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The Salutary Role of *Allium cepa* Extract on the Liver Histology, Liver Oxidative Status and Liver Marker Enzymes of Rabbits Submitted to Alcohol-induced Toxicity

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ABSTRACT

Alcohol is currently recognized as the most prevalent known cause of abnormal human health. Furthermore, the liver remains the most commonly affected organs following alcohol abuse. The effect of *Allium cepa* against alcohol-induced hepatic damage in rabbits was investigated in the present study. Rabbits were divided into four groups; The *Allium cepa*-alone group received physiological saline 5 mL kg⁻¹ b.wt., daily per oral (p.o) for 60 days followed by *Allium cepa* 100 mg kg⁻¹ b.wt., daily p.o for another 60 days. The alcohol-alone group was given alcohol 5 mg kg⁻¹ b.wt., daily p.o for 60 days followed by saline 5 mL kg⁻¹ b.wt., daily p.o for another 60 days. The alcohol plus *Allium cepa* group were similarly given alcohol, but had *Allium cepa* 100 mg kg⁻¹ b.wt, daily p.o post-treatment for another 60 days. Another group of rabbits were given peanut oil (the vehicle) 100 mg kg⁻¹ b.wt., daily p.o, for 60 days, after saline 5 mL kg⁻¹ b.wt., daily p.o for 60 days to serve as the control. The gross anatomical parameters of the liver and liver histology were assessed. Liver oxidative stress was evaluated by liver Superoxide dismutase (SOD), catalase (CAT), Glutathione Peroxidase (GPx), reduced glutathione (GSH) and malondialdehyde (MDA) assays. In addition, the activities of the biomarker enzymes of the liver (alanine transaminase, aspartate transaminase, alkaline phosphatase and gamma-glutamyl transpeptidase) were assayed. An assessment of the histological profiles of the liver showed a derangement of the liver cytoarchitecture following alcohol abuse and a marked improvement was observed after *Allium cepa* administration. Similarly, *Allium cepa* improved the reduction of antioxidant parameters (SOD, CAT, GPx and GSH) and the increased MDA and serum hepatic markers levels caused by alcohol ingestion. It was concluded that *Allium cepa* may offer protection against free radical mediated oxidative stress of rabbits with alcohol-induced hepatotoxicity.

Key words: Alcohol-induced liver damage, oxidative stress, antioxidants, *Allium cepa*

INTRODUCTION

Alcoholic Liver Disease (ALD) is one of the most serious consequences of chronic alcohol abuse in the world (Diehl, 2002). The disease is often progressive and is considered to be a major cause of morbidity and mortality (Sherlock, 1995). Various studies have been carried to elucidate the pathogenesis of ALD (Lieber, 2004; Seitz *et al.*, 2005; Tilg and Day, 2007; Seth *et al.*, 2008). The

main mechanism, by which alcohol abuse causes hepatotoxicity has been reported to involve increased oxidative stress, reduced antioxidative status and nitrosative stress (Lu and Cederbaum, 2008).

The chief reason why alcohol abuse is frequently associated with liver pathology is because approximately 80% of ingested alcohol is metabolized in the liver by a process that generates many reactive oxygen species. Firstly, alcohol is metabolized into the highly toxic acetaldehyde by alcohol dehydrogenase in the liver, then acetaldehyde is oxidized to acetate by aldehyde oxidase or xanthine oxidase giving rise to Reactive Oxygen Species (ROS) via cytochrome P450 2E1 (Tuma and Casey, 2003). Furthermore, chronic alcohol consumption increases Nitric Oxide (NO) level which may lead to toxicity by peroxynitrite, a potent oxidant (Venkatraman *et al.*, 2004). Thus, overproduction of reactive nitrogen species/ reactive oxygen species (RNS/ROS) may occur when its generation in a system exceeds the systems ability to neutralize and eliminate them.

The resulting oxidative stress following chronic alcohol ingestion results in enhanced lipid peroxidation and change in structure and functions of other important cellular components, such as protein and DNA (Rouach *et al.*, 1997). Alcohol metabolism does not only produce liver oxidative stress which causes further lipid peroxidation that damages membranes of cells and organelles, it could also lead to the release of reactive aldehydes which possess potent pro-inflammatory and profibrotic properties (Lieber, 2004).

Allium cepa (onion), also known as the bulb onion, common onion and garden onion, is the most widely cultivated species of the genus *Allium* (Fritsch and Freisen, 2002). It has a globose bulb that is an underground part of the stem, it is biennial and perennial and it is widely distributed in the temperate regions. *Allium cepa* (AC) is used commonly in foodstuff and as a traditional remedy in the treatment of a variety of disorders. The pharmacological evidence for the use of AC as an anti-asthmatic, anti-hypertensive, anti-hyperglycemic, anti-hyperlipidemic and anti-tumor agent has been reported (Augusti, 1996; Stajner and Varga, 2003).

Active ingredients in AC include phenolic compounds (flavonoids, antocyanins, phenolic acids and flavonols), organosulphur compounds, vitamins and some minerals (Teyssier *et al.*, 2001; Kamal and Daoud, 2002; Furusawa *et al.*, 2003; Campos *et al.*, 2003; Gabler *et al.*, 2003; Ismail *et al.*, 2003; Wang *et al.*, 2005). These compounds may mediate the pharmacological effects of *A. cepa*. Thus, phenolic acids, such as caffeic, chlorogenic, ferulic, sinapic, p-coumaric acids, vanillic, syringic and p-hydroxybenzoic appear to be active antioxidants (Larson, 1988; Ibrahim *et al.*, 2004). Its vitamins, especially vitamin C have a protective function against oxidative damage and a powerful quencher of singlet oxygen (O₂), hydroxyl (OH) and peroxy (RO₂) radicals (Niki, 1991; Saalu, 2010).

In recent years there has been considerable interest in the use of natural plant products in the management of liver diseases since there is no reliable antihepatotoxic drug available in modern medicine (Reddy *et al.*, 2010). Thus, the aim of this study is to investigate the hepatoprotective and antioxidant potentials of *Allium cepa* on alcohol-induced liver injury in rabbits.

MATERIALS AND METHODS

Chemicals: Ethanol of E. Merck, Darmstadt, Germany was obtained from Biotechnology Co. Ltd, Yaba Lagos in the month of October, 2010. All reagents used in this research were of analytical grade.

Plant material and its extraction: Twenty fresh mature *Allium cepa* fruit weighing 200 g were bought at sabo market, ogbomosho, Oyo state Nigeria on 12th December, 2010. The botanical

identification and authentication of the plant sample was done at the Herbarium Section, Department of Pure and Applied Biology, Ladoko Akintola University of Technology, Nigeria (Voucher No. 20).

Aqueous extract of *Allium cepa* fruit was obtained using the method described by Azu *et al.* (2007). Briefly, the fruit were thoroughly washed in water and blended by a locally made blender and left to stand for 24 h so as to release the active contents. The juice obtained was then squeezed out using clothing mesh and the crude extract which weighed 45 g was stored at a temperature of 4°C for the experiment.

Animals: A total of thirty adult Rabbits (15 females and 15 males) were obtained from a breeding stock maintained in the animal house of the college of health sciences, Ladoko Akintola University of Technology (LAUTECH), Ogbomosho, Nigeria. The animals were housed in well ventilated wire wooden cages in the animal facility of the department of Anatomy, Ladoko Akintola University of Technology (LAUTECH), Ogbomosho, Nigeria. The rabbits were maintained under standard natural photoperiodic condition of twelve hours of light alternating with twelve hours of darkness (i.e., L: D; 12:12 h photoperiod) at room temperature (25-26°C) and humidity of 65±5%.

The rabbits were allowed unrestricted access to water and rabbit chow, they were acclimatized for 20 days before the commencement of the experiment. The weights of the animals were estimated at procurement, during acclimatization, at commencement of the experiments and after the experiment was completed using an electronic analytical and precision balance (BA210S, d = 0.0001 g).

Experimental procedures involving the animals and their care were conducted in conformity with international national and institutional guidelines for the care of laboratory animals in biomedical research and use of laboratory animals in bio-medical research promulgated by the National research council of animal care (National Research Council, 1996).

Acute oral toxicity study of *Allium cepa* extract: The acute oral toxicity study for *Allium cepa* extract was conducted using the Organization for Economic Cooperation and Development (OECD, 2000), Guidance Document on Humane End points that should reduce the overall suffering of animals used in this type of toxicity test. The test used was the limit dose test of the up and down procedure.

Briefly, 5 animals were weighed and individually identified. The first animal was given the test dose-*Allium cepa* extract 2000 mg kg⁻¹ body weight. The second and third animals were concurrently dosed and the fourth and fifth animals sequentially dosed.

The results were evaluated as follows (S = Survival, X = death). The animals were observed individually at least once during the first 30 min after dosing, periodically during the first 24 h (with special attention given during the first 4 h) and daily thereafter for a total period of 14 days. All observations were systematically recorded with individual records maintained for each animal.

Animals grouping and treatment: Twenty adult rabbits, 10 males and 10 females weighing 1500-1800 g were randomly allocated into four groups (A, B, C, D), n = 5.

Group A rabbits were given peanut oil (the vehicle) 100 mg kg⁻¹ b.wt., daily per oral (p.o), for 60 days, after saline 5 mL kg⁻¹ b.wt., daily p.o for 60 days to serve as the control.

Group B rabbits (the *Allium cepa*-alone group) received physiological saline 5 mL kg⁻¹ b.wt., daily p.o for 60 days followed by *Allium cepa* 100 mg kg⁻¹ b.wt., daily p.o for another 60 days.

Group C rabbits (the alcohol-alone group) were given alcohol (25% ethanol) 5 mg kg⁻¹ b.wt., daily p.o for 60 days followed by saline 5 mL kg⁻¹ b.wt., daily p.o for another 60 days (Hussein *et al.*, 2007).

Group D rabbits (the alcohol plus *Allium cepa* group) were similarly given alcohol, but had *Allium cepa* 100 mg kg⁻¹ b.wt, daily p.o post-treatment for another 60 days.

Animal sacrifice and sample collection: Each rabbit was at the time of sacrifice first weighed and then anaesthetized by placing it in a closed jar containing cotton wool sucked with chloroform anaesthesia. The abdominal cavity was opened up through a midline abdominal incision to expose the liver. Then the liver was excised and trimmed of all fat. The liver weight of each animal was evaluated with an electronic analytical and precision balance (BA 210S, d = 0.0001-Sartoriusen GA, Goettingen, Germany). The liver volume was measured by water displacement method.

A portion of the median lobe of the liver was dissected and fixed in fixed in 10% formol-saline for histological examination. The remaining parts of the liver were frozen quickly in dry ice and stored at -25°C for biochemical analysis.

Histological procedures and analysis: This was done as described by Saalu *et al.* (2008). Briefly, the organs were cut on slabs about 0.5 cm thick and fixed in 10% formol saline for a day after which they were transferred to 70% alcohol for dehydration. The tissues were passed through 90% alcohol and chloroform for different durations before they were transferred into two changes of molten paraffin wax for 20 min each in an oven at 57°C. Serial sections of 5 µm thick were obtained from a solid block of tissue and were stained with haematoxylin and eosin stains, after which they were passed through a mixture of equal concentration of xylene and alcohol. Following clearance in xylene, the tissues were oven-dried. Photomicrographs were taken with a JVC colour video digital camera (JVC, China) mounted on an Olympus light microscope (Olympus UK Ltd., Essex, UK).

Assay of liver enzymatic antioxidants

Assay of catalase (CAT) activity: Catalase activity was measured according to the method of Aebi (1983). The 0.1 mL of the liver homogenate (supernatant) was pipetted into cuvette containing 1.9 mL of 50 mM phosphate buffer, pH 7.0. Reaction was started by the addition of 1.0 mL of freshly prepared 30% (v/v) hydrogen peroxide (H₂O₂). The rate of decomposition of H₂O₂ was measured spectrophotometrically from changes in absorbance at 240 nm. Activity of enzyme was expressed as units mg⁻¹ protein.

Assay of superoxide dismutase (SOD) activity: Superoxide dismutase activity was measured according to the method of Winterbourn *et al.* (1975) as described by Rukmini *et al.* (2004). The principle of the assay was based on the ability of SOD to inhibit the reduction of nitro-blue tetrazolium (NBT). Briefly, the reaction mixture contained 2.7 mL of 0.067 M phosphate buffer, pH 7.8, 0.05 mL of 0.12 mM riboflavin, 0.1 mL of 1.5 mM NBT, 0.05 mL of 0.01 M methionine and 0.1 mL of enzyme samples. Uniform illumination of the tubes was ensured by placing it in air aluminum foil in a box with a 15 W fluorescent lamp for 10 min. Control without the enzyme source was included. The absorbance was measured at 560 nm. One unit of SOD was defined as the amount of enzyme required to inhibit the reduction of NBT by 50% under the specific conditions. It was expressed as µ mg⁻¹ protein.

Assay of glutathione peroxidase (GPx) activity: Glutathione peroxidase activity was measured by the method described by Rotruck *et al.* (1973). The reaction mixture contained 2.0 mL of 0.4 M Tris-HCl buffer, pH 7.0, 0.01 mL of 10 mM sodium azide, 0.2 mL of enzyme. 0.2 mL of 10 mM glutathione and 0.5 mL of 0.2 mM H₂O₂. The contents were incubated at 37°C for 10 min followed by the termination of the reaction by the addition of 0.4 mL 10% (v/v) TCA, centrifuged at 5000 rpm for 5 min. The absorbance of the product was read at 430 nm and expressed as nmol mg⁻¹ protein.

Assay of liver non-enzymatic antioxidants

Assay of liver reduced glutathione (GSH) concentration: GSH was determined by the method of Ellman (1959). 1.0 mL of supernatant was treated with 0.5 mL of Ellmans reagent (19.8 mg of 5, 5'-dithiobisnitro benzoic acid (DTNB) in 100 mL of 0.1% sodium nitrate) and 3.0 mL of phosphate buffer (0.2 M, pH 8.0). 0.4 mL of distilled water was added. The mixture was thoroughly mixed and the absorbance was read at 412 nm, expressed as nmol mg⁻¹ protein.

Estimation of lipid peroxidation (malondialdehyde): Lipid peroxidation in the liver tissue was estimated colorimetrically by thiobarbituric acid reactive substances TBARS method of Buege and Aust (1978). A principle component of TBARS being malondialdehyde (MDA), a product of lipid peroxidation. In brief, 0.1 mL of tissue homogenate (Tris-HCl buffer, pH 7.5) was treated with 2 mL of (1:1:1 ratio) TBA-TCA-HCl reagent (thiobarbituric acid 0.37%, 0.25 N HCl and 15% TCA) and placed in water bath for 15 min, cooled. The absorbance of clear supernatant was measured against reference blank at 535 nm. Concentration was calculated using the molar absorptive of malondialdehyde which is 1.56×10⁵ M⁻¹ cm⁻¹ and expressed as nmol mg⁻¹ protein.

Estimation of liver marker enzymes: The alanine transaminase, aspartate transaminase, alkaline phosphatase and Gamma-Glutamyl transpeptidase activities were all determined according to the methods of Retiman and Frankel (1957).

Statistical analysis: All data were expressed as Mean±SD of number of experiments (n = 5). The level of homogeneity among the groups was tested using Analysis of Variance (ANOVA) as done by Snedecor and Cochran (1980). Where heterogeneity occurred, the groups were separated using Duncan Multiple Range Test (DMRT). A value of p<0.05 was considered to indicate a significant difference between groups (Duncan, 1957).

RESULTS

Acute oral toxicity studies: There were no deaths of rabbits dosed 3000 mg kg⁻¹ body weight of the plants extract both within the short and long outcome of the limit dose test of Up and Down method (Table 1). The LD50 was calculated to be greater than 3000 mg kg⁻¹ body weight/orally.

Body weight changes: Figure 1 shows that rabbits in the control and *Allium cepa* alone groups significantly (p<0.05) increased in weight when compared to their initial mean live weight. Both the alcohol-administered groups lost weights when compared with their initial weights. However the weight loss by the alcohol-administered alone rabbits was higher than the losses by the group that received *Allium cepa* post-treatment after alcohol abuse.

Table 1: Results of acute toxicity test for *Allium cepa* (AC) extract (up and down procedure) in rabbits

Serial No.	Identity mg kg ⁻¹	Test animal dose of ac short term results long term results	
		(48 h)	(14 days)
1 REP	2000	S	S
2 LEP	2000	S	S
3 TC	2000	S	S
4 RLT	2000	S	S
5 I	2000	S	S

S: Survival, REP: Right ear pierced, LEP: Left ear pierced, TC: Tail cut, RDC: Right leg tagged, I: Intact rabbit

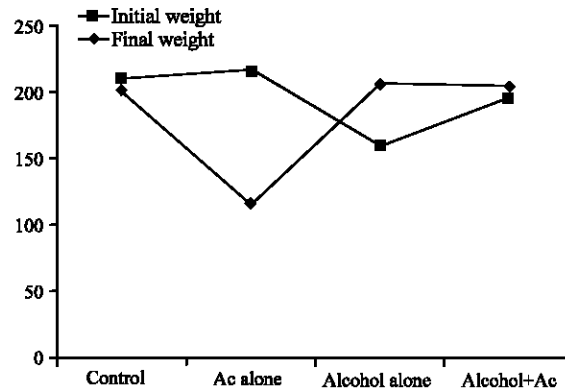


Fig. 1: The body weight changes of rabbits

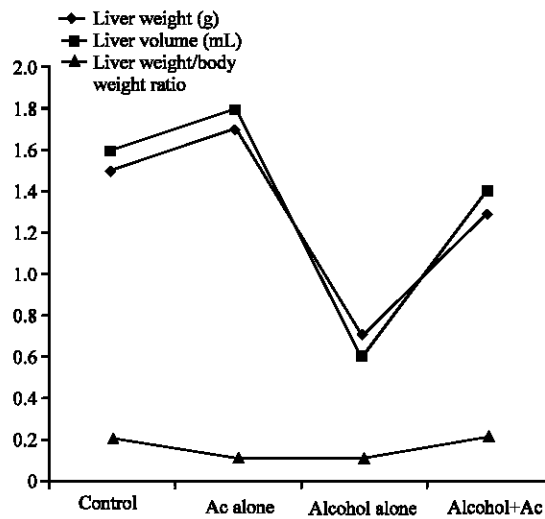


Fig. 2: Liver weight, liver volume and liver weight, body weight ratio of rabbits

Weights and volumes of liver: The liver weights, liver weight/body weight ratio and liver volumes of the alcohol-alone rabbits were the least, being significantly lower ($p < 0.001$) compared to the mean liver weights, liver weight/body weight ratio and volumes of the alcohol administered rabbits that in addition had *Allium cepa*, which in turn were also lower but not significantly ($p > 0.05$) lower than those of the control and *Allium cepa*-alone rabbits (Fig. 2).

Liver histology: An evaluation of the histological profiles of the livers showed that the control group of rabbits demonstrated normal liver architecture comprising of hepatocytes oriented in cords radiating from a central vein in an astomosing manner to form a sponge work (Fig. 3).

Following chronic administration of alcohol, there was a marked distortion and degeneration of the liver paraencyma. There was necrosis of cells and with presence of fibrosis as evidenced by formation of irregular collagenous fibers (Fig. 4).

As shown in Fig. 5, the livers of the group that had AC treatment post alcohol administration demonstrated a remarkable preservation in their histological profiles with a near absence of fibrosis.

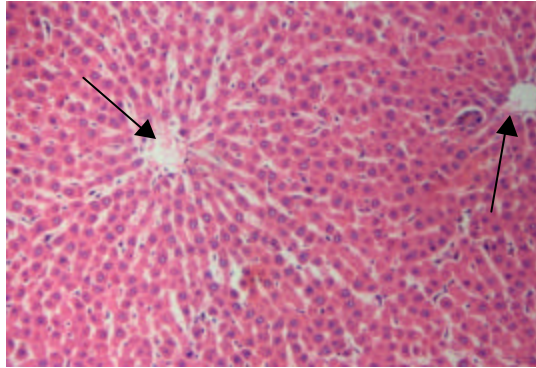


Fig. 3: A representative section of an untreated control rabbit liver administered peanut oil (the vehicle) $100 \text{ mg kg}^{-1} \text{ b.wt.}$, daily p.o, for 60 days, after saline $5 \text{ mL kg}^{-1} \text{ b.wt.}$, daily p.o for 60 days. Showing the normal structure of liver tissue composing of hepatocytes arranged in cords radiating from a central vein (arrowed). (X100 magnification, hematoxylin and eosin stain)

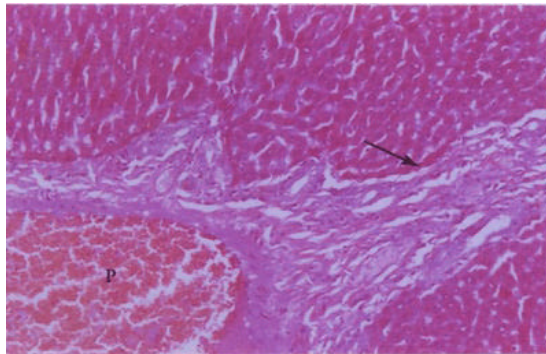


Fig. 4: A sectional view of the liver of rabbit which received alcohol (25% ethanol) $5 \text{ mg kg}^{-1} \text{ b.wt.}$, daily p.o for 60 days followed by saline $5 \text{ mL kg}^{-1} \text{ b.wt.}$, daily p.o for another 60 days. Showing hepatocytes damage and degeneration. There are also irregular collagenous fibers with fibrocytes (arrowed) and dilatation of the portal vein (p). (X100 magnification, hematoxylin and eosin stain)

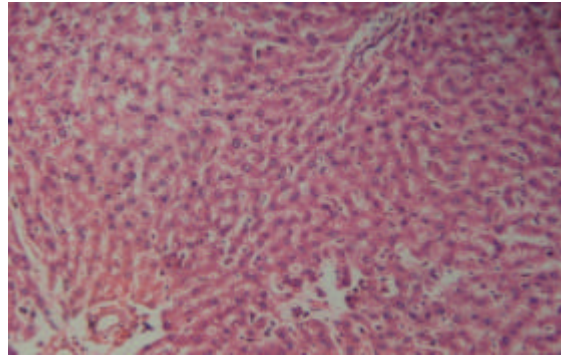


Fig. 5: A representative section of an untreated control rabbit liver administered alcohol (25% ethanol) 5 mg kg⁻¹ b.wt., daily p.o for 60 days followed by *Allium cepa* 100 mg kg⁻¹ b.wt., daily p.o post-treatment for another 60 days. Showing marked improvement in liver pararenal degenerative changes, absence of fibrosis. (X 100 magnification, hematoxylin and eosin stain)

Liver oxidative stress

Activities of liver enzymes- superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx): Treatment with of *Allium cepa* (AC) alone caused no significant change in liver SOD activity, whereas, alcohol-alone administration in rabbits showed a statistically significant decrease in SOD activity compared to control animals. Treatment with combined alcohol and AC significantly increased the liver SOD activity compared to animals that received alcohol alone (Fig. 6).

As shown in Fig. 7, the liver activities of CAT after AC alone dosing were comparable to that of the control values. Alcohol-alone administration, however, resulted in a statistically significant reduction in liver CAT activity compared to control rabbits. Co- administration of alcohol and AC significantly increased the liver CAT activity when compared to alcohol alone-challenged animals. The CAT activity was in this group approximately comparable to normal control values.

The GPx activities following AC administration approximated that of the control animals. Alcohol, however, markedly decreased the enzyme activity compared to control values. Administration of both alcohol and AC significantly increased the GPx activity in liver tissue compared to animals treated with alcohol alone (Fig. 8).

Liver content of glutathione (GSH) and malondialdehyde (MDA): Following treatment with AC, the liver GSH level was not significantly different from the control group. A remarkable reduction in GSH content was, however, observed after alcohol-alone treatment when compared to the control animals. Administration of both alcohol and AC significantly elevated the liver content of GSH compared to animals that were given alcohol alone (Fig. 9).

As shown in Fig. 10, AC had no effect on the liver content of lipid peroxides (products of lipid peroxidation) expressed as MDA when compared to control animals. Alcohol however, significantly elevated the liver MDA by about five folds as compared to the control value.

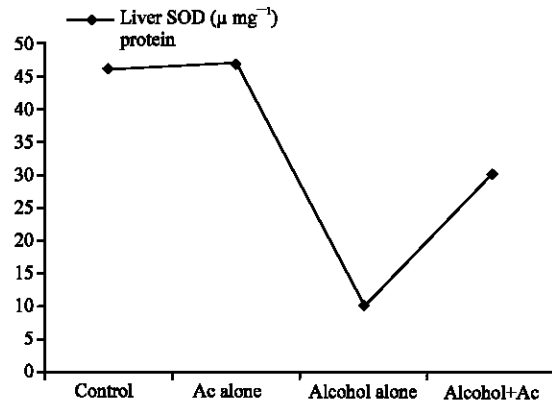


Fig. 6: Liver SOD of rabbits

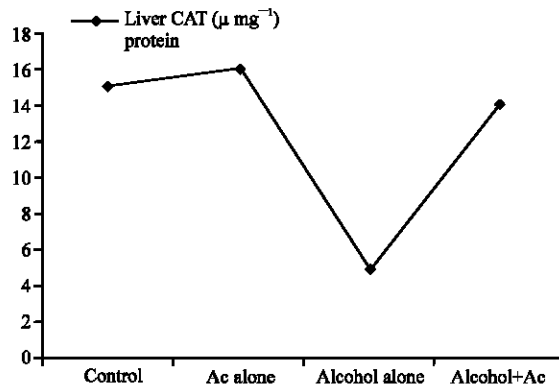


Fig. 7: Liver CAT of rabbits



Fig. 8: Liver GPX of rabbits

Co-administration of alcohol and AC exhibited a notable reduction in the liver MDA level compared to alcohol alone treated rabbits.

The activities of serum hepatic biomarker enzymes: As shown in Fig. 11-14, alcohol administration increased serum alanine transaminase (ALT), aspartate transaminase (AST),

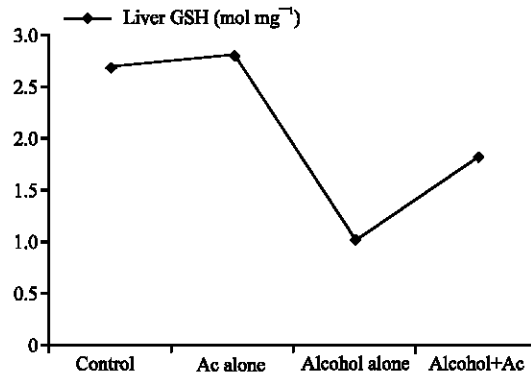


Fig. 9: Liver contents of GSH

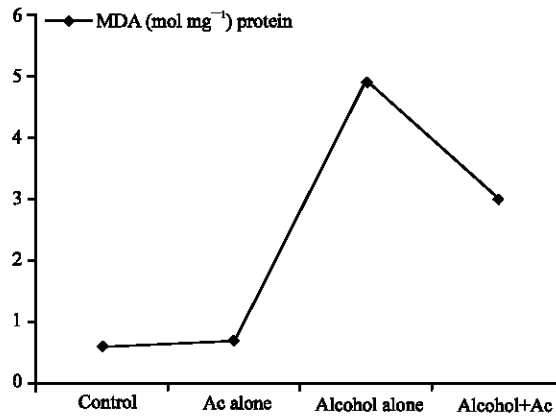


Fig. 10: Liver contents of MDA

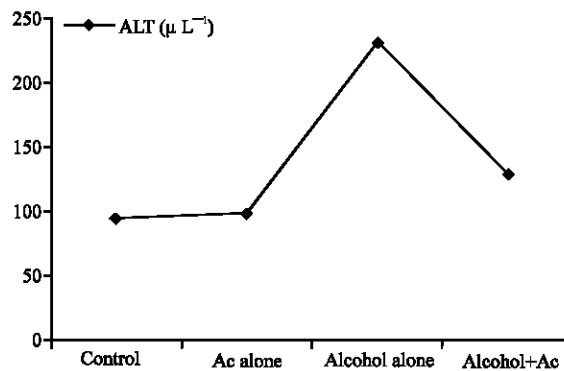


Fig. 11: The activities of serum liver ALT

alkaline phosphatase (ALP) and Gamma-Glutamyl transpeptidase (GGT). This indicated severe liver damage. Treatment with AC after alcohol abuse however, showed a significant reduction of these liver biomarker enzymes to near control values.

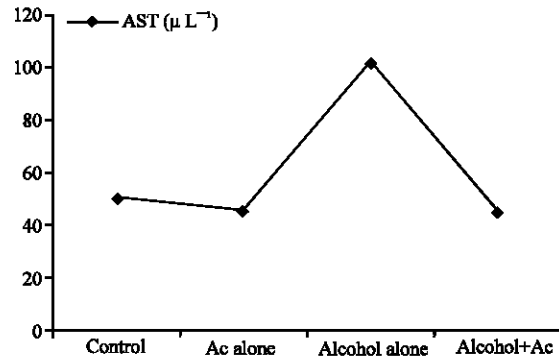


Fig. 12: The activities of serum liver AST

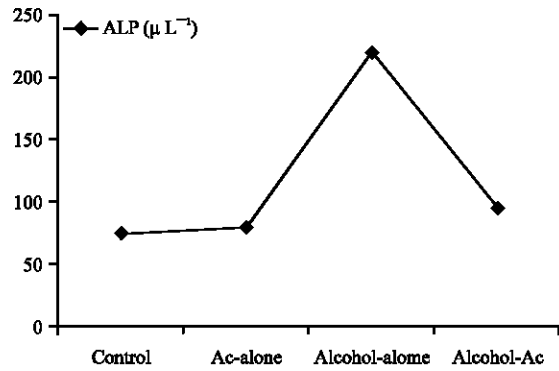


Fig. 13: The activities of serum, liver ALP

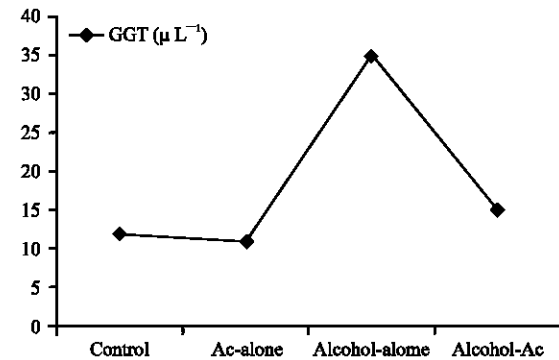


Fig. 14: The activities of serum, liver GGT

DISCUSSION

Alcohol-induced liver disease is currently a major health burden in Nigeria just like it is in most parts of the world. The liver remains the most susceptible to damage in chronic alcohol ingestion because the portal vein drains the intestines directly to the liver and due to the fact that approximately 80% of ingested alcohol is metabolized in the liver (Tuma and Casey, 2003). The mechanism by which alcohol exerts hepatotoxicity is not yet clearly understood. However, there have been various plausible postulations. One of the main pathogenetic pathways is based on the fact that alcohol is metabolized into the highly toxic acetaldehyde by alcohol dehydrogenase in the

liver, then acetaldehyde is oxidized to acetate by aldehyde oxidase or xanthine oxidase giving rise to Reactive Oxygen Species (ROS) via cytochrome P450 2E1 (Tuma and Casey, 2003). Furthermore, chronic alcohol consumption increases Nitric Oxide (NO) level which may lead to toxicity by peroxynitrite, a potent oxidant (Venkatraman *et al.*, 2004; Pacher *et al.*, 2007). The present study was therefore designed to evaluate the potential hepatoprotective effect of *antioxidant-rich Allium cepa* extract following chronic alcohol abuse in rabbits.

The findings from this study demonstrate that chronic alcohol abuse decreased the absolute testicular weights, testicular weight/body weight ratio and testicular volumes of rabbits. The animals that had co-administration alcohol and *Allium cepa* however, showed a fairly preserved testis weights, testis weight/body weight ratio and testis volumes.

An assessment of the liver histological profiles of all the groups of rabbits that received alcohol indicates varying alterations of the liver cytoarchitecture as was the case in various other earlier studies (Sillanauke, 1996; Nanji *et al.*, 2001; Lieber, 2004). Further, as was the case with the gross anatomical parameters and for probably similar reasons, co-treatment with *Allium cepa* showed a remarkable improvement in the liver histological profiles.

Estimation of lipid peroxidation, GSH content as well as SOD, CAT, GPx and other antioxidant enzyme activities in biological tissue have been always used as markers for tissue injury and oxidative stress (Chularojmontri *et al.*, 2005; Prahalathan *et al.*, 2005; Atessahin *et al.*, 2006; Saalu *et al.*, 2007; Saalu *et al.*, 2009; Saalu *et al.*, 2010). In the present study, liver derangement and oxidative stress induced by alcohol administration are also manifested by a significant increase in the activities of antioxidant enzymes, SOD, CAT, GPx and the liver content of MDA and a significant decrease of GSH. Remarkably, co-administration of laboratory animals with extract of *Allium cepa* strikingly ameliorated the oxidative stress induced by alcohol abuse.

The most prominent result of liver damage is the release of intracellular enzymes such as ALT, AST, ALP and GGT into the blood stream. This leads to an increase in serum levels of these enzymes, therefore their serum levels can serve as indicators of liver status (hence they are termed liver biomarker enzymes). In the present study, alcohol intake significantly increased liver enzymes (ALT, AST, ALP and GGT). These findings are in agreement with Pari and Karthikesan (2007), who indicated that chronic alcohol intake leads to many cellular and tissue abnormalities such as alteration in liver enzymes (ALT, AST and ALP), which could be due to the increased permeability, damage and/or necrosis of hepatocytes (Sarananan *et al.*, 2006). The results of our present study demonstrated that administration of *Allium cepa* to rabbits after alcohol abuse remarkably reduced the serum levels of these liver biomarker enzymes.

Several studies (Tuma and Casey, 2003; Venkatraman *et al.*, 2004; Pacher *et al.*, 2007) indicate that free radicals or reactive oxygen species such as a hydroxyl ethyl radical, superoxide and hydroxy radicals are responsible for alcohol induced liver oxidative stress and hepatotoxicity. Also, Prakash *et al.* (2007), reported that *Allium cepa* (onion) is a rich source of polyphenols with promising antioxidant and free radical scavenging potentials and has the ability to provide protection against DNA damage caused by reactive oxygen and reactive nitrogen species.

In conclusion, this study showed clearly the beneficial effects of *Allium cepa* extract in protecting animals against alcohol induced liver oxidative damage. This protective potential of *Allium cepa* could be at least in part due to its free radical scavenging capabilities.

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