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Effect of Aqueous Extract of *Zingiber officinale* (Ginger) on Some Biochemical Parameters in Streptozotocin-induced Diabetes Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Author CDL designed the study, performed the statistical analysis. Author NP wrote the protocol and the first draft of the manuscript. Author MKJ managed the analyses and the literature of the study. Author CEM managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Appreciable number of medicinal plants are used for the treatment of diabetes in Nigeria.
Aim of the Study: The present study aimed to investigate the antidiabetic activity of *Zingiber officinale* extracts and its potential mechanisms in streptozotocin-induced diabetic rats.
Study Duration: The period of the study was done on 30th September, 2018 at the Department of Biochemistry, Faculty of Basic Medical Sciences, university of Jos, Nigeria.
Methodology: Albino rats of Wistar strain weighing between 130 g to 160 g were induced with single freshly prepared streptozotocin (55 mg/kg body weight). Diabetes was confirmed after forty eight hours in streptozotocin -induced rats showing fasting blood glucose levels > 10 mmol/l. The rats were randomly divided into four (4) experimental groups (n = 4). A (Control diabetic group fed with normal feed), Group B (Normal control fed with normal feed), Group Group C (Diabetic rats treated with 400 mg/Kg body weight extract of ginger and Group D, (Diabetic rats are treated with 400 mg/Kg body weight of metformin). After 8 days the animals were sacrificed and blood samples

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were collected for biochemical and hematological analysis. Changes in the animal body weights were also measured within the period.

Results: From the results, it was observed that treatment of rats with extract of ginger compensates for the reduction of body weight, and caused an increase in the body weight of the treated rats (+11.5%) in contrast to 24.8% reduction observed in diabetic control. In the same order, serum glucose significantly decreased ($p<0.05$) after the 8-day treatment compared to diabetic control. The extent of reversal of hyperglycemia in the ginger extract treated animals compared well with the metformin treated group. The results, therefore, showed that ginger extract has a significant ($p<0.05$) hypoglycemic effect in diabetic rats and moreover, elevations in the measured biochemical parameters were significantly ($p<0.05$) attenuated in rats treated with ginger extract.

Conclusion: *Zingiber officinale* extracts has a significant effect on some biochemical parameters and hematological assays. These provide scientific evidence to confirm the traditional use of *Z. officinale* in the treatment of diabetes mellitus.

Keywords: Antidiabetic; hematological assay; medicinal plant; Zingiber officinale.

1. INTRODUCTION

Diabetes mellitus is a metabolic disorder characterized by the presence of hyperglycemia due to defective insulin secretion, defective insulin action or both [1]. The chronic hyperglycemia of diabetes is associated with relatively specific long-term micro vascular complications affecting the eyes, kidneys and nerves, as well as an increased risk for cardiovascular disease (CVD) [2] The diagnostic criteria for diabetes are based on thresholds of glycemia that are associated with micro vascular disease, especially retinopathy [3]. Human bodies possess enzymatic and non-enzymatic antioxidative mechanisms which minimize the generation of reactive oxygen species, responsible for many degenerative diseases including diabetes [4]. The disease is rapidly increasing worldwide and affecting all parts of the world. Due to deficiency of the insulin people suffering from diabetes have high blood glucose level [5]. Type 2 diabetes or non-insulin-dependent diabetes mellitus, is the most common form of the disease, accounting for 90%–95% of cases in which the body does not produce enough insulin or properly use it [6]. According to World Health Organization the diabetic population is likely to increase up to 300 million or more by the year 2025 [7]. Currently available therapies for diabetes include insulin and various oral antidiabetic agents such as sulfonylureas, biguanides and glinides. Many of them have a number of serious adverse effects; therefore, the search for more effective and safer hypoglycemic agents is one of the important areas of investigation [8]. Aldose reductases, a key enzyme in the polyol pathway catalyze the reduction of glucose to sorbitol. Accumulation of sorbitol in the body causes various complications including cataract, neuropathy and nephropathy [9]. The hypoglycemic effect of several plants used as antidiabetic remedies has been confirmed, and the mechanisms of hypoglycemic activity of these plants are being studied. Natural products having antidiabetic potential which acts through either insulin mimetic or secretagogues properties are reviewed here. This review also focuses on the role of traditional therapeutic and natural medicines from traditional medicinal plants for diabetes. Traditional medicines from readily available medicinal plants offer great potential for the discovery of new antidiabetic drugs [10].

The consequence of this disorder differs in etiology and symptoms. Diabetes can be seriously debilitating initially leading to constant fatigue, blurred vision, nerve deterioration, blindness, limb amputation, heart disease, organ damage, hypertension, coma and death [11]. The magnitude of cardiovascular risk associated with diabetes is illustrated by its position as a coronary heart disease risk equivalent [12]. Complications related to neuropathy are vast, often working in concert with vascular abnormalities and resulting in serious clinical consequences such as foot ulceration [13]. Increased understanding of the natural history of this disorder has generated the potential to intervene and halt pathological progression before overt disease ensues, after which point management becomes increasingly challenging [14].

In modem medicine, no satisfactory effective therapy is still available to cure Diabetes Miletus [15]. There is increasing demand by patients to

use natural products with anti-diabetic activity due to side effects associated with the use of insulin and oral hypoglycemic agents [16]. There are numerous traditional medicinal plants reported to have hypoglycemic properties such as *Allium Sativum* (Garlic), *Vincarosen* (Nayantara), (Fenngreek), (Bitter ground), *Ocimum Santum* (Tulsi). The universal role of plants in treating diseases is shown by their use in all major systems of medicine irrespective of the underlying philosophical premise [17]. The use of medicinal plants as a fundamental component of the African traditional healthcare system is perhaps the oldest and the most assorted of all therapeutic systems [18]. In many parts of Africa, traditional healers recommending medicinal plants are the most cost effective and are easily accessible health resource available to the local community and most times, the only therapy that subsist. Nonetheless, there is still paucity of updated comprehensive compilation of promising medicinal plants from the African continent [19].

2. MATERIALS AND METHODS

2.1 Plant Materials and Chemicals

Fresh ginger were purchased from Farin-Gada market in Jos Plateau state, Nigeria and authenticated at the Plant Science and technology Department, University of Jos.

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 Ginger

An amount of 100 g of ginger was soaked in 500 ml of water for three days. The water was then sieved collecting the ginger juice extract and the pellets discarded. The extract was stored at room temperature in a refrigerator at the laboratory of biochemistry university of Jos to avoid any form of fermentation and growth of microorganism and also maintain its potency.

2.3 Experimental Animal

Male albino wistar strain rat was bought from animal farm at pharmacology unit university of Jos and feed on a standard feed on daily basis until they reach the weight which range of 130 to 160 g.

2.4 Experimental Design

Twenty male albino wistar rats are distributed into four groups five each, the groups are;

Diabetic control (A).
Normal control (B).
Metformin control (C) (Standard drug).
Extract of *Zingiber officinale* (D)

2.4.1 Streptozotocin Administration (STZ)

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 [20].

2.4.2 Plant and metformin (Drug) administration

400 mg/kg/day of the dissolved paste were administered for 8 days orally with constant feed and water. 400 mg/kg/day of metformin were administered orally for 8 days with constant feed and water.

2.5 Sample Collection

After the 8 days of treatment the blood glucose level was checked and weight of the experimental rat were taken before they are sacrifice. The blood was collected into two different bottle, the plain and the EDTA bottle for analysis. The blood collected in the EDTA bottle are for hematological analysis, while that of plain bottle is for chemical pathology analysis [21].

Enzymatic glucose kits (Human Gesellschaft für and Diagnostica mbH, Germany) was used for estimation of blood glucose. Serum level of liver enzymes including ALT, AST and alkaline phosphatase (ALP) was estimated. Lipid profile including, triglyceride, total cholesterol, low-density lipoprotein, and high-density lipoprotein cholesterol was determined.

2.6 Biochemical Analysis

Serums were separated by centrifugation of whole blood at 3000 g for 15 minutes at 4ºC and used for measurement of serum glucose and insulin concentration [22]. Fasting blood glucose concentration was determined using the commercial available colorimetric kit (Pars Azmoon co, Tehran, Iran) with an automatic biochemical analyzer. Serum insulin

concentration was determined using a commercial available rat insulin ELISA kit (Thermo Scientific Inc., Rockford, IL).

3. RESULTS

Zingiber officinale extracts has a significant effect on some biochemical parameters and hematological assays as indicated from the Tables below:

4. DISCUSSION

Diabetes mellitus was induced in experimental rats by direct administration of streptozotocin intraperitoneally (Abdominal region) at 55 mg/kg body weight of rat. Hyperglycaemia was confirmed 48 hours after administration of streptozotocin by existence of high blood glucose concentration. After 2 days, the blood glucose level when comparing the groups of the experimental design was increased from 3.46±0.147 Mmol/L in normal control group to 17.46±0.07 Mmol/L in diabetic control group.

Treatment with ginger root extract produced a time dependent decreased concentration in blood glucose level and other biochemical parameters [23]. Total protein, total cholesterol

Table 1. Effect of administration of extract of ginger extract of lipid profile parameters

Samples	Glucose (mmol/L)	TB (μmol/L)	DB (μmol/L)	Total Chol. (mmol/L)	Triglyceride (mmol/L)	HDL (mmol/L)
Normal	3.46±0.147	9.48±0.0.068	3.37±0.141	3.17±0.010	1.54±0.540	2.12±0.347
Diabetic	17.46±0.147^{b}	37.51±0.256^{b}	20.83±0.072^{b}	5.24±0.064^{b}	2.97±0.752^{b}	17.46±0.147^{b}
Drug control	4.55±0.1079^{bc}	14.72±0.072^{bd}	4.94±0.023^{bc}	4.10±0.073^{bc}	2.07±0.673^{bc}	1.98±0.673^{bd}
Ginger extract	4.35 ±0.062^{bc}	15.47±0.126^{bd}	4.37±0.080^{bc}	4.48±0.109^{bc}	1.94±0.787^{bc}	1.96±0.778^{bd}

TB = Total bilirubin; DB = Direct bilirubin; HDL= high density lipoprotein; Values are expressed as mean ± SEM, n = 4; [a]Values are significantly low when compared with normal control (p < 0.05); [b]Values are significantly high when compared with normal control (p >0.05); [c]Values are significantly low when compared with diabetic control (p<0.05); [d]Value are significantly high when compared with diabetic control (p>0.05)

Table 2. Effect of administration of extract of ginger extract on some level of some biochemical parameter

Samples	Protein (g/L)	Albumin (g/L)	UA (μmol/L)	UR (mmol/L)	Cr(μmol/L)
Normal	72.66±0.286	36.89±0.031	138.98±0.540	3.95±0.037	69.24±0.245
Diabetic	57.36±0.035^{a}	27.58±0.036^{a}	521.92±1.073^{b}	30.01±0.206^{b}	473.18±2.086^{b}
Drug control	67.69±0.023^{ad}	32.51±0.023^{ad}	143.48±0.968^{bc}	5.56±0.287^{bc}	78.20±0.188^{b}
Ginger extract	68.72 ±0.032^{ad}	33.02±0.014^{ad}	229.23±0.592^{bd}	5.03±0.00=26^{bc}	75.81±0.240^{bc}

UA = uric acids, UR = urea, Cr = creatinine; Values are expressed as mean ± SEM, n = 4; [a]Values are significantly low when compared with normal control (p < 0.05); [b]Values are significantly high when compared with normal control (p >0.05); [c]Values are significantly low when compared with diabetic control (p<0.05); [d]Value are significantly high when compared with diabetic control (p>0.05)

Table 3. Effect of administration of extract of ginger extract on serum level of enzymes

Samples	ALT(U/L)	AST (U/L)	ALP (U/L)
Normal	11.06±0.089	15.16±0.288	133.90±0.473
Diabetic	59.26±0.622^{b}	82.86±0.388^{b}	419.39±0.560^{b}
Drug control	15.06±0.193^{bc}	17.74±0.144^{bc}	149.76±0.374^{bc}
Ginger extract	13.15 ±0.150^{bc}	16.71±0.0170^{bc}	140.71±0.330^{bc}

ALT = Alanine transaminase, AST = Aspartate transaminase, ALP = Alkalinephosphatase; Values are expressed as mean ± SEM, n = 4; [b]Values are significantly high when compared with normal control (p >0.05); [c]Values are significantly low when compared with diabetic control (p<0.05)

Table 4. Effect of Administration of extract of ginger extract of on serum level of some hematological parameter

Samples	PCV (%)	Hb (g/dl)
Normal	42.12±0.107	14.07±0.038
Diabetic	30.07±0.053[a]	10.09±0.065[a]
Drug control	39.09±0.061[ad]	13.04±0.033[ad]
Ginger extract	36.05 ±0.032[ad]	12.04±0.029[ad]

PCV = Packed - cell volume, Hb = Haemoglobin; Values are expressed as mean ± SEM, n = 4; [a]Values are significantly low when compared with normal control (p < 0.05); [b]Values are significantly high when compared with normal control (p >0.05); [c]Values are significantly low when compared with diabetic control (p<0.05); [d]Value are significantly high when compared with diabetic control (p>0.05)

Table 5. Effect of administration of extract of ginger extract of on some level of some electrolytes

Samples	Na^+ (g/L)	Albumin (g/L)	UA (μmol/L)	UR (mmol/L)
Normal	108.90±35.245	3.51±0.120	144.05±0.032	27.13±0.099
Diabetic	101.90±32.222[a]	5.98±0.250[b]	96.05±0.026[a]	14.07±0.040[a]
Drug control	105.29±33.764[ad]	4.22±0.085[bc]	108.05±0.035[ad]	25.07±0.055[ad]
Ginger extract	106.12 ±33.940[ad]	4.71±0.140[bc]	110.07±0.065[ad]	24.06±0.034[ad]

Na = Sodium ion, UA = Uric Acids, UR = Urea; Values are expressed as mean ± SEM, n = 4; [a]Values are significantly low when compared with normal control (p < 0.05); [c]Values are significantly low when compared with diabetic control (p<0.05); [d]Value are significantly high when compared with diabetic control (p>0.05)

and Liver enzymes (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase).

Table 1 shows the result of the analysis of biochemical parameters, the glucose concentration of the normal control had no significant change in the concentrations, considering the diabetic + drug and diabetic + ginger root extract treatment group, which was shown to be significantly different when compared respectively to the diabetic control group ($p<0.05$). As compared generally, the results shows that administration of ginger extracts was effective in reducing blood glucose level after 21 days of treatment, as earlier observed in the same research carried out utilize ginger extract which tested for antihyperglycaemic activity in alloxan induced hyperglycemic rats [24].

Table 2 showed the result of the analysis of total protein and albumin on experimental rats. After 21 days of treatment. It was observed that the concentration of the total protein of the treated rat increases within the normal range of total protein which is between 60 g/L to 80 g/L. However, results indicates the ability ginger extracts to be effective in enhancing the level of total protein observed in the extraction groups of pod when compared with the diabetic group, as also seen in the table ($p<0.05$). Also, after 21 days, it was observed that the concentration of serum albumin when compared with the normal control group seemed to be significantly different from the diabetic + ginger group ($p<0.05$). As earlier observed in the same research carried out utilizing blood samples were collected and used for estimation of plasma glucose, Total proteins. Albumin, fibrinogen which tested In the study of type 2 diabetics plasma albumin levels were decreased compared to controls and plasma fibrinogen, total protein levels were statistically significantly increased compared to controls [25].

The increase in total cholesterol level of the diabetic group was due to the hyperglycemia confirmed in the diabetic group [26]. Ginger extracts were able to improve lipid metabolites generally including the correction of the High density lipoproteins known as good cholesterol which aids as carriers for the removal of low density lipoproteins and triglyceride from the blood to prevent the blockage, results indicates the ability of ginger extracts to be effective in correction of these levels of metabolites in experimental rats diabetic and treated respectively.

Also the same Table 2 shows the result of the analysis of biochemical lipid profile parameters (Total cholesterol, triglyceride, high density lipoproteins and low density lipoproteins) on experimental rats. In consideration of the groups of the experimental rats (experimental design) the result of the serum total cholesterol, shows that ginger extracts is effective in significantly reducing the level of serum total cholesterol for

diabetic control group ($p<0.05$). Comparing the diabetic + drug and diabetic + ginger extract groups. After 21 days, it was observed that the concentration of the triglyceride and low density lipoproteins when compared with the diabetic control groups, which showed a significant decrease ($p<0.05$) on treatment with drug in the diabetic + ginger extract, which reflects that the ginger root is effective in reducing the concentration of triglyceride and low density lipoproteins (which is harmful in the blood generally), Also, the result of the high density lipoproteins concentration after 21 days of treatment with the ginger extracts, in the comparison with the diabetic group also shows that there is an increase in the level of the concentration of the high density lipoproteins in the diabetic + drug and diabetic + ginger groups respectively ($p<0.05$).

Table 3 showed the result of the analysis of some biochemical liver function test parameters (alanine aminotransferase. aspartate aminotransferase and alkaline phosphatase) on experimental rats. Generally, elevated levels of serum liver marker enzymes; AST, ALT and ALP are indicative of cellular leakage [27]. And loss of functional integrity of the cell membrane in liver. This could be a result of hepatotoxicity [28].

Considering the groups of experimental rats it was observed that the concentration of the liver enzyme (serum ALT, AST and ALP) in normal control group increased significantly when compared to that of the diabetic control group ($p<0.05$). After 21 days of the treatment with pod extracts, there was a decrease in the diabetic + pod treatment group respectively of each of the enzymes. Generally this shows that ginger extracts were effective in reduction of liver damage [29].

Table 5 showed the result of the analysis of some other biochemical parameters (Such as Creatinine, Urea and Uric acid) on experimental rats. Considering the groups of experimental rats it was observed that the concentration of the Creatine. Urea and Uric acid in diabetic control group increased significantly when compared to the normal control group ($p<0.05$).

After 21 days of the treatment with ginger extract extracts and drug, there was a decrease in the diabetic + extract treatment group and the diabetic + drug treatment group ($p<0.05$). Generally this shows that ginger extracts were effective in reducing Creatinine, Urea and Uric acid levels in the blood which aids in the reduction of kidney disease and dysfunction [30].

Table 5 also shows the result of the analysis of some other biochemical electrolytes parameter (Such as Sodium, Potassium and calcium) on experimental rats. It was observed that the concentration of all the electrolytes exceptPotassium in normal control group reduced significantly respectively of each the serum electrolytes, when compared with that of the diabetic control group ($p<0.05$) but that of potassium rather increased from (3.11±0.084) to (5.10±0.121) for normal and diabetic respectively.

Also, after 21 days of treatment of the of diabetes in experimental rats, it was observed that the concentration of all the electrolytes except potassium was regulated and there was an increase from the initial reduced diabetic group, in the diabetic + drug treatment group respectively of each of the serum electrolytes, and the diabetic + ginger treatment group also. Potassium was partial regulated to (5.10±0.121) and (3.31±0.265) for diabetic + drug treatment group and the diabetic + extract treatment group respectively. The result shows that both diabetic + drug and diabetic + pod treatments were effective in reducing electrolyte imbalance which may have occurred due to hormonal or endocrine disorders, kidney disease and dysfunction [31].

Aqueous extracts from ginger had no significant effects on haemoglobin in all treated groups. However, significant effects were recorded in White Blood Cell (WBC) and platelets count. Extracts considerably improved the platelet counts [32] at the end of the administration period when compared to the diabetes untreated.

5. CONCLUSION

The results of this study show that aqueous extract of ginger possessed antidiabetic properties as shown in its ability to reduce blood glucose level of streptozotocin induced diabetic rats. This confirmation justifies its use in ethno medical for the treatment of diabetes.

CONSENT

It is 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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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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