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Effect of *Terminalia catappa* Seed Extract on Liver Enzymes and Lipid Profile in Male Wistar Rat

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

The traditional use of plant-derived natural substances has continued to gain traction in the last few decades and has gradually become the mainstay of human pharmacotherapy. The present study evaluated the effect of *Terminalia catappa* seed extract on the lipid profile and serum liver enzymes of male Wistar rats. Fresh, ripe fruits of *T. catappa* were sourced locally from the University of Port Harcourt and the dried seeds were extracted using methanol and used for the study. Fifteen (15) male Wistar rats (160 – 180g) were grouped into three (3) of five (5) animals per group and used for the study. Group I served as the control and received distilled water whiles groups II and II received 500 and 1000mg/kg of ethanolic seed extract of *T. catappa* (TCE) by oral gavage for twenty-eight (28) days. Animals were anaesthetized, blood was collected by cardiac puncture and analyzed for serum liver enzymes: aspartate transaminase (AST), alanine Transaminase (ALT), and alkaline phosphatase (ALP) and lipid profile: total cholesterol (TC), triglycerides (TG), high-density lipoproteins (HDL) and low-density lipoproteins (LDL) using standard laboratory methods. Results obtained from the study indicate that serum ALT and LDL were significantly reduced among rats that received TEC compared to the control ($p<0.05$). The study concludes that TEC exhibited possible hepatoprotective properties and modulation of lipid profile and hence may be effective against liver injury and protection against cardiovascular and neurogenerative diseases.

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Keywords: Terminalia catappa; liver enzyme; lipid profile; hepatoprotection; lipid peroxidation.

1. INTRODUCTION

Terminalia catappa is among the most common trees found in Nigeria. The generic name *terminalia* originates from "terminalis", a Latin word that refers to the way the leaves team at the end of the shoots. It belongs to the family of Combretaceae. The tree can grow up to 35 meters tall and has a broad, spreading canopy. Its leaves are large, glossy, and oval-shaped, and can range in colour from green to red to copper. The tree produces small, white flowers that grow in clusters, which are followed by oval-shaped fruits that contain a hard, woody shell surrounding a seed, which can be eaten raw [1,2]. They are grown for ornamental and medicinal purposes. In Nigeria, the almond tree is found in foremost towns and villages where the trees serve as shades with the seed highly sought by children who consume them as a foraged snack and by some rural dwellers as a protein supplement in local delicacies and the preparation of local herbs [3-5].

Several cultivated almond varieties display a different chemical profile in their leaves, barks, fruits and seeds due to genetic and ecological factors, as well as processing conditions [1,6,7]. They typically contain lipids, carbohydrates, proteins and other bioactive compounds. The leaves of T.*catappa* contain glucose, phenols, tannins, flavones, xanthones, alkaloids, flavonoids and triterpene steroids [8-11]. The fruit contains proteins, carbohydrates, β-carotene, glucose, tannin, oil and vitamin C [2,11], while the bark is rich in glycoside, cardiac tannins, volatile oil, saponin and phenols. The fruit also contains protein, carbohydrates, β-carotene, glucose, tannin, oil and vitamin C [11]. The seed is rich in fixed oils, olein, stearin, crude fibre, protein, fat and carbohydrate and phytochemicals such as terpenoids, alkaloids, tannins, steroids, flavonoids, saponin, glycosides, phenols, anthraquinones and phlotabinnins [11-13] and in other minerals such as calcium, iron, phosphorus, potassium, magnesium, copper and zinc [14]. These diverse phytochemical constituents confer on various plant parts, several applications in folk remedies. The leaves, barks and roots are used in traditional medicine. Fallen leaves of *T. catappa* are used to treat headaches, liver diseases, and colic and as a diuretic [15]. In Ayurveda, the fruit is referred to as the "king of medicine" and used in the treatment of inflammation, asthma, ulcer, diarrhoea and allergies [16]. The seeds are thought to possess aphrodisiac activity and have been found effective in the treatment of sexual malfunction and premature ejaculation [17,18]. Documented research evidence has shown the seeds of *T. catappa* to possess anthelmintic [19], antioxidant [20,21], aphrodisiac [18], antidiabetic and hypolipidaemic potentials [22].

The leaves, bark and fruit of *T. catappa* have been evaluated for their pharmacological actions [23-27]. However, the seed (or nut/kernel) has remained minimally explored for potential effects on biochemical parameters. The present study, therefore, is aimed at evaluating the effect of *T. catappa* seed extract on the lipid profile and serum liver enzymes of Wistar rats to plug the knowledge gap on the safety and efficacy of the medicinal use of seeds of *T. catappa* and shed more light on their effect on lipid metabolism.

2. MATERIALS AND METHODS

2.1 Source and Preparation of Plant Material

Fresh, ripe fruits of *T. catappa* were collected from host trees at the University of Port Harcourt, Port Harcourt, Nigeria from February through April 2022. The fresh fruit of *T. catappa* was identified at the Department of Plant Science and Biotechnology, Faculty of Science, University of Port Harcourt and deposited with a herbarium number UPH/P/267. The fruits were meticulously cracked open to expose the seed within. Seeds of *T. catappa* were shed dried for 4 weeks and then ground into a coarse powder. The ground seeds were then extracted by the method of Soxhlet [28]. The *T. catappa* seed extract (TCE) was refrigerated at 5ºC pending administration.

2.2 Research Animals

Fifteen (15) male Wistar rats (160 – 180g) were locally sourced from the animal house of the Department of Human Physiology and used for the study. The animals were housed in standard rat cages under hygienic animal husbandry conditions: temperature, 25 - 28ºC; humidity 40 – 60% while maintaining a 12hr light/dark cycle. The animals were allowed to acclimatize for four (4) weeks to their new environment before the commencement of the study. During this period, they were allowed a standard rat chow and water a*d libitum*.

2.3 Experimental Design

The fifteen (15) male Wistar rats were randomly grouped into three (3) groups of five (5) animals each. Group I served as the control and received distilled water, while groups II and III served as the experimental groups and received a methanolic seed extract of *T. catappa* at 500 and 1000mg/kg respectively by oral gavage. Daily oral administration of distilled water and seed extracts of *T. catappa* lasted for 28 days between 8 – 10 am. The animals were weighed before and after the experiment using a digital weighing scale (SF400 Shenzhen Jufengcai Electronic Technology Co., LTD, China). The animals were then anaesthetized with sodium thiopental (50 mg/kg, i.p.) and blood was collected via cardiac puncture into plain sample bottles for laboratory analysis.

2.4 Laboratory Analysis

Blood samples were centrifuged at 3000rpm (Xiangtian 800-1, China). The supernatant serum was carefully collected using an automatic micropipette (Rong Tai Biochemical Engineering Co., Ltd, China). Lipid profile: total cholesterol (TC), triglycerides (TG) and high-density lipoproteins were determined using standard laboratory kits (Randox, UK) while low-density lipoproteins (LDL) were estimated using Friedewald's equation [29]. Liver enzymes: aspartate transaminase (AST), alanine transaminase (ALT), and alkaline phosphatase (ALP) were determined using colourimetric methods (Randox, UK).

2.5 Statistical Analysis

Data obtained from laboratory investigations in the study were analyzed using IBM Statistical Product and Service Solutions (SPSS version 25). The mean and standard error of the mean were calculated for each parameter. The mean values obtained for the experimental groups (II & III) were compared to the control (Group I) using the analysis of variance (ANOVA) followed by a least significant difference (LSD) posthoc analysis (ANOVA). A p-value less than 0.05 ($p<0.05$) was considered statistically significant.

3. RESULTS

Table 1 shows the effect of 28 days of administration of methanolic extract of *T. catappa* on the serum liver enzyme of male Wistar rats. The results indicate that there was a significant reduction in the mean values of serum ALP among the animals that received 1000mg/kg of *T. catappa* compared to the control ($p<0.05$). Though the mean serum values of AST and ALT showed a dose-dependent reduction among the 500 and 1000mg/kg when compared with the control, it was not statistically significant ($p>0.05$).

Table 2 shows the effect of 28 days of administration of methanolic extract of *T. catappa* on the liver profile of male Wistar rats. Our results indicate that there was a dose-dependent reduction in the mean values of serum LDL among animals that received 500 and 1000mg/kg of *T. catappa* compared to the control ($p<0.05$). Though the mean serum values of TC and TG showed a gradual dose-dependent reduction among the 500 and 1000mg/kg when compared with the control, it was not statistically significant. Similarly, the mean values of serum HDL were observed to show a dose-dependent non-significant increase among the experimental groups compared to the control ($p>0.05$).

Table 1. The effect of *T. catappa* on serum liver enzymes of male Wistar rats

Groups	Treatment	AST (iu/L)	ALT (iu/L)	ALP (iu/L)
I	Distilled water	36.20 ± 1.66	18.00 ± 0.77	93.60 ± 6.30
II	500 mg/kg TCE	35.80 ± 8.22	19.40 ± 1.60	84.20 ± 5.68
III	1000 mg/kg TCE	31.00 ± 4.23	17.80 ± 0.80	50.20 ± 3.25*

*values expressed as mean ± standard error of mean;*significant difference compared to control (P<0.05)*

Table 2. The effect of *T. catappa* on the serum lipid profile of male Wistar rats

Groups	Treatment	TC (mmol/L)	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
I	Distilled water	3.61 ± 0.23	0.43 ± 0.13	2.47 ± 0.21	0.92± 0.10
II	500 mg/kg TCE	3.24 ± 0.19	0.34 ± 0.34	2.89 ± 0.76	0.20 ± 0.14*
III	1000 mg/kg TCE	3.12 ± 0.51	0.31 ± 0.25	2.84 ± 0.55	0.14 ± 0.10*

*values expressed as mean ± standard error of mean;*significant difference compared to control (P<0.05)*

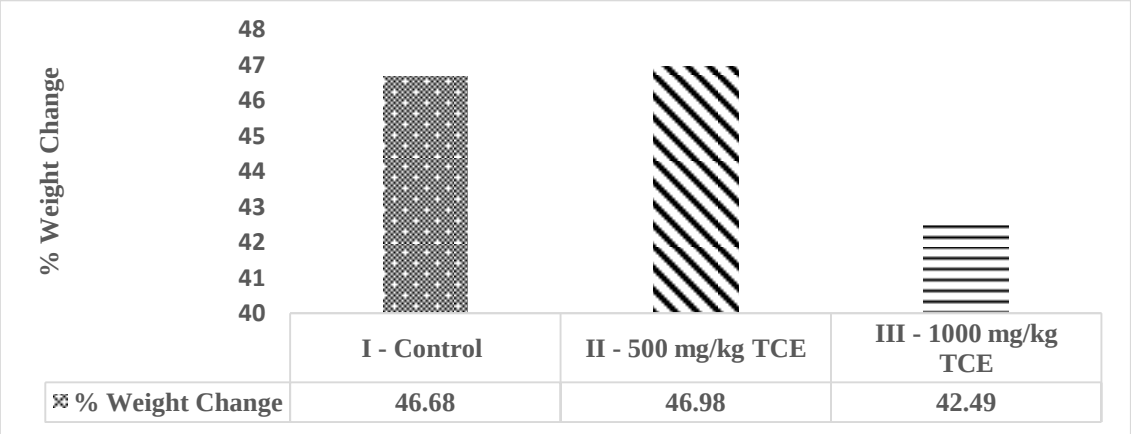

Fig. 1. The effect of *T. catappa* on percentage weight changes of male Wistar rats

Data on the percentage weight gain of weight of male Wistar rats following a 28 days administration of methanolic *T.catappa* seed extract is shown in the bar chats above. Data obtained showed that group II animals (500mg/kg) had the highest percentage increase in their weight gain (46.98%) followed by group I (control) (46.68%) and group III (1000mg/kg) (42.9). However, there were no significant changes among the groups when the experimental groups were compared with the control.

4. DISCUSSION

The traditional use of plant-derived natural substances has continued to gain traction in the last few decades and has gradually become the mainstay of human pharmacotherapy [30-33]. The present study investigated the effect of the oral administration of *Terminalia catappa* seed extract (TCE) on liver enzymes and lipid profile of male Wistar rats.

4.1 Effect on Liver Enzymes

Results obtained from this study show that the oral administration of TCE caused a significant reduction in the mean values of serum ALP among the animals that received 1000mg/kg of *T. catappa* compared to the control ($p<0.05$) (Table 1). Data also indicate that the mean serum values of AST and ALT showed a dose-dependent reduction among the animals that received 500 and 1000mg/kg of TCE when compared with the control, however. it was not statistically significant. The liver functions in many metabolic processes in the body and hence it is the primary target of most toxicants. It plays a role in clearing and transforming toxicants and other chemicals [34]. Routine measurement of liver function includes the measurement of serum AST, ALT and ALP. They are often used as indicators of liver function and can be affected by liver damage or disease [35-37]. Though they are all found in the kidney, muscle and liver, they are predominately used to access liver function. The observed significant reduction in ALP and the marginal reduction in AST and ALT could be attributed to the hepatoprotective potential of TCE. The seed extract of *T.catappa* has been shown to contain significant quantities of flavonoids and phenols [11-13] which possess potent hepatoprotective ability [38-40]. Also, TCE has been demonstrated to have antioxidant activity [20,21] which has the ability to attenuate liver enzymes [38]. Similarly, the leaf extract of *T. catappa* has been shown to reverse chemically induced liver injury in experimental models [11,41,42]. The present study, therefore, hypothesizes that TCE has potent hepatoprotective potential and could be useful in the treatment of toxin-induced liver injury.

4.2 Effect on Lipid Profile

The result of the present study shows that there was a dose-dependent reduction in the mean values of serum LDL among animals that received 500 and 1000mg/kg of TCE compared to the control ($p<0.05$) (Table 2). Also, serum TC and TG showed a marginal dose-dependent reduction among the 500 and 1000mg/kg when compared with the control, although not statistically significant. On the other hand, serum HDL was observed to show a dose-dependent increase among the experimental groups (II and III) compared to the control. The possible TCE-attenuating effect on lipid profile is attributable to

its antioxidant property [20,21] and its ability to prevent lipid peroxidation. Lipid peroxidation is a process that occurs when free radicals react with lipids in cell membranes, resulting in damage to the cell membrane and the release of harmful byproducts [43,44]. This process is implicated in the aetiology of cardiovascular and neurodegenerative diseases, and cancer [45,46]. Flavonoids and other antioxidant phytochemicals contained in TCE can help to prevent lipid peroxidation by neutralizing free radicals and protecting cell membranes from damage and inhibiting the formation of reactive oxygen species (ROS) [47-49]. They also enhance the activity of antioxidant enzymes, such as superoxide dismutase (SOD), glutathione peroxidase (GPx) and catalase (CAT) which can further protect cells from oxidative damage [38,49]. Also, Flavonoids are known to impact lipid metabolism by reducing cholesterol synthesis or increasing LDL receptor expression [50,51]. Also, saponins have been shown to suppress cholesterol absorption, increase lipid peroxidation and depress the rates of intestinal hepatic and intestinal cholesterol synthesis [51-54]. Likewise, leaf extracts of *T. catappa* have been shown to possess anti-hyperlipidaemic properties in experimentally induced hyperlipidaemia and diabetes [22,55,56]. Besides the significant reduction in LDL, the present study hypothesizes that *T. catappa* can attenuate lipid metabolism by marginally reducing TG and TC and increasing HDL.

4.3 Effect on Body Weight

There was no significant change in the body weight of animals treated with TEC as the data obtained showed that group II animals (500mg/kg) had the highest percentage increase in their weight gain (46.98%) followed by the group I (control) (46.68%) and group III (1000mg/kg) (42.90%). This could be due to the short duration of the administration of TEC. However, the leaves of *T. catappa* have shown potent anti-obesity activity in experimentally induced obesity animal models [55,56].

5. CONCLUSION

In light of the paucity of data regarding the pharmacological effects of the seed extract of *T. catappa*, the present study evaluated the effects of TCE on liver enzymes and lipid profile using Wistar rat models. The study concludes that TEC exhibited possible hepatoprotective properties and modulation of lipid profile. This study shows that *T. catappa* may be effective against liver injury and protection against cardiovascular and neurogenerative diseases due to the reduction of LDL. Hence the consumption of *T. catappa* seeds as a dietary supplement is recommended.

ETHICAL CONSIDERATIONS

Animals used for the study were housed and handled in compliance with standard guidelines and care of the use of laboratory animals [30, 31]. The research design and protocol were approved by the institutional research ethics committee.

COMPETING INTERESTS

The authors have declared that no competing interests exist.

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