical software Minitab v14 (Minitab Inc.). $p<0.05$ was taken as statistical significant value.

## 3. Results and Discussion

Arsenic exposure produces free radicals that cause damage to lipid, protein, and DNA of the body [11]. Though the exact mechanism by which arsenic exposure brings about deterioration of kidneys is still not known but ROS production may be one of the causes and is also observed in this present work with both doses of arsenic. Arsenic treatment led to a significant increase in MDA content as compared to control (Figure 2). Increased lipid peroxidation is thought to be the consequence of oxidative stress which occurs when the dynamic balance between peroxidant and antioxidant mechanism is impaired [12]. The amount of ROS in cells is dependent on both the production of ROS by the mitochondrial electron transport chain and their removal by ROS-detoxifying enzymes. Recently, some researchers have evaluated the effects of arsenic intermediate metabolites (monomethylarsonous acid, MMA III, and trivalent dimethylarsinous acid, DMAIII) on the induction of ROS. It has been clearly confirmed that the generation of ROS is specifically induced in the endoplasmic reticulum by exposure to DMA III, while previous studies have shown that MMA III induces ROS generation specifically through inhibition of the activities of complexes II and IV in mitochondria [13-14]. Increased lipid peroxidation has been reported even at low doses of arsenic treatment in rats [15]. Arsenic attaches to the glomerular membrane due to its lipophilicity and increases lipid peroxidation [16].

Further, Arsenic exposure leads to significant decrease in superoxide (SOD) and Catalase (CAT) content in kidneys (Figure 3). Antioxidant enzymes are considered to be the first line of cellular defense against oxidative damage. SOD is an antioxidant metalloenzyme that reduces superoxide radicals to water and molecular oxygen [17]. CAT is a haemoprotein, which reduces hydrogen peroxide to molecular oxygen and water gutteridge [18]. Arsenic intoxicated kidneys in experimental mice showed decreased activities of antioxidant enzymes in the present study. SOD is an important antioxidant enzyme responsible for the elimination of superoxide radical and plays an important role in maintaining cellular ROS balance. A marked decrease in activity of SOD ($p<0.05$) was observed in mice administered with 6mg/kg body weight of arsenic as compared to Group I control mice and is probably due to the over production of free radicals in the kidney [19-20]. A decrease in the activity of SOD can be owed to an enhanced superoxide production during arsenic metabolism [21]. SOD catalyzes the dismutation of superoxide anions and prevents the subsequent formation of hydroxyl radicals [22].

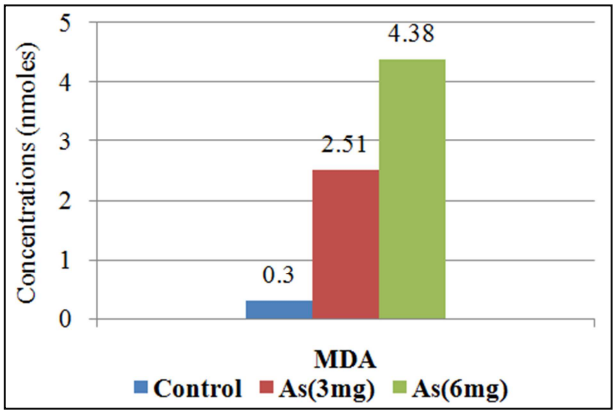


***Figure 2.*** *Concentration of MDA in control and arsenic treated groups.*

Wang et al. [23] also reported decreased SOD activity in serum, liver and kidneys of pigs after arsenic intoxication and suggested that the accumulation of superoxide anion radicals

might be responsible for increased lipid peroxidation. They also observed decreased CAT activity in kidneys which may be due to impaired ability of catalase to detoxify overproduction of $H_2O_2$ in arsenic exposed pigs. Use of MDA in assessing oxidative stress has been validated by different researchers [24, 25]. In one of our previous study, MDA has also been found to increase under higher oxidative stress conditions, even in humans [26]. Therefore, it is concluded that the arsenic exposure leads to varying degree of changes in antioxidant defense mechanisms and tissue architecture.

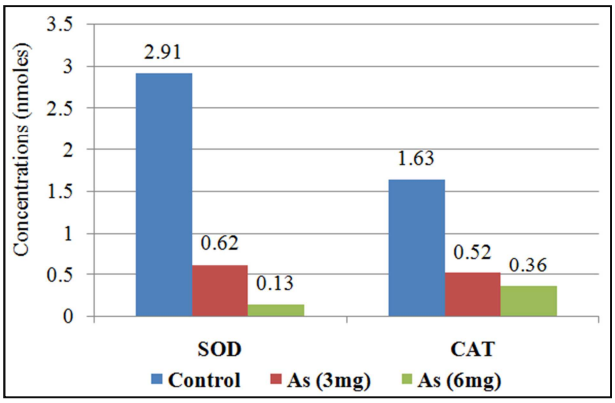


***Figure 3.*** *Concentration of SOD and CAT in control and arsenic treated groups.*

## 4. Ethical Permission

Ethical permission for the present study was taken from the institutional ethical committee vide letter no. 107/99/CPCSEA/2013-03.

## Acknowledgements

The authors gratefully acknowledge the Department of Zoology & Environmental Sciences, Punjabi University, Patiala, for providing the necessary facilities to pursue the research work and UGC for providing financial assistance in the form of RGNF fellowship [F1-17.1/2013-14/RGNF-2013-14-SC-PUN-40235/(SA-iii/website)] to pursue this research work.

## References

[1] T. S. Singh and K. K. Pant (2004) Equilibrium, kinetics and thermodynamic studies for adsorption of As (III) on activated alumina. Sep. Purif. Technol, 36: 139-147.

[2] P. H. Patra, S. Bandyopadhyay, M. C. Bandyopadhyay, T. K. Mandal (2013) Immunotoxic a genotoxic potential of arsenic and its chemical species in goats. Toxicol. Int, 20: 6-10.

[3] D. Ghosh, S. Ghosh, S. Sarkar, A. Ghosh, N. Das, K. Das, Saha (2010) Quercetin in vesiculardelivery systems: Evaluation in combating arsenic-induced acute liver toxicity associated gene expression in rat model. Chem. Biol. Interact, 186: 61-71.

[4] P. B, Tchounwou, A. K, Patolla, J. A, Centeno (2003) Carcinogenic and systemic health effects associated with arsenic exposure-acritical review. Toxicol. Pathol 31: 575-88.

[5] P. H. Patra, S. Bandyopadhyay, R. Kumar, B. K. Datta, C. Maji, S. Biswas (2012) Quantitative imaging of arsenic and its species in goat following long term oral exposure. Food Chem. Toxicol, 50: 1946-50.

[6] M. F. Hughes (2002) Arsenic toxicity and potential mechanisms of action. Toxicol. Letters, 33: 1-16.

[7] S. Singh, Z. Singh, S. S. Hundal (2015) Toxicological aspects of arsenic in different animal models: A Review. Int. J. Anal. Pharma. Biol. Sci., 4 (2): 6-15.

[8] S. M. Keyse, R. M. Tyrell (1989) Heme oxygenase is the major 32-kDa stress protein induced in human skin fibroblasts by UVA radiation, hydrogen peroxide and sodium arsenite. Proc. Natl. Acad. Sci, USA, 86: 99-103.

[9] T. S. Wang, H. Huang (1994) Active oxygen species are involved in the induction of micronuclei in XRS-5 cells. Mutagenesis, 9: 253-257.

[10] S. X. Liu, M. Athar, I. Lippai, C. Waldren, T. K. Hei (2001) Induction of oxygen radicals by arsenic: implications for mechanism of genotoxicity. Proc. Natl. Acad. Sci, 98: 1643-1648.

[11] P. Manna, M. Sinha, P. C. Sil (2008) Arsenic-induced oxidative myocardial injury: Protective role of arjunolic acid. Arch. Toxicol, 82: 137-49.

[12] S. J. Flora, S. Chouhan, G. M. Kannan, M. Mittal, H. Swarnkar (2008) Combined administration of taurine and monoisoamyl DMSA protects arsenic induced oxidative injury in rats. Oxid. Med. Cell. Longev, 1: 39-45.

[13] H. Naranmandura, S. Xu, S. Koike (2012) The endoplasmic reticulum is a target organelle for trivalent dimethylarsinic acid (DMA*III*)-induced cytotoxicity. Toxicol. App. Pharmacol., 260: 241–249.

[14] H. Naranmandura, S. Xu, T. Sawata (2011) Mitochondria are the main target organelle for trivalent monomethylarsonous acid (MMA III)-induced cytotoxicity. Chem. Res. Toxicol., 24: 1094–1103.

[15] A. N. Chaudhuri, S. Basu, S. Chattopadhyay, S. D. Gupta (1999) Effect of high arsenic content in drinking water on rat brain. Indian. J. Biochem. Biophys, 36: 51-4.

[16] E. O. Farombi, O. A. Adelow, Y. R. Ajimoko (2007) Biomarkers of oxidative stress and heavy metals levels as indicators of environmental pollution in African cat fish (*Clarias gariepinus*) from Nigeria ogun river. Int. J. Environ. Res. Public Health, 4: 158-65.

[17] J. M. McCord, B. B. Keele, I. Fridovich (1976) An enzyme based theory of obligate anaerobis: The physiological functions of superoxide dismutase. Proc. Natl. Acad. Sci, 68: 1024-31.

[18] J. M. Gutteridge (1995) Lipid peroxidation and antioxidants as biomarkers of tissue damage. Clin. Chem., 41: 1819-28.

[19] A. M. Al-Attar (2011) Antioxidant effect of vitamin E treatment on some heavy metals – induced renal and testicular injuries in male mice. Saud. J. Biol. Sci, 18: 63-72.

[20] C. G. Alimba, A. A. Bakare, O. O. Aina (2012) Liver and kidney dysfunction in wistar rats exposed to municipal landfill leachate. Res. Enivron., 2: 150‑63.

[21] A. J. Searle, R. Wilson (1980) Glutathione peroxide effect ofhydroxyl and bromine free radicals on enzyme activity. Int. J. Radiat. Biol, 37: 213-217.

[22] J. A. Imlay, S. Linn (1988) DNA damage and oxygen radical toxicity. Sci, 240: 1302-1309.

[23] L. Wang, Z. R. Xu, X. Y. Jia, J. F. Jiang, X. Y. Han (2006) Effects of Arsenic (AsIII) on Lipid Peroxidation, Glutathione Content and Antioxidant Enzymes in Growing Pigs. Asian-Aust. J. Anim. Sci, 19: 727-733.

[24] Z. Singh, I. P. Karthigesu, P. Singh, R. Kaur (2014) Use of malondialdehyde as a biomarker for assessing oxidative stress in different disease pathologies: A Review. Iranian J. Pub. Health 43 (3): 7-16.

[25] Z. Singh, P. Chadha, S. Sharma (2013) Evaluation of oxidative stress and genotoxicity in battery manufacturing workers occupationally exposed to lead. Toxicol. Int., 20 (1): 95-100.

[26] Z. Singh, P. Chadha (2013) Oxidative stress assessment among iron industry grinders. Biochem. Cell. Arch., 12 (1): 65-68.