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Protective role of lycopene against arsenic induced renal toxicity In male mice

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The present work was designed to evaluate the protective role of lycopene against renal histopathological changes due to arsenic toxicity. The animals were divided into four groups with six in each: Group I: served as control animals received saline, Group II: receive lycopene (5 mg/kg b.w). Group III: received once daily sodium arsenite at a dose of 5 mg/kg b.w. Group IV: receive once daily sodium arsenite plus lycopene. Histological examinations revealed that sodium arsenate caused glomeruli hypercellularity, disappearance of Bowman's capsule, lymphocytic infiltrations, interstitial hemorrhages among the renal tubules. Sodium arsenate treated animals showed positive reaction to Bax in renal tubules as compared with controls. Co-administration with lycopene decrease and improve pathological changes in the kidney.

Keywords: Sodium arsenite, Kidney, Lycopene, Histopathology, Immunohistochemistry, Mice

INTRODUCTION

Arsenic (As) is a naturally occurring toxic metalloid, present in food, soil and water. As is found in the environment in both forms inorganic and organic. Inorganic As (iAs) is the most occurance form of As in underground water stock (Paul et al., 2007). Arsenite (the trivalent form) and arsenate (the pentavalent form) are the most common forms of arsenic in water-soluble. Trivalent arsenic is more toxic than pentavalent arsenic and its inorganic forms are more toxic than organic forms (Bertolero et al., 1987). Environmental arsenic exposure mainly occurs from arsenic-contaminated drinking water, burning high arsenic coal and use of arsenic-containing herbicides, insecticides and preservatives (Flora et al., 2008). The World Health Organization (WHO) has set the standard limit for arsenic to 10 parts per billion (ppb) (Kayajanian, 2003). However, millions people are exposed to levels of inorganic arsenic concentrations above 10 ppb the drinking water (IARC, 2004). Inorganic arsenic is a human carcinogen associated with skin, lung and urinary bladder cancer and potentially linked to cancer of the kidney, liver and prostate. Umit et al., (2016) illustrated the protective effects of thymoquinone against apoptosis and oxidative stress by arsenic in rat kidney. (Chu and Crawford-Brown, 2006) reported that bladder cancer was associated with exposure to concentration as low as 10 ppm of inorganic arsenic. (Tchounwou et al., 2003 and Navas-Acien et al., 2006) found that there was a strong correlation between chronic arsenic exposure and various noncancer human diseases, such as diabetes, atherosclerosis, and chronic pulmonary diseases. In addition, there is a considerable debate about several non-cancerous effects that may result from exposure to arsenic such as hypertension, cardiovascular disease, anemia, neurologic disorder, and liver and kidney diseases (Szymanska-Chabowska et al., 2002). The

dissolved arsenic compounds are readily absorbed after ingestion and affects nearly entire organs of the body. kidney is an important target organ for arsenic toxicity (Guha Majumdar, 2005). Wang, X. et al., 2014 described Nephroprotective effect of astaxanthin against trivalent inorganic arsenic-induced renal injury in wistar rats. Many authors have demonstrated that acute and chronic exposure to Arsenic can cause kidney injury, apoptosis and increase the risk of renal cancer (Nandi et al., 2006; Pastoret et al., 2012; Anwar-Mohamed et al.,2012; Yajima et al. (2012); Xu et al., 2012; Ranaa et al., 2018).

Plant products are known to exert their protective effects by scavenging free radicals and modulating antioxidant defense system. Lycopene is a natural pigment synthesized by plants and predominantly found in tomato, watermelon and grapefruit. It is the most prevalent carotenoid in the western diet. Lycopene has been shown to have the highest antioxidant activity among the carotenoids in cell protection against free radicals (Atessahin et al., 2006; Mure and Rossman, 2001). Recently, lycopene has become a focus of interest because of its highly efficient antioxidant scavenging activity against singlet-oxygen and free radicals. Lycopene is one of the most effective antioxidants in the carotenoid family (Amarowicz, 2011; Yonar and Sakin, 2011; Yonar, 2012). Lycopene has been suggested to have strong antioxidant potency in vitro, almost being 100 times more efficient in quenching singlet oxygen (1O2) than vitamin E (Mordente et al., 2011). Many studies has been demonstrated the anticancer activity of Lycopene, such as prostate, stomach, breast and lung cancer (Mahmooduzzafar et al., 2007; Atessahin et al., 2006). It has been suggested that lycopene can prevent carcinogenesis by protecting vital biomolecules including DNA, proteins, enzymes and lipids (Scolastici et al., 2007). Lycopene was found to be protective against chemotherapeutic-induced renal damage in several studies (Atessahin et al., 2005; Dogukan et al., 2011; Wang et al., 2010).

Therefore, this study was designed to investigate the possible protective role of lycopene against the histopathological changes in the renal tissue of mice administered sodium arsenate.

MATERIALS AND METHODS

Chemicals

Sodium arsenite (NaAsO2) and Lycopene were purchased from Sigma Chemical Company, St Louis, USA.

Animals

Twenty-four healthy adult male Swiss albino mice weighing 25-30 g were used in this study. Animals were left to acclimatize in the laboratory for at least one week at a conditions of photoperiod (12 h light: 12 h dark) and a room temperature of 23 ± 2 ◦C before the experiments. They were maintained on a standard diet and water was available ad libitum.

Experimental design

Animals were divided randomly into four groups of six animal each.

Group1 (control group): animals received 0.5 ml normal saline solution + 0.5 ml corn oil orally by gavage for 30 consecutive days.

Group 2 (Lycopene group): were administered by lycopene suspended in corn oil by gavage at the doses of (5 mg/kg b.w/day.)

Group 3 (arsenic group): were received sodium arsenite ($NaAsO_2$) at a dose of 5 mg/kg b.w/day by gavage for 30 consecutive days. The dose of $NaAsO_2$ and the period of treatment were selected based on previous studies (Yousef et al., 2008).

Group 4 (arsenic and Lycopene group): were received daily with both sodium arsenite (5 mg/kg b.w.) plus Lycopene (5 mg/kg b.w.) by gavage. The total doses of sodium arsenite given to animals were 150 mg/kg b.w. At the end of experimental period, animals were sacrificed by decapitation, kidneys were immediately removed and parts were fixed into 10% formalin for overnight fixation to perform histopathological examinations.

Histopathological examination:

Small parts of fixed kidney tissue from each animal were processed for routine light microscopy. Paraffin blocks were prepared and 5 µm thick sections were taken. Routine hematoxylin and eosin (H&E) staining was used then sections were examined under light microscope.

Immunohistochemistry

Immunolocalization for Bax was performed using the avidin-biotin complex method. Slides were deparaffinized and blocked for endogenous peroxidase with hydrogen peroxide in methanol for 20 mm, antigen retrieval for 15 mm. The slides

were allowed to cool. The monoclonal antibody was applied overnight followed by the biotinylated secondary antibody and the ABC complex. Diaminiobenzidine (DAB) was applied for 20 min at room temperature as chromogen. Slides were counterstained with hematoxylin, dehydrated, and covered by coverslip. In negative control slides, the same system was applied with replacement of the monoclonal antibody by diluted normal bovine serum. Bax immunostaining was performed using polyclonal rabbit-anti-human at a dilution of 1:50.

RESULTS

Histopathological changes in kidney tissues of mice are shown in Fig. 1. The kidney in the control animals showed normal histological structure in glomeruli, proximal and distal tubules (Fig.1A). After 4 weeks of sodium arsenite exposure (Figs. 1B&C)), there were glomeruli dilation and hypercellularity, disappearance of Bowman's capsule, glomerular capillaries and cellular proliferation. Some of the renal tubules were degenerated, lymphocytic infiltrations were observed. There were interstitial hemorrhages and necrosis among the renal tubules. After 4 weeks of lycopene plus sodium arsenite-treatments, there were improvements in both glomerular and renal tubules pathological changes (Fig. 1D)

Immunohistochemical observation

Histopathological changes in the kidneys exposed to sodium arsenite were in accordance with the distribution of Bax immunoactivity. In control treated animals, kidney sections showed negative immune reaction to Bax (Fig.2A). sodium arsenite treated animals (Fig. 2B) showed more positive reaction to Bax in renal tubules as compared with controls. Sodium arsenite plus lycopene treated animals showed less reaction to Bax (Fig. 2C).

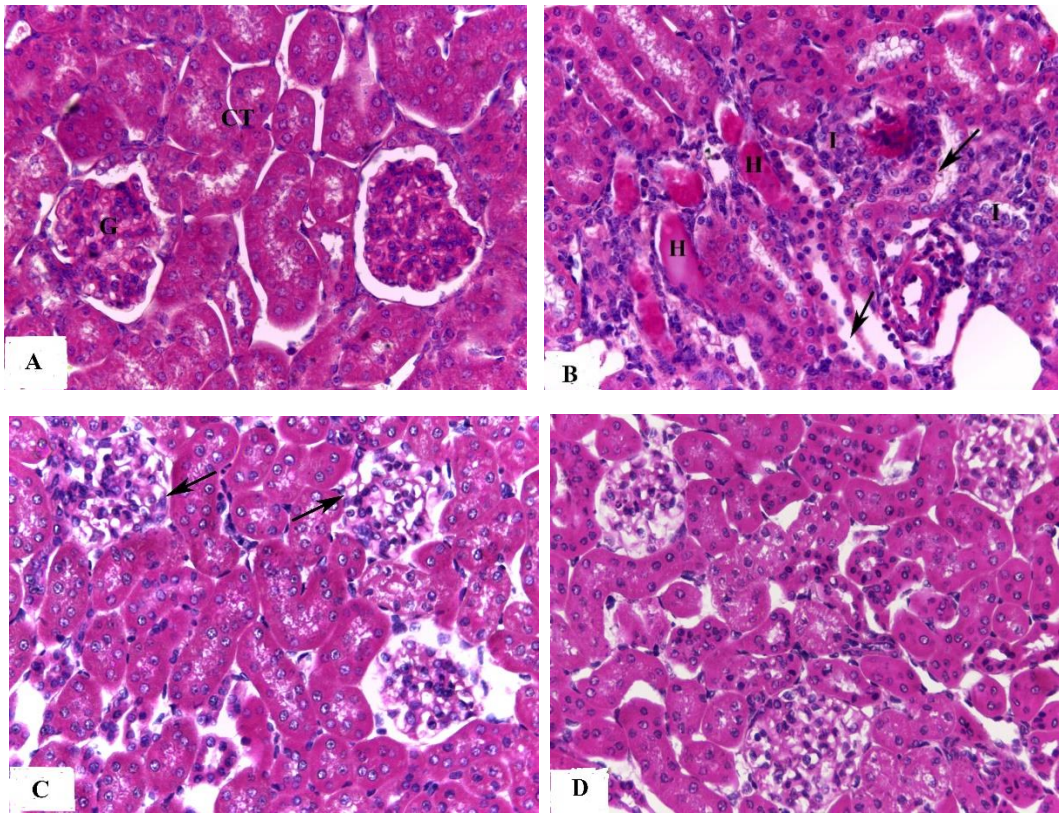

Figure1. A: Photomicrograph of kidney sections of control mice showing glomerulus (G) and convoluted tubules (CT), H&E, X200). B: Photomicrographs of mice kidney section exposed to sodium arsenite displaying lymphocytic infiltration (I), interstitial hemorrhage (H) and degeneration of convoluted tubules (arrows), H&E, X200). C: Photomicrographs of mice kidney section exposed to sodium arsenite showing dilated corpuscle (arrows), H&E, X200). D: Photomicrographs of mice kidney section exposed to sodium arsenite plus lycopene treatment. (H&E, X200).

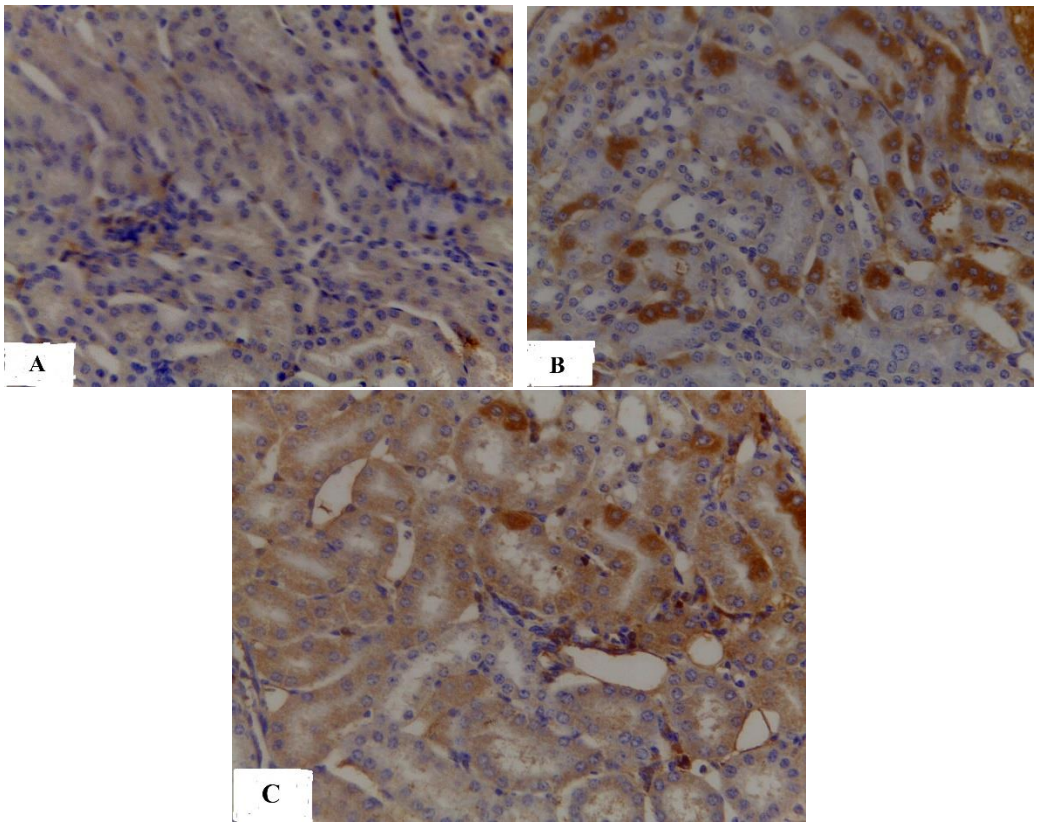

Figure 2: Immunohistochemical localization of Bax in the renal tissue of mice. Control (A), sodium arsenite (B) and sodium arsenite plus lycopene treated animals (C).

DISCUSSION

Arsenic is present in the environment as a heavy metal. Arsenic responsible for the generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Results of the present work suggest that kidney may be a target of arsenic toxicity. Chronic arsenic exposure causes various disease and abnormalities in the several organs like kidney (Chowdhury, 2001). Chronic kidney disease is closely associated with exposure to arsenic, which can be characterized with decrease estimated glomerulus filtration rate and inflammation (Ranaa et al., 2018). Results of the present study demonstrated that mice treated for 4 weeks with sodium arsenate showed many histopathological changes in kidney such as dilation of glomerular capillaries and tubules, hemorrhage, lymphocytic infiltration and degeneration of convoluted tubules. Results of this study are in accordance with Sinha et al. (2008) who reported that when the renal tissue of mice received sodium arsenate, histopathological results of swollen and necrosis were observed in renal epithelial cells of convoluted tubules which are more sensitive to arsenic due to their reabsorptive activity. Many studies revealed that pathological changes in mice kidney exposed to arsenic is due to oxidative stress, which is the important feature of cell apoptosis and necrosis.

Results of the present study are in agreement with Qureshi et al., (2009) who stated that the renal corpuscles in animals treated with sodium arsenate showed congestion and dilatation of glomerular capillaries and hypercellularity and obliteration of the capsular space. Apoptosis is a common feature of renal toxicity induced by chemicals or drugs. The Bax gene was the first identified pro-apoptotic member of the Bcl-2 protein family. In this study, sodium arsenite produced high Bax protein expression. The immunoactivity of Bax in the kidney tissue was mainly concentrated in the epithelial cells of renal tubules.

CONCLUSION

The results of this investigation shows that

arsenic cause histopathological changes in mice kidney and lycopene co-treatment ameliorates arsenic-induced renal damage in male mice.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

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AUTHOR CONTRIBUTIONS

Gamal H. Abdel-Rahman designed the study, prepared the Figures and wrote the manuscript. Abdallah M. Sliai performed the experiments. The authors read and approved the final version.

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