Original Article

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Histomorphological Profile of Liver and Kidney Tissues of Albino Wistar Rats Following Exposure to Cadmium-Induced Damage and Ascorbic Acid Supplementation

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Abstract

Introduction: Cadmium is a common heavy metal toxicant that can cause diverse tissue toxicities and pathologies. Conversely, ascorbic acid is a natural anti-oxidant that can ameliorate cytotoxic effects of tissue toxicants. In this study, the objective was to assess the histomorphological profile of liver and kidney tissues of albino Wistar rats after exposure to cadmium-induced damage and ascorbic acid supplementation. **Subjects and Methods**: 24 animals were divided into four groups (1-4) comprising of six animals each (n=6). Normal control group 1 was given distilled water, test control group 2 given 5 mg/kg Cadmium chloride and test groups 3 and 4 given 5 mg/kg Cadmium chloride + 100 mg/kg ascorbic acid and 5 mg/kg + 200 mg/kg ascorbic acid respectively. The route of the 21 days administration was oral. Thereafter, the liver and kidney of experimental animals were harvested, weighed and processed. **Results:** Only the test control group 2 showed significant ($p < 0.05$) reduction in mean organ weight compared to normal control group 1. Similarly, only the test control group 2 animals showed significant alterations in the liver and kidney histomorphological profile compared to normal control group 1. **Conclusion:** The ascorbic acid exhibited prominent ameliorative effect against damaging effect of cadmium exposure leading to relative reparation of liver and kidney histomorphology in albino Wistar rats.

Keywords: Liver histomorphology, Kidney histomorphology, Cadmium, Ascorbic acid, Wistar rats.

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Introduction

Environmental toxicants have become a major source of health hazards to humans thereby impacting negatively on the health and overall well-being of exposed individuals. Among these environmental toxicants, heavy metals stand out as major cause various tissue pathologies and threat to health status of an individual.[1] During exposure to tissue toxicants including heavy metals, the liver and kidney tissues are among the most susceptible bodily tissues to their toxic effects.[2,3] One of such heavy metal is cadmium whose exposure has been linked with various tissue toxicities including nervous, respiratory, reproductive, cardiovascular, hepatic and renal tissues.[4-6]

Cadmium is a non-biodegradable heavy metal which possesses a relatively long half-life and readily accumulates in bodily tissues wherein it produces tissue toxicities leading to tissue dysfunction.[7-10] The cadmium exposure and accumulation in these tissues cause significant reduction of activities of certain anti-oxidant enzymes and induced membrane lipid peroxidation and oxidative damage.[11-13] The oxidative tissue damage that follows cadmium exposure have been described to results from generation of reactive oxygen species such as hydrogen peroxide and thiobarbituric acid reactive substances that act to impair the anti-oxidant defence system.[14-16]

On the other hand, anti-oxidants, such as ascorbic acid, act to ameliorate the cytotoxic effects of tissue toxicants. It functions as electron-carrier similar to other free radical scavengers such as glutathione, β-carotene and Vitamin E.[17,18] This anti-toxic property of ascorbic acid invariably translates into cytoprotection of histomorphology of biological tissues particularly hepatic and renal tissue.

Therefore, the objective of this study was to assess the histomorphological profile of liver and kidney tissues of albino Wistar rats after exposure to cadmium-induced damage and ascorbic acid supplementation.

Subjects and Methods

Experimental animals

This study involved twenty four (24) albino Wistar rats with body weight ranging between 150 g – 185 g. The experimental animals were procured from and housed at the Central Animal House Facility of Igbinedion University,

Okada, Edo State, Nigeria where the study was subsequently conducted. During the study period, the animals were kept in cages under hygienic conditions, at 24±20C room temperature, 57±2% relative humidity and 12-12 hour light-darkness cycle. The experimental animals were allowed regular access to animal feed and drinking water ad libitum.

Experimental design

The experimental animals were randomly grouped into four groups (1 – 4) comprising six (6) animals per group (n=6).

Groups	Description	Number of animals (n)	Exposure	Dosage/Body weight
1	Normal control	6	No induction, No treatment	5 mL/kg distilled water
2	Test Control	6	Induced + No treatment	5 mg/kg Cadmium chloride in drinking water
3	Test group	6	Induced + treated	5 mg/kg Cadmium chloride in drinking water + 100 mg/kg ascorbic acid
4	Test group	6	Induced + treated	5 mg/kg Cadmium chloride in drinking water + 200 mg/kg ascorbic acid

All administrations were conducted orally using an orogastric gavage coupled to a calibrated hypodermic syringe, everyday for 21 days.

Tissue processing, sectioning and staining

After the study period, experimental animals were sacrificed and their liver and kidney tissues harvested, weighed and processed for histological staining. During tissue processing, 10% Neutral Buffered Formalin was used to fixed the tissue, alcohol was used as dehydrating agent and xylene was used as clearing agent. Processed liver and kidney tissues of experimental animals were embedded in molten paraffin wax and allowed to solidify to form tissue blocks. The liver and kidney tissue blocks were sectioned at 5 µ thickness and stained by Haematoxylin and Eosin (H & E) technique for subsequent histomorphological study.

Histopathological study

Stained liver and kidney tissue sections were viewed under microscope and photomicrograph of each section generated for further analysis. The histomorphological profile of the liver and kidney tissues of experimental animals was assessed and observable histopathological changes were quantified using the image-J software (National Institute of Health, Bethesda, MA, USA). All data generated during the study were recorded and statistically analyzed.

Statistical analysis

The data obtained during this study were presented as mean ± standard error of mean (SEM) following their analysis using the IBM-SPSS (version 20, IBM Corp., NY, USA). Comparison of statistical results was done using t-test and analysis of variance (ANOVA) with the level of statistical significance set at $p < 0.05$.

Results

Assessment of weight of experimental tissues

The mean weight values of liver tissue of experimental animals in normal control group 1, test control group 2 and treated groups 3 and 4 were given in [Figure 1] while the mean weight values of kidney tissue of experimental animals in corresponding groups were given in [Figure 2]. From these findings, the mean weight values of liver and kidney tissues of experimental animals showed significant ($p < 0.05$) decrease in test control group 2 but an insignificant decrease among the test groups 3 and 4 when compared to the normal groups 1.

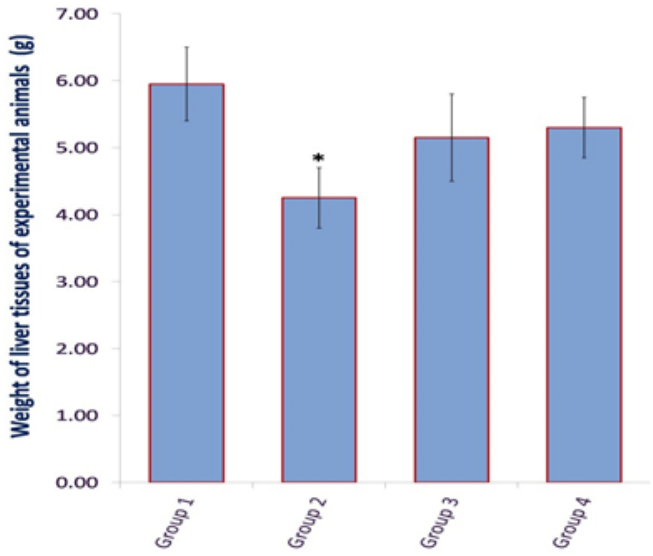

Figure 1: Mean weight values of liver tissues of experimental animals in normal control group 1, test control group 2 and treated groups 3 and 4 (* indicates significant difference at $p < 0.05$ in comparison to Groups 1).

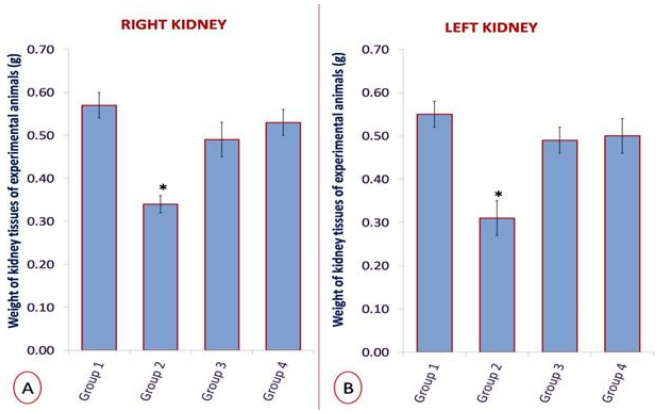

Figure 2: Mean weight values of Right (A) and Left (B) kidney tissues of experimental animals in normal control group 1, test control group 2 and treated groups 3 and 4 (* indicates significant difference at $p < 0.05$ in comparison to Groups 1).

Histopathological results

The microscopic examination of liver and kidney tissue of experimental animals showed the histomorphological profile of normal control group 1, test control group 2 and treated groups 3 and 4 animals [Figures 3 & 4]. The quantified histomorphological alterations in liver tissues included necrosis, inflammation and steatosis [Figure 5] while that of

the kidney tissues included necrosis, inflammation and glomerular congestion [Figure 6].

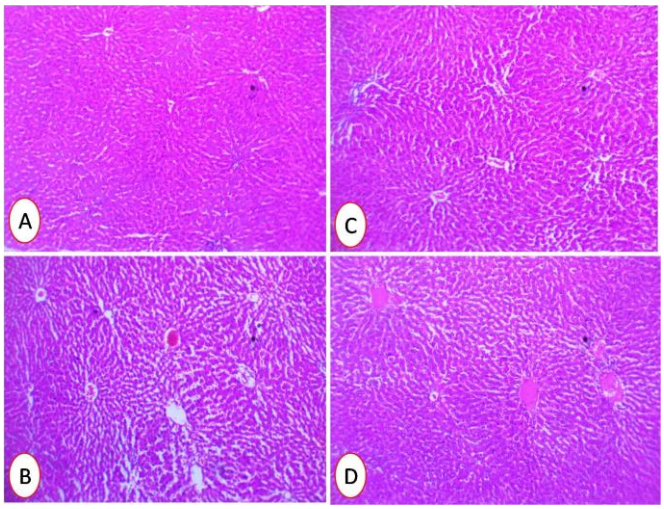

Figure 3: Micrograph showing liver tissue histomorphology of experimental animals in normal control group 1 (A), test control group 2 (B) and treated groups 3 (C) and 4 (D).

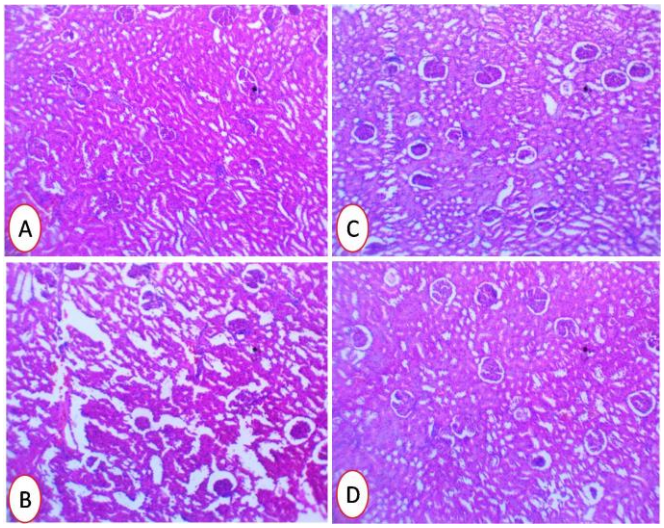

Figure 4: Micrograph showing kidney tissue histomorphology of experimental animals in normal control group 1 (A), test control group 2 (B) and treated groups 3 (C) and 4 (D).

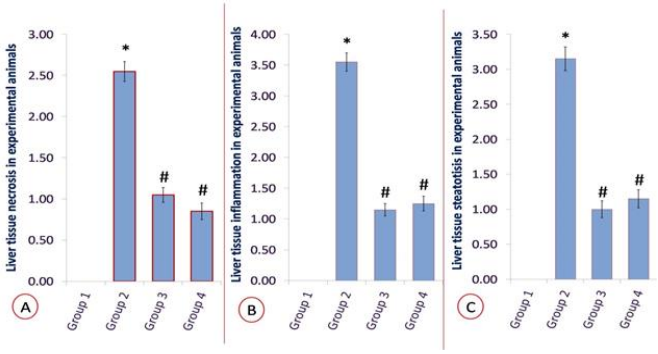

Figure 5: Evaluation of liver tissue necrosis (A), inflammation (B) and steatosis (C) in normal control group 1, test control group 2 and treated groups 3 and 4 experimental animals (* and # indicate significant difference at p < 0.05 in comparison to Groups 1 and 2 respectively).

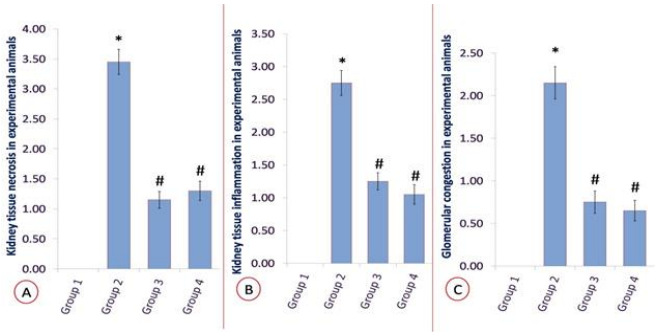

Figure 6: Evaluation of kidney tissue necrosis (A), inflammation (B) and glomerular congestion (C) in normal control group 1, test control group 2 and treated groups 3 and 4 experimental animals (* and # indicate significant difference at p < 0.05 in comparison to Groups 1 and 2 respectively).

Discussion

The potency of cadmium as tissue toxicant affecting wide range of bodily tissues including the liver and kidney has been widely reported.[19-21] Such cadmium-induced toxicity can adversely impact the weight of distinctly exposed tissues and the overall body weight.[22,23] According to the results of this study [Figures 1&2], test control group 2 animals, exposed to cadmium only, showed significant reduction of mean weight of liver and kidney tissues relative to normal control group 1 animals. In test groups 3 and 4 animals, due to ascorbic acid supplementation, the mean weight of liver and kidney tissues showed marginal, non-significant reduction compared to the normal control group 1.

Furthermore, the cadmium-induced tissue toxicity has been indicated by altered haematological and biochemical parameters.[24,25] Asides the significant alterations in different haematological and biochemical indicators of cadmium-induced hepato-renal tissue toxicity, cadmium exposure may also leads to pathological changes in the histomorphology of exposed tissue. However, the ascorbic acid has been described as a potent antioxidant that can ameliorate adverse or deleterious effects of tissue toxicant such as cadmium exposure. Studies by Rehka et al.[26] and Sharaf et al.[27] reported that protective activity of ascorbic acid against toxic effects of heavy metals such as cadmium is characterized by modulation of heamatological and biochemical markers of tissue toxicity and resultant histomorphological reparation of the exposed tissue.

According to the findings of this study [Figures 3&5], cadmium exposure resulted in significant inflammatory response in the hepatic tissue of experimental animals as well as other histomorphological changes such as necrosis and steatosis. Also, the exposure resulted in significant inflammatory response in kidney tissue of experimental animals and other histomorphological changes such as necrosis and glomerular congestion [Figures 4&6]. Conversely, the treatment of experimental animals with variable dosage of ascorbic acid showed prominent reparation of histomorphology of exposed liver and kidney tissues.

During tissue toxicity, including cadmium-induced toxicity, free radicals generated by oxidative damage to membrane lipids and lipoproteins can cause cellular damage and

apoptosis.[20,28] This can further culminate into pathological changes in the histomorphology of exposed tissues. However, ascorbic acid is a natural antioxidant that can potently cause inhibition or scavenging of free radicals thereby ameliorating the damaging effects of tissue toxicants.[29] It is an essential vitamin and anti-toxin which potently functions to reduces the deleterious effects of toxic agents in biological tissues. Each molecule of ascorbic acid contains two hydrogen atoms that bear two high-energy electrons which can be readily donated to reduce oxidation by free radicals thereby neutralizing or ameliorating the deleterious effects of tissue toxins.[18,30,31]

These previous studies highlighted the anti-oxidant and cytoprotective activity of ascorbic acid which corroborated the findings of this study on ameliorative activity of ascorbic acid against damaging effect of cadmium exposure on histomorphology of liver and kidney tissues of experimental animals.

Conclusion

The findings of this study affirmed the potency of cadmium exposure in pathological alteration of histomorphology of bodily tissues including the liver and kidney as well as the anti-toxicant activity of ascorbic acid leading to amelioration of the damaging effects of cadmium exposure on the hepato-renal histomorphological profile.

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