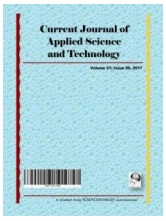

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Effect of Aqueous Extract of *Dodonaea viscosa* Linn on Some Biochemical Parameters in Alloxan-induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration between all authors. Author CDL designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors GI and MG managed the analyses of the study. Authors GI and NSJ managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

This study evaluates the effect aqueous leaf extracts *Dodonaea viscosa* Linn on alloxan-induced diabetic rats. Sixty grams of *Dodonaea viscosa* Linn leaf that has initially been pulverized was used to produce the aqueous extract. Sixteen male albino rats were randomly divided into four groups of four rats per group. Three groups were induced with experimental diabetes using alloxan monohydrate at a graded dose of 150 mg/kg body weight. Group A rats were given feed and water; Group B rats were not given any form of treatment for 14 days. Group C rats were treated with *Dodonaea viscosa* Linn extract at 400 mg/kg body weight for 14 days. Group D rats were treated with metformin at 400 mg/kg body weight for 14 days. All administration were done orally through intragastric tube method. At the end of 14 days, blood samples of all rats in each group were collected for liver function test, lipid profile, kidney function test and uric acid. The results obtained were analyzed statistically using a one way analysis of variance (ANOVA) tool at $p<0.05$. Results of the analysis showed that aqueous leaf extract of *Dodonaea viscosa* Linn is a potential candidate for the management of diabetic mellitus and its associate complications.

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1. INTRODUCTION

Diabetes mellitus (DM) is a chronic disorder caused by decreased insulin production in the pancreas, or by the ineffectiveness of the insulin action on target tissues; this result in increased concentrations of glucose in the blood, which in turn damage many of the body's systems, particularly the blood vessels and nerves [1]. The classical symptoms of diabetes include polyuria, glycosuria, polydipsia, polyphagia and weight loss [2]. Derangements of carbohydrate metabolism in diabetes lead to chronic hyperglycemia in diabetes, which is associated with long-term damage, dysfunction and failure of various organs, especially the heart, eyes, blood vessels, kidneys, and nerves [3].

Plants have been of tremendous help to animals from time immemorial plants have been used by animals especially human beings as sole source of energy in the form of food and also medicine and beautification; the most important of these been the green plants. *Dodonaea viscosa* Linn. Commonly called the ''sticky hop bush'' is a member of the sapindaceae family that has a cosmopolitan distribution in tropical, subtropical and warm temperate regions of Africa, Asia, and Australia. *Dodonaea viscosa* Linn is a shrub growing 1-3 m tall. The leaves are variable in shape; generally obovate but some of them are lanceolate [4]. *Dodonaea viscosa* Linn species have a pointed apex and secrete resinous substances. The flowers are yellow to orange in colour and are produced in the panicles. The flowers may only be male or female ones, and one plant bears either male or female flowers. However, sometimes (in rare cases), they are observed to bear flowers of both sexes. The fruit of *Dodonaea viscosa* Linn is a capsule 1.5 cm broad, red ripening brown with 2-4 wings [5]. *Dodonaea viscosa* Linn is a shrub that can grow well on poor soil and rocky site. Seedling, wildling and direct sowing are the methods used for the propagation of giant hop bush (*Dodonaea viscose* Linn). It is a fast growing shrub that requires little or no management once it is established. Seeds are viable for about one year if properly stored and pretreatment of seeds before sowing is not always necessary [4]. Also hop bush can be propagated by taking cuttings; this method can be used to obtain female plants for the aesthetic value of the winged fruits. The World Health Organization (WHO) consultative group defined a medicinal plant as any plant which in one or more of its organs contains substances that can be used for therapeutic purposes or are starting materials (precursors) for the synthesis of useful drugs which can either be through infusions or decoctions. These include spices, perfumery, food, plants including microscopic plants like fungi and actimycetes used for the isolation of drugs especially antibiotics and fiber plants e.g. cotton, flax, jute, used for application in surgical wound areas. Medicinal plants are group of plants captured the interest of mankind from time immemorial due to its cosmetic, pharmaceutical and nutritional application.

2. MATERIALS AND METHODS

2.1 Plant Materials

Fresh leaf of *Dodonaea viscosa* Linn was obtained at *Angwan Rukuba, Jos* North Plateau State, Nigeria during the rainy season. The plant was identified and authenticated at Federal College of Forestry Jos and assigned the voucher specimen number 13.

2.2 Experimental Animals

Sixteen (16) white male albino rats (wistar rats) were purchased from the animal house of the University of Jos. The animals initially weighing 40-65 grams were fed with standard feed for 10 weeks until their weight is between 160-220 grams. All experiments on animals were in accordance with the guidelines of both the University's ethical committee and the international guidelines for handling of laboratory animals [6].

2.3 Treatment of Experimental Animals

The experimental rats were grown to the required weight of 160-220 grams. The animals were randomly selected (to avoid bias) and divided in four (4) groups of 4 animals per group.

Group 1: Diabetic control (diabetic animals given standard feed and water)
Group 2: Normal control (normal animals given standard feed and water)
Group 3: Diabetic animals given *Dodonaea viscosa* Linn extract through intra-gastric tube for 14 days

Group 4: Diabetic animals were given metformin standard drug through intra-gastric tube for 14 days.

Group 3 animals were administered 400 mg/kg body weight of *Dodonaea viscosa* Linn extract through intra-gastric tube for 14 days. Group 4 animals were administered 400 mg/kg body weight of metformin standard drug through intra-gastric tube for 14 days. Prior to each study, the animals were made to fast for 14 hours but had free access to water [7].

2.4 Induction of Experimental Diabetes Mellitus

Experimental diabetes was induced in group 1 (diabetic control), group 3 (diabetic animals given *Dodonaea viscosa* Linn extract) and group 4 (diabetic animals given metformin standard drug) by a single intra-peritoneal injection of 150 mg/kg body weight of alloxan monohydrate. 1 gram of alloxan monohydrate was dissolved in 10ml of distilled water and was used at once. Experimental diabetes was confirmed through intragastric tube touch Glucometer when fasting blood glucose levels reach 126 mg/dl and accompanied with positive hyperglucosuric test [8].

2.5 Preparation of Plant Extract

The leaf of *Dodonaea viscosa* Linn collected was air-dried at room temperature under shade until properly dried. The dried leaf was pounded to obtain the powder using piston and mortar. The powder was sieved with a sieve and the fined powder obtained was stored in an air-tight plastic container. Phytochemicals were extracted using sixty (60) grams of the fine powder in 1500 ml (1.5 L) of water and allowed to stand overnight for 24 hours; to ensure maximum extraction of the phyto-chemicals. It was then filtered using whatman No. 1 filter paper. The filtrate was transferred into a beaker and dried in the oven at 60ºC until properly dried.

2.6 Collection of Animal Blood Samples

After 14days of administration, all the animals were fasted for 12 hours before they were sacrificed by decapitation. The blood was collected in plain tubes and allowed to properly clot centrifuging at 3500 rpm for 5 minutes. The serum was separated and analyzed within 18 hours.

2.7 Phytochemical Screening of Plant Extract

The phytochemical test of the fine powder aqueous extract was carried out using standard qualitative methods [9]. The aim is to test the presence of the plant secondary metabolites in *Dodonaea viscosa* Linn extract.

2.8 Phytochemical Screening

Phytochemical screening of aqueous extract of peels of *Dodonaea viscosa* Linn was carried out using standard qualitative procedure [9].

2.9 Test for Alkaloids (Dragendorff's Reagent Test)

Procedure: To 2.0 ml of the extract, few drops of the reagent were added and observed for yellow colouration.

2.10 Test for Flavonoids Using Lead Acetate

Procedure: To 2.0 ml of the extract, add few drops of 10% lead acetate, the formation of cream or light yellow indicate the presence of flavonoids.

2.11 Test for Saponins

Procedure: To 2.0 ml of the extract, 4 ml of distilled water was added and vigorously shaken for 2 minutes. Frothing which persist on warming was taken as a preliminary evidence for the presence of saponins.

2.12 Test for Resins

Procedure: To 2.0 ml of the extract, 2.0 ml of acetic anhydride was added followed by the addition of few drops of concentrated H_2SO_4 and the solution was observed for violet coloration to confirm the presence of resin.

2.13 Test for Cardiac Glycosides (Salkowsky's Test)

Procedure: 0.5 g of the extract was dissolved 2.0 ml of chloroform; sulphuric acid was carefully added to form a lower layer. A reddish-brown precipitate at the interphase shows the presence of cardiac glycosides.

2.14 Test for Steroids and Terpenes (Liebermann's Test)

Procedure: To 2.0 ml of the extract, 1 ml of acetic anhydride and concentrated sulphuric acid are carefully added down the side of the test tube and observed for reddish brown color at the interphase, indicating the presence of terpenes and steroids.

3. RESULTS

The result of phytochemical screening of *Dodonaea viscosa* Linn is shown below:

Table 1. Phytochemical screening

Phytoconstituents	Result
Alkaloids	+
Flavonoids	+
Tannins	+
Saponons	+
Terpenes and steroids	_
Cardiac glycosides	_
Balsam	+
Carbohydrates	+
Phenol	+
Resins	+

Key: Present: +; Absent: _

4. DISCUSSION

Alloxan is a toxic glucose analogue which selectively destroys the insulin-producing cells of the islet of langerhans (β-cells) of the pancreas [10]. The destruction of the pancreas results in the utilization of non-carbohydrate moieties such as protein for the synthesis of glucose. In the present study, diabetes induced in the experimental animal by alloxan produced significantly decreased in body weight [11]. The loss in weight in the diabetic groups is attributed to the alloxan that was injected into the animals. Alloxan is known to destroy the beta-cells of the islets of the Langerhans of the pancreas that function in insulin regulation, producing type 1 diabetes [12]. The loss of structural proteins in increased gluconeogenesis together with increased lipolysis and increased synthesis of ketone bodies results in severe weight loss [13]. In this research, a sharp increase in blood glucose was observed in group B, C and D animals after alloxan-induction compare to normal animal. This high blood glucose is chiefly due to the destruction of the insulin-producing cells of the pancreas, glycogenolysis and gluconeogenesis [14,15]. The continuous treatment of these hyperglycemic animals with *Dodonaea viscosa* Linn extract for 14 days reduces their blood glucose bringing it close to the fasting blood glucose of normal animals. This anti-hyperglycemic effect may be due to stimulation of the few undamaged β-cells to produce insulin or regeneration of some β-cells. Also, the antihyperglycemic effect of metformin(standard drug) treated animals (group D) further strengthens the above explanation.

In this study, alloxan causes a hike decrease in body weight of all alloxan-induce animals diabetic control group (group B) continue to lose weight drastically but all diabetic animals that were treated with metformin and *Dodonaea viscosa* Linn extract have only minimal weight loss; this reflect improvement in the health status of these animals. Normal control (Group A) animals continue to gain weight indicative of their healthy status.

Table 2. Effect of plant extract on body weight in grams

Group	Treatment	Initial weight (Day 1)	Final weight (Day 14)	Difference
A	Normal Control	160.50	181.80	+21.30
B	Diabetic Control	200.06	140.3	-59.76
C	Diabetic + treated E	190.30	170.70	-19.60
D	Diabetic + STD D	220.10	197.90	-22.20

Where E is extract, STD is standard and D is drug

Table 3. Effect of plant extract on serum glucose, protein and albumin

Group	Treatment	Glucose (mmol/L)	TP (g/L)	ALB (g/L)
A	Normal Control	5.15±0.12	38.02±017	31.42±0.17
B	Diabetic Control	16.95±0.12[a]	53.02±017[a]	37.27±0.22[a]
C	Diabetic + treated E	9.25±0.12[ab]	49.47±0.22[ab]	23.30±0.25[ab]
D	Diabetic + STD D	8.55±0.12[ab]	50.67±0.17[ab]	31.30±0.25[ab]

Where E is extract, STD is standard and D is drug
Values are expressed as Mean ± SD, n= 4 for each group.
[a]Values are significantly different when compared with normal control (p<0.05).
[b]Values are significantly different when compared with diabetic control (p<0.05).

Table 4. Effect of plant extract on lipid profile

Group	Treatment	T. CHOL (mmol/L)	TRIG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
A	Normal control	2.72±0.12	0.55±0.12	1.25±0.12	0.65±0.12
B	Diabetic control	3.35±0.17[a]	4.05±0.12[a]	0.45±0.12[a]	2.65±0.12[a]
C	Diabetic + Treated E	1.82±0.17[ab]	2.35±0.12[ab]	0.85±0.12[ab]	1.25±0.12[ab]
D	Diabetic + STD D	2.52±0.17[ab]	0.75±0.12[ab]	1.15±0.12[ab]	1.15±0.12[ab]

Where E is extract, STD is standard and D is drug
Values are expressed as Mean ± SD, n= 4 for each group.
[a]Values are significantly different when compared with normal control (p<0.05).
[b]Values are significantly different when compared with diabetic control (p<0.05)

Table 5. Effect of plant extract on some liver biomarkers (ALT, AST and ALP)

Group	Treatment	ALT (U/L)	AST (U/L)	ALP (U/L)
A	Normal control	23.15±0.12	7.15±0.12	82.45±0.12
B	Diabetic control	39.98±0.12[a]	13.15±0.12[ab]	128.65±0.12[a]
C	Diabetic + Treated E	40.08±0.12[ab]	18.45±0.22[ab]	129.93±0.09[ab]
D	Diabetic + STD D	33.15±0.12[ab]	12.57±0.17[ab]	88.25±0.12[ab]

Where E is extract, STD is standard and D is drug
Values are expressed as Mean ± SD, n= 4 for each group.
[a]Values are significantly different when compared with normal control (p<0.05).
[b]Values are significantly different when compared with diabetic control (p<0.05)

Table 6. Effect of plant extract on serum urea, creatinine and uric acid

Group	Treatment	Urea (mmol/L)	CREATININE (mmol/L)	URIC Acid (µmol/L)
A	Normal control	13.25±0.12	131.50±0.12	131.35±0.12
B	Diabetic control	4.05±0.12[a]	105.15±0.12[a]	80.35±0.12[a]
C	Diabetic + Treated E	8.25±0.12[ab]	111.95±0.12[ab]	93.65±0.12[ab]
D	Diabetic + STD D	7.15±0.12[ab]	109.15±0.12[ab]	96.25±0.12[ab]

Where E is extract, STD is standard and D is drug
Values are expressed as Mean ± SD, n= 4 for each group.
[a]Values are significantly different when compared with normal control (p<0.05).
[b]Values are significantly different when compared with diabetic control (p<0.05)

Table 7. Effect of plant extract on serum electrolytes (Na^+, K^+, $Cl^-HCO_3^-$) in mmol/L

Group	A	B	C	D
Treatment	Normal control	Diabetic control	Diabetic + Treated E	Diabetic + STD D
Sodium (Na^+)	133.65±0.12	121.15±0.10[a]	141.15±0.12[ab]	139.15±0.12[ab]
Potassium (K^+)	4.25±0.12	5.55±0.12[a]	5.05±0.12[ab]	4.65±0.12[ab]
Chloride (Cl^-)	99.15±0.12	100.75±0.12[a]	90.15±0.17[ab]	100.65±0.12[ab]
Bicarbonate (HCO_3^-)	21.75±0.12	18.15±0.12[a]	22.25±0.12[ab]	23.15±0.12[ab]

Where E is extract, STD is standard and D is drug
Values are expressed as Mean ± SD, n= 4 for each group.
[a]Values are significantly different when compared with normal control (p<0.05).
[b]Values are significantly different when compared with diabetic control (p<0.05)

From Table 3, the effect of *Dodonaea viscosa* Linn extract on serum glucose, total protein and albumin shows a decreasing order of diabetic treated with *Dodonaea viscosa* Linn extract (Group C) at a significant level (P<0.05) reduction in blood glucose, total protein and albumin when compared to diabetic control (group B) animals. From table 4, effect of plant extract on serum lipid profile shows a decrease in diabetic treated with *Dodonaea viscosa* Linn extract at a significance (P<0.05). Reduction in total cholesterol, triglycerides and low density lipoproteins (LDL) and an increasing order of high density lipoprotein (HDL) when compared to diabetic control (group B) animals. In the present study, alloxan induced diabetic untreated rats showed significantly increased serum lipid profiles except HDL compared with the control rats. The elevated TG, TC, LDL level and decreased HDL level in alloxan -induced diabetic rats observed in this study is in agreement with the previous reports regarding alteration of these

parameters under diabetic condition [16]. This may be due to the increase in the mobilization of free fatty acids (FFA) from the peripheral depots, since insulin inhibits the hormone sensitive lipase [17]. Serum FFA concentration are a result of the balance between the release from lipolysis, neosythesis and disposal and represent the major determinant of insulin effect on FFA oxidation and non-oxidative metabolism [18] From table 5, effect of plant extract on some liver biomarkers shows an increasing order in diabetic treated with *Dodonaea viscosa* Linn extract (group C) at a significance ($P<0.05$), increase in ALT, AST and ALP when compared to diabetic control group. The increase in ALT, AST and ALP is indicative of the fact that the extract did not mitigate the damage done to the liver. From table 6, effect of plant extract on urea, creatinine and uric acid shows an increase in diabetic treated with *Dodonaea viscosa* Linn extract (group C) at a significance ($P<0.05$), increase in urea, creatinine, and uric acid when compared to diabetic control (group B) animals. From table 7, effect of plant extract on serum electrolyte, it shows anincrease Cl^- and a decrease in K^+, Na^+ and $HCO3^-$ in diabetic treated with *Dodonaea viscosa* Linn extract at a significant level ($P<0.05$) when compared to normal control group.

5. CONCLUSION

In conclusion, it may be stated that diabetes is an important metabolic disorder afflicting many from various walks of life in different countries, especially the urban areas of developing countries. Recently, there has been an exponential growth in the field of herbal medicine to cure various diseases including diabetes and cancer. In this regard, the species of *Dodonaea viscosa* Linn are among the potential natural source to manage type 2 diabetes. This has been suggested to be mediated by a number of bioactive compounds present in the plant extract. *Dodonaea viscosa* Linn may play a vital role on future in mitigating the health complications associated with diabetes. Further study is recommended to find out its mechanism of hypoglycemia as well as for the isolation and identification of the hypoglycemic agent. Also, further comprehensive pharmaco-logical investigations may be carried out to assess the likely toxic agent(s) in this plant since it has shown in this research to elevated serum concentration of liver enzymes, urea, creatinine and misbalances serum electrolytes.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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