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Keywords: Ascorbic acid; Lipid profile; Electrolyte; *Massularia acuminata*; Aluminium chloride



Research Article



Synergistic Assessment of Supplementation of Ascorbic Acid and *Massularia acuminata* Extracts on Serum Electrolyte and Lipid Profile Indices of Dyslipidemia in Adult Wistar Rats Exposed to Aluminum Chloride Toxicity

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Abstract

Background: Aluminum chloride (AlCl₃) toxicity is a growing concern due to its prevalence usage in various industrial and environmental settings. Prolonged exposure to aluminum chloride can lead to oxidative stress, electrolyte imbalances, and alterations in lipid metabolism. This study aimed to investigate the effects of supplementation of ascorbic acid and *Massularia acuminata* extracts on electrolyte function and lipid profile parameters in adult Wistar rats exposed to aluminum chloride toxicity.

Methodology: The stem barks of *Massularia acuminata* were air-dried at room temperature for thirty (30) days and were mechanically ground into fine powder by using an electrical mill. The powder was kept in air-tight container until use. Six hundred (600 g) of the dried powders was dissolved in 4 litres of 80 % (v/v) of methanol, ethanol and butanol respectively for 72 h with occasional agitation using sterile rod. The resulting mixture obtained was then filtered using pieces of white cotton gauze and concentrated in a rotary evaporator following by dryness under vacuo at 40 °C in a rotary evaporator. The extracts that were obtained were then concentrated to dryness 'in vacuo' to yield the respective solvent extracts For the animal study, then, fifty Adult Wistar rats was randomly divided into several groups, including a control group, an aluminum chloride-exposed group, and treatment groups supplemented with ascorbic acid, *Massularia acuminata* extracts, and combination of both in varied doses. The dosage of supplementation was determined based on preliminary experiments and relevant literature. The rats in the aluminum chloride-exposed group and the treatment groups received oral administration of aluminum chloride at a specific dose of (34 mg/kg) for a defined duration to induce toxicity. The control group received a placebo. The treatment groups received supplementation of Ascorbic Acid and *Massularia acuminata* extracts received daily oral supplementation of ascorbic acid, *Massularia acuminata* extracts, or a combination of both, while the control and aluminum chloride-exposed groups received a placebo.

Results: The result showed that there was a significant ($p < 0.05$) decrease in the lipid profile of Total Cholesterol (TC), Very Low-Density Lipoprotein (VLDL) and a non-significant decrease in High Density Lipoprotein (HDL) treated with vitamin C while a significant decrease in the level of HDL, VLDL, LDL and cholesterol were observed from the groups treated with the various plant extracts.

Conclusion: From the study, it can therefore be concluded that ethanol leaf extract of *Massularia acuminata* has protective effect against aluminium chloride induced hepatotoxicity, oxidative stress and alterations in lipid and electrolyte profile in Wistar rats.

Introduction

Dyslipidemia is on the rise in young people in both developed and developing countries. It is believed that with increasing prevalence of sedentary life styles and dietary

changes, hyperlipidemia is emerging as an important cause of adverse health outcomes including cardiovascular complications, obesity, metabolic disorders, infertility and so on [1]. According to an estimate global infertility range between 10% - 15% of couple, affecting 50-80 million people all over

the world. Male infertility has a substantial share of the total infertility burden [2]. Over the years, a number of population-based studies have highlighted a trend towards deterioration of semen quality [3]. Due to environment contamination and change of life style, the infertility rate is going to increase in future. Lipids have an important role in the functional activity of sperm cells, sperm viability, maturity, capacitation and fertilization [4,5]. Excessive intake of high cholesterol or high fat diet may induce hypercholesterolemia/hyperlipidemia and disturb cholesterol homeostasis in the body which may adversely affect normal male reproductive functions. Several animal and clinical studies have been conducted to focus on the association of hyperlipidemia/hypercholesterolemia with male infertility. However, these studies show some variation in the results and also the exact molecular mechanism(s) of action are still poorly known. Therefore, the purpose of this review is to critically explore the links between hypercholesterolemia/hyperlipidemia and male infertility, to address how it disrupts the male reproductive function and fertility. Lipids play multiple roles that either individually or collectively influence many cell processes. Cholesterol is one of the most important bio-molecule in animals and has significant role in cellular function and integrity. It is essential for membrane composition, permeability, fluidity, endocytosis and intracellular signaling. It is also a precursor of all sexual hormones [6,7]. Cholesterol has crucial functions in the area of male and female reproductive physiology, from sex differentiation to gamete formation. The sperm membrane is composed from heterogeneous mixture of phospholipids, glycolipids and sterol and plays an important role in sperm capacitation and fertilization [8,9]. It is known that the acrosome reaction and sperm-oocyte fusion both are membrane associated events [10,11]. Besides this, the lipids of the spermatozoa have been suggested to be important for viability, maturation and function of spermatozoa [12,13]. Cholesterol's ability to other saturated phospholipids contributes to the formation of rafts that have distinctive protein composition and are supposed to play an important role in signal transduction pathway [14,15]. Spermatozoa leaving testes are neither mobile nor fertile. As spermatozoa transverse through the epididymis and female genital tract, they undergo multiple biochemical and physiological modifications, such as the removal of seminal plasma proteins/glycoproteins absorbed to the surface of ejaculated spermatozoa, as well as modification and reorganization of sperm plasma membrane molecules [16-18]. As spermatozoa travel through the epididymis, modification in the content of cholesterol and different phospholipids takes place to promote membrane fluidity [19,20].

Massularia acuminata

Massularia acuminata (Ma) is an aphrodisiac herb from Yoruba medicine of Nigeria. The plant appears to contain a

mixture of alkaloids, anthraquinones, saponins, phenolics, flavonoids, and tannins. *Massularia acuminata* (G. Don) Bullock ex Hoyl. (Rubiaceae) known as pako ijebu or orin ijebu (Yoruba-Western Nigeria), is a tree growing up to 5 m high. It is distributed from Sierra Leone through Nigeria to Democratic Republic of Congo. The large leaves are practically stalkless, elliptic, acuminate and almost glabrous. Phytoconstituents of the aqueous extract of *M. acuminata* stem included alkaloids (0.22%), saponins (1.18%), anthraquinones (0.048%), flavonoids (0.032%), tannins (0.75%) and phenolics (0.066%). The juice from the fruit is used as antibiotics for the treatment of eye infections in Sierra Leone. The stems are used as chewing stick for oral hygiene in Nigeria. The decoction or infusion of the stem has also been claimed to be used as aphrodisiac and anticarcinogenic. Previous studies have reported that the alkaloidal content of *M. acuminata* stem was responsible for the antibacterial and anti-inflammatory activities of the plant. Furthermore, a recent study by Yakubu, et al. 2008 [21] have also validated the aphrodisiac claim of aqueous extract of *M. acuminata* root at 100, 300, and 500 mg/kg body weight in male rats. In addition, Yakubu, et al. [22] have also reported that the aqueous extract of *M. acuminata* stem at the doses of 250, 500, and 1000 mg/kg body weight exhibited dose related androgenic and gonadotropic effects in male rats. Thus, it is logical to investigate the acclaimed aphrodisiac potential of the plant stem in a complete randomized design at the same doses used previously by Yakubu, et al. [21]. In several replicated rat studies, *Massularia acuminata* (Ma) has been shown to increase parameters of sexuality in males. It did increase testosterone, but did so at a level corresponding with sexual activity and lesser than the control (Viagra); these increases may be vicarious of increased sexual activity rather than from the compound itself. Lower doses seem more effective than higher, with 50 mg/kg bodyweight increasing sexuality and testosterone more than 100 mg/kg and 200 mg/kg. Although this relationship appears to be reversed at dosages of 500 mg/kg and 1000 mg/kg bodyweight, in which sexuality and testosterone levels begin to become elevated again. The 1000 mg/kg group had a spike above the expected value, and was nearly double the control. These studies were conducted in otherwise healthy rats. When 1000 mg/kg in rats is converted into a human dosage based on Body Surface Area it results in a 160 mg/kg bodyweight dosage of *Massularia acuminata*; the lower dose, 50 mg/kg, correlates to 8mg/kg bodyweight and is more feasible.

Aluminium chloride

Aluminium (Al) is an abundant element in the earth's crust, existing primarily as polymorphous alumina silicates in combination with oxygen, silicon, fluorine, and other elements in soil, rocks, clays, and gems. Aluminium utensils are widely used throughout the world and for a long time it has been considered to exist predominantly in forms

not biologically available to humans and animals. When aluminium cutlery is used with salty, acidic, or alkaline foods, the individual's aluminium exposure can increase significantly [23,24]. In the medicine field, aluminium compounds are now widely used being in the composition of numerous pharmaceutical conditionings (e.g., antacids, phosphate binders, buffered aspirins, vaccines, or antiperspirants), making them a potential threat [25-27]. To date, the main known toxicological effects of aluminium included anaemia [28], neurodegenerative disorders such as Alzheimer disease and dementia [29], amyotrophic lateral sclerosis [30,31], hepatotoxicity [32,33], or diverse reproductive disorders [34-36]. The toxic effects associated with aluminium are due, in most situations, to generation of Reactive Oxygen Species (ROS) [37,38], conducting to cellular lipidic proteinic and/or DNA oxidative deterioration [39,40]. Aluminium ingestion in excessive amount leads to accumulation in target organs and has been associated with damage of testicular tissues of both humans and animals. Alteration in the histology of testis [41] deterioration in spermatogenesis and sperm quality; enhancement of free radicals and alterations in antioxidant enzymes [36,42]; interruption in sex hormone secretion [43,44]; and biochemical changes in testis and other accessory reproductive organs [45] are some of the aspects suggested that Aluminium exposure causes adverse impact on male reproduction.

Ascorbic acid

Ascorbic acid, commonly known as vitamin C, is a water-soluble vitamin and a vital micronutrient essential for various physiological processes [46,47]. It is a potent antioxidant, playing a significant role in neutralizing free radicals, supporting immune function, and facilitating the biosynthesis of collagen, L-carnitine, and certain neurotransmitters [48]. Since humans lack the enzyme *gulonolactone oxidase*, which is necessary for ascorbic acid synthesis, it must be obtained from dietary sources or supplements [49,50].

Rationale of the research

Although individual studies have explored the therapeutic effects of ascorbic acid and *Massularia acuminata*, their combined efficacy remains underexplored. This study addresses the following gaps:

1. The extent to which the co-supplementation of ascorbic acid and *Massularia acuminata* mitigates dyslipidemia and electrolyte imbalances.
2. The biochemical mechanisms underlying their synergistic effects on oxidative stress and lipid metabolism.
3. The potential of natural remedies to provide an affordable and effective alternative to synthetic drugs in managing $AlCl_3$ -induced toxicity.

Materials and methods

Study area and design

The study was carried out at was conducted in the Department of Biochemistry laboratory, Faculty of Science, Adekunle Ajasin University, Akungba Akoko, Ondo state, Nigeria.

Animal ethical considerations and approval

The research procedure for handling of experimental animals for this study was approved by the Adekunle Ajasin University, Akungba Akoko Central Research Committee on Animal Ethics with the approval number of AAUA/SC/BCH/RS0402 prior to commencement of research. All procedures followed were in accordance with the ethical standards of Ministry of Health, Nigeria Declaration of 1975.

Sample collection and storage

Fresh leaves and stem barks of *Massularia acuminata* were collected from Ute, in Owo Local Government of Ondo State. The plant was identified and authenticated at the University Herbarium, Department of Plant Science, Adekunle Ajasin University Akungba Akoko, Ondo State, Nigeria. Then similar voucher specimen was again re-deposited and re-authenticated for cross-confirmation at Obafemi Awolowo University Herbarium and the specimen identified with herbarium voucher number given as IFE 17568. The animals were sacrificed after two weeks of treatments, whole blood was collected into EDTA bottle and the organs were collected into plain bottle for analysis. Five mL venous blood sample was collected from antecubital vein of each of the experimental rats and control subjects in a metal-free sterile tube, between 7 and 8 am after an overnight fasting and after 2 h. The blood was then allowed to clot at room temperature for 30 min and centrifuged at 3000 rpm for 15 min to extract the serum. The serum was taken in Eppendorf tube and stored at $-20\text{ }^{\circ}\text{C}$ until analysis. Blood collection and serum separation were carried out in a dust-free environment.

Preparation of samples of *massularia acuminata* stem barks

The stem of the plant was first weighed after which it was sliced into pieces and oven-dried at $40\text{ }^{\circ}\text{C}$ to a constant weight. This was then pulverized using an electric grinding machine. A known amount (500 g) was percolated in 1 litre of distilled water with intermittent shaking and kept in the refrigerator for 48 hours. The solution was thereafter filtered using Whatman No 1 filter paper and the filtrate concentrated on a water bath to give a yield of 25.50 g representing a percentage yield of 5.10%.

Extraction and preparation of solvent extracts of *massularia acuminata* stem bark

The stem barks of *Massularia acuminata* were air-dried at room temperature for thirty (30) days and were mechanically ground into fine powder by using an electrical mill. The powder was kept in air-tight container until use. Six hundred (600 g) of the dried powders was dissolved in 4 litres of 80 % (v/v) of methanol, ethanol and butanol respectively for 72 h with occasional agitation using sterile rod. The resulting mixture obtained was then filtered using pieces of white cotton gauze and concentrated in a rotary evaporator following by dryness under vacuo at 40 °C in a rotary evaporator. The extracts that were obtained were then concentrated to dryness 'in vacuo' to yield the respective solvent extracts. The respective solvent extracts that were obtained were screened for *in vitro* antioxidant to establish their potency and used for further analyses.

Determination of the yield of *Massularia acuminata* stem bark

An empty clean and dry glass peptri dish was weighed and later the extract was poured into it. The glass peptri dish was weighed after the extract has been concentrated to constant weight. The weight of the extract was calculated as follows:

$$\text{The Percentage Yields of Extracts (\%)} = \frac{W}{w} = \frac{(\text{Weight of Glass Peptri dish and Extract} - \text{Weight of Empty Peptri Dish})}{\text{Weight of Plant materials}} * 100$$

Measurement of biochemical parameters

Fasting and after breakfast glucose level was determined by Glucose Oxidase–Peroxidase method [51], cholesterol by Cholesterol Oxidase–Peroxidase method [52], triglycerides by Trinders Glycerol Phosphate Oxidase–Peroxidase method [53,54], HDL by Poly ethylene glycol [PEG] precipitation method [55], LDL cholesterol was calculated according to Freidewald Formula [56]. The electrolytes were analyzed on Beckman Coulter DXC auto analyzer. Other biochemical parameters were determined by enzymatic process using assay kit those were adapted for experimental analysis of these parameters.

Determination of lipid profile parameters

Total triglycerides assay: Serum total triglycerides concentration was measured by the Tietze (1990) method, as described in the manual of the Randox Total triglycerides kit (Randox Laboratories Limited, United Kingdom).

Total cholesterol assay: Serum total cholesterol level was measured by the Trinder (1969) method, as described in the manual of the Randox Total cholesterol kit (Randox Laboratories Limited, United Kingdom).

HDL-Cholesterol assay: Serum HDL-cholesterol concentration was measured by the NIHCDCS (1992) method, as described in the manual of the Randox HDL-cholesterol kit (Randox Laboratories Limited, United Kingdom).

Experimental animals

A total number of 50 male Wister rats of average weight 140 g were obtained from the animal house of the Institute of Advanced Medical Research and Training, (IAMRAT), University College Hospital (UCH) Ibadan, Oyo state, Nigeria, and were allowed to acclimatize to experimental condition for two weeks. They were housed and grouped in a temperature and humidity-controlled environment under a 12 hours light/dark cycle, with their normal rat pellet ration (Top Feeds, Nigeria) and portable water available ad libitum. All experiments involving animals were conducted in the animal house of the Biochemistry Department of Adekunle Ajasin University, Akungba-Akoko. Animals were handled according to the local rules and regulation of experiment of A.A.U.A, Nigeria.

Experimental design

The rats used were divided into ten groups with five rat per groups. First group was positive control (animals not infected with aluminium chloride), while other four groups were infected with aluminium chloride and treated with solvent extract of *Massularia acuminata* and supplemented with ascorbic acids. After about one week of acclimatization, the administration of various dose of the solvent extract took place. The first group was not infected (negative control), the second group was treated with 34 mg/kg per body weight of aluminium chloride, Aluminium chloride serves as the toxicant, the third group was treated with Ascorbic acid (200 mg/kg), Vitamin C (ascorbic acid) is a potent antioxidant widely used in experimental studies to combat oxidative stress and lipid peroxidation caused by toxins such as aluminum chloride. The 200 mg dose was selected based on the following considerations: Studies have demonstrated that doses of vitamin C in the range of 100–200 mg/kg body weight effectively scavenge free radicals and enhance the body's antioxidant defense system without causing toxicity. The selected dose ensures adequate antioxidant action to neutralize the Reactive Oxygen Species (ROS) generated by aluminum chloride. As a water-soluble vitamin, excess vitamin C is readily excreted through urine, making it a safe choice for supplementation. A dose of 200 mg/kg is within the effective range and minimizes the risk of side effects, such as gastrointestinal disturbances; the fourth group received Ascorbic acid (200 mg/kg) + Aluminum chloride (34 mg/kg), the fifth group was administered with Ethanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminum chloride (34 mg/kg), the last group was treated with 500 mg per body

weight of the aqueous extract of *Massularia acuminata*, the sixth group received Ethanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminum chloride (34 mg/kg), the seventh group equally received Methanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminum chloride (34 mg/kg), the eighth group also received Methanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminum chloride (34 mg/kg), while the ninth group received Butanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminum chloride (34 mg/kg), and the tenth group received Butanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminum chloride (34 mg/kg). The choice of 50 mg and 100 mg doses of *Massularia acuminata* extract stems from its phytochemical composition, known pharmacological effects, and prior studies investigating its safety and efficacy in animal models which were confirmed from the LD50 toxicity determination while the combination of 200 mg of vitamin C with 50 mg and 100 mg doses of *Massularia acuminata* extract is designed to maximize the synergistic antioxidant effects of both agents. Vitamin C directly scavenges free radicals, while *Massularia acuminata* enhances antioxidant enzyme activity, lipid metabolism, and electrolyte balance through its phytochemical constituents. This combined approach provides a robust defense against aluminum chloride-induced oxidative damage and dyslipidemia, enabling a comprehensive evaluation of their protective effects.

The different groups of rats were treated as follows;

Group 1: Control,

Group 2: Aluminum chloride (34 mg/kg),

Group 3: Ascorbic acid (200 mg/kg),

Group 4: Ascorbic acid (200 mg/kg) + Aluminum chloride (34 mg/kg),

Group 5: Ethanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminum chloride (34 mg/kg),

Group 6: Ethanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminum chloride (34 mg/kg),

Group 7: Methanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminum chloride (34 mg/kg),

Group 8: Methanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminum chloride (34 mg/kg),

Group 9: Butanolic extract of *Massularia acuminata* (50 mg/kg) + Aluminum chloride (34 mg/kg),

Group 10: Butanolic extract of *Massularia acuminata* (100 mg/kg) + Aluminum chloride (34 mg/kg).

Procedures for lipid profile test

Total cholesterol: Three test tubes were labeled; Reagent Blank, Standard, Sample respectively. 10 µl of Distilled water

and 1000 µl of reagent was added using micropipette into test tube labeled Reagent Blank, into test tube labeled Standard 10 µl of sample and 1000 µl of reagent was added. The mixture was mixed by shaking. Incubated for 5 mins at 37 °C. Absorbance was measured against the reagent blank at 500 nm.

Calculation:

$$\text{Total Cholesterol} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} * \text{Concentration of Standard}$$

Triglyceride

Three test tubes were labeled; Reagent Blank, sample respectively. 1000 µl of Reagent 1 was added using micropipette into test tube labeled Blank, into test tube labeled Standard 10 µl of standard and 1000 µl of Reagent 1 was added. The mixture was mixed by shaking.

Incubated for 5 mins at 37 °C. Absorbance was measured against the Reagent Blank at 500 nm.

Calculation:

$$\text{Triglyceride} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} * \text{Concentration of Standard}$$

LDL-cholesterol

Three test tubes were labeled; Reagent Blank, Sample respectively. About 100 µl of Distilled water and 1000 µl of reagent was added using micropipette into test tube labeled reagent blank, into test tube labeled Standard 100 µl of sample and 1000 µl of reagent was added. The mixture was mixed by shaking. Incubated for 5 mins at 37 °C. Absorbance was measured against the reagent blank at 500 nm.

Calculation:

$$\text{LDL - Cholesterol} = \frac{\text{Absorbance of Sample}}{\text{Absorbance of Standard}} * \text{Concentration of Standard}$$

Statistical analysis

All data were subjected to statistical analysis. Statistical analysis was performed using SPSS version 20.0 (IBM, U.S.A). The data were analyzed using one-way analysis of variance (ANOVA) and significant differences were determined using post Hoc Duncan multiple comparison test ($p < 0.05$). Data are expressed as mean ± SEM. Comparisons between different groups were done using one-way analysis of variance (ANOVA) followed by Turkey – Kramer multiple comparisons test using the software Graph Pad Prism. A probability level of less than 0.05 was accepted as statistically significant. Values were expressed as mean ± SEM. Comparison of data between patient and control groups was performed by one-way ANOVA analysis. p - values < 0.05 were considered statistically significant, p - value < 0.01 were considered statistically highly

significant and p - value < 0.001 were considered statistically very highly significant. The results were considered significant at 95% confidence level. The values are represented as mean \pm standard deviation.

Results

The total yield from the extraction of 600 g of dried stem bark of *Massularia acuminata* weighed 25.50 g which represents 5.10% of the starting material. The results in Figures 1-4 summarize the effects of oral vitamin C and various extracts of *Massularia acuminata* administration on electrolyte profiles (mmol/L). There was a significant decrease in the potassium and chloride level of the groups induced with $AlCl_3$ without treatment compared to the control and the treated groups. A significant increase in sodium and calcium level of the groups treated with plant extract and ascorbic acid compared to the control group were observed. The effects of oral administration of extracts of *Massularia acuminata* and ascorbic acid on lipid parameters (mmol/L) of Wistar rats induced with *aluminium chloride* are presented in Figures 5-9. The result indicates that there was no significant change in the values of HDL and TG of the test groups relative to the control but there was significant ($p < 0.05$) decrease in total serum

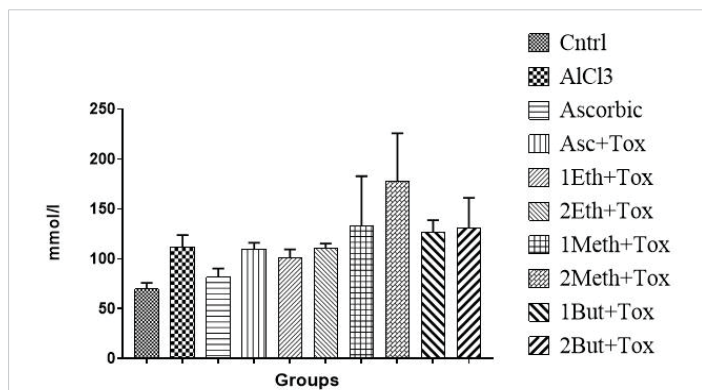


Figure 1: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum Sodium Level of Rats Exposed to Aluminium Chloride.

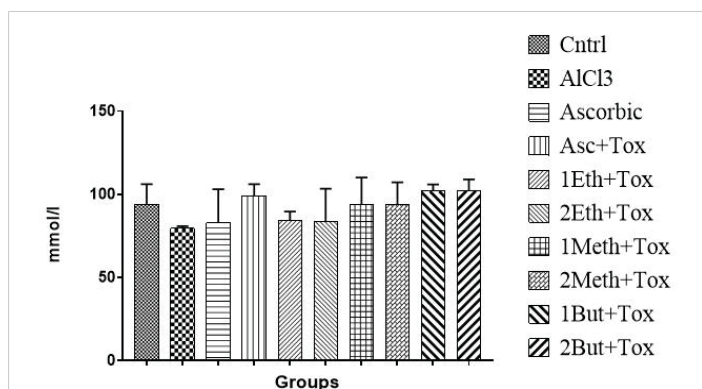


Figure 2: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum Chloride Level of Rats Exposed to Aluminium Chloride.

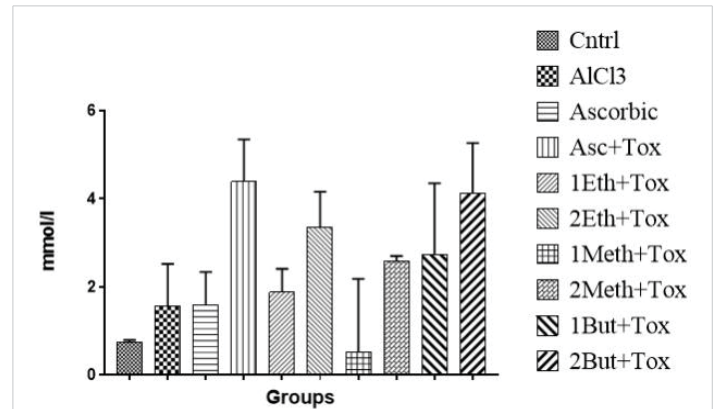


Figure 3: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum Calcium Level of Rats Exposed to Aluminium Chloride.

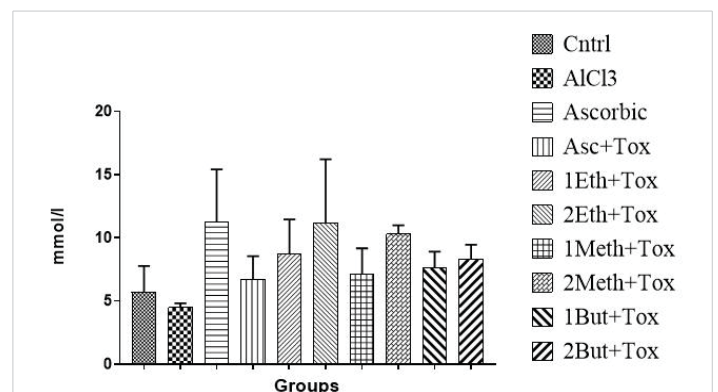


Figure 4: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum Potassium Level of Rats Exposed to Aluminium Chloride.

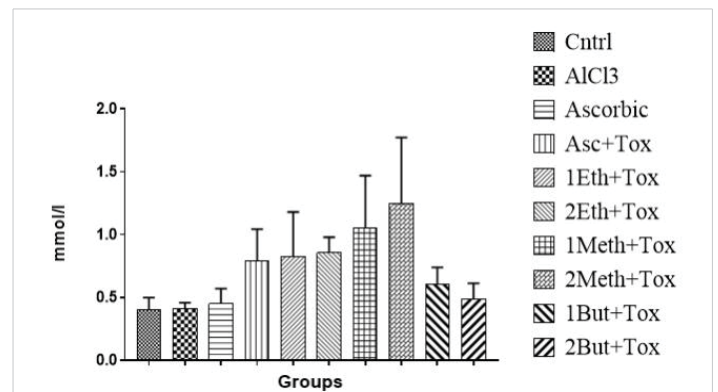


Figure 5: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum VLDL Level of Rats Exposed to Aluminium Chloride.

cholesterol, VLDL and LDL in the treatment group compared with the control. There was no effect shown in VLDL, HDL and TG induced with aluminium chloride when compared with the control.

Discussion

The leaf extract of *Massularia acuminata* is reported to be hepatoprotective and to possess antioxidant properties [57]. It has also been observed that the hepatotoxic effect

of aluminium chloride is mediated by the generation of free radicals via oxidative stress [58,59]. Hence, this study evaluated the protective potentials of various leaf extracts of *Massularia acuminata* against aluminium chloride induced toxicity adult Wistar rats. The effects of oral administration of extracts of *Massularia acuminata* and ascorbic acid on serum lipid profile and electrolyte induced with aluminium chloride were investigated in albino Wistar rats. The result showed that there was a significant ($p < 0.05$) decrease in the lipid profile

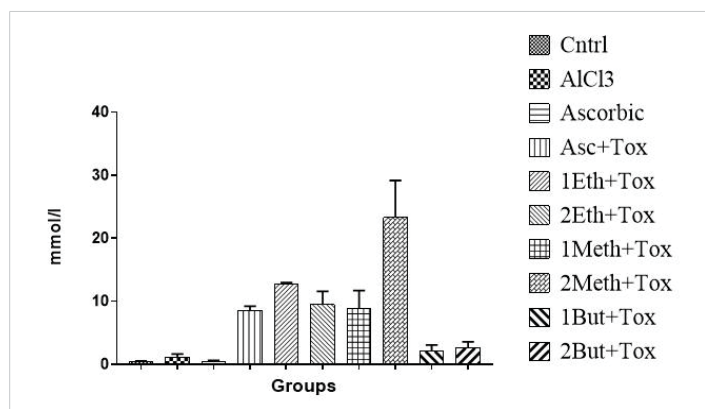


Figure 6: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum LDL Level of Rats Exposed to Aluminium Chloride.

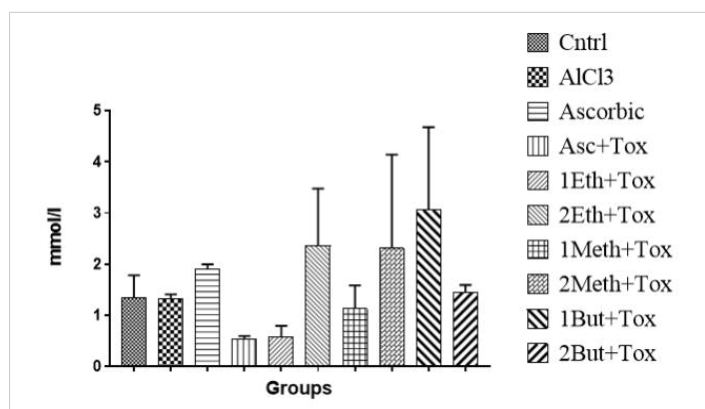


Figure 7: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum HDL Level of Rats Exposed to Aluminium Chloride.

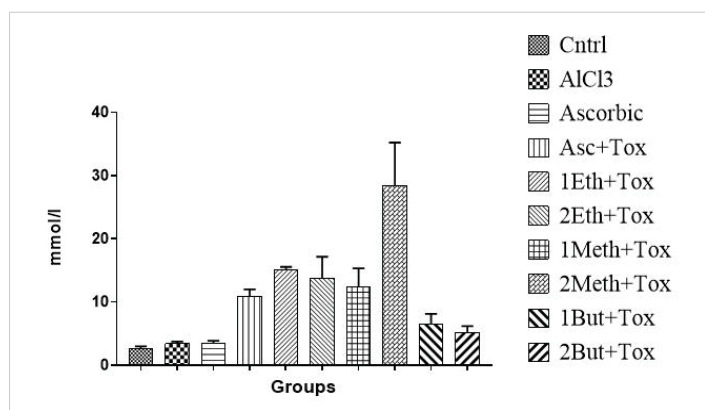


Figure 8: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum Cholesterol Level of Rats Exposed to Aluminium Chloride.

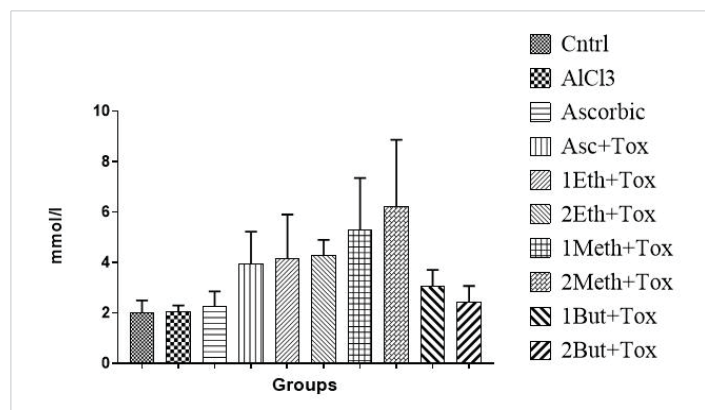


Figure 9: Effects of Extract of *Massularia acuminata* and Ascorbic Acid on Serum Triglyceride Level of Rats Exposed to Aluminium Chloride.

of Total Cholesterol (TC), very low-density lipoprotein (VLDL) and a non-significant decrease in High Density Lipoprotein (HDL) treated with vitamin C while a significant decrease in the level of HDL, VLDL, LDL and cholesterol were observed from the groups treated with the various plant extracts. The present result agrees with previous reports as documented by Chatterjea and Shinde [60] which observed a reduction in serum cholesterol in experimental animals administered with vitamin C, and of recent, the ability of the vitamin to inhibit the oxidation of HDL even in humans [61]. A plausible explanation for the observed effect on serum lipids may be due to the activation of the enzyme 7 α -hydroxylase by ascorbic acid or other metabolite found in *Massularia acuminata* which enhances the conversion of plasma cholesterol into bile acid hence resulting in a decrease in serum levels of cholesterol. In fact, Mayes [62] observed that deficiency of vitamin C inhibits 7 α hydroxylase leading to the block in bile acid synthesis and accumulation of cholesterol in serum with subsequent atherosclerosis in scorbutic Guinea pigs. Steroid hormones synthesis requires cholesterol as the precursors and vitamin C plays a role in hydroxylating the steroid hormone in the adrenal glands. It also directly meditates through a rate limiting hydroxylation of side chains, the conversion of cholesterol into steroid hormones as documented by White, et al. [63,64]. The reduction in LDL-cholesterol points to the fact that adequate vitamin C intake can reduce the incidence of atherosclerosis. Both Anderson, et al. [65] and Bsoul and Terezhalmly [66] noted that animal fed on vitamin C had reduced risk of coronary heart disease [66]. The observed decrease in total cholesterol, VLDL and most significantly the ability to reduce the levels of the atherogenic predisposing factor (serum - LDL cholesterol) yet desirably decreasing the level of HDL implies that dietary vitamin C and *Massularia acuminata* on account of its effect on lipid profile in which aluminium chloride may have a resulting effect to arteriosclerosis. Sodium (Na^+) ion and chloride (Cl^-) ion excretion from the body is a function of arterial blood pressure [67]. Sodium (Na^+) ion depletion stimulates rennin release and subsequence production of Angiotensin II, a potent vasoconstrictor [68,69]. Increased plasma sodium (Na^+)

ion levels inhibit rennin release from the juxtaglomerular cells and consequent withdrawal of angiotensin II [70,71]. When modulation of the rennin-angiotensin system is pharmacologically prevented, changes in salt intake markedly affect long term levels of arterial blood pressure [72,73]. There is therefore a need to strike a balance in the levels of plasma (Na^+) and (Cl^-) to avoid either of the extreme of hypotension or hypertension. The electrolyte profile result also obtained from this study showed a significant decrease in serum (Na^+) level for treated with 200mg of vitamin C and 50 mg of ethanolic extract of *Massularia acuminata* compared to the AlCl_3 induced untreated group. Aldosterone, a steroid hormone produced by the adrenal cortex in the zona glomerulosa, plays a crucial role in regulating sodium and potassium balance in the body [74]. Its primary function is to promote sodium reabsorption and potassium excretion in the renal tubules, maintaining fluid balance and blood pressure. Increased sodium levels in the body have a significant impact on aldosterone secretion and activity. Increased sodium levels exert a negative feedback effect on aldosterone secretion primarily through the inhibition of the RAAS pathway and the direct suppression of the adrenal cortex. This regulatory mechanism is vital for maintaining electrolyte balance, fluid homeostasis, and normal blood pressure. Disruptions in this feedback loop can lead to significant clinical consequences, emphasizing the importance of aldosterone's role in sodium and potassium balance. A small increase in plasma K^+ as small as 0.1 meq/L stimulates production of aldosterone whereas a similar decrease reduces aldosterone production and secretion. Increase in serum K^+ leads to hyperaldosteronisms, however the increases in potassium ion level in this study were significant. Vitamin C administration does not adversely impact on plasma electrolytes and therefore does not predispose to hypertension. Ca^{2+} is known to be an important constituent of bones and teeth, to be participated in the biochemical blood clotting process and to be responsible for proper nerve and muscle function [75]. The calcium result obtained from this study showed a significant decrease in serum (Ca^{2+}) level treated with 200 mg of vitamin C and 50 mg of methanolic extract of *Massularia acuminata* compared to the AlCl_3 induced untreated group. An excessive increase in serum calcium ion level can lead to hypercalcemia which can affects many bodily systems while too much decrease in calcium ion level which may lead to hypocalcemia which can reverse coronary heart failure [76-83].

In conclusion on account of the ability of vitamin C and *Massularia acuminata* extract (at high dose) to lower the atherogenic predisposing factor (serum LDL cholesterol) as well as alleviating HDL cholesterol coupled with its impact on electrolyte profile, we conclude that moderate to high intake of vitamin C and ethanolic/ methanolic extract of *Massularia acuminata* produce hypocholesterolemia effect and do not adversely affect serum electrolyte profile. It can therefore be

concluded that ethanol leaf extract of *Massularia acuminata* has protective effect against aluminium chloride induced hepatotoxicity, oxidative stress and alterations in lipid and electrolyte profile in Wistar rats.

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