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Original Article

Ameliorating effects of vitamin E and coriander (*Coriandrum sativum*) seed extract on lead-induced renal damage in Swiss albino mice

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A B S T R A C T

Ameliorating effects of vitamin E and coriander (*Coriandrum sativum* L.) seed extract on lead-induced renal damage in Swiss albino mice were investigated in the present study by gross and histological studies. Intoxication with a particular dose of lead acetate was done for 42 days through the oral route. The intoxicated mice were divided into three groups for treatment purposes. The first, second and third groups of mice were treated orally with the vitamin E, coriander seed extract and both the vitamin E & coriander seed extract, respectively. Treatment was done for 42 days. In the present study, the weight of the left kidney was significantly ($p<0.05$) reduced in lead-intoxicated mice in comparison to the control group. Lead acetate was found to cause nodular lesions as well as epithelial cast in the kidney. Vitamin E and coriander seed extract were found effective in the treatment of lead intoxicated mice. Kidneys were found normal in the vitamin E and coriander seed extract treated groups. These results of this study suggested that vitamin E and coriander seed extract are being used to protect against lead-induced kidney injuries.

Introduction

Humans and animals are exposed to various types of environmental pollutants present in our surroundings. The use of toxic chemicals or xenobiotics or certain synthetic compounds, like heavy metal compounds, is responsible for this situation (Jagadeesan and Pillai, 2007). Cadmium (Cd), copper (Cu), arsenic (As), nickel (Ni), mercury (Hg), lead (Pb), zinc (Zn), chromium (Cr) and aluminium (Al) and other hazardous metals are included in this list of heavy metals (Sullivan *et al.*, 2002). Experimental studies have shown that many heavy metals have induced renal failure associated with significant histopathological and physiological changes (Suradkar *et al.*, 2009; Soudani *et al.*, 2010). Lead toxicity is one of the major environmental health threats (Juberg *et al.*, 1997). Pathogenesis of lead toxicity is mainly attributed to lead-induced oxidative stress. Chronic lead exposure disrupts the pro-oxidant/antioxidant balance existing within the mammalian cells (Senapati *et al.*, 2001). Lead is reported to cause oxidative stress by generating the release of reactive oxygen species (ROS) such as superoxide radicals, hydrogen peroxide and hydroxyl radicals and lipid peroxides (El-Nekeety *et al.*, 2009).

Many studies found that lead has a wide range of toxic biochemical and histological effects where it deposits in soft organs like the kidney (Loumbourdis, 2003), ovary (Taupeau *et al.*, 2001), liver (Galleano and Puntarulo, 1997), brain (Schwartz *et al.*, 2002) and endocrine system (Gorbel *et al.*, 2002). Our previous study found that lead acetate causes morphological deformities of seminiferous tubules and irregular arrangement of spermatogenic cells in the seminiferous tubules of mice testis (Islam *et al.*, 2019). We also found that lead acetate causes nodular lesions and congestion in the central vein in mice's liver (Jahid *et al.*, 2020). Lead causes serious harmful effects on the kidney. Most lead-associated renal effects or toxicity result from the ongoing chronic or current high acute exposure (Moniem *et al.*, 2010). It has been reported that chronic lead nephropathy is an irreversible renal disease that develops over months or years of excessive exposure (Lin *et al.*, 2001). The lead was also found to cause dilation of tubules, sloughing of tubular epithelium, the disintegration of tubules, glomerular shrinkage, widened urinary space of the Bowman's capsule and swollen proximal convoluted tubules (Kansal *et al.*, 2012).

Vitamins are essential to maintain normal metabolic activities and homeostasis in the body. Vitamin C and vitamin E are low molecular mass antioxidants that scavenge or quench free radicals (Janisch *et al.,* 2005). Antioxidants like vitamin C (Hsu *et al.,* 1998) and vitamin E (Patra *et al.,* 2011) are used to prevent the incidence and lessen oxidative stress in tissues. Vitamin E has an antioxidant function, and other functions include enzymatic activities, gene expression, and neurological function (Songthaveesin *et al.,* 2004). It also functions as a free radical scavenger, scavenging superoxide, hydrogen peroxide and hydroxyl radicals (Makker *et al.,* 2009).

The coriander seed is one of the most popular spices in the world. Coriander is also popular for its antioxidant properties. It has been found that the antioxidative property of coriander seed is related to the large amounts of tocopherols, carotenoids and phospholipids (Ramadan and Morsel, 2004). The antioxidant property of coriander extracts could be directly related to the scavenging function against ROS, and the elevation of antioxidant make up. It removes harmful mineral residue such as lead and mercury from the body through the faces and urine. Coriander (*Coriandrum sativum*) increases chloramphenicol acetyltransferase, salicylate dioxygenase functions and glutathione content and decreases lipid peroxidation level in lead-induced tissues of mice. Coriander extract increases antioxidant enzymes' activities (glutathione peroxidase, catalase) but reduces the formation of lipid peroxides in rats (Chithra and Leelamma, 1999).

There has been a considerable number of study on chemical treatment for lead poisoning (Marija *et al.,* 2004). However, there is a scarcity of research on treatment of lead intoxication by natural products (Ashour, 2002). Furthermore the exact role of vitamin E and coriander seed extract is not clearly elucidated and the relationship between vitamin E, coriander seed extract and renal cells still requires further investigation. Therefore, the present study investigated the beneficial effect of vitamin E and coriander seed extract on lead-induced renal injuries in the kidney of mice.

Materials and methods

Animals

The study was conducted in the Department of Anatomy and Histology, Faculty of Veterinary Science, Bangladesh Agricultural University, Mymensing-2202 during the period from January, 2017 to December, 2017. The experimental Swiss albino mice (male) were collected from the Department of Pharmacy, Jahangirnagar University, Dhaka. The collected mice were six weeks of age and about 25-28 grams at the time of collection. All mice were raised under confinement as an intensive system. Mice were kept in cages at room temperature. Water and feed were supplied *ad libitum* to the mice. All experimental protocols were approved by the Animal Welfare and Ethical Committee, Faculty of Veterinary Science, Bangladesh Agricultural University.

Chemicals

Lead (II) acetate trihydrate and Vitamin E were purchased from Merck (Darmstadt, Germany). Aqueous coriander extract was prepared in the Department of Pharmacology, Faculty of Veterinary Science, Bangladesh Agricultural University, Mymensingh. Coriander extract was prepared according to previous research (Kansal *et al.,* 2012).

Experimental design

Adult Swiss albino male mice were divided into different groups according to the experimental design and treated by oral gavages as follows-

Group I: Control group, 10 mice were fed with only standard rat diet and tap water for 6 weeks. After six weeks, samples were collected from 5 mice and the remaining 5 mice were kept as a control for the next 6 weeks.

Group II: Lead intoxicated group, 25 mice were treated with 60 mg/kg b.w. dose of lead acetate by oral gavage once daily for 6 weeks. After six weeks, samples were collected from 5 mice and 5 mice were further intoxicated upto the end of the experiment. Other 15 mice of the intoxicated group were divided into three groups (Group III, IV and V) each having 5 mice.

Group III: Mice were treated with 150 mg/kg b.w. vitamin E (diluted in soya oil) by oral gavage once daily for 6 weeks.

Group IV: Mice were treated with 300 mg/kg b.w. coriander extract (diluted in distilled water) by oral gavage once daily for 6 weeks.

Group V: Mice were treated with both 150 mg/kg b.w. vitamin E (diluted in soya oil) and 300 mg/kg b.w.coriander extract (diluted in distilled water) by oral gavage once daily for 6 weeks.

The dose of lead acetate, vitamin E and coriander seed extract was selected based on a previous study (Kansal *et al.,* 2012; El-Tohami and Ali, 2014). After completion of the experiment, the animals were given a one-day rest and were killed under light chloroform anaesthesia. The right and left kidneys were collected from all the mice of different groups.

Gross and histology

In the gross study, parameters such as color, weight and length were taken into consideration. All kinds of abnormalities were also observed. The color of the kidney was compared with the color of the kidney of the control group by eye observation. Weight was measured in grams by electronic balance. The length of the kidney of different groups was measured by a graded scale. The unit of length measurement was millimeters. After gross observation, samples were preserved in 10% formalin and Bouin's fluid. After proper fixation, samples were processed for histological study. Hematoxylin and Eosin (H& E) staining protocol was applied. The detailed histological study was done using a light microscope.

Photomicrographs

Photographs for the present study were taken according to a previous study performed in the same laboratory (Jannat *et al.,* 2018). Necessary photomicrographs were taken with Olympus BX 51 photographic light microscope and placed to illustrate the result better.

Statistical analysis

The collected data were then analyzed using the Statistical Package for Social Sciences (SPSS) for Windows version 12.0 software. All data were represented as mean ± standard error (SE). Data were subjected to one-way analysis of variance (ANOVA) followed by Student's *t*-test. Statistical probability of $P < 0.05$ was considered to be significant.

Results

Gross observation

The reddish-brown with a smooth and shiny surface of kidneys were found in the control group of mice (Fig. 1A).

Kidneys of other groups were also reddish-brown. However, nodular lesions and abnormal shape were found in the lead intoxicated group. Massive changes were found in the periphery of cortex of kidney due to nodular lesion (Fig. 1B). The kidney's appearance was found normal in the vitamin E treated group, coriander seed extract-treated group, and vitamin E and coriander seed extract (combined) treated group. The nodular lesion was not observed in these groups (Fig. 1 C-E).

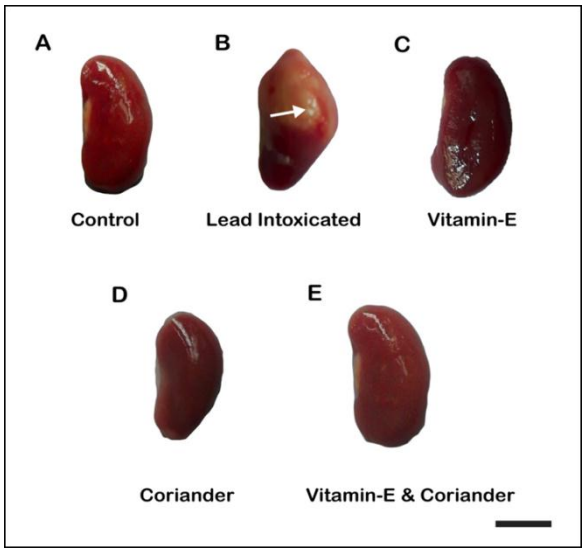

Fig. 1 (A-E): Gross observation of the left kidney in mice*. Normal appearance of kidney was found in the control group (A). Nodular lesion (white arrow) and abnormal shape were found in the lead intoxicated group (B). The appearance of the kidney was found normal in the vitamin E treated group (C), coriander extract-treated group (D), and vitamin E and coriander extract-treated group (E). Scale bar = 10 mm. *Only left kidneys of different groups are presented here because there was no gross difference between the left and right kidney.

Effects on weight and length of kidney

The mean weight of left and right kidney in the control group, intoxicated group, vitamin E treated group, coriander seed extract-treated group, and vitamin E and coriander seed extract (combined) treated group was 0.30 ± 0.01 g, 0.24 ± 0.01 g, 0.27 ± 0.01 g, 0.27 ± 0.01 g, 0.26 ± 0.02 g, and 0.30 ± 0.01 g, 0.27 ± 0.01 g, 0.28 ± 0.01 g, 0.28 ± 0.01 g, 0.28 ± 0.01 g, respectively (Fig. 2 A-B). The weight of the left kidney in the lead intoxicated group was significantly ($p<0.05$) reduced compared to the control group.

The mean length of the left and right kidney in the control group, intoxicated group, vitamin E treated group, coriander seed extract-treated group, and vitamin E and coriander seed extract (combined) treated group was 10.86 ± 0.34 mm, 10.36 ± 0.18 mm, 11.07 ± 0.25 mm, 10.50 ± 0.31 mm, 10.79 ± 0.26 mm and 10.75 ± 0.27 mm, 10.29 ± 0.15 mm, 10.93 ± 0.23 mm, 10.43 ± 0.20 mm and 10.86 ± 0.26 mm, respectively (Fig. 2 C-D). There was no significant difference observed between the control and treated groups.

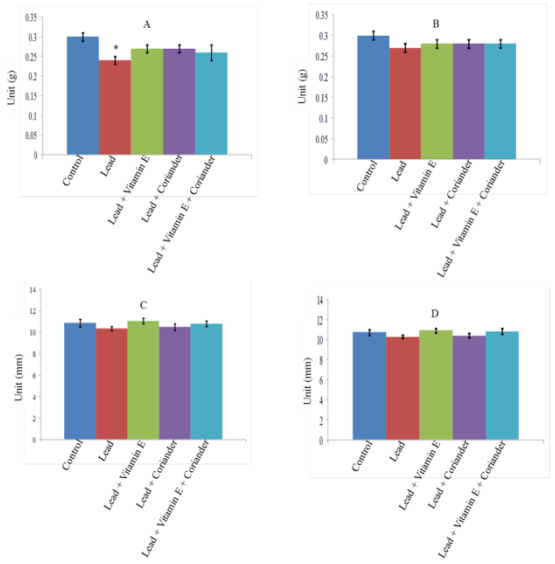

Fig. 2 (A-D): Weight of the left kidney (A), the weight of the right kidney (B), length of the left kidney (C) and length of the right kidney (D) of mice in different groups (Mean ± standard error).* Significant in comparison to the control group. Significant at 5% ($p<0.05$) level.

Histological observation

In the present study, the kidney was found with normal histological architecture in the control group (Fig. 3A). In the lead intoxicated group, the epithelial cast was found in the urinary space (Fig. 3B). However, the epithelial cast was not observed in the urinary space in vitamin E treated group, coriander seed extract-treated group, and vitamin E and coriander seed extract (combined) treated group (Fig. 3 C-E). In these groups, the kidney's appearance was found in normal. Glomeruli were found normal surrounded by the Bowman's capsule, a proximal convoluted tubule, descending and ascending portions of the straight loop of Henle, and a distal convoluted tubule.

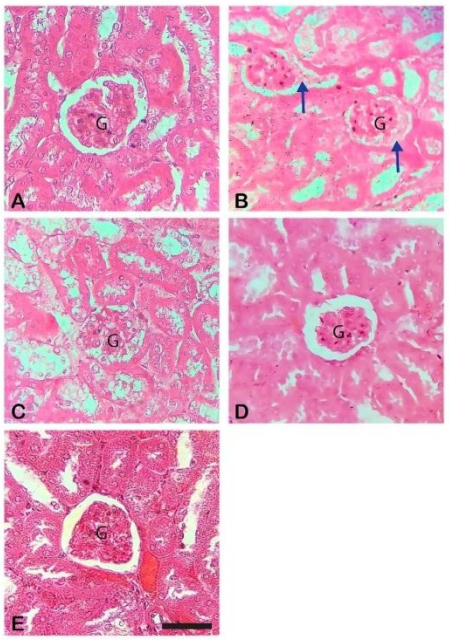

Fig. 3(A-E): Histological observation of kidney in mice (H&E)*. Normal appearance of kidney was found in the control group (A). Epithelial cast (blue arrow) was found in urinary space in the lead intoxicated group (B). The appearance of the kidney was found normal in the vitamin E

treated group (C), coriander extract-treated group (D), and vitamin E and coriander extract-treated group (E). *Histological observation of the left kidney is presented here because there was no histological differentiation between the left and right kidney. G=Glomerulus. Scale bar: 1 µm.

Discussion

Heavy metals are widely distributed in the environment, and it is well known that most of them can create physiological, biochemical and histological turbulence. Humans may be exposed to all these metals from a variety of sources, including polluted air, water, soil and food. The evaluation of the potential toxicity of heavy metals is, therefore, necessary for the risk assessment of human beings who have been normally exposed to these substances. Various scientific research have shown that the degree of toxicity of different metals depends on the dosage, duration, administration route and other physiological factors, especially nutritional factors (Chowdhury, 2009). The present study shows that mice chronically intoxicated with a mixture of some heavy metals show a marked impairment in the function of the kidneys, confirmed by histopathological changes.

In the present study, the kidneys of all mice were reddish-brown in color. Nodular lesions and abnormal shape were found grossly in the lead intoxicated group. There was no report regarding nodular lesions in the kidney of mice. The actual mechanism of nodule formation is unknown. However, this may be due to increased cellular activity and nuclear interruption in the mechanism of lead detoxification. An abnormal shape of the kidney was found due to the formation of a large nodule.

The kidney was found in normal in the vitamin E treated group, coriander seed extract treated group, and vitamin E and coriander extract (combined) treated group after lead intoxication. The nodular lesion was not observed in these groups. This is due to the antioxidant properties of vitamin E and coriander seed extract. The findings of other researchers support this. It has been reported that vitamin E plays the role of ideal antioxidant to increase tissue protection from oxidative stress (Flora *et al.,* 2012). It has also been stated that aqueous and ethanolic extracts of *Coriandrum sativum* can prevent or slow down the oxidative damage induced by lead in mice (Kansal *et al.,* 2012). More probably, these antioxidative properties played an important role in ameliorating the pathology of the nodular lesion.

The weight of the left kidney in the lead intoxicated group was significantly ($p<0.05$) reduced compared to the control group. This is partially supported by the findings of other researchers who found that lead caused a decrease in rats' growth rate when fed with lead (Nabil *et al.,* 2012). More probably, the decreased weight of the kidney is due to reduced body weight.

In the lead intoxicated group, the epithelial cast was found in the kidney's urinary space in the present study that is similar to a previous report that found casts in the kidney of lead nitrated exposed mice (Kansal *et al.,* 2012). The kidney histology regained the normal architecture after treated with the vitamin E, coriander seed extract, and vitamin E and coriander seed extract (combined) in lead intoxicated mice. Glomeruli were found normal surrounded by the Bowman's capsule, a proximal convoluted tubule, descending and ascending portions of the straight loop of Henle, and a distal convoluted tubule. There was no epithelial cast in the urinary space in these groups. This is due to the antioxidative properties of vitamin E and coriander seed extract, which is strongly supported by the previous studies showing that vitamin E, a chain-breaking antioxidant, not only scavenges oxygen radicals from the membrane but also intercepts pyroxyl and alkoxyl radicals which are generated during the conversion of lipid hydroperoxides that fuel the peroxidative chain reaction thereby preventing this damaging process from propagating through the plasma membrane (Nadia *et al.,* 2013).

Conclusion

Lead is the most abundant toxic metal in the environment. The present findings revealed that lead has detrimental effects on the kidneys of mice. In the kidney, lead was found to cause nodular lesion as well as epithelial cast in the urinary space. Treatment with vitamin E and coriander seed extract was found effective in lead intoxicated mice. Nodular lesions and epithelial cast were diminished in the kidney after individual and combined vitamin E and coriander seed extract treatments. In conclusion, the present study showed that vitamin E and coriander seed extract have ameliorating effects on lead metals-induced renal injuries. This study, therefore, suggested that vitamin E and coriander seed extract could be a useful preventive agent against the effects of the heavy metals.

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Authors' contribution

MR Islam designed the experiment, and MA Jahid performed the experiment. MA Jahid and U Ayman analyzed the data and wrote the draft. I Hasan, M Afrin, MZI Khan and MR Islam critically revised the manuscript. MR Islam supervised the project.

Conflict of interest

The author declares that no conflict of interest exists.

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