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RESEARCH ARTICLE

PROTECTVE EFFICACY OF GINGER AGAINST ARSENIC INDUCED HEPATOTOXICITY IN SWISS ALBINO MICE

Suman Sharma and Anjali Singh Gill

Department of Zoology and Environmental Sciences, Punjabi University, Patiala-147002, Punjab, India.

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Corresponding Author

Suman Sharma

Abstract

Arsenic is an ubiquitous element in the environment and it causes potential threat to human as well as animal health due to its carcinogenic activities. The present study was conducted to evaluate the protective role of ginger against arsenic induced hepatotoxicity in albino mice. Albino mice were divided into three groups. **Group I** were control mice, **group II** received an acute dose of arsenic (5 mg/kg bw) orally, **group III** received an acute dose of arsenic followed by daily administration of ginger (20mg/kg bw) orally. Autopsies were done on 15 days post treatment. Arsenic treatment leads to increase in weight of liver. Biochemical analysis of treated group showed decrease in antioxidant enzymes i.e. SOD and CAT but increased MDA content in liver as compared to control group. Ginger administration to mice decreased the weight of mice and showed significant protection in the alleviation of arsenic induced liver injury.

INTRODUCTION

Exposure to heavy metals has become a common problem throughout the world due to contaminated drinking water, food and air. Arsenic is one of the most important metalloids and persists in organic, inorganic and elemental form in nature. Trivalent arsenic species are most toxic than pentavalent arsenic compounds (Chowdary et al., 2008). A chronic exposure through contaminated drinking water has become an increasing global problem of public health concern. Epidemiological studies have shown that inorganic arsenic exposure may lead to cancer of the liver, kidney, bladder, prostate, skin, lung, colon and nasal cavity (Jin et al., 2004). The liver is a major target organ for both arsenic metabolism and toxicity. Arsenic induced hepatic injury is known to be exerted through excess production of reactive oxygen species. The harmful expressions of arsenic are primarily due to an imbalance between pro-oxidant and antioxidant homeostasis in physiological system and also due to its fascination to bind sulfhydryl groups of proteins and thiols of glutathione (GSH) (Mathews et al., 2012).

Several classes of antioxidant dietary compounds have been suggested to present health benefits, and there is evidence that consumption of these products leads to reduction in the expression of various oxidative stress biomarkers (Peng et al., 2000; Halliwell et al., 2002; Jacob et al., 2003). A positive correlation has also been established between dietary supplementation with certain vegetables and plants and the reduction of toxic effects of various toxicants, environmental agents including heavy metals (Nandi et al., 1997).

Ginger rhizome, having a pleasant aroma and pungency, has been used as a spice and medicine for thousands of years. It contains the pungent principles, gingerols and shogoals. which are phenolic in nature and pharmacologically are the most active components of ginger (Afzal et al., 2001). Ginger extract possesses antioxidative characteristics, since it can scavenge superoxide anion and hydroxyl radicals. It contains a host of compounds which includes acid resins, vitamin C compounds [folic acid, inositol, choline and panthotenic acid]

(Arfeen, 2000), gingerol, sesquiterpene, vitamin B3 and B6, volatile oils and bio-trace elements [Ca, Mg, P and K] (Ernst and Pittler, 2000). The medicinal values of ginger have been intensively reported.

Therefore in the present investigation, protective effects of ginger against arsenic induced biochemical changes in the liver of Swiss albino mice have been studied.

MATERIALS AND METHODS

Animals: Swiss albino mice weighing 20±2g were procured from CRI, Kasuali. They were kept and acclimatized to the laboratory conditions for 15 days under optimal conditions of light and temperature. They had *ad libitum* access to tap water. The animals were handled with human care in accordance with the guidelines of the Institutional Animal Ethical Committee.

Chemicals: Arsenic trioxide was bought from Qualikems Fine Pvt. Limited, New Delhi. It was dissolved in double glass distilled water and administered orally to mice. **Ginger** was obtained from local market and aqueous extract was prepared by the method of Hussein (2012) and was also administered orally to mice.

Experimental Design: The mice were divided into three groups of six mice each. **Group I –** Control animals were given distilled water. **Group II** – Animals were administered an acute dose of 5mg/kg bw of arsenic orally for 15 days. **Group III** –Animals were injected with an acute dose of 5 mg/kg bw of arsenic followed by a daily dose of 20 mg/kg bw of ginger for 15 days. Autopsies were done on 15 days post treatment.

Tissue analysis: Liver homogenates were prepared with the help of tissue homogenizer in 3 ml of phosphate buffer and used for estimation of antioxidant enzymes. The catalytic activity of hepatic catalase (CAT) enzyme was estimated from the rate of decomposition of H_2O_2 by the method of Aebi (1983). SOD activity in liver was determined by the method of Das et al. (2000). Lipid peroxidation was measured as malondialdehyde a thiobarbutaric acid reacting substance, using the method of Wilbur et al. (1949).

Statistical analysis: The data was analyzed by using Student's *t*-test.

RESULTS AND DISCUSSION

Arsenic is highly toxic and corrosive to gastrointestinal tract resulting into partial anorexia and gastro-intestinal disturbances followed by loss of body weight in arsenic intoxicated animals as compared to control animals. Gora et al. (2015) evaluated that arsenic at high doses causes acute hepatic injury and hepatocellular necrosis causing leakage of hepatocellular enzymes into blood Further, they observed that the extent of injury to the hepatocytes is generally detected by the activity of antioxidant enzymes. In the present study, it is observed that the relative weight of liver was more in arsenic exposed mice in comparison to control mice. This observation is in confirmation with the study of Shiguang and Beynen (2001), they also reported that liver weight significantly increased in male rats fed with 100 mg/kg arsenic diet for a period of 2 weeks. As liver is a very active site of metabolism, it is the main site of arsenic intoxication, where arsenic methyltransferase enzymes mediate the methylation process with *S*-adenosylmethionine as the methyl donor and GSH as an essential co-factor (Mazumder, 2005).

The measurement of lipid peroxidation byproducts and the status of antioxidant enzymes like SOD and CAT are appropriate indirect ways to assess the proxidant-antioxidant status in the tissues and the estimation of MDA, a by-product of lipid peroxidation, continues to be a reliable method to assess the degree of peroxidative damage to cell membrane. In the present investigation, lipid peroxidation was enhanced, while the activities of SOD and CAT were significantly decreased in the liver of treated mice (Bouaziz et al. 2015). The liver can accumulate arsenic with repeated exposures. Liver is the main site of synthesis of proteins, therefore hepatic damage caused by arsenic leads to decrease in the levels of antioxidant enzymes with arsenic trioxide. Recent studies have clearly demonstrated that arsenic compounds during their metabolism in cells generate reactive oxygen species like superoxide anion, hydroxyl radical and hydrogen peroxide leading to oxidative stress. Liu et al (2001) suggested Enhanced production of free radicals and inhibition of antioxidant enzymes as possible mechanisms to explain arsenic induced oxidative damage.

A significant reduction in SOD levels was observed in both the experimental groups (group II and III) as compared to control group. Gora *et al*. (2015) suggested that superoxide dismutase is an important antioxidant enzyme responsible for the elimination of superoxide radical. The exhausted SOD levels observed in this study might be due to overproduction of free radicals in the body. A decrease in the activity of SOD can be owed to an enhanced superoxide production during arsenic metabolism (Searle and Wilson, 1980). SOD catalyzes the dismutation of superoxide anions and prevents the subsequent formation of hydroxyl radicals (Imlay et al. 1988). In the present study, the decreased SOD activity in liver of mice suggested that the accumulation of superoxide anion

radical might be responsible for increased lipid peroxidation following arsenic treatment (Maiti and Chatterjee, 2000).

In the present study a decrease in catalase activity in liver. Kono and Fridovich (1982) reported that superoxide radical also inhibited the activity of catalase. Exposure to arsenic decreased the catalase activity (Kirkman and Gaetani, 1984). Lee and Ho (1995) also observed that Arsenic inhibited the catalase activity in human fibroblast cells. CAT catalyzes the removal of H_2O_2 formed during the reaction catalyzed by SOD. So, the present study, the decreased CAT activity indicated that exposure to arsenic may result in impaired ability to detoxify H_2O_2 via catalase and accumulation of H_2O_2 occured in liver of mice.

A significant increase in Lipid peroxidation in arsenic treated group as compared to control. It is well known that tissue retention of arsenic increases with the length of exposure due to the lesser rate of excretion of arsenic than exposure which causes its accumulation in tissues. Liver being the main workhouse of metabolism, arsenic was accumulated at high concentration in liver of the arsenic exposed groups in the present study. Ramos et al. (1995) demonstrated a tendency for a positive correlation between arsenic concentration and lipid peroxidation level in liver, kidney and heart of rats following acute exposure to arsenic. Flora et al. (2002) reported that GaAs induced lipid peroxidation in blood, liver and kidney of rats. Their study indicated that the lipid peroxidation was increased by high arsenic level and duration of exposure. Arsenic induced MDA production could be due to the impairment of cells natural protective system. In this study, there was an inhibition of peroxidative damage as evidenced by reduced MDA level, and elevation of CAT and SOD activities in the arsenic and ginger co-treated mice. This finding is consistent with previous findings that ginger significantly lowered lipid peroxidation Morakinyo et al. (2008) by maintaining the of the antioxidant enzymes; SOD, CAT and GSH in the rat testes activities Ahmed et al. (2002)

Recently, much attention has been focused on the protective effects of antioxidants and the possibility of using antioxidants in the treatment of hepatocytic toxicity. Accumulating evidences suggest that the effects of ginger against oxidative damage may be attributed to its antioxidant properties (Katiyar et al., 1996; Vimala et al., 1999). The prevention of arsenic trioxide induced oxidative stress in mice by ginger shown by the results obtained from this study, suggests the protective effects of ginger against arsenic trioxide induced toxicity. Thus, ginger supplementation aids in amelioration of hepatotoxicity induced by arsenic in albino mice.

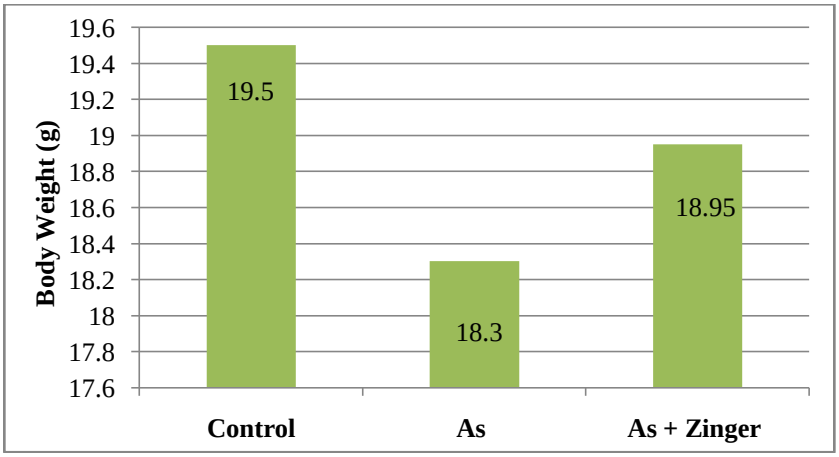

Fig.1 Body weight of mice in control and treated groups.

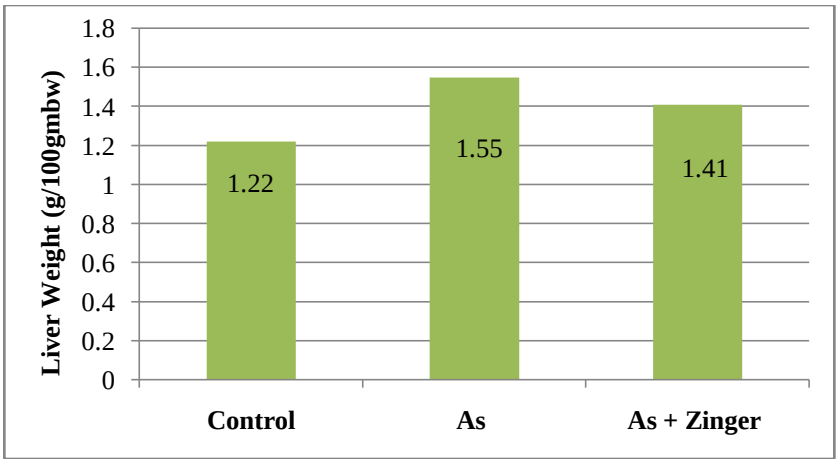

Fig.2 Weight of liver in control and treated groups.

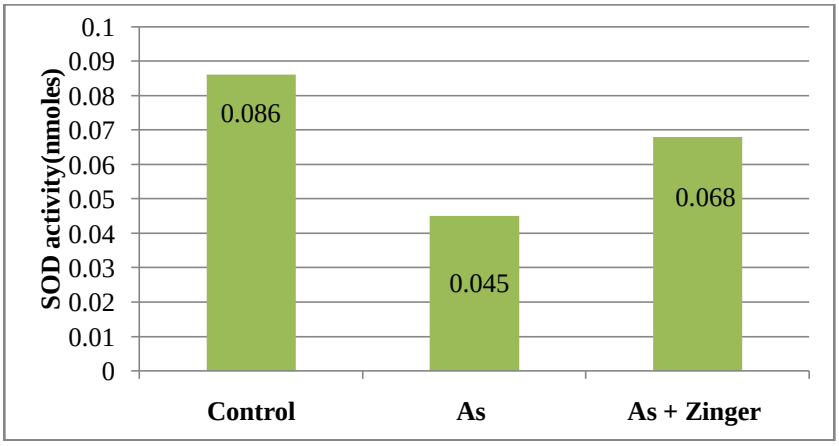

Fig.3 SOD activity in liver of control and treated group.

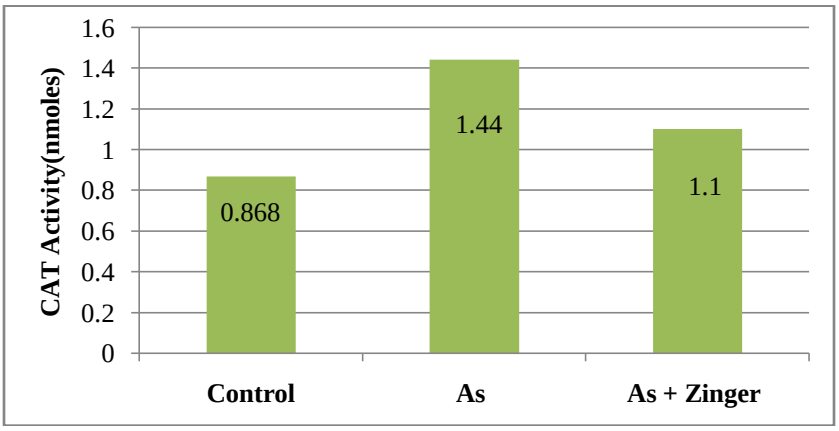

Fig.4 CAT activity in liver of control and treated group.

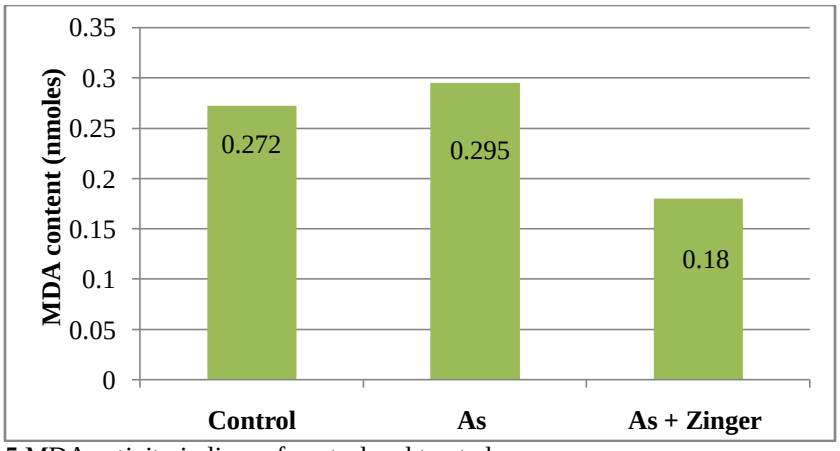

Fig.5 MDA activity in liver of control and treated group.

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