

***Crinum glaucum* bulb extract improves the lipid profile of endotoxin-induced Wistar rats**

ABSTRACT

Background and Objective: Medicinal plants are widely known as sources of potential that are used in traditional medicine. The effect of *Crinum glaucum* (*C. glaucum*) aqueous extract on the lipid profile in endotoxin, lipopolysaccharide (LPS) induced-rats was evaluated. **Methodology:** Fifty Wistar rats (male and female) were divided randomly into five groups (n = 5) each. Group 1 is the control group. Group 2 was administered with *C. glaucum* aqueous extract (1000 mg/kg body weight). Group 3 was exposed to an LPS dose (1 ml/kg body weight) only for 2 hours. Group 4 was administered LPS (4 hours) and *C. glaucum* aqueous extract. Group 5 was administered aqueous extract + LPS + 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 of using a spectrophotometric method. **Results:** The reduction of cholesterol, triglyceride, and phospholipid concentrations was the hallmark of LPS as revealed in this study. The administration of *C. glaucum* significantly ($p < 0.05$) increases the lipid profile in all the groups. Data also revealed that while LPS causes a reduction in lipid profile, the administration of *C. glaucum* reverses the effect. **Conclusion:** The finding suggests that *C. glaucum* has an ameliorative and therapeutic effect in preventing lipid dysfunction.

Key words: *Crinum glaucum*, Lipid profile, 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]. They are cellular membrane structural elements that 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. Homeostasis disturbances of these lipids result in dyslipidemia, which is connected to a variety of clinical conditions, including diabetes, heart disease, inflammation, and obesity [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 Department of Botany 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 (LD₅₀) of *C. glaucum* bulb aqueous extract was determined by oral route using the modified method of Ogunrinola *et al.*, (2022) [5] and Adu *et al.*, (2021) [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 of the Department of Biochemistry, Faculty of Science, Lagos State University, Ojo, Lagos State, Nigeria. Prior to 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.

2.6 Study design: The rats were randomly divided into 5 groups (n = 5) for both male and female.

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 anesthetic. 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°C until analysis. 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 [20].

2.7 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]. 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].

2.8 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 \pm SEM of 3 replicates. The

level of homogeneity at $p < 0.05$ among the groups was tested for 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, triglycerides, and phospholipid of endotoxin-induced male Wistar rats. The induction of endotoxin with LPS significantly ($p < 0.05$) reduced the concentration of cholesterol, triglycerides, and phospholipid in all the compartments. The administration of *C. glaucum* bulb aqueous extract significantly ($p < 0.05$) decreased the 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 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 of the compartments had varying levels of cholesterol/phospholipid.

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

Treatment dose		Group 1	Group 2	Group 3	Group 4	Group 5
Parameters						
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		31.26±2.33 ^a	23.28±0.44 ^b	15.25±1.28 ^c	21.53±1.52 ^d	22.38±0.78 ^c
Heart		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 ^c
Kidney		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		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		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		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		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		15.35±0.58 ^a	17.28±0.87 ^b	8.02±0.83 ^c	13.12±0.89 ^d	18.43±1.00 ^c
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		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		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		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 ^c
Kidney		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

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).

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, triglycerides, and phospholipid of endotoxin-induced female wistar rats is depicted in Table 2. The administration of *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 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 triglycerides by endotoxin was reversed by the pre- and post-treatment with 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 phospholipid concentration in all the compartments 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		Group 1	Group 2	Group 3	Group 4	Group 5
Parameters						
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	mg/dl	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	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	mg/g	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	tissue	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	tissue	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	mg/dl	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	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	mg/g	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	tissue	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	tissue	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	mg/dl	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	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	mg/g	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	tissue	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	tissue	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	mg/dl	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	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	mg/g	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	tissue	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	tissue	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 \pm SEM for 5 rats in each group; values having different superscripts within a row differ significantly from each other ($p < 0.05$).

4. DISCUSSION

Triglycerides, phospholipids, and cholesterol partake in numerous biochemical reactions and integrate different 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, triglycerides, 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 down-regulates the activities of some lipid metabolic enzymes. Triglycerides 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 tryglycerides. While cholesterol functions as the precursor of steroid hormones, phospholipids 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, triglycerides, and phospholipid in the various compartments of the animal. This action of *C. glaucum* can be interpreted in several ways: The enhanced cholesterol may 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 the upregulation of the activity of cholesterol-7 α -hydroxylase, a cytochrome P-450 enzyme that is located in the endoplasmic reticulum and the rate-limiting enzyme in bile acid biosynthesis [28,32-33]. In addition, lysosomal phospholipase activity is activated, as is 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 an increase in membrane fluidity with the LPS but that *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 as 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 the plasma, erythrocyte, and organ lipid metabolism dysfunction in endotoxin-induced-rat.

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