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Garlic (*Allium sativum* L.) Protects Hepatic and Renal Toxicity of Alloxan in Rats

J. S. Aprioku[1*] and F. S. Amah-Tariah[2]

[1]Department of Experimental Pharmacology and Toxicology, Faculty of Pharmaceutical Sciences, University of Port Harcourt, P.M.B. 5323, Port Harcourt, Nigeria.
[2]Department of Human Physiology, Faculty of Basic Medical Sciences, University of Port Harcourt, P.M.B. 5323, Port Harcourt, Nigeria.

Authors' contributions

This work was carried out in collaboration between both authors. Author JSA designed the study, wrote the protocol and wrote the first draft of the manuscript. Both authors performed the statistical analysis, managed the analyses of the study and literature searches. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Aims: *Allium sativum* (Garlic) possesses antioxidant principles and is consumed widely as a nutritional agent and for medicinal purposes. This work investigated the effects of aqueous Garlic bulb extract on alloxan-induced plasma elevations of hepatic enzymes and renal biochemical indices in Wistar rats.
Study Design: Twenty rats were divided randomly into three experimental groups, labelled I, II and III) and a control group (group IV) each containing five animals. Experimental groups were given alloxan and different dose levels of Garlic extract, while control group was given vehicle. Plasma levels of renal and kidney markers obtained in experimental animals were compared with control animals.
Place and Duration of Study: Department of Pharmacology, Faculty of Basic Medical Sciences, University of Port Harcourt, Nigeria, in 2015-2016.
Methodology: Group I was injected intraperitoneally, single dose of alloxan (100 mg/kg). Group II and III rats were injected single dose alloxan (100 mg/kg) followed by treatment with aqueous Garlic extract (100 or 200 mg/kg/day, given by oral gavage) for 21 days. Group IV was

**Corresponding author: E-mail: sydaprio@yahoo.com;*

administered distilled water. The animals were sacrificed and plasma levels of urea, creatinine, albumin, aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphate (ALP) were analyzed.
Results: There was significant (P< .05) elevation in the plasma levels of creatinine (25.8%), urea (35.4%), AST (336.7%) and ALT (118.5%) in alloxan alone treated rats compared to control. In Garlic treated rats, plasma levels of all parameters measured were not altered compared to control.
Conclusion: The result suggests that *Allium sativum* has protective effects on alloxan-induced elevations of plasma biochemical factors of renal and hepatic functions.

Keywords: Alloxan; ALT; AST; biochemical indices; creatinine; garlic.

1. INTRODUCTION

Garlic (*Allium sativum* L.), which belongs to the Family, Liliaceae is used widely as a flavoring agent in dishes and in traditional medicine to treat many diseases. As reviewed by Saddique et al. [1], garlic and its constituents prepared by various means have diverse biological activities, including, antitumor, antimicrobial, antioxidant, antihypertensive, and antiplatelet. The plant has been shown to have antidiabetic activity over a long period of time [2-4]. Further, animal studies and some early investigational studies in humans, have suggested possible beneficial cardiovascular effects of garlic [5]. Garlic supplementation has been demonstrated to reduce accumulation of cholesterol or deposition of plaques in the blood vessels in animals [6,7]. Other studies have shown that garlic extract exhibit insecticidal property [8] and inhibits the growth of different species of bacteria, fungi, virus and protozoa [8-10]. Garlic has equally been demonstrated to possess antioxidant properties [11-13].

Garlic is very popular among many in developed and developing countries and used frequently for a large array of medical conditions because of its high medicinal value. Although, the plant has been reasonably studied, investigation of its biological properties has not been exhausted. Recently, garlic has been reported to exhibit antioxidant and pro-oxidant properties, depending on the dose [14]. The present study investigates the effects of aqueous extract of garlic bulb on alloxan-induced elevations of plasma hepatic and renal biochemical indices in Wistar rats.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Chemicals/Kits

Chemicals used include, alloxan (Sigma -Aldrich, UK) and diethylether (Loba-Chemie PVT. Ltd., Mumbai, India). Commercially available test kits for alkaline phosphatase (QCA, S.A, Amposta / Spain); alanine transaminase, aspartate transaminase, albumin, urea and creatinine (Randox Lab. Ltd., UK) were used in the study.

2.1.2 Animals

A total number of 20 adult male Wistar rats, weighing 180 to 200 g and aged about 12 weeks, were obtained from the Animal House of our institution and allowed to acclimatize. The rats were fed with standard rodent feeds, allowed free access to clean tap water and maintained under natural temperature and lighting conditions. Animals were handled carefully and all experimental procedures were approved by our institution's Animal Research Ethics Committee.

2.2 Methods

2.2.1 Preparation of garlic aqueous extract

Fresh garlic bulbs were obtained from a local botanical garden and authenticated by a botanist at the Department of Plant Science and Biotechnology of our institution. After authentication, the outer skin was removed and remaining seed was ground to powder after shade-drying for 2 weeks. The garlic powder was then macerated in distilled water for 24 h and exhaustively extracted. The solution was thereafter filtered and evaporated using a steam bath at temperature of 45°C to obtain a pasty extract.

2.2.2 Experimental design

The rats were randomly distributed into 4 groups (I, II, III and IV) containing 5 per group. Group I animals were administered alloxan (100 mg/kg, ip). Group II and III animals were each given single dose of alloxan (100 mg/kg, ip) followed by garlic extract (100 or 200 mg/kg, po). Group IV (control) group was administered the vehicle (distilled water). Garlic and the vehicle were

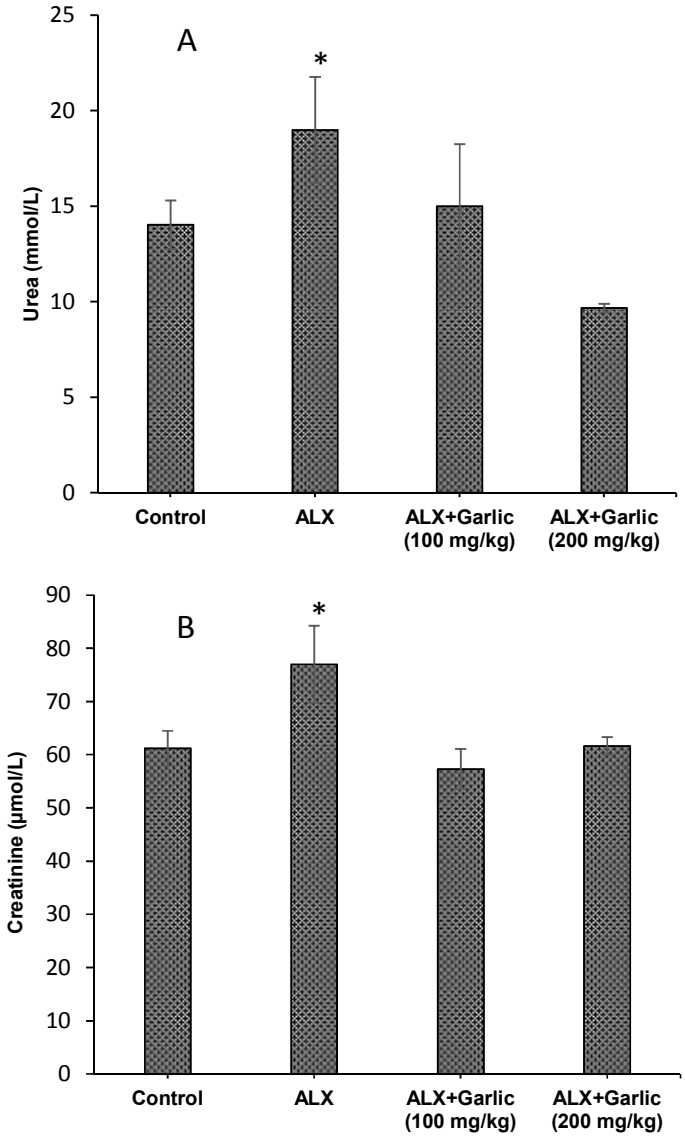
administered once daily for 21 consecutive days by oral gavage. The animals were anesthetized with diethylether and sacrificed by cervical dislocation at the end of the treatments. Blood was collected by cardiac puncture into lithium heparinized specimen bottles. Blood plasma was separated and assayed to measure alanine transaminase, aspartate transaminase, alkaline phosphatase, albumin, urea and creatinine levels using a Chemistry Autoanalyzer (Model: BS-800 m; Guangzou Shihal Medical Equipment Co. Ltd., China).

2.2.3 Statistical analysis

Data were analyzed using one way analysis of variance (ANOVA) followed by Dunnette's test and values were expressed as mean±standard error of mean (mean±SEM). The software that was used to perform data analysis was GraphPad Prism Version 6 and probability was set at $P< 0.05$.

3. RESULTS AND DISCUSSION

There was a significant ($P< .05$) increase in serum urea level in alloxan alone treated rats compared to control (Fig. 1A). Conversely, there was no significant change in urea levels of garlic administered rats compared to the control (Fig. 1B). In addition, there was a significant ($P< .05$) increase in creatinine level in alloxan alone treated rats, whereas the levels obtained in rats that received garlic were not altered (Fig. 1B).



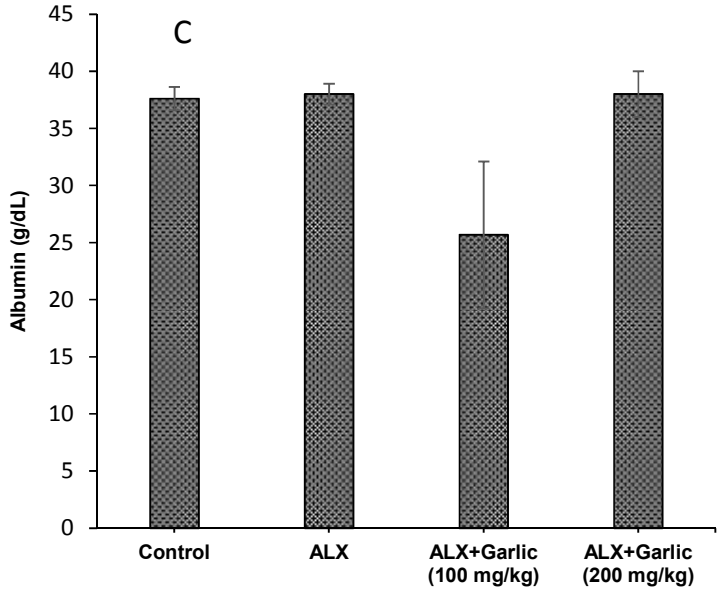
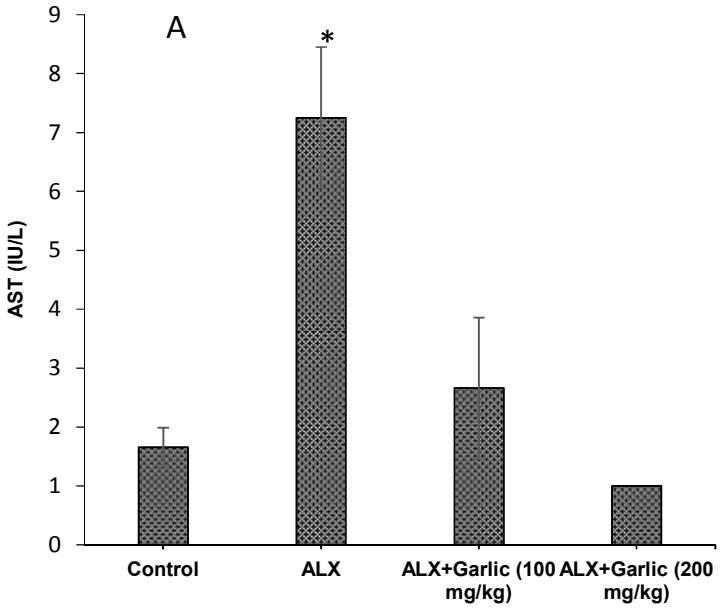


Fig. 1. Plasma levels of (A) urea, (B) creatinine and (C) albumin following single dose alloxan (ALX, 100 mg/kg) and 21 days Garlic treatment in Wistar rats

Data are expressed as mean±SEM, n = 5 per group.
** Represents values significantly different compared to control at (P < .05)*

Plasma level of albumin was not altered in alloxan treated rats, as well as rats that received garlic treatment (Fig. 1C). Furthermore, alloxan treated rats showed elevated plasma levels of aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP), but only the AST and ALT values were significant (*P*< .05) when compared to control (Fig. 2A-C). Plasma levels of AST, ALT and ALP in garlic treated rats were not significantly different compared to control (Fig. 2A-C).



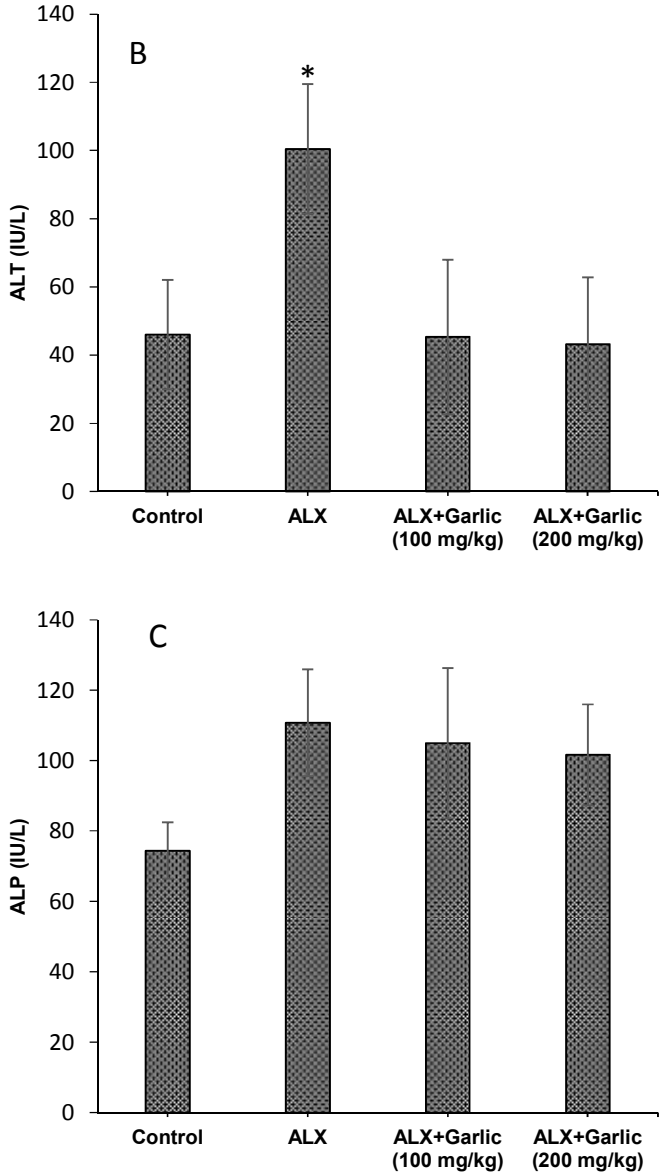


Fig. 2. Plasma levels of (A) aspartate transaminase (AST), (B) alanine transaminase (ALT), and (C) alkaline phosphatase (ALP) following single dose alloxan (ALX, 100 mg/kg) and 21 days Garlic treatment in Wistar rats

Data are expressed as mean±SEM, n = 5 per group
** Represents values significantly different compared to control at (P < .05)*

Plasma levels of urea and creatinine are used routinely for assessment of renal function [15]. Increased levels is strongly related to alteration of renal function which may result from damage to renal cells and tissues [15-17]. The results of this study showed that garlic treatment inhibited elevation of urea and creatinine levels by alloxan. Consistent with our result, previous studies have also shown elevation of serum creatinine level by alloxan [18]. Thus, garlic may protect alloxan-induced toxicity on the kidney.

Furthermore, aspartate transaminase (AST), alanine transaminase (ALT) and alkaline phosphatase (ALP) are biochemical markers of hepatic function. They are hepatic enzymes and their elevations in serum or plasma have been attributed to their leakage from liver cytosol into

the blood stream as a result of hepatotoxicity [19, 20]. ALT is specifically produced by hepatic cells [21,22], while AST is a less specific marker of liver function as it is produced by other organs as well. Elevation of ALT and AST is indicative of hepatic injury [20], thus, elevation of plasma levels of these enzymes by alloxan is suggestive of toxicity to hepatic cells. This finding agrees with the results of Yuniarti et al. [18] and Saei et al. [23]. Further, the non-significant elevation in alkaline phosphatase by alloxan suggests that higher dose levels of alloxan could possibly cause damage to biliary structures in the liver. The results obtained therefore give a strong indication that alloxan would induce hepatotoxic effect in rats. The elevation of the hepatic enzymes by alloxan was prevented by garlic treatment as the plasma levels became lower than the alloxan induced levels and equally comparable with those of the control.

The alloxan-mediated effects in this study may be related to its ability to induce oxidative stress in biological tissues [24,25]. On the other hand, garlic has been shown to contain phytochemicals that possess potent antioxidant activity [11,12] and this may be attributed to the observed protective effect of garlic in this study.

4. CONCLUSION

Allium sativum (garlic) bulb inhibits elevations of biochemical markers of hepatic and renal functions by alloxan in rats. The protective role of garlic may be due to antioxidant activity of phytochemical constituents that are present in it.

CONSENT

It is not applicable.

ETHICAL APPROVAL

All authors hereby declare that standard international guidelines for care and use of laboratory animals were strictly adhered to. All experiments were examined and approved by our Institutional Research Ethics Committee.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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