

Original Research Article

Antilipidemic and Hepatorenal Effects of Aqueous Extracts of *Terminalia catappa* on Streptozotocin-induced Diabetic Rats

ABSTRACT

Aims: Diabetes mellitus, a condition characterized by glucose receptor abnormalities affecting glucose uptake, affects approximately 600 million individuals globally as of 2021. This study aimed to assess the antilipidemic and renal effects of aqueous extracts from the root bark and flowers of *Terminalia catappa* on streptozotocin-induced diabetic rats.

Methodology: Twenty-five Albino rats weighing 160 – 300g were divided into five groups: A - normal control, B - diabetic control, C - diabetic treated with root bark extract, D - diabetic treated with flower extract, E - diabetic rats treated with glibenclimide. Diabetes was induced using streptozotocin (55mg/kg). The extracts (200mg/kg) were orally administered for 14 days, after which lipid profiles, renal and liver function tests were conducted.

Results: There was a significant ($p < 0.05$) increase in total cholesterol, serum liver enzymes, and kidney markers in the diabetic control group compared to the normal control group. Treatment with the *Terminalia catappa* extracts for 14 days decreased the urea, creatinine and uric acid concentration by more than 20%. There was also a significant reduction in the serum liver enzymes, in the *Terminalia catappa* extract-treated groups when compared with the diabetic control group. The extent of hepatoprotective capacity in the root bark extract treated animals compared well with the glibenclimide treated group. The extracts also decreased the concentration of total cholesterol, triglyceride, and low-density lipoproteins by 3%, while significantly increasing the high-density lipoproteins. The study suggests that *Terminalia catappa* extracts exhibit hypolipidemic and hepatoprotective properties in streptozotocin-induced diabetic rats.

Conclusion: The aqueous root bark and flower extracts of *Terminalia catappa* demonstrate potentials for managing diabetes mellitus at the specified dosage.

Keywords: Diabetes mellitus, *Terminalia catappa*, liver enzymes, kidney biomarkers, lipid profile

1. INTRODUCTION

Diabetes is a serious, chronic condition that occurs when raised levels of blood glucose occur because the body cannot produce any or enough of the hormone insulin or cannot effectively use the insulin it produces [1]. A lack of insulin, which is needed for the conversion of glucose to energy or stored, or the inability of cells to respond to insulin, leads to high levels of blood glucose, a condition known as hyperglycaemia, a clinical indicator of diabetes. About 600 million people are suffering from diabetes globally today and this number is projected to reach 783 million by 2045 [1]. As the disease progresses, it causes damage to the vascular tissues, leading to such complications as neuropathy, nephropathy, retinopathy, cardiovascular complications and ulceration [2].

There are several other types of diabetes, including the monogenic diabetes, type 1 and type 2 diabetes [3]. Monogenic diabetes, which represents about 2% of all diabetes cases, results from a single gene [4]. Type 1 diabetes is caused by an autoimmune process in which the body's immune system attacks the insulin producing beta-cells of the pancreas. As a result, the body produces very little or no insulin [5]. Type 2 diabetes is considered the most prevalent type of diabetes, with

over 90% of cases. It results from initially, the inability of the body's cells to respond fully to insulin, a condition termed insulin resistance. Thereafter, the insulin is less effective and, in due course, prompts an increase in insulin production. Over time, inadequate production of insulin can develop as a result of failure of the pancreatic beta cells to keep up with demand. The causes of type 2 diabetes are not completely understood but there is a strong link with overweight, and obesity, increasing age, ethnicity, and family history [6]. As with type 1 diabetes, contributors to type 2 diabetes risk are thought to include polygenic and environmental triggers [1].

Economic burden of diabetes on countries, health systems, people with diabetes, and their families is significant [1, 7-10]. According to the International Diabetes Foundation Atlas report of 2021, it is estimated that the total diabetes-related health expenditure will reach USD 1.03 trillion by the year 2030. The increasing cost of treatment associated with modern medicine, coupled with the unsatisfactory outcome [11], has prompted many researchers to begin looking in the direction of medicinal plants for alternative therapeutic measures [12].

Plants have formed the basis for the treatment of disease in traditional medicine for many years. Among these are the medicinal plants which possess compounds that have therapeutic properties or exert pharmacological effects on the human body [13]. Though there are known antidiabetic drugs available in the market, herbal mixtures have become the go-to alternatives to treat diabetes [14]. The use of traditional medicine in developing countries have been attributed to multiple factors, such as accessibility, familiarity, and tradition; inadequate access to modern health care systems; high cost of modern medicine; and perceived safety or comparatively less toxicity to synthetic drugs, among other factors [15]. Different parts of *Terminalia catappa*, a widely grown large tropical tree in the leadwood tree family, Combretaceae, native to Asia, Australia, the Pacific, Madagascar and Seychelles [16] have been investigated for their physiological properties. Different extracts of the leaves of this plant have been reported to possess anticancer, anti-HIV reverse transcriptase, hepatoprotective, and anti-inflammatory effects, among other biological effects [2, 17]. The antidiabetic activities of its fruit have also been reported in other study [18]. Therefore, the current study was aimed to determine the antilipidemic and hepatorenal effect of *T. catappa* root bark and flower in an STZ-induced animal model.

2. MATERIAL AND METHODS

2.1 Plant Materials and Chemicals

Fresh *Terminalia catappa* root bark and flower were harvested from Old Jos University Teaching University compound, Jos, Plateau state, Nigeria and authenticated at the Plant Science and Technology Department, University of Jos (identification number: UJH16000249). Streptozotocin was purchased from Sigma Chemical Co. (St Louis, MO, USA). A one-touch glucometer was purchased from Roche Diagnostics GmbH (Mannheim, Germany) for the analysis of blood glucose (BG). All other chemicals were of analytical grade.

2.2 Extraction of the root bark and flower of *Terminalia catappa*

An amount of 100 g of root bark and flower of *Terminalia catappa* was separately soaked in 500 ml of water for 72 hours. The water was then sieved collecting the *Terminalia catappa* extract and the pellets discarded. The extract was stored at room temperature in a refrigerator within the laboratory of the Department of Biochemistry, University of Jos pending use.

2.3 Experimental Animal

Twenty-five (25) male albino rats were acquired from Animal House Unit, Department of Pharmacology, University of Jos. The rats acclimatized to the laboratory condition for two weeks before any experimental work was undertaken. At the time of experiment, the rats were weighing between 160 g and 300 g.

2.4 Experimental Design

Twenty-five male albino rats were distributed into five (5) groups. The groups are; Normal control (A), diabetic control (B), diabetic rats treated with root bark extract (C), diabetic rats treated with flower extract (D), and diabetic rats treated with glibenclimide (E).

2.4.1 Streptozotocin Administration (STZ)

A dose of 55 mg/kg of STZ was administered to three groups (via intra-peritoneal (IP) with the exception of normal control group. The blood glucose leveled was checked after 48hours using on call plus glucose strip [19].

2.4.2 Plant extracts and glibenclimide (standard drug) administration

200 mg/kg/day of the extracts were administered for 14 days orally with constant feed and water ad libitum. 2.5 mg/kg of glibenclimide were administered orally for 14 days with constant feed and water.

2.5 Sample Collection and Biochemical Analysis

After the 14 days of treatment, the blood glucose level was checked and weight of the experimental rats were taken before they were sacrificed. The blood was collected into two different bottles as described in Jiyil et al., 2019 [20]. Serum level of liver enzymes including ALT, AST and alkaline phosphatase (ALP) was estimated by using the commercially available test kits. Lipid profiles including, triglyceride, total cholesterol, low density lipoprotein, and high-density lipoprotein cholesterol were determined.

2.6 Statistical Analysis

All statistical analyses were conducted by using the statistical package SPSS version 22.0 (Chicago, IL). Values were compared by one-way analysis of variance (ANOVA). Results were expressed as mean \pm standard deviation with p value <0.05 considered significant.

3. RESULTS AND DISCUSSION

For decades, several natural compounds obtained from different plants, possessing significant pharmacological effects have been utilized in the treatment and management of various chronic diseases [21]. Today, about 10,000 phytochemicals made up of tannins, flavones, triterpenoids, steroids, saponins, and alkaloids have been acknowledged, and many more are yet to be identified [22]. The present study assessed the anti-diabetic and renoprotective effect of the flower and root bark of *T. catappa* (200mg/kg) using STZ-induced diabetic model in experimental rats.

Terminalia catappa extracts possess a significant effect on some biochemical parameters and hematological assays as indicated from the Tables below:

Table 1. Effect of administration of extract of *Terminalia catappa* on some level of biochemical parameter.

Group	Treatment	Urea (Mmol/L)	Creatinine (Mmol/L)	Uric Acid (μ mol/L)
A	Normal Control	4.61 \pm 0.15	80.19 \pm 1.20	199.01 \pm 0.46
B	Diabetic control	18.18 \pm 0.50 ^a	343.56 \pm 12.72 ^a	570.54 \pm 9.37 ^a
C	Diabetic treated RB	11.58 \pm 0.40 ^{ab}	223.94 \pm 15.54 ^{ab}	413.55 \pm 15.26 ^{ab}
D	Diabetic treated F	13.92 \pm 0.75 ^{ab}	266.30 \pm 30.18 ^{ab}	440.62 \pm 40.00 ^{ab}
E	Glibenclimide	12.71 \pm 0.73 ^{ab}	233.00 \pm 134.18 ^{ab}	438.90 \pm 017.43 ^{ab}

Values are expressed as Mean \pm SD, n= 5 for each group.

^aValues are significantly different when compared with normal control (p<0.05).

^bValues are significantly different when compared with diabetic control (p<0.05).

RB: *Terminalia catappa* root bark; F: *Terminalia catappa* flower

As shown in Table 1, aqueous extracts of the root bark and flower obtained from *Terminalia catappa* induced a significant reduction in the serum protein when compared with the diabetic rats following the administration of *T. catappa* root bark or flower extract. The activities of these enzymes decreased gradually, suggesting an improvement in the streptozotocin-induced diabetic effect in rats. Furthermore, the study found that in streptozotocin-treated animals, there was an elevation in urea, uric acid, and creatinine levels (Table 1), indicating impaired renal function in response to streptozotocin treatment. Urea and creatinine are kidney markers that are raised under diabetic conditions [23]. High serum uric acid level has also been associated with metabolic syndrome in both normal subjects and diabetic patients [24]. However, since the levels of urea and creatinine were decreased in the *T. catappa* (200 mg/kg) treated groups, this suggests that *T. catappa* root bark and flower may have prevented the streptozotocin-induced biochemical alterations and did not cause renal damage.

Table 2. Effect of administration of *Terminalia catappa* extract on serum level of liver function enzymes

Group	Treatment	ALT (U/L)	AST (U/L)	ALP (U/L)
A	Normal Control	12.61 \pm 0.54	17.52 \pm 0.52	158.93 \pm 0.96
B	Diabetic control	36.96 \pm 0.73 ^a	58.56 \pm 0.68 ^a	493.12 \pm 5.36 ^a

C	Diabetic treated RB	15.52±0.71 ^{ab}	19.25±0.81 ^{ab}	188.50±5.00 ^{ab}
D	Diabetic treated F	25.98 ±3.67 ^{ab}	43.45±1.50 ^{ab}	365.08±13.80 ^{ab}
E	Glibenclimide treated	6.24±0.57 ^{ab}	19.51±0.52 ^{ab}	204.29±6.54 ^{ab}

Values are expressed as Mean ± SD, n= 5 for each group.

^aValues are significantly different when compared with normal control (p<0.05).

^bValues are significantly different when compared with diabetic control (p<0.05).

RB: *Terminalia catappa* root bark; F: *Terminalia catappa* flower

Under diabetic conditions induced by streptozotocin, liver marker enzymes such as AST, ALP, and ALT were elevated (Table 2). These enzymes, which are key indicators of hepatic function, are found in various tissues including the liver, cardiac muscle, skeletal muscle, kidney, brain, pancreas, lungs, leukocytes, and erythrocytes [25]. The increase in enzyme activity in the blood suggests increased permeability and damage or necrosis of liver cells [26]. The liver is a vital organ for glucose regulation in physiological and pathological states such as diabetes mellitus. Dyslipidaemia in diabetes mellitus has been considered to play an important role in the accumulations of free fatty acids and lipids in the liver that leads to excessive ROS production and lipid peroxidation. These processes enhance the oxidative stress and damage in liver resulting to increase the liver enzymes in serum of diabetic subjects [27]. However, following the administration of *T. catappa* root bark or flower extract, the activities of these enzymes decreased gradually, suggesting an improvement in the streptozotocin-induced diabetic effect in rats.

Table 3. Effect of aqueous root bark and flower extracts of *Terminalia catappa* extracts on serum lipid profile of both normal and streptozotocin induced diabetic rats.

Group	Treatment	Total chol. (mmol/L)	TRIG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
A	Normal Control	3.73±0.16	0.89±0.64	1.23 ± 0.07	1.83±0.07
B	Diabetic control	5.80 ±0.21 ^a	2.41±0.03 ^a	0.41± 0.03 ^a	2.41±0.03 ^a
C	Diabetic treated RB	4.43±0.32 ^{ab}	1.57±0.15 ^{ab}	0.66±0.03 ^{ab}	2.34±0.09 ^{ab}
D	Diabetic treated F	4.96±0.49 ^{ab}	1.75±0.15 ^{ab}	0.58±0.04 ^{ab}	2.32±0.16 ^{ab}
E	Glibenclimide-treated	4.55±0.24 ^{ab}	1.44± 0.15 ^{ab}	0.83±0.04 ^{ab}	2.26 ±0.12 ^{ab}

Values are expressed as Mean ± SD, n= 5 for each group.

^aValues are significantly different when compared with normal control (p<0.05).

^bValues are significantly different when compared with diabetic control (p<0.05).

RB: *Terminalia catappa* root bark; F: *Terminalia catappa* flower

Furthermore, Table 3 shows the result of the analysis of biochemical lipid profile parameters (Total cholesterol, triglyceride, high density lipoproteins and low-density lipoproteins) on experimental rats. Lipid profiles have been demonstrated to be another significant predictor of many diseases, including diabetes [28-29]. In this study, administration of aqueous extract of *T. catappa* root bark and flower caused antihyperlipidaemia, as the serum total cholesterol, triglyceride and low density lipoproteins, were significantly reduced, coupled significant increase in high density lipoprotein, when compared with the diabetic control group. Our results corroborate the findings of previous investigations within our laboratory regarding the antidiabetic effects of plant extracts [29-31], and shows the efficacy of *T. catappa* root bark and flower extracts in ameliorating the diabetes-induced damages.

4. CONCLUSION

Administration of *Terminalia catappa* root bark and flower aqueous extracts decreased the concentration of total cholesterol, triglyceride, and low-density lipoproteins, and increased the good lipoproteins, high density lipoprotein in streptozotocin induced diabetic rats. Therefore, the flower and root bark have antihyperlipidemic effects. The study also showed that *T. catappa* flower and root bark extracts possess hepatoprotective characteristics.

CONSENT

Not applicable

ETHICAL APPROVAL

The experimental design was conducted in accordance with the guidelines approved by the institutional animal ethical committee of University of Jos, Nigeria.

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