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The Effect of Aqueous Extract of *Citrus sinensis* Peel on Some Biochemical Parameters in Normal and Alloxan-Induced Diabetic Wister Rats

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Abstract

The effect of aqueous extract of *Citrus sinensis* peel on some biochemical parameters in alloxan-induced diabetic rats was investigated. Sixteen (16) adult male albino rats (181 g to 206 g) were randomly divided into four groups (A-D). 150 mg/kg body weight of alloxan was administered intra-peritoneally to the rats to induce diabetes. A normal control group, diabetic group, treated group with the aqueous extract (400 mg/kg of body weight) and metformin (500 mg/kg of body weight) were separated. Treatment was done for 21 consecutive days. The result of the study showed significant variation in blood concentrations of glucose, liver enzymes, creatinine, urea, uric acid, electrolytes, total protein, total bilirubin, lipid profile high density lipoprotein and albumin between the normal control and diabetic control groups ($P<0.05$). The result of this study revealed a significant role of the extract of *Citrus sinensis* peel and metformin in restoring blood glucose, liver enzymes and lipid profile to levels approximate to or below the normal control groups ($P<0.05$). However, metformin has more profound effect in restoring blood glucose compared with the extract of *Citrus sinensis* at the employed dosage. Other results of the study showed that *Citrus sinensis* peel extract increased blood urea, potassium, total bilirubin to values approximate to normal control and decreased creatinine and sodium to values approximate to normal control ($P<0.05$). The effects of the extract on other biochemical parameters differ significantly from the normal control ($P<0.05$).

Keywords: *Citrus sinensis*; Alloxa; Diabetes mellitus

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Introduction

Oranges probably originated from south East Asia, and were cultivated in China by 2500 BC [1], where it was referred to as ''Chinese'' apple [2]. Today, it is grown almost all over the world as a source of food for humans because of its high nutritional values, source of vitamins and other uses. Though Nigeria is not well noted for the exportation of citrus fruits, she has the potential to produce more for both local and international markets. Of all the citrus fruits, sweet orange is the commonest and the most widely cultivated and consumed in the major 15 citrus growing states in Nigeria, namely: Cross River, Imo, Anambra, Osun, Ondo, Lagos, Ogun, Oyo, Kwara, Benue, Abia, Plateau, Kogi, Kaduna, Enugu and Bauchi states. *Citrus sinensis* is consumed all over the world as an excellent source of vitamin C, which is a powerful natural antioxidant that builds the body's immune system [3]. It has been used traditionally to treat ailments like constipation, cramps, colic, diarrhea, bronchitis, tuberculosis, cough, cold, obesity, menstrual disorder, angina, hypertension, anxiety, depression and stress [4]. The human diet contains important micronutrients namely vitamins C and E, carotenoids and flavonoids, essential for maintenance of human health. Multiple dietary sources of these compounds are present virtually in all plant material [5]. The nutritional importance of foods is due to the presence of these functional food ingredients and antioxidant nutraceuticals or phytochemicals. Phytochemicals are present in edible fruits and vegetables and when eaten potentially modulate human metabolism in a favourable manner, thereby prevent chronic and degenerative diseases [6]. Increase in fruits and vegetables

consumption protects against degenerative pathologies such as cancer and therosclerosis [7]; as epidemiological surveys had shown an inverse relationship between dietary flavonoid intake from citrus and cardiovascular diseases [8]. Citrus fruits are the main source of important phytochemical nutrients and for long have been valued for their wholesome nutritious and antioxidant properties. It is scientifically proven that oranges being rich in vitamins and minerals have many health benefits. Moreover, it is now appreciated that other biologically active, non-nutrient compounds found in citrus fruits such as phytochemical antioxidants, soluble and insoluble dietary fibres are known to be helpful in reducing the risk for cancers, many chronic diseases like arthritis, obesity and coronary heart diseases [9]. Diabetes mellitus is a very wide prevalent disease in both developed and developing countries, and its world prevalence has been estimated as 25% of the world population [10]. Diabetes mellitus results from disturbed carbohydrate metabolism, and this is associated with either insufficient blood insulin or insulin insensitivity [11]. Irrespective to witnessing progress in treating diabetes using oral synthetic agents, there still a need to find out new medications because of the limitations of available medications. On the other hand, there is a need to formulate herbal plants with potential use as antidiabetic therapy [12]. Diabetes is not a single disease, but rather, a group of metabolic diseases. It leads to diabetic complications. Antidiabetic herbs act through increasing insulin secretion, enhance glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver [13]. Liver has a significant role in glucose homeostasis and acts to retain normal glucose levels during fasting and in the postprandial period [14]. The role of liver in developing of type II diabetes has attracted much interest. Furthermore, it is thought that abnormal function of liver attributed to insulin-resistance syndrome may lead to development of type II diabetes [15]. Liver function test is assessed through using liver enzymes aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase (ALP) [16]. Both AST and ALT are considered markers of hepatocellular health **(Figure 1).** ALT is considered the most specific biomarker of liver pathology and is found mainly in liver [17]. Because AST and ALP can be found in other tissues, they are thought to be less specific biomarkers of liver function [18]. The relationship between concentrations of liver enzymes and the incidence of type II diabetes has been investigated through several studies. Some studies showed a significant relationship between serum AST and diabetes [19,20]. Other studies have investigated the relationship between AST and ALT and risk of type II diabetes, with varied results [21-24]. Another study by Tibi et al. [25] showed that liver ALP was significantly higher in the diabetic control compared to normal control group. Long before the cause of diabetes was known and its present therapeutic discoveries, traditional herbal medicine practitioners manage diabetic patients by prescribing concoctions, decoctions, infusions and other forms of plants preparation. Myrcia, the first registered use of antidiabetic drugs was a herbal extract used by Indians in the Amazon basin for the treatment of type II diabetes and today promoted as vegetable insulin, though, not formally an insulin analog. Animal studies have shown that walnut leaf and garlic can significantly reduce fasting blood glucose level in rats with alloxan induced diabetes. Some plants have been described to have hypoglycemic properties. One example of such plants is *Buchholzia coriacea* seeds [26].

Materials and Methods

Collection of plant material

Fresh *Citrus sinencis* fruits were obtained from Paul Gindiri farm and Hayi farm located at Farin Gada, Jos, Plateau State and were identified at the department of Plant Science and Technology, University of Jos.

Collection of experimental animals

Sixteen young male Wister strain albino rats were purchased from the Animal House Unit, University of Jos. The rats were fed

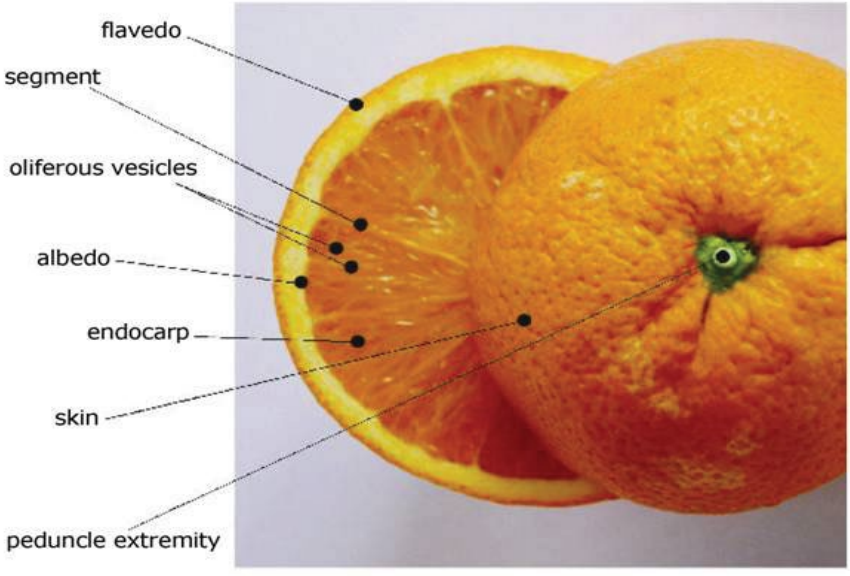

Figure 1 Structure of Citrus fruit [28].

with standard feed (vital growers mesh) from Grand Cereals and Oil Mills limited and distilled water until a weight range of 161 g-206 g were obtained. The feed nutrient composition includes; crude protein 14.5%, fat 7.0%, crude fiber 7.4%, calcium 0.8%and phosphorus 0.4%.

Methods

Extraction from *Citrus cinensis* peel: The peel from fresh *Citrus sinensis* fruits was obtained using a laboratory knife. The peel was cut in pieces and air dried at room temperature under a shade until a constant weight was obtained. The dried peel was pulverized 100 g of the powdered peel was dissolved in 500 ml of distilled water and allowed for 24 hours with intermittent shaking. Afterwards, the mixture was then stirred vigorously and filtered with Whatman No. 1 paper and then concentrated in an oven at 60°C. Extract to be administered is freshly reconstituted in distilled water daily to give the required dose (400 mg/kg body weight) used in this study. The reconstituted extract was administered orally to the rats orally.

Phytochemical screening: Phytochemical screening of aqueous extract of peels of *Citrus sinensis* was carried out using standard qualitative procedure [27].

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.

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.

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.

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.

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.

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.

Preparation of alloxan solution: One gram of alloxan monohydrate (Sigma chemical USA) was dissolved in 10 ml of distilled water and used as stock.

Preparations of *Citrus sinensis* extract: Eight grams of dried *Citrus sinensis* extract was dissolved in 80 ml of distilled water.

Preparation of standard drug: Standard drug; 500 mg of metformin was dissolved in 80 ml of distilled water. Induction of diabetes in experimental animals, Experimental diabetes was induced by a single intraperitonial injection of alloxan at a dose of 150 mg/kg body weight. Diabetes was confirmed in the animals after 48 hours using a glucometer. Animals with blood glucose level greater than 120 mg/dl were selected and used for the experiment.

Administration of extract: Extract was prepared and administered; 400 mg/kg body weight of *Citrus sininsis* peel extract was given orally on a daily basis. This was carried out for 21 consecutive days after the induction of diabetes in the rats.

Administration of standard drug: Standard drug was prepared and administered; 500 mg/kg body weight of metformin was given orally on a daily basis. This was carried out for 21 consecutive days after the induction of diabetes in the rats.

Experimental grouping: The rats were divided into four groups of four animals each and allowed to acclimatize for three days before the commencement of the experiment. They were kept in wide normal cages. They had free access to feed and water throughout the period of the experiment. The experimental groupings were A, B, C, and D. Diabetes was induced in groups A, B, and C by intraperitonial injection of freshly prepared alloxan (150 mg/kg body weight /day) while animals in group D were not induced. The groupings and administration of alloxan, extract, and standard drug were as follows: The administration was done for 21 consecutive days. Rats in groups A and D served as control while those in groups B and C were treated orally with 400 mg/kg body weight and 500 mg/kg body weight of *Citrus sinensis* and standard drug respectively.

Collection of blood sample: At the end of the experiment, the rats were fasted for 24 hours before they were sacrificed by decapitation. The blood was collected in clean dry centrifuge tubes and was allowed to clot. It was then spun at 5,000 rpm for 10 minutes. The serum was collected and used for the analysis. All analysis was carried out using Cobas C111 Chemistry Analyzer (Roche).

Preparation of Alloxan: One gram of Alloxan was weigh and dissolved in 10 ml of distilled water into a beaker and was shaken thoroughly.

Administering of the Alloxan: The Alloxan solution of dosage 150/kg was administered to the albino rats intra peritorially per body weight.

Plant fruits collection and processing

Collection of blood sample: The rats were placed in desiccators containing chloroform. The chloroform allows the rats to die gradually. Note: The rats must not be allowed to die completely but should be removed immediately they go unconscious because if they die, the heat would stop pumping blood and this can affect the collection of blood sample because blood will not be available for collection, but when they are unconscious, they still pumps. To the unconscious rats, using a dissecting knife cut the throat of the rats then placed the plain tube to collect the blood gushing out from the cut section. Allow the blood to stand for about 10-15 minutes for the content to settle i.e., the serum will be above in the tube and the red blood cells settles below.

Separate the serum into another plain tube then it's ready for analysis. While the EDTA container is used to collect blood for hematological parameters.

Statistical analysis: Data were expressed as mean ± standard deviation (SD). Comparison of the data from test control groups of animals were analyzed by One Way Analysis of Variance (ANOVA) at the confidence limit of 95% was used to determine significant results, differences between groups were considered statistically significant at $p<0.05$.

Results

Phytochemical screening

Results of phytochemical screening carried out on the aqueous extract of *Citrus sinensis* peel are shown in **Table 1.**

Discussion

Exposure to hyperglycemia for a long period is recognized as the major factor in pathogenesis of diabetic complications as well as inducing large alterations in vascular tissue that potentially promote atherosclerosis [28,29]. The present study was conducted to investigate the effects of aqueous extract of *Citrus cinensis* peel on alloxan induced diabetic rats. This effect was compared with diabetic untreated and normal experimental rats. Results of this study showed a significant variations in blood glucose, creatinine, urea, uric acid, electrolytes, total protein (TP), total bilirubin (TBIL) and lipid profile between the normal control, treated and diabetic control groups except HDL and albumin (ALB) in which normal control did not differ significantly from the treated ($P<0.05$). Results of phytochemical screening showed that *Citrus sinensis* peel extract contains flavonoids, saponins, resins, cardiac glycosides, terpenes and steroids. The result shows the absence of alkaloids. The determination of blood glucose concentration among others is a useful quantitative parameter for diabetes [30]. The increase in the blood glucose levels of the rats to a chronic state and its subsequent reduction by the administration of extract of *Citrus sinensis* in this study suggests anti-hypoglycemic effect of the plant extract. The probable mechanisms of action of plant extract could be via several mechanisms which are linked to either potentiation of insulin from beta cells, increasing peripheral glucose uptake, slowing down the absorption of sugar from the intestinal gut or by decreasing the release of glucose from the liver [31,32]. The reduction in the blood glucose of the rats by extract of *Citrus sinensis* in this study is similar to the previous work of Vinuthan et al. [33]. Concentration of glucose in the normal control group significantly increased when compared to diabetic control group ($P<0.05$). Treatment with the extract of *Citrus sinensis* (400 mg/kg body weight) decreased the concentration of glucose significantly ($P<0.05$). Also, treatment with metformin (500 mg/kg body weight) decreased the concentration of glucose significantly ($P<0.05$). Albumin is a major protein of human plasma and represents about 25% of total hepatic protein synthesis and half its secreted proteins. Its synthesis is depressed in variety of diseases, particularly those of the liver [34]. **Table 2** shows that there was a significant decrease in the concentration of albumin and total serum protein of the untreated alloxan induced diabetic rats when compared with the control and the treated groups. This observation may be attributed to numerous effects of hyperglycemia in alloxan-induced diabetes. Hyperglycemia increases gluconeogenesis and as such leads to excess protein breakdown as well as excess loss of nitrogen resulting in negative nitrogen balance [34]. A decline in total protein level in diabetic rats have been attributed to inhibition of oxidative phosphorylation which leads to decrease in protein synthesis, increase in catabolic processes and reduction in protein absorption [35]. Also, decrease in the total protein of alloxan induced rat, might may due to decrease due to microproteinurea which are important clinical markers of diabetic nephropathy [36], and/or may be due to increased protein catabolism [37] as a result of insulin deficiency from free radical generation due to alloxan induction, since it has been established that insulin stimulates the incorporation of amino acids into protein [37]. The results showed that administration of the extracts caused a remarkable increase in the serum total protein and albumin levels in the diabetic rats. These observations may be due to the presence of some compounds which help in provision of a reserved store of protein [38]. The concentration of TP in the normal control differs significantly when compared to diabetic control. Treatment with the extract of *Citrus sinensis* (400 mg/kg body weight) increased the concentration of TP and it differs significantly from the normal and diabetic controls ($P<0.05$). Metformin treatment group also increased the concentration of TP and it differs significantly when compared with normal and diabetic control ($P<0.05$). Concentration of ALB in the treatment group was not significantly different when compared with normal and diabetic control group ($p<0.05$). The effect of treatment with metformin did not differ significantly when compared with both the normal control group ($p<0.05$). 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 [39]. 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 [40]. 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 nonoxidative metabolism [41]. Oral administration of *Citrus sinensis* to the diabetic rats significant reduced the level of TG, TC, and LDL and significantly increases the level of HDL as shown in **Table 3.** The activities of AST, ALT and ALP have been reported to increase in alloxan-induced diabetic rats [42,43]. In this study, we reported significant ($p<0.05$) increase in the activities serum AST, ALT and ALP alloxanized diabetic untreated rats when compared

Table 1 Phytochemical Analysis.

Phytochemicals	Results
Alkaloids	-
Flavonoids	+
Saponins	+
Resins	+
Cardiac glycosides	+
Steroids	+
Terpenes	+

Table 2 Glucose, Total Protein and Albumin Levels.

Group ALB	Treatment	Glucose	TP	ALB
A	Normal control	92.50 ± 2.08	61.50 ± 1.29	33.02 ± 4.67
B	Diabetic control	392.50 ± 2.08a	31.42 ± 1.99a	32.52 ± 2.04a
C	Diabetic+treated E	106.75 ± 2.50ab	65.50 ± 1.29ab	41.50 ± 2.64ab
D	Diabetic+STD D	102.50 ± 2.08ab	60.40 ± 1.45ab	32.59 ± 2.08cd

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); [C]Values are not significantly different when compared with normal control (p<0.05)

Table 3 Blood Lipid Profile in Normal and diabetic Rats Groups.

Group ALB	Treatment	TOT. CHOL	TRIG	HDL	LDL
		mmol/L	mmol/L	mmol/L	mmol/L
A	Normal control	2.80 ± 0.18	1.30 ± 0.18	0.92 ± 0.22	1.80 ± 0.18
B	Diabetic control	3.30 ± 0.18a	1.85 ± 0.12ab	0.82 ± 0.17a	2.57 ± 0.17a
C	Diabetic+treated E	2.30 ± 0.18ab	65.50 ± 1.29ab	1.12 ± 0.29ab	1.77 ± 0.78ab
D	Diabetic+STD D	2.67 ± 0.17ab	1.12 ± 0.22ab	1.12 ± 0.22ab	1.72 ± 0.22ab

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).

with the control **(Table 4).** Measurement of the activities of "marker" enzymes or biomarkers in body fluids can be used to access the degree of assault and the toxicity of a chemical compound on organs/tissues [44,45]. Such measurements can also be used to indicate tissue cellular damage caused by a chemical compound long before it is revealed by histological techniques [46]. In **Table 4**, concentrations of ALT, AST and ALP in increased significantly in the diabetic groups (P<0.05). Treatment with the extract of *Citrus sinensis* (400 mg/kg body weight) decreased the concentrations of ALT, AST and ALP significantly (P<0.05) compared with diabetic control group. Also, treatment with metformin (500 mg/kg body weight) decreased the concentrations of ALT, AST and ALP significantly (P<0.05) compared with normal and diabetic controls. This study revealed a significant role of the extract of *Citrus sinensis* and metformin in restoring blood glucose to levels approximates to or below the normal control groups. Within this context, it is plausible to share other researchers that there is a need to formulate herbal plants with potential use as antidiabetic therapy [12]. It is also possible that the extract of *Citrus sinensis* acts through increasing insulin secretion, enhance glucose uptake by adipose or muscle tissues and inhibit glucose absorption from intestine and glucose production from liver [13]. This study also showed that metformin has more profound effects in restoring blood glucose compared with the extract of *Citrus sinensis*. In **Table 5**, in normal control groups, concentrations of urea, creatinine, and uric acid values were significantly different when compared with the diabetic groups (p<0.05). Results of treatment with the extract of *Citrus sinensis* peel (400 mg/kg body weight) on the concentrations of urea and creatinine differ significantly when compared with normal control. In the case of uric acid, results of treatment with the plant extract differ significantly from diabetic and normal control with the diabetic control higher than normal control and treatment group. Treatment with metformin (500 mg/kg body weight) increased the concentration of urea significantly compared with diabetic control and differ significantly when compared with normal control (P<0.05). The increased volume and metabolites excretions via the kidneys, usually in excess of normal thresholds give rise to imbalance in homeostasis with respect to electrolytes [47]. It imperative that the increased electrolytes and water levels usually observed in diabetes could lead to depletion of the extracellular fluid electrolyte and thus lead to the excretion of electrolyte by parietal and non-parietal cells [48], which may account for the observed significant decrease in the serum Na^+ and K^+ of diabetic untreated rat when compared with normal control **(Table 6).** However, the reduction of the electrolytes following oral administration of extract suggests that the extract could effectively attenuate the altered extracellular fluid electrolytes levels of the diabetic treated rats. Concentration of sodium in normal control group and diabetics control significantly increased. Treatment with the extract of *Citrus sinensis* peel (400 mg/kg body weight) decreased the concentration of sodium significantly (P<0.05). Treatment with metformin (500 mg/kg body weight) increased the concentration of sodium significantly (P<0.05). Concentration of potassium in normal control group differs significantly compared to diabetic control group (P<0.05). Treatment with the extract of Citrus sinensis peel (400 mg/kg body weight) increased the concentration of potassium significantly (P<0.05). Treatment with metformin (500 mg/kg body weight) decreased the concentration of potassium significantly (P<0.05). The results are as shown in **Table 6.** In **Table 7**, concentration of gamma-glutamyltransferase in normal control group significantly increased compared to diabetic control group (P<0.05). Treatment with the extract of *Citrus sinensis* peel (400 mg/kg body weight) decreased the concentration of gamma-glutamyltransferase significantly (P<0.05). Concentration of bilirubin in normal control group differs significantly when compared to diabetic control group (P<0.05) as shown in **Table 8.** Treatment with the extract of *Citrus sinensis* peel (400 mg/kg body weight) increased the concentration

Table 4 Liver Enzyme Activity in Normal and diabetic Rats Groups.

Group ALB	Treatment	ALT	AST	ALP
		(U/L	(U/L)	(U/L)
A	Normal control	116.25 ±2.98	230.25 ± 4.78	1302.80 ± 2.21
B	Diabetic control	142.75 ± 2.21a	314.50 ± 1.29a	3431.10 ± 2.39a
C	Diabetic+treated E	71.50 ± 2.46ab	192.75 ± 2.21ab	767.75 ± 2.21ab
D	Diabetic+STD D	35.55 ± 2.00ab	214.35 ± 1.53ab	1289.00 ± 2.54ab

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); [c]Value is not significantly different when compared with diabetic control (p<0.05)

Table 5 Differences in Urea, Creatinine and Uric acid Levels.

Group ALB	Treatment	Urea	Creatinine	Uric acid
		mmol/L	mmol/L	mmol/L
A	Normal control	7.82 ±3.25	0.57 ± 0.22	44.00 ± 1.82
B	Diabetic control	4.32 ± 1.57a	6.57 ± 0.22a	92.80 ± 2.13a
C	Diabetic+treated E	8.62 ± 1.10cb	0.67 ± 0.22cb	74.25 ± 1.70ab
D	Diabetic+STD D	7.95 ± 0.82cb	4.42 ± 0.17ab	32.92 ± 1.93ab

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); [c]values are not significantly different when compared with normal control (p<0.05)

Table 6 Differences in Electrolyte Levels.

Group ALB	Parameter	Sodium (Na^+)	Potassium (K^+)
A	Normal Control	102.75 ± 1.70	6.32 ± 0.22
B	Diabetic control	111.50 ± 2.08a	5.72 ± 0.22a
C	Diabetic+treated E	104.25 ± 1.70cb	7.10 ± 0.25ab
D	Diabetic+STD D	139.25 ± 1.70ab	4.10 ± 0.25ab

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); [c]Value is not significantly different when compared with normal control (p<0.05)

Table 7 Differences in Gamma-glutamyltransferase and Total Bilirubin Levels.

Group ALB	Parameters	GGT (U/L)	T/Bil (umol/L)
A	Normal Control	5.30 ± 0.25	11.10 ± 0.29
B	Diabetic control	6.50 ± 0.25a	12.50 ± 0.25a
C	Diabetic+treated E	5.47 ± 0.35cb	14.67 ± 0.17ab
D	Diabetic+STD D	6.17 ± 0.17ab	12.45 ± 0.12ab

Table 8 The groupings and administration of alloxan, extract, and standard drug.

Group	Title	Number of rats	Treatment
A	Normal Control	4	Feed+Distilled water
B	Diabetic Control	4	Feed+Distilled water
C	Diabetic+Extract	4	Feed+Distilled water+Extract
D	Diabetic+Std drug	4	Feed+Distilled water+Std drug

of bilirubin significantly (P<0.05). Treatment with metformin (500 mg/kg body weight) differs significantly when compared with diabetic control (P<0.05).

Conclusion

In alloxan-induced diabetic rats, the peel extract of *Citrus sinensis* has shown some antidiabetic and hypolipidemic properties as it reduced serum concentrations of glucose, total cholesterol, triglyceride and low density lipoprotein. It decreased the serum concentrations of liver enzymes. This suggests that *Citrus sinensis* peel extract may not have toxic effect on the liver at the employed dosage. Based on these findings, *Citrus sinensis* peel extract could be used in the treatment and management of diabetes mellitus. It could also be used to reduce the risks of coronary heart disease and obesity as it has hypo-lipidemic properties.

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