INTERNATIONAL JOUNAL OF: SCIENCE RESEARCH AND TECHNOLOGY

TIMBOU-AFRICA ACADEMIC PUBLICATIONS
INTERNATIONAL JOURNAL, FEBRUARY, 2023 EDITIONS
VOL. 12 NO. 9 ISSN: 2623-7861

METHANOL EXTRACT OF *LAGENARIA BREVIFLORA* (BENTH.) FRUITS AMELIORATES HYPERGLYCEMIA USING NORMAL AND ALLOXAN-INDUCED DIABETIC RATS

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ABSTRACT

The fruit of *Lagenaria breviflora* had been reported through folklore medicine for its anti-diabetic activity and other medicinal uses in South Western part of Nigeria. The present study aimed to evaluate the phytochemical and anti-diabetic activity of the methanol extract of *Lagenaria brevilora* fruit. Twenty adult experimental rats (*Rattus norvegicus*) were used for this study. The animals were grouped as Group I (normal control which received 1 ml distilled water), Group II (diabetic control received 1 ml distilled water), Group III

INTRODUCTION

Diabetic is a metabolic disorder of human that leads to hyperglycemic condition in individuals. It is a disease caused by the inability of the pancreas to secrete insulin (Type 1) or the inactivity of the secreted insulin to break down blood glucose (Type 2). Among the two forms of diabetes mellitus that exist in individuals, Type 2 diabetes is the most prevalent with about 95 % occurrence in individuals (Chen *et al*., 2020). Type 2 diabetes is a multifactorial disease, considered as a polygenic disorder, as it is associated with multiple gene inheritance (Ali, 2013). The disease is accompanied by chronic hyperglycemia and lowered metabolism in carbohydrate, fat and protein. Diabetes mellitus is one of the most typical chronic disorders in the world, accounting for about 387 million cases reported in the 2014 (**Khadke *et al*., 2015**).

Several therapeutic strategies are currently available for the treatment of this diabetes, including the stimulation of endogenous insulin secretion, enhancement of insulin action at the target tissues, inhibition of dietary starch and lipid degradation, and treatment with oral hypoglycemic agents (Birari and Bhutani, 2007). The limitations

(diabetic and treated group that received 1 ml of 400 mg/Kg body weight of methanol extract of *L. breviflora* fruit), Group IV (normal treated group and received 1 ml of 400 mg/Kg body weight of methanol extract of *L. breviflora* fruit). The rats were fasted for 12 hours followed by induction of diabetes with alloxan through intraperitoneal route. The initial weight of the animals was taken, while subsequent weight was recorded on the 14th and 28th day of the experiment. The administration of the extract was performed for 28 days, then the animals were sacrificed and blood samples were collected for biochemical analyses such as blood glucose, total protein, albumin, total cholesterol, high density lipoprotein, low density lipoprotein and triacylglyceride. The result of phytochemical screening revealed the presence of flavonoids, saponins, alkaloids, tannins, coumarin and anthraquinones. The methanol extract of *L. breviflora* fruit showed significant decrease (p<0.05) in the level of serum glucose level, low-density lipoprotein (LDL), triglycerides (TG) and total cholesterol, while the levels of total protein, albumin, high density lipoprotein and body weight were significantly elevated compared to the diabetic untreated rats. The findings from the present research suggests that the methanol extract of *L. breviflora* fruit alleviated diabetes and related complications.

Keywords: Alloxan, Biochemical indices, Blood glucose, Diabetes, Lipid Profile and *L. breviflora* Fruit.

associated with those therapeutic strategies have led to a determined search for more efficient and cost-effective alternatives (Aloulou *et al.,* 2012). Complementary and alternative medicine applications have attracted special attention in recent research because they offer new promising opportunities for the development of efficient, side effect-free and lower cost alternatives to existing synthetic hypoglycemic agents (Aloulou *et al.*, 2012; Rao and Nammi 2006). A wide range of medicinal plants have been used by various cultures to treat diabetes mellitus because of their hypoglycaemic properties (Adesokan *et al.,* 2009).

***Lagenaria breviflora* is an indigenous African plant used for the traditional treatment of diseases as well as management of disease disorders. Lagenaria is a seasonal creeping gourd plant that belongs to the family** Asteraceae (Aladekoyi *et al*., 2020). The plant has been exploited locally in the management of malaria, infections and also, it has been used in folklore medicine in West Africa for the treatment of measles, wound antiseptics, digestive disorders, and also for the treatment of coccidiosis and Newcastle disease in livestock farms in South Western Nigeria (Adedapo *et al*., 2013). Considering the numerous health benefits reported on this plant, this research work was therefore conducted to investigate the antidiabetic activity of the methanol extract of *Lagenaria breviflora* fruit in normal and alloxan induced diabetic rats.

Material and Methods

Plant Material

The fruit of *Lagenaria breviflora* (Benth.) was obtained from Sherri hill in Jos South local government area of Plateau State. The fruit was taken to the herbarium unit of Federal College of

Forestry, Jos where it was identified, authenticated and voucher specimen deposited and voucher number (FHI-285593) obtained.

Chemicals

Alloxan monohydrate was gotten from Sigma-Aldrich Chemical Company, St. Louis, U.S.A. Every other chemical and reagents used for this experiment were of standard and analytical grade and were prepared according to standard methods.

Experimental Animals

Adult Wistar (male and female) albino rats (20) weighing between 180-185g were obtained from the experimental animal house of University of Jos, Plateau State. The animals were kept in standard aluminum cages under normal room temperature. They were acclimatized for a period of two weeks before the commencement of the experiment and were given standard animal pellets and water *ad libitum*. Ethical clearance for the use of laboratory animals was obtained from the University of Jos Ethical Committee on Institutional Animal Care and Use (IACU) for the use of Experimental animals, where a voucher number of UJ/FPS/F17-00379 was obtained.

Extract Preparation

The fruit was harvested after which it was washed under running water. The pod was cut open and sliced into smaller pieces after which it was blended to obtain a jelly-like form. About 2 kilograms was weighed and 4 L of methanol was added and the content was thoroughly mixed by shaking after which it was left for 48 hours. The juice from the percolated sample was squeezed using clean muslin cloth and later filtered with Whatman No1 filter paper. The filtrate was then concentrated in a rotary evaporator (Model: RE-52A, PEC MEDICAL USA) to obtain 4.48g of the extract.

Phytochemical Analysis

Phytochemical analysis was carried out using the methods described by Trease and Evans (1989) and Sofowora (1993). The phytochemicals analyzed include alkaloids, flavonoids, saponins, tannins, coumarins, anthraquinones, amino acids and phlobatannins.

Induction of Diabetes

The animals were fasted overnight and diabetes was induced by a single intraperitoneal injection of a freshly prepared Alloxan monohydrate (150 mg/kg body weight) in ice cold 0.9% NaCl solution. The animals were allowed 5% glucose solution overnight *ad libitum* to overcome the drug-induced hypoglycemia. Control (normal) rats and normal treated rats were not injected with alloxan and were placed on normal saline alone. After 24 hours, rats with blood glucose level >126.13 mg/dL were considered to be diabetic and grouped into diabetic experimental groups (Group B and C).

Experimental Design

The animals were randomly selected into their various groups and were acclimatized to their new animal house conditions. The animals were fed with standard rat feeds consisting of 68.4% carbohydrate, 12.50% protein, 8.2% fat, 9.60% fibre and 1.30% minerals. The animals were

randomized into 4 groups of 5 animals in each of the groups. Group I were the normal control and were given 1.0 mL of distilled water, Group II were the diabetic control and they received 1 mL of distilled water, Group III were the diabetic treated group and they received 1 mL of 400 mg/Kg body weight of extract, while group IV were the normal treated group and they received 1 mL of 400 mg/Kg body weight of the extract.
Administration of the drug was done daily for a period of 28 days.

Blood Sample Collection

The methods described by Yakubu *et al.* (2003) was adopted in the blood sample collection and serum preparation. Briefly, the animals were placed under diethyl ether anaesthesia in a jar container with the neck area shaved quickly in order to expose the jugular veins. The veins were sharply cut with a sterile razor. Blood sample was then collected into EDTA sample bottles for haematological assay while some quantities were collected in a clean sample bottle and was allowed for clotting after 30 minutes. This sample was later centrifuged at 33.5 g for 15 minutes using a Uniscope Laboratory Centrifuge (Model: WN-4C). The sera were aspirated using a Pasteur pipette after which it was stored and allowed to freeze until when needed.

Biochemical Assays

The total protein content of the serum was determined using the Biuret method of Henry *et al*. (1974). The albumin (ALB) level was determined as described by Grant and Kacchman (1987). Serum glucose, total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL) and triglyceride (TG) were determined by the method of Trinder (1969), Friedrickson *et al*. (1967), Albers *et al*. (1978), Assman *et al*. (1984), Jacob and Van Demark (1960) respectively.

Statistical Analysis

Data obtained were analyzed using statistical package for social Sciences (SPSS Version 23). Data were presented as mean±standard deviation of five values using analysis of variance (ANOVA) to calculate the mean between the variables. Where differences occurred in the mean, Duncan Multiple Range Test was used to separate the means.

Result

Phytochemical Screening

The result of the phytochemical analysis of methanol fruit extract of *L. breviflora* is as displayed in Table 1. The result showed that important biological phytochemicals are present in the extract and they include flavonoids, saponins, alkaloids, tannins, coumarins and phenols. Other phytochemicals profile such as amino acids, anthraquinones and cardiac glycosides were however observed to be absent.

Table 1: Phytochemical analysis of Methanolic fruit extract of *Lagenaria breviflora*

Phytochemical	Reagents	Inference
Orange Yellow colouration	1 mL Extract stock + 2N NaOH	Flavonoids presesnt
Formation of 1.5 cm foam layer	2 mL Extract stock + 2 mL water + vigorous Shaking	Saponin present

Reddish-brown precipitate	2 ml Extract stock + Dragendorff's reagent	Alkaloids Present
Greenish-black colouration	2M of 5% ferric chloride + 1 ml Extract stock	Tannins Present
No colour change	0.25% w/v ninhydrin + 2 ml extract stock + heat 30°C for 10 minutes	Amino acids Absent
Appearance of cloudy solution	2 drops 1% NaOH + heat for 3 minutes + 4 drops of 2% HCl	Coumarins Present
No colour change	2ml extract stock + dil. H_2SO_4+ heat. After 10 minutes, filtrate + benzene + 5 ml NH_3	Anthraquinones Absent
Development of Bluish-green colouration	5 ml extract stock + 10 ml water + 2 ml $NH_4(OH)$ + 5 ml conc. Amyl alcohol + 30 minutes	Phenols Present
No colour change	2 ml extract stock + drops Glacial acetic acid + drop 10% $FeCl_3$ + Conc. H_2SO_4	Cardiac glycosides Absent

Mean Body Weight

Table 2 shows the result of the extract effect on the body weight of normal and alloxan induced diabetic rats at 14th day and 28th day. The result showed a significant decrease ($p \geq 0.05$) in the body weight gain of diabetic untreated rats when compared to the normal control. This effect was more pronounced on the 28th day.

Table 2: Effect of Methanol Fruit Extract of *L. breviflora* on the Weight Gain of Normal and Alloxan-Induced Diabetic Rats

Groups	Initial Weight (g)	Weight at 14th Day (g)	Weight at 28th Day (g)
Control	182.73±0.31^{a}	188.53±0.60^{a}	197.46±0.82^{a}
Diabetic Control	184.23±0.31^{a}	174.20±1.87^{b}	167.04±0.57^{c}
Diabetic + Extract	181.77±0.21^{ab}	187.17±0.65^{a}	192.49±1.66^{b}
Normal + Extract	180.43±0.11^{ab}	189.49±1.00^{a}	196.27±0.51^{a}
L.S	*	*	*

Means within the same column having different superscript alphabets are significantly different. Values are expressed as Mean±S.D, where n=5.

Blood Glucose Parameters

The result of the effect of methanol extract of *L. breviflora* fruit on the blood glucose, protein and albumin of rats is as presented in Table 3. The result showed that significant increase ($p \leq 0.05$) occurred in the blood glucose of the diabetic control group when compared with the normal control. The administration of 400 mg/Kg body weight of the extract was observed to have normalized the blood glucose level of the diabetic treated group. The result of the protein concentration and total albumin showed that significant decrease ($p \leq 0.05$) occurred in the diabetic untreated group when compared with the normal control. The result also showed that the

plant extract was able to control the protein and albumin concentration of the diabetic treated group.

Table 3: Effect of Methanol Fruit Extract of *L. breviflora* on Hematological Parameters of Albino Rats

Groups	Blood Glucose (mg/dL)	Protein (g/L)	Albumin (g/L)
Normal Control	105.40±1.01^{b}	68.93±3.76^{a}	35.34±0.72^{a}
Diabetic Control	179.45±3.14^{a}	60.49±1.26^{b}	28.74±0.62^{b}
Diabetic + Extract	107.40±1.22^{b}	68.15±2.23^{a}	34.08±0.64^{a}
Normal + Extract	105.00±2.25^{b}	70.02±2.49^{a}	33.81±0.69^{ab}

Means within the same column having different superscript alphabets are significantly different. Values are expressed as Mean±S.D, where n=5.

Lipid Profile

Table 4 showed the effect of methanol fruit extract of *L. breviflora* in normal and alloxan-induced diabetic rats. The result showed that significant increase ($p \leq 0.05$) was recorded in the total cholesterol, triacylglycerol and low-density lipoprotein on the rats at 28th day. The 400 mg/Kg body weight of the plant extract was, however, able to significantly ameliorate the total cholesterol, triacylglyceride and low-density lipoprotein of the rats. On the other hand, a significant decrease ($p \geq 0.05$) was observed in the high-density lipoprotein result in the diabetic untreated rats. The plant extract was also able to

Table 4: Effect of Methanol Extract of *L. breviflora* Fruit on the Serum Lipid Profile of Normal and Alloxan-Induced Diabetic Rats

Groups	Lipid Profile (mg/dL)			
	Total Cholesterol	**Triacylglyceride**	**LDL**	**HDL**
Normal Control	168.12±0.28^{c}	106.67±1.75^{d}	123.75±0.39^{c}	124.94±0.40^{b}
Diabetic Control	358.83±3.13^{a}	250.87±0.67^{a}	267.01±0.71^{a}	78.55±0.57^{d}
Diabetic + Extract	175.37±0.81^{b}	147.73±1.15^{b}	138.77±0.26^{b}	118.16±0.32^{c}
Normal + Extract	167.23±0.40^{c}	123.17±0.35^{c}	114.72±0.48^{d}	133.12±0.50^{a}

Means within the same column having different superscript alphabets are significantly different. Values are expressed as Mean±S.D, where n=5.

Discussion

Prior to the advent of orthodox medicine, plants have been used as a source of treatments for various forms of ill-health. The use of orthodox medicine have been reported, though to be effective, some side effects have been experienced by the patients who use them. This has brought about reverting to the use of medicinal plants as cheap and affordable source of medicine after much scrutiny. A good number of medicinal plants have been reported to have the ability to lower blood sugar level in experimental rats (Idu *et al*., 2021; Ajiboye *et al*., 2018; Olatunde *et al*., 2014^{a}; Olatunde *et al*., 2014^{b}; Mishra *et al*., 2010).

In the recent times many traditionally used medicinally important plants were tested for their antidiabetic potentials by various investigators in experimental animals. These properties were attributed to different formulations, extracts and active principles. Continuous ingestion of hyperglycemia rich diet is regarded as the major contributing factor to the pathogenesis of the disease and its related complications such as atherosclerosis (Aronson & Rayfield, 2002). The extract of *L. breviflora* at a dose of 400 mg/Kg body weight was effective in exhibiting hypoglycemic properties in rats when compared to the control. This effect might have been due to the presence of certain phytochemicals present in the fruit extract of the plant. Previous researchers have reported the possible antidiabetic effect of plants such as *Stachytarpheta jamaicensis* (Idu *et al*., 2021), *Vitellaria paradoxa* stem bark (Miaffo *et al*., 2019) through the various phytochemicals like flavonoids, tannins, saponins, alkaloids present in them.

There is increasing evidence that alloxan causes diabetes by rapid depletion of cells, through DNA alkylation and accumulation of cytotoxic free radicals that is suggested to result from initial islet inflammation, followed by infiltration of activated macrophages and lymphocytes in the inflammatory focus. It leads to a reduction in insulin released thereby a drastic reduction in plasma insulin concentration leading to stable hyperglycemic states (Chia *et al*., 2018). In this study, significant hyperglycemia was achieved within 48 hours after alloxan (150mg/kg b.w. i.p) injection. The antidiabetic activity of this plant extract might have also been due to the ability of plants to possess hypoglycemic properties, their ability to stimulate the secretion of insulin from the β-cells of the islet of Langerhans in the pancreas and their ability to absorb the existing glucose in the peripheral tissues. This in-turn reverses the action of alloxan through stimulation of hypoglycemia (Xi *et al*., 2007; Youn *et al*., 2004).

One of the major features of diabetes mellitus is the decrease in animal weight as a result of metabolic disorders (Ajiboye *et al*., 2018). The loss of weight experienced in the diabetic control group might have been due to the effect of protein wastage in the experimental animals, since the major source of energy for the body metabolic processes is (glucose) is not available for use. This brought about the body system diverting to another source of energy through the use of protein in a process known as gluconeogenesis (Zhang *et al*., 2019).

Proteinuria and albuminuria are regarded as important attributing features of diabetes nephropathy (Ajiboye *et al*., 2018). Albumin is an important plasma protein which represents about 25% of the total hepatic protein synthesis (Olatunde *et al*., 2014[a]). Depletion in the plasma protein and albumin in the result of the diabetic control rats can be attributed to the gluconeogenesis usage of protein in the diabetic rats. Yassin *et al*. (2004) stated that a decline in the level of plasma protein in diabetes can be attributed to the inhibition of oxidative phosphorylation, leading to increased catabolism, reduction in protein absorption and hence, decrease in protein synthesis.

Some researchers have indicated that diabetes brings about elevated serum lipid such as high cholesterol, triacylglycerides and HDL and this affects the normal metabolic function witin the system (Joel *et al*., 2014; Mishra *et al*., 2010; Idu *et al*., 2021; Adeneye *et al*., 2007). The result of the lipid profile in the diabetic control rat group showed that high cholesterol, high triacylglycerides, high HDL and low LDL occurred as compared to the control group. This effect can be attributed to the fact that diabetes is usually accompanied with variety of derangements in the normal metabolic and regulatory processes within the body system. This brings about accumulation of

cholesterol, triacylglycerides and low-density lipoprotein (LDL) as a result of mobilization of free fatty acid from the peripheral fat depots (Joel *et al*., 2014)

Conclusion

In conclusion, the methanol fruit extract of *L. breviflora* was able to reduce the hyperglycemic activity in alloxan-induced diabetic rats when compared with the normal control rats. The extract also brought about significant amelioration in the metabolic imbalance conditions associated with diabetes at the end of the 28th day of receiving the extract. Further search will be suggested on the exact biomolecule(s) responsible for the antidiabetic activity and the possible mechanism of action of this plant on its antidiabetic role.

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