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Allium cepa Mitigates Aluminum Chloride-Induced Hepatotoxicity in Male Wistar Rats

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Abstract

Allium cepa (Common Onion), one of the most widely grown crops in world, is believed to possess medicinal potency. The present study was designed to investigate the effect of Allium cepa (ACE) administration on oxidative stress-mediated hepatotoxicity following aluminum chloride (AlCl₃) administration. 24 adult male wistar rats weighing 175 g were randomly divided into vehicle-treated (control), ACE, aluminum chloride (AlCl₃) and ACE+AlCl₃ groups. Rats were given single oral administrations of 100mg/kg body weight of AlCl₃ and 1 mL/0.1 kg body weight of ACE for four weeks. When compared with vehicle-treated, AlCl₃ administration caused a significant decrease in serum total protein (TP) and an increase in serum levels of alanine transaminase (ALT), aspartate transaminase (AST) and total bilirubin. On the other hand, ACE treatment significantly improved serum TP but depressed serum levels of ALT, AST and total bilirubin. There was no significant change in these biomarkers of liver function in ACE+AlCl₃ group compared with the vehicle-treated group. Furthermore, while AlCl₃ group was characterized by a significant rise in hepatic malondialdehyde (MDA) and a decrease in hepatic superoxide dismutase (SOD) and catalase activities, ACE group exhibited a significant low hepatic MDA and a high hepatic SOD and catalase activities. However, none of these antioxidant markers changed in ACE+AlCl₃ group compared with vehicle-treated. Therefore, we conclude that ACE mitigates hepatotoxic effect of AlCl₃ administration through regulation of hepatic oxidant/antioxidant system.

Keywords Hepatotoxicity; *Allium cepa*; Catalase; Aspartate transaminase; Alanine transaminase bilirubin

Introduction

Within the ecosystem, interaction between living organisms and environmental borne factors such as dusts and chemicals is inevitable [1]. Human exposure to chemicals, most especially aluminum occurs through natural processes such as weathering

of rocks and erosion [2]. Dietary and occupational exposures to the mineral are also sources of aluminum in humans and animals [2,3]. During normal breathing, at least 1.4 µg of aluminum in particulate was reported to be inhaled per day [3]. With a significant aluminum load, the excretory capacity of the kidney is exceeded leading to deposition of the minerals in various tissues including the liver and consequently resulting in hepatotoxicity [2,4,5].

In animal studies, experimental hepatotoxicity was associated with alterations in liver function test such as total plasma protein, plasma liver enzymes (ALT, AST and alkaline phosphatase) and plasma bilirubin [6-8]. A study by Ige et al. (2011) [6] on cadmium-induced hepatic damage showed a decrease in total serum protein and significant increases in serum ALT and AST activities in male rats. Arsenic and mercury loading were also associated with increases in plasmatic activities of AST, ALT and alkaline phosphatase in rats [7,9]. Interestingly, a high oxidant/antioxidant ratio was a common feature characterizing these reports, indicating the plausible role of oxidative stress in the liver damage.

Amelioration of damage and prevention of diseases have always been linked with nutritional status and dietary factors [10]. Many food stuffs especially flavonoid-containing types have been shown to play important role in the prevention of tissue damage and management of diseases [11,12]. *Allium cepa*, an example of flavonoid-containing vegetable [13] has been shown to exhibit high therapeutic efficacy against atherosclerotic conditions and organ toxicity in cadmium-intoxicated rats [14]. It also prevented obesity related malignancy [15] and averted hyperglycemia in diabetic rats [16]. We have demonstrated in our previous study that Allium cepa ameliorated aluminum chloride induced reproductive dysfunctions in male rats [17]. The present study was designed to investigate the effect of Allium cepa administration on oxidative stress-mediated hepatotoxicity in male wistar rats following aluminum chloride exposure.

Materials and Methods

Animals care and management

Twenty adult male wistar rats weighing 175 g were used for the research work. They were divided into four groups consisting of five animals each. These rats were kept in four different cages with a wire mesh covering. They were fed pelletized grower's mash ad libitum, provided water through drinking trough and kept under 12 hour light and 12 hour darkness at room temperature.

Ethical certification

The study was conducted in line with the guidelines of United State National Institute of Health (NIH) Guidelines for the use of laboratory rats.

Experimental procedure

The rats were weighed and randomly grouped into;

Group A: received distilled water for four weeks.

Group B: received a single daily administration of 100 mg/kg body weight of $AlCl_3$ (P.O.) for four weeks

Group C: received a single daily administration of 1 ml/0.1 kg body weight of Allium cepa (P.O.) for four weeks.

Group D: received single daily administrations of 100mg/kg body weight of $AlCl_3$ (P.O.) and 1 ml/0.1 kg body weight of Allium cepa (P.O.) for four weeks.

Preparation of Allium cepa extract

Allium cepa was prepared following procedures from previous studies [6,14]. Briefly, fresh common onion (Allium cepa) bulbs were rinsed thoroughly in distilled water, air dried, and 200 g was then blended. The resulting paste was allowed to stand for 24 hrs. Juice was then filtrated and squeezed out of it using a tight sieve. The filtrate/juice was prepared on weekly basis following the same procedure and kept at 4°C. This is to prevent it from losing its potency.

Sample collection

At the end of the experiment, blood samples were collected via cardiac puncture. Livers of rats were harvested, weighed and homogenized in phosphate buffer for determination of oxidative stress.

Determination of total serum protein, total serum bilirubin, and serum liver enzymes

Total serum protein and bilirubin were assayed using a standard enzymatic calorimetric method with standard laboratory kits (LABKIT, Barcelona-Spain) as reported by Ige et al.

(2011) [6]. Serum liver enzymes (ALT and AST) were also determined using standard kit (Biosystems S.A Barcelona-Spain).

Determination of liver superoxide dismutase (sod), catalase activities and malondialdehyde (mda) levels

At the end of the experiment, the livers were excised, cleaned and weighed. A portion of each liver was washed in normal saline (0.9% NaCl), homogenized in phosphate buffer (1 g tissue/4ml). The homogenate were then centrifuged and aliquots of the supernatant were obtained for biochemical analysis. Liver SOD, catalase activities and MDA levels were determined as reported by Fridovich (1986) [18], Sinha (1972) [19] and Varshney and Kale (1990) [20] respectively.

Statistical analysis

Results are presented as mean \pm SEM. Significant difference was set at $P < 0.05$. Data were analysed by using a one-way analysis of variance (ANOVA) followed by unpaired Student's t-test.

Result

Effect of Allium cepa on the liver weight of Aluminum treated rats

Figure 1 shows the liver weight across the groups. $AlCl_3$ treated group has non-significant increase liver weight while Allium cepa, Al +Allium cepa and control liver weight were comparable.

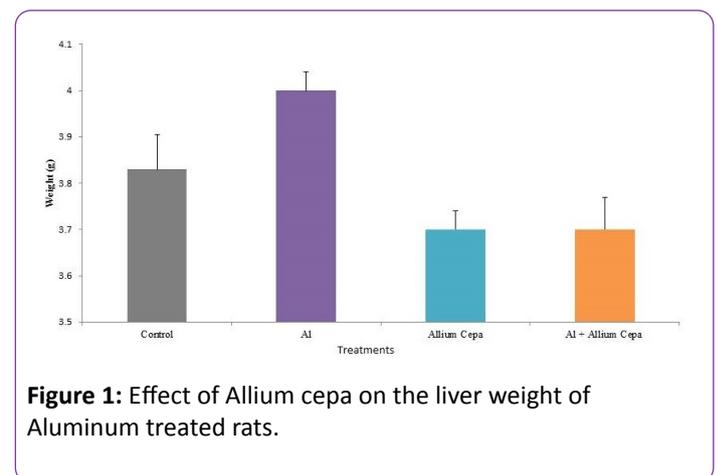


Figure 1: Effect of Allium cepa on the liver weight of Aluminum treated rats.

Effect of Allium cepa on some liver function parameters

There was significant decrease serum total protein level and increase serum total bilirubin, ALT and AST in the $AlCl_3$ treated group when compared with control. The Allium cepa alone treated group showed a significant increase in serum total protein level and decrease serum total bilirubin, ALT and AST when compared with control group. There was no significant difference in serum total protein level, serum total bilirubin, ALT

and AST of AI+ Allium cepa group when compared with control (Table 1).

Table 1: Effect of Allium cepa on some liver function Parameters.

Parameters	Control	AI	Allium cepa	AI+Allium cepa
Total Serum Protein (g/dl)	35.75 ± 2.55	26.08 ± 2.92*	60.9 ± 3.66*	30.2 ± 1.00
Total Serum Bilirubin (mg/dl)	0.82 ± 0.02	1.02 ± 0.02*	0.68 ± 0.02*	0.84 ± 0.01
ALT(IU/L)	18.3 ± 0.30	28.12 ± 3.75*	16.4 ± 6.40*	17.5 ± 0.50
AST(IU/L)	54 ± 0.32	60.6 ± 0.400	50.6 ± 0.40	53 ± 0.32

*p=0.05 vs. control

Effect of Allium cepa on some Antioxidant Activities and Hepatic Lipid peroxidation

Aluminum administration caused a significant decrease in SOD, catalase activities and increase in MDA level (marker of lipid peroxidation). While Allium cepa treatment caused significant increase in SOD, catalase and decrease MDA. There was no significant difference in SOD, catalase and MDA of AI +Allium cepa animals when compared with the control (Figure 2 and Table 2).

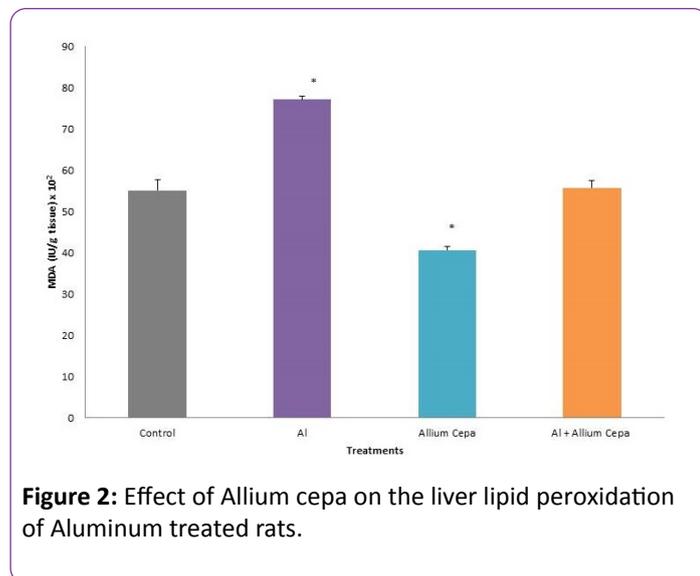


Figure 2: Effect of Allium cepa on the liver lipid peroxidation of Aluminum treated rats.

Discussion and Conclusion

Liver, one of the largest organs in the body [21,22] plays an indisputable role in catabolic and anabolic processes, storage, synthesis and detoxification [21-23]. Alteration in liver function test is characterized by increase in serum ALT, AST, ALP, total bilirubin and liver weight and decrease in total protein [24,25]. The present study demonstrated that administration of AlCl₃ led to hepatotoxicity. Many studies have documented that administration of cadmium, arsenic acid and AlCl₃ impaired liver function [6,7,8,26]. The change in serum ALT, ALP, bilirubin and total protein levels in this study clearly indicated a significant

damage of hepatocytic cell membranes [4] resulting in leakage of these chemical substances into the systemic circulation and attenuation of synthetic capacity of the organ.

Table 2: Effect of Allium cepa on some antioxidant activities.

Antioxidants	Control	AI	Allium cepa	AI+Allium cepa
SOD (IU/g tissue)	1.29 ± 0.02	0.75 ± 0.03*	1.66 ± 0.04*	1.33 ± 0.01
CAT (IU/g tissue) × 10 ³	15 ± 0.58	6 ± 0.57*	19 ± 5.7*	13 ± 1.5

*p,0.05 vs. control

There was an insignificant rise in liver weight of AlCl₃ group. This is inconsistent with previous study [27] where significant increase in liver weight was observed. Dissimilarity observed in this study might be due to the short duration of AI treatment. There was also comparable liver weight in control, Allium cepa alone and AlCl₃+Allium cepa rats. This confirms the non-toxic effect of Allium cepa as earlier reported [28].

In this study, the least activity of antioxidant enzymes (SOD and catalase) and the highest level of MDA were observed in AlCl₃ group. MDA, a reactive metabolite, produced during peroxidation of polyunsaturated fatty acid tends to bombard tissue borne molecules [29,30], resulting in a high MDA/antioxidant enzyme ratio, oxidative stress and tissue deterioration. As far as this study is concerned, AlCl₃ induced hepatotoxicity was mediated by oxidative stress.

Researchers have found that Allium cepa essential oil, Allium cepa flesh and Allium cepa juice exerted a positive influence on health [11,12,31]. The present study corroborated this report. We noticed a decrease in ALT, AST, total protein and an elevated total protein in ACE group. On the other hand, the hepatic tissue displayed a low level of MDA and high activities of SOD and catalase. This indicated that the positive influence of Allium cepa on liver function biomarkers was mediated by a low MDA/antioxidant enzyme ratio.

Studies have reported the beneficial effect of Allium cepa on arsenic acid induced- and cadmium-induced hepatic damage in rats [5-7,26]. Exposure of human beings to both Allium cepa and aluminum chloride is insurmountable [2]. The present study showed that there was an insignificant change in ALT, AST, total bilirubin and total serum protein in Allium cepa+AlCl₃ group. This implied that administration of Allium cepa may exert a mitigating effect on the hepatotoxic effect of AlCl₃. Also, we observed that there was no change in hepatic MDA and hepatic antioxidant enzymes. This also indicated that the mitigating influence of Allium cepa involves restoration of hepatic MDA and hepatic antioxidant. However; subsequent study will be needed to clarify the mode of action of Allium cepa on aluminum chloride-induced hepatotoxicity. In conclusion, the result of the study showed that Allium cepa mitigated aluminum chloride-induced hepatotoxicity through regulation of hepatic oxidant/antioxidant system.

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