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Crinum glaucum Bulb Extract Improves the Lipid Profile of Endotoxin-Induced Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author OOO designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors RIK and GAA contributed to conception and design, analysis and interpretation of data and critical review of the manuscript. Authors OAO and KOO managed the analyses of the study, literature searches and interpretation of data. Authors AOF and AJS managed the analyses of the study and literature searches. Authors OBA and BOE supervised the work and contributed intellectual idea in the discussion and overall presentation of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Background and Objective: Medicinal plants are widely known as sources of potential that are used in traditional medicine. The effect of C*rinum glaucum* (*C. glaucum*) aqueous extract on the lipid profile of endotoxin-induced rats was evaluated.
Methodology: Fifty Wistar rats (male and female) were divided randomly into five groups (n = 5). Group 1 is the control group. Group 2 was administered *C. glaucum* aqueous extract (1000 mg/kg body weight). Group 3 was endotoxin-induced with 1 ml/kg body weight single dose of lipopolysaccharide (LPS) for 4 hours. Group 4 was given LPS (4 hours) and treated with *C. glaucum* aqueous extract. Group 5 was administered *C. glaucum* aqueous extract, LPS, and *C. glaucum* aqueous extract. At the end of administration, blood and organs (brain, heart, lungs, liver, and kidney) were harvested for the lipid profile (triglyceride, cholesterol, and phospholipid) assay analysis using a spectrophotometric method.
Results: The reduction of cholesterol, triglyceride, and phospholipid concentrations is the hallmark of endotoxin, as revealed in this study. While *C. glaucum* administration significantly ($p<0.05$) reduced cholesterol concentrations, there was an up- or down-regulation of triglyceride and phospholipid concentrations in the male compartments compared to the control. A similar trend was observed in the female compartment. Data also revealed that while LPS causes a reduction in lipid profiles, the administration of *C. glaucum* reverses the effect.
Conclusion: The findings of the research suggest that *C. glaucum* has an ameliorative and therapeutic effect in improving lipid dysfunctions.

Keywords: Crinum glaucum; lipid profiles; lipopolysaccharide; therapeutic; ameliorative; dysfunction.

1. INTRODUCTION

Lipid molecules such as cholesterol, phospholipids, and triglycerides are transported through the blood as lipoproteins for vital metabolic functions [1-6]. Cellular membrane structural elements contain protein complexes like ion channels, receptors, and scaffolding complexes [3]. For energy balance, reproductive and organ physiology, as well as many other aspects of cellular biology, lipids are crucial [3-6]. Homeostasis disturbances of these lipids result in dyslipidemia, which is connected to a variety of clinical conditions, including diabetes, heart disease, inflammation, and obesity [7-10]. The administration of endotoxin, a lipopolysaccharide (LPS), component of gram-negative bacteria, causes septic shock, leading to these health conditions [11-12].

Traditional use of medicinal plants has gained awareness as a source of bioactive compounds that can change metabolic processes and lower the risk of human and animal health issues [6,13-14]. The medicinal plant, *Crinum glaucum*, is a rigid bulbous plant belonging to the Amaryllidaceae family. It is commonly known as 'Isumeri' (Yoruba language), 'Ede Chukwu' (Igbo language), 'Albasar kwa'adi' (Hausa language) and 'umNduze' (Zulu language). The English names include river lily, string-lily, swamp-lily, *Crinum* lily, and spider lily. Traditional medicine used the plant for the treatment of several ailments such as asthma, cough, and convulsions, renal and hepatic conditions, as anthelmintics and emetics, and in the treatment of sores, sexually transmitted diseases, and backaches [15-17].

The objective of the present study was to investigate the effect of *Crinum glaucum* bulb extract on the lipid profile of endotoxin-induced Wistar rats.

2. MATERIALS AND METHODS

2.1 Plant Collection, Identification and Preparation of *C. glaucum* Bulb Crude Aqueous Extract

The *Crinum glaucum* bulbs were purchased from Iyana-iba axis of Ojo Local Government area, Lagos State, Nigeria in March 2021, authenticated at the Department of Botany, Faculty of Science, Lagos State University, Ojo, Lagos State, Nigeria and deposited in the herbarium. The bulbs were rinsed in water, drained of excess water, sliced, and then weighed. 12.5 g of the bulbs were soaked in distilled water for 72 hours in a plastic container. The crude extract was collected through filtration and stored in the refrigerator for further use.

2.2 Acute toxicity studies

The acute toxicity (LD_{50}) of *C. glaucum* bulb aqueous extract was determined by oral route using the modified method of Ogunrinola et al. [5] and Adu et al. [18].

2.3 Preparation of Lipopolysaccharide (LPS)

"The LPS (Sigma Aldrich Chemical Company, St Louis, MO, USA), due to its high level of the toxin, was prepared in a solution by diluting with dextrose (2:1 w/v) and the solution was administered at 4 ml/kg body weight" [19].

2.4 Experimental Animals

Fifty (50) Wistar rats, male (25) and female (25) weighing between 100 g and 200 g, were used for the experiment. The rats were kept in the animal house. Before the experiment, the rats underwent a fourteen (14) day acclimatization period during normal day and night settings and were given free access to a standard diet (Livestock Feeds, Plc, Lagos, Nigeria) and water *ad libitum*. The study was carried out at the Department of Biochemistry, Drug Discovery Lab, Faculty of Science, Lagos State University, Ojo from March to April, 2021.

2.5 Study Design

The rats were randomly divided into 5 groups (n = 5) for both male and female. This is to understand the effect of *C. glaucum* bulb aqueous extract on sex differences.

Group 1: Water and animal feed only.
Group 2: *C. glaucum* bulb aqueous extract (1000 mg/kg body weight) for 7 days.
Group 3: Lipopolysaccharide (LPS) for 4 hours before they were sacrificed.
Group 4: LPS for 4 hours + *C. glaucum* bulb aqueous extract (1000 mg/kg body weight) for 7 days.
Group 5: 7 days of *C. glaucum* bulb aqueous extract + 4 hours of LPS + 7 days of *C. glaucum bulb* aqueous extract (1000 mg/kg body weight) body weight.

After the induction and treatment, the animals were starved for an entire night before being killed under a light anaesthetic. Blood was drawn from the animals' hearts into heparinized tubes, and the brain, heart, lung, kidney, and liver were removed. The blood and organs were processed as previously described by Ogunrinola et al., (2019; 2022) [4,5] and kept at -20^{o}C until analysis [20].

2.6 Biochemical Analysis

Lipids were extracted from the erythrocytes, brain, heart, lung, liver, and kidney according to the modified method of Axelsson and Gentili, (2014) [21]. Briefly, the erythrocytes and organ lipids were extracted with a 2:1 v/v chloroform-methanol mixture and shaken vigorously for a few seconds. The supernatant (lipid extract) was stored for further analysis. The commercially available kits were used to determine the cholesterol, triglycerides, and phospholipid concentrations in the plasma, lipid extracts from erythrocytes, brain, heart, lung, kidney, and liver, respectively [4-6,22].

2.7 Statistical Analysis

The IBM SPSS version 21.0 Statistical Software (IBM Corp., Armonk, NY, USA) was used for the analysis. Results are expressed as Mean ± SEM of 3 replicates. The level of homogeneity at $p < 0.05$ among the groups was tested using One-way analysis of variance (ANOVA).

3. RESULTS

3.1 Acute Toxicity Studies

C. glaucum bulb aqueous extract is not toxic because no death was recorded during the experiment.

3.2 The Effect of *Crinum glaucum* Bulb Aqueous Extract on the Lipid Profile of Endotoxin-Induced Male Wistar Rats

Table 1 shows the results of the effect of aqueous extract of *Crinum glaucum* bulb on cholesterol, triglyceride, and phospholipid of endotoxin-induced male Wistar rats. The induction of endotoxin with LPS significantly ($p < 0.05$) reduced the concentration of cholesterol, triglyceride, and phospholipid in all the compartments. The administration of *C. glaucum* bulb aqueous extract (group 2) significantly ($p < 0.05$) decreased concentration of cholesterol in the plasma, erythrocytes, brain, heart, lung, liver, and kidney compared to the control. While LPS decreased cholesterol concentration in groups 4 and 5, *C. glaucum* treatment significantly ($p < 0.05$) increased the cholesterol concentration. The triglyceride concentration increased with the administration of *C. glaucum* bulb aqueous

Table 1. Effect of *Crinum glaucum* bulb aqueous extract on the lipid profile of endotoxin-induced male wistar rats

Treatment dose / Parameters		Group 1	Group 2	Group 3	Group 4	Group 5
Cholesterol Concentration						
Plasma	mg/dl	200.60±21.73[a]	152.99±36.03[b]	70.22±5.89[c]	198.95±11.39[d]	193.11±7.16[e]
Erythrocytes	mg/dl	146.41±14.65[a]	142.76±6.07[b]	32.61±4.21[c]	49.69±2.88[d]	58.69±6.00[e]
Brain	mg/g tissue	31.26±2.33[a]	23.28±0.44[b]	15.25±1.28[c]	21.53±1.52[d]	22.38±0.78[e]
Heart	mg/g tissue	16.20±1.44[a]	17.48±1.57[b]	9.22±0.82[c]	21.21±0.67[d]	23.51±1.74[e]
Lung	mg/g tissue	20.31±1.14[a]	15.45±1.34[b]	8.59±0.72[c]	12.26±0.85[d]	17.33±1.40[e]
Liver	mg/g tissue	15.76±1.04[a]	14.50±1.06[b]	6.41±0.78[c]	12.68±0.79[d]	13.70±0.82[e]
Kidney	mg/g tissue	41.17±3.27[a]	28.39±1.11[b]	11.89±0.53[c]	16.57±1.01[d]	18.48±0.84[e]
Triglyceride Concentration						
Plasma	mg/dl	118.05±4.53[a]	200.78±5.06[b]	51.55±3.62[c]	163.61±17.05[d]	201.93±5.07[e]
Erythrocytes	mg/dl	87.03±12.74[a]	227.42±12.01[b]	55.30±4.84[c]	215.94±4.13	243.24±4.22
Brain	mg/g tissue	37.99±1.60[a]	41.97±1.89[b]	13.74±1.26[c]	24.72±1.39[d]	26.07±0.96[e]
Heart	mg/g tissue	36.64±5.99[a]	30.80±2.30[b]	8.47±0.70[c]	20.87±1.84[d]	25.34±0.57[e]
Lung	mg/g tissue	19.80±1.58[a]	26.06±0.85[b]	8.15±0.38[c]	15.82±1.80[d]	18.80±1.08[e]
Liver	mg/g tissue	27.93±3.01[a]	32.16±2.91[b]	8.54±0.92[c]	13.84±1.00[d]	16.56±0.44[e]
Kidney	mg/g tissue	34.05±2.05[a]	35.85±2.56[b]	7.37±0.59[c]	15.18±1.68[d]	21.51±2.60[e]
Phospholipid Concentration						
Plasma	mg/dl	15.76±0.86[a]	18.16±0.79[b]	9.04±0.69[c]	15.43±1.33[d]	18.34±0.51[e]
Erythrocytes	mg/dl	86.63±12.55[a]	104.70±2.98[b]	43.30±4.82[c]	49.99±4.60[d]	71.72±6.03[e]
Brain	mg/g tissue	15.30±0.79[a]	13.50±0.80[b]	9.35±0.62[c]	13.44±1.04[d]	15.77±0.69[a]
Heart	mg/g tissue	15.35±0.58[a]	17.28±0.87[b]	8.02±0.83[c]	13.12±0.89[d]	18.43±1.00[e]
Lung	mg/g tissue	12.90±0.37[a]	16.19±0.53[b]	8.66±0.64[c]	11.80±0.52[d]	14.61±0.72[e]
Liver	mg/g tissue	14.45±1.53[a]	15.11±0.72[b]	8.68±0.58[c]	12.16±0.58[d]	12.90±0.69[e]
Kidney	mg/g tissue	16.22±0.34[a]	16.97±0.90[b]	7.83±0.84[c]	12.72±0.66[d]	16.27±0.72[e]
Cholesterol/Phospholipid Ratio						
Plasma	mg/dl	12.94±1.70[a]	8.42±1.91[b]	8.17±1.44[c]	13.04±0.53[d]	10.56±0.49[e]
Erythrocytes	mg/dl	1.77±0.15[a]	1.36±0.06[b]	0.75±0.06[c]	1.05±0.15[d]	0.83±0.09[e]
Brain	mg/g tissue	2.05±0.15[a]	1.74±0.09[b]	1.68±0.22[c]	1.63±0.16[d]	1.42±0.05[e]
Heart	mg/g tissue	1.06±0.11[a]	1.00±0.06[b]	1.21±0.17[c]	1.64±0.11[d]	1.29±0.09[e]
Lung	mg/g tissue	1.59±0.13[a]	0.95±0.07[b]	0.99±0.05[c]	1.04±0.08[d]	1.19±0.10[e]
Liver	mg/g tissue	1.13±0.12[a]	0.97±0.09[b]	0.76±0.11[c]	1.05±0.07[d]	1.08±0.10[e]
Kidney	mg/g tissue	2.56±0.24[a]	1.69±0.12[b]	1.57±0.13[c]	1.32±0.13[d]	1.14±0.09[e]

The values are the mean ± SEM for 5 rats in each group; values with different superscripts within a row differ significantly from each other ($p < 0.05$)

extract compared with the control. The significantly reduced triglyceride concentration by LPS induction was increased by the aqueous extract of *C. glaucum* bulb treatment. The administration of aqueous extract of *C. glaucum* bulb resulted in significant ($p < 0.05$) increases in the plasma, brain, heart, lung, and liver phospholipid but a reduction in erythrocyte phospholipid and no significant changes in the kidney phospholipid compared to the control. The treatment with aqueous extract of *C. glaucum* bulb in groups 4 and 5 leads to an increased or decreased phospholipid concentration. All the groups had varying levels of cholesterol/phospholipid in the different compartments.

3.3 The Effect of *Crinum glaucum* Bulb Aqueous Extract on the Lipid Profile of Endotoxin-Induced Female Wistar Rats

The effect of aqueous extract of *Crinum glaucum* bulb on cholesterol, triglyceride, and phospholipid of endotoxin-induced female Wistar

rats is depicted in Table 2. *Crinum glaucum* significantly ($p < 0.05$) reduced the cholesterol concentration in the plasma, erythrocytes, brain, heart, lung, and liver but increased kidney cholesterol compared to the control. The induction of endotoxin caused a significant ($p < 0.05$) reduction of the concentration of cholesterol in all the compartments, and the treatment with an aqueous extract of *C. glaucum* bulb significantly ($p<0.05$) reversed the effect. When compared to the control, triglyceride concentrations increased in plasma, erythrocytes, brain, and kidney but decreased in the heart, lung, and liver.. The significant reduction of triglyceride by endotoxin was reversed by the pre- and post-treatment with an aqueous extract of *C. glaucum* bulb in all the compartments. Aqueous extract of *C. glaucum* bulb caused an increase in phospholipid concentration, while endotoxin revealed decreased in phospholipid concentration in all the compartment compared to the control. The post and pre-treatment with aqueous extract of *C. glaucum* bulb increased the phospholipid concentration, respectively. It was observed that there was up/down cholesterol/phospholipid concentration in all the compartments and in all the groups.

Table 2. Effect of *Crinum glaucum* bulb aqueous extract on the lipid profile of endotoxin-induced female wistar rats

Treatment dose / Parameters		Group 1	Group 2	Group 3	Group 4	Group 5
Cholesterol Concentration						
Plasma	mg/dl	222.52±12.29^a	192.70±14.10^b	159.70±6.19^c	166.47±4.30^d	166.56±4.18^e
Erythrocytes		168.62±6.78^a	137.46±14.96^b	49.89±4.18^c	83.30±5.96^d	101.39±3.23^e
Brain		68.39±2.40^a	60.90±2.56^b	36.92±8.18^c	75.02±6.13^d	92.60±6.96^e
Heart	mg/g tissue	12.81±1.29^a	12.22±0.52^a	6.96±1.19^c	11.25±0.49^d	12.03±0.41^a
Lung		7.60±1.08^a	6.96±0.72^b	4.02±0.47^c	5.90±0.52^d	6.85±0.80^b
Liver		44.32±6.03^a	36.91±3.92^b	14.33±0.93^c	16.64±1.75^d	18.86±1.10^e
Kidney		40.51±2.52^a	42.58±1.23^b	16.89±1.43^c	27.24±0.82^d	28.92±0.95^e
Triglyceride Concentration						
Plasma	mg/dl	131.98±6.33^a	171.88±11.72^b	119.13±8.31^c	165.58±18.03^d	186.24±14.79^e
Erythrocytes		120.02±5.45^a	155.52±17.56^b	75.34±9.82^c	121.81±5.11^d	124.50±4.82^e
Brain		39.19±1.68^a	61.04±5.15^b	24.38±3.42^c	37.87±6.34^d	49.80±9.20^e
Heart	mg/g tissue	15.33±0.56^a	13.64±1.07^b	7.30±0.85^c	10.58±0.40^d	12.22±0.88^e
Lung		61.37±8.01^a	32.80±3.06^b	25.61±1.57^c	51.83±5.63^d	60.68±4.43^a
Liver		31.09±3.27^a	26.17±1.32^b	14.75±1.15^c	17.29±0.77^d	22.19±0.73^e
Kidney		42.40±1.91^a	44.25±2.21^b	29.23±0.51^c	36.36±1.04^d	40.38±0.61^e
Phospholipid Concentration						
Plasma	mg/dl	122.76±5.95^a	150.74±1.58^b	102.96±2.17^c	148.76±3.25^d	166.57±5.45^e
Erythrocytes		147.00±4.03^a	153.60±3.60^b	61.60±2.24^c	115.21±8.23^d	118.11±4.87^e
Brain		16.66±1.61^a	20.13±1.43^b	11.86±0.53^c	18.34±2.08^d	19.66±1.14^e
Heart	mg/g tissue	15.78±0.61^a	14.60±0.39^b	10.92±0.68^c	12.94±0.83^d	13.60±0.67^e
Lung		1.30±0.03^a	1.73±0.16^b	0.67±0.19^c	1.18±0.06^d	1.45±0.04^e
Liver		14.55±0.89^a	19.03±0.75^b	12.64±0.62^c	14.95±0.99^a	15.94±0.44^d
Kidney		16.16±0.50^a	18.73±0.84^b	11.94±0.40^c	15.52±0.30^d	18.06±0.59^e
Cholesterol/Phospholipid Ratio						
Plasma	mg/dl	1.85±0.18^a	1.27±0.08^b	1.55±0.06^c	1.12±0.05^d	1.00±0.03^e
Erythrocytes		1.16±0.08^a	0.89±0.09^b	0.81±0.08^c	0.73±0.07^d	0.86±0.03^e
Brain		4.25±0.41^a	3.10±0.31^b	3.09±0.61^b	4.28±0.57^a	4.76±0.42^c
Heart	mg/g tissue	0.80±0.06^a	0.84±0.02^b	0.63±0.11^c	0.88±0.06^d	0.89±0.03^e
Lung		5.81±0.80^a	4.18±0.59^b	9.49±3.62^c	5.13±0.68^d	4.76±0.58^e
Liver		3.15±0.55^a	1.97±0.24^b	1.15±0.09^c	1.13±0.14^d	1.18±0.06^e
Kidney		2.50±0.15^a	2.29±0.11^b	1.42±0.13^c	1.76±0.08^d	1.60±0.017^e

Values are mean ± SEM for 5 rats in each group; values having different superscripts within a row differ significantly from each other ($p < 0.05$)

4. DISCUSSION

"Triglyceride, phospholipid, and cholesterol partake in numerous biochemical reactions and integrate metabolic pathways. Any alteration in the lipids will affect the other metabolites that are directly or indirectly connected with them" [5,3]. "They are structural components of the cellular membrane" [3,23]. Essential components of the plasma membrane involved in maintaining its structure-function properties are lipids. These include rigidity and permeability; the formation of membrane microdomains; and precursors for steroids and bile acids [24-25]. Septic shock, resulting in tissue injury and metabolic imbalances in humans and animals, is caused by endotoxins [12]. Studies have shown that endotoxin inducement alters lipid metabolism [5,12,26]. As observed in this study, both male and female animals, induced with LPS, had reduced cholesterol, triglyceride, and phospholipid concentrations in the different compartments of the organism, which might alter the structure/functional properties of the plasma membrane and cause metabolic imbalance. This is supported by Khan et al., (2000) [12,26]. These data suggest that endotoxin downregulates the activities of some lipid metabolic enzymes. Triglyceride serve as the stored energy of the organism, while phospholipid and cholesterol act as building blocks in the cell structures of living organisms [27]. "Transportation of hydrophobic constituents in and out of cells involves cholesterol and triglyceride. While cholesterol functions as the precursor of steroid hormones, phospholipid function as emulsifying agents to maintain the proper colloidal state of the cytoplasm" [28]. The study shows that *C. glaucum* is not toxic. Our findings on the likely mechanism of the protective and ameliorative effects of *C. glaucum* aqueous bulb extract revealed a reversal in the concentrations of cholesterol, triglyceride, and phospholipid in the various compartments of the animal." This action of *C. glaucum* can be interpreted in several ways: The increased cholesterol could be attributed to the activation of 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase and HMG CoA synthase (the two rate-limiting enzymes in cholesterol synthesis) or it may be due to feedback inhibition by pre-/post-administration of aqueous bulb extract of *C. glaucum"* [6,28-31]. "Another interpretation is that the activity of cholesterol-7α-hydroxylase, a cytochrome P-450 enzyme found in the endoplasmic reticulum and the rate-limiting enzyme in bile acid biosynthesis, is increased" [28,32-33]. In addition, lysosomal phospholipase activity is activated, as well as lysosomal enzyme transport and phospholipid biosynthesis [29,34].

One of the indices of membrane fluidity is the ratio of cholesterol to phospholipid, and an increase in the ratio indicates a decrease in membrane fluidity [35-37]. Our findings revealed that LPS increased membrane fluidity, but *C. glaucum* decreased the membrane fluidity. The mechanism of action of *C. glaucum* bulb dwells in the presence of bioactive constituents-alkaloids, flavonoids, and phenols, which afford the protective and ameliorative properties observed in this study [38].

5. CONCLUSION

The results of this study revealed that treatment with the aqueous extract of *C. glaucum* bulb has the potential to prevent and ameliorate plasma, erythrocyte, and organ lipid metabolism dysfunction in endotoxin-induced rats.

ETHICAL APPROVAL

The Ad Hoc Animal Ethical Committee of the Department of Biochemistry at Lagos State University, Ojo, Lagos, Nigeria, approved the research, and all procedures followed the Ethical guiding principles of laboratory animal care

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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