Evaluation of Antidiabetic Potentials of *Ficus capreifolia* Extract in Alloxan-induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

The study evaluated the antidiabetic potentials of *Ficus Capreifolia* extract in an alloxan-induced diabetic rats. The study used animal models (albino rats) and daily administration of the extract at various dosages. The study took place at the University of Port-Harcourt, Choba, Rivers State, Nigeria and its environs between June to November, 2020. Diabetes mellitus was induced by a single intraperitoneal injection of freshly prepared alloxan (150 mg/kg body weight) except group 1 which was negative control (NC). Diabetes was confirmed after 48 hours in all the rats with fasting blood glucose levels above 250 mg/dl. The experimental animals were grouped into 5 of 10 rats each. Group 1 was non-diabetic rats used as normal control, group 2 consisted of diabetic control rats that received no treatment. Group 3, 4 and 5, rats were diabetic rats but treated with Co-mepiryl (SD), FC_{500}, and FC_{200} (*ficus capreifolia* at 500,200 mg/kg). Blood were collected after 14 days and 28 days of treatment for biochemical assay of fasting plasma glucose, renal, lipid profile and hepatic parameters. The dose dependent treatment significantly lowered ($P<0.05$) fasting glucose level, atherogenic indices, lipid profile (except in the case of High density lipoprotein which was significantly increased, ($P<0.05$) and hepatic biomarkers when compared with the positive control. It showed their antidiabetic potential by reduction in elevated glucose level, amelioration of dyslipidaemia, reduction in hepato-renal biomarkers and showed protective effect against coronary heart disease. All these, supports the use of the extract for the management of diabetes mellitus in African traditional health care practices.

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1. INTRODUCTION

Ficus capreifolia (Moraceae) is a fig shrub that grows in the tropical regions of Africa. The plant (also known as sandpaper fig) grows to about 7 cm in height [1].

Ficus capreifolia is a useful multipurpose plant providing not only fiber, planting material and sand-paper but also a range of other products such as food and traditional medicines. It is used to treat various ailments in some part of Nigeria including Rivers State such as diabetes, cough, diarrhea, skin infection, ulcer, stomach disorders, liver disease and even infertility [2]. Despite it several medicinal values, the plant is grossly underused coupled with the limited literature available on the use of the plant [3].

Diabetes mellitus is regarded as a syndrome, a group of illnesses characterized by hyperglycemia and glucose intolerance, which can be caused by insulin shortage, insulin ineffectiveness, or a combination of these factors [4]. The progressive nature of this disease condition necessitates constant reassessment of glycaemic control in people with diabetes and appropriate adjustment of therapeutic regimens [3]. The World Health Organization has stated that preventing diabetes and its complications is not only a huge task for the future, but also a serious one now [5], but essential if health for all is to be an attainable target, and strongly emphasize the optimal, rational use of traditional and natural indigenous medicines [6]. Hence the study, to evaluate the antidiabetic potentials of *Ficus capreifolia* (a commonly used antidiabetic plant in Aluu and Bodo communities in Rivers State, Nigeria) in alloxan-induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Chemicals and Reagents

All chemicals/reagents and materials used for the work were commercially made available and the manufacturers standard operating procedures was strictly followed while using them for the work.

2.2 Plant Material

Ficus capreifolia was obtained from Bodo City in Gokhana Local Government Area and Aluu in Ikwerre Local Government Area of Rivers State, Nigeria. The plant was identified and authenticated in the Herbarium of the Department of Plant Science and Biotechnology, Rivers State University, Port Harcourt as *Ficus capreifolia.*

2.3 Sample Preparations

To remove dirt, fresh *Ficus caprecfolia* leaves were thoroughly cleaned with deionized water. The leaves were dried and pulverised in a warring blender at room temperature. The extraction was done using Soxhlet extractor in a continuous extraction Process (BDH Chemicals) for72 hours using Methanol as extracting solvents. A weighed portion of the pulverized samples (200 g) was used against 1000 ml of absolute methanol. The extract weas concentrated using rotary evaporator set at 60°C. Different concentrations (250mg/kg and 500 mg/kg) of the extract and reference drug (Co-Mepiryl) were prepared using distilled water.

2.4 Acute Toxicity Test of the Extract

This was done using the Fixed Dose Procedure (OECD, 2001), with the aim of determining the LD_{50} of the Extract formulation. Three rats were grouped into a group. The rats were fasted overnight, and then given 2000mg/kg of *Ficus Capreifolia.* They were observed for three days for signs of toxicity and there was none.

2.5 Experimental Animals

A total of fifty (50) Albino rats weighing between 120-309g were used for the study. The animals were obtained from the Animal House of the Department of Pharmacology, faculty of Basic Medical Science, University of Port-Harcourt, Choba, Rivers State. All the animals were housed in the animal house, Department of Pharmacology, University of Port-Harcourt, Abuja campus using standard cages at room temperature. They were allowed access to feed (finisher) manufactured by TopFeeds Nig. Ltd and water *ad libitum*.

After their baseline weight was recorded, they were acclimatised for two weeks prior to the trial and marked for easy identification and monitoring. All animal handling procedures and techniques were carried out according to conventional procedures and in accordance with

the National Institute of Health's guidelines (CIOMS, 1985).

2.6 Determination of Therapeutic Dose

The rat doses of the extract formulation and orthodox drugs were extrapolated from the human therapeutic doses based on body surface area ratio, using the Paget and Barnes (1964) conversion table, which is based on 70kg as the weight of adult human, and 200g as the weight of rat.

The rat dose for each drug was calculated using the formula:

Quation1. Rat dose (mg/kg) = Human dose (mg) x 0.018 x 5 [7].

The daily dose of both the standard drug and the Extract formulation were determined based on Organization for Economic Co-operation and Development's Guidelines (OECD, 2001). The drug and Extract formulation were dissolved in water and administered to the rats according to OECD's Guideline.

2.7 Experimental Design and Diabetes Inductions

The acclimatized albino rats were sorted according to their weights into five groups of ten (10) rats each. Diabetes was induced by a single intraperitoneal injection of freshly prepared alloxan (150 mg/kg body wt.) (apart from the group 1) dissolved in physiological saline, after a 6 hour fast. Diabetes was confirmed after 48 hours in all the rats, with fasting blood glucose levels above 14mmol/L (250 mg/dl). Treatments were administered daily according to the grouping by means of oral administration for 14 and 28 days respectively.

Group 1: Negative control (NC) group fed with the normal rat feed and water.
Group 2: Diabetic rats (PC, Positive control) was fed with feed and water without treatment.
Group 3: Diabetic rats (SD) treated with Standard drug (Co-Mepiryl) 500mg/kg body weight.
Group 4: Diabetic rats (FC$_{500}$) treated with *Ficus capreifolia* Extract (500mg/kg body weight).
Group 5: Diabetic rats (FC$_{200}$) treated with *Ficus capreifolia* Extract (200mg/kg body weight).

All animals were allowed access to water and food for 14 and 28days periods respectively.

2.8 Sacrificing of Animals and Collection of Blood Samples.

All animals from the groups were sacrificed at the end of the treatment period of 14 and 28 days respectively. The animals were incapacitated with chloroform in a dessiccator. Under this condition, the rats were dissected using dissecting tools and the blood were collected and put in plain bottles for biochemical analysis.

2.9 Determination of Body Weight

Prior to the administration of the samples after acclimatization, the animals were weighed to have the initial weights (IW). Subsequently, weekly weights were determined at 14 and 28 days respectively.

2.10 Determination of Blood Glucose Level

Glucose level was determined using Accu-chek active electronic glucometer (One touch Ultra easy Blood glucometer, Life scan, USA) with glucose strips. The blood for this was collected via the tail vein and the assay done instantly.

2.11 Data Analysis

Data from this study was analyzed using SPSS (statistical package for social sciences) version 23. ANOVA(Analysis of Variance) statistic followed by Tukey and Posthoc analysis was used to compare the means of the parameters. P-values less than 0.05 ($P<0.05$) were considered statistically significant in this study.

3. RESULTS AND DISCUSSION

Despite the discovery of a variety of medications that can alleviate the symptoms of the ailment, a therapeutic cure for diabetes mellitus has remained elusive [8,9]. Phytotherapies have maintained a rich source of drug discovery around the world [10,1] and have played an essential role in the management of diabetics for decades, particularly in resource-constrained nations. Alloxan acts as a diabetogen by destroying -cells in the Langerhans islets, resulting in a substantial drop in insulin release and hyperglycemia [9]. Insulin deficiency leads to various metabolic alternations in the animals [11,7].

Table 1. Mean ± SEM of Plasma Glucose Profile of normal and alloxan-induced diabetic rats after 14 and 28 days

S/N	Group	Initial Glucose level (mmol/l)	Glucose Level after induction (mmol/l)	Glucose Level after 14days of treatment (mmol/l)	Glucose Level after 28 days of treatment (mmol/l)
1.	NC n = 5	4.84 ± 0.27^a	4.56 ± 0.53^{ac}	5.40 ± 0.25^{ac}	5.40 ± 0.24^{ac}
2.	PC n = 5	4.56 ± 0.018^a	15.82 ± 3.80^{ac}	12.54 ± 3.05^a	15.28 ± 1.20^{ac}
3.	SD n = 5	4.68 ± 0.08^a	16.62 ± 8.75^{ac}	7.34 ± 6.41^a	7.34 ± 6.41^{aci}
4.	FC$_{500}$ n = 5	4.58 ± 0.26^a	18.32 ± 5.0^{ac}	14.18 ± 4.20^{ac}	6.66 ± 5.73^a
5.	FC$_{200}$ n = 5	4.58 ± 0.08^a	11.48 ± 1.40^{ac}	7.20 ± 5.53^a	6.56 ± 4.33^a

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 1 shows mean ±SEM of plasma glucose profile of normal and alloxan-induced diabetic rats after 14 and 28 days of treatment. After 48 hours of intraperitoneal injection of freshly prepared alloxan, elevated glucose level was observed as compared with the negative control (confirming diabetic condition). However, after 14 and 28 days of treatments, there was a significant reduction in glucose level of the treated rats as compared with the positive control (untreated rats) at P<0.05. Knowing that diabetes mellitus induced by alloxan, is usually known by decrease insulin level, hyperglycemia, elevated triglycerides and total cholesterol and decreased high density lipoprotein [10]. Therefore, the reduction in plasma glucose levels produced by the extract support the use of the plant in the management of diabetes mellitus.

Table 2 shows the mean ±SEM of the body weight of normal and alloxan-induced diabetic rats after 14 and 28 days of treatment. There was significant weight gain by the diabetic rats as compared with the negative control. However, after 14 and 28 days of treatment, there was significant weight gain by groups treated with FC$_{500}$ as compared with the control rats at **P<0.05**, while there was reduction in weight of groups treated with SD and FC$_{200}$ as compared with the positive control. Hence, Relationships between hyperglycaemia and increase in body weight of the experimental animals have been reported [12]. In this study, there was significant increase in body weight of the diabetic rats when compared with their initial weight. This is an indication of obesity in the diabetic rats [13], but in the treated ones from 14-28 days, may be as a result of improved glycaemic control.

Table 2. Mean ±SEM of the body weight of normal and alloxan-induced diabetic rats after 14 and 28 days of treatments

S/N	Group	Initial Weight (g)	Weight after 14 days of treatment (g)	Weight after 28 days of treatment (g)
1.	NC n = 5	122.80 ± 5.93^{ac}	161.20 ± 14.92^{ac}	161.20 ± 14.92^{ac}
2.	PC n = 5	174.80 ± 30.88^{ac}	188.40 ± 30.37^{ad}	190.80 ± 21.51^{ad}
3.	SD n = 5	179.60 ± 32.50^{ac}	155.60 ± 26.20^{ae}	148.80 ± 8.17^{ae}
4.	FC$_{500}$ n = 5	184.20 ± 39.30^{ac}	204.20 ± 20.66^{acei}	249.40 ± 22.65^{acdei}
5.	FC$_{200}$ n = 5	132.80 ± 6.06^a	144.60 ± 14.06^{adi}	151.20 ± 22.79^{ai}

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 3. Mean ± SEM of Renal Parameters in albino Rats after 14 Days of Treatment

S/N	Groups	Biocarbonate (mmol/l)	Potassium (mmol/l)	Sodium(mmol/l)	Urea (mmol/l)	Creatinine (µmol/l)	Chloride(mmol/l)
1	NC n=5	25.60± 1.67[a]	3.58 ± 0.83[ac]	116.60± 5.08[aci]	6.12±1.11[ac]	110.40±10.62[ac]	56.20±2.17[a]
2	PC N=5	28.40±2.19[ac]	4.36± 0.16[acd]	135.60±4.67[acd]	10.14±0.32[a]	158.20±15.39[a]	62.80±2.68[ac]
3	SD n=5	23.60±1.67[ad]	3.26±0.17[ade]	104.60±2.88[acdi]	7.80±0.78[a]	122.20±7.22[a]	54.60±1.67[ac]
4	FC 500 n = 5	24.00±2.45[a]	3.64±0.15[ade]	116.20±1.64[ads]	8.10±1.12[ac]	127.80±18.44[aci]	58.20±1.09[aci]
5	FC 200 n = 5	26.80±2.68[a]	3.56±0.17[ad]	114.20±4.55[ad]	9.90±2.77[a]	99.60±9.59[aie]	49.80±4.50[aci]

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 4. Mean ± SEM of Renal Parameters in albino rats after 28 days of treatment

S/N	Groups	Biocarbonate (mmol/l)	Potassium (mmol/l)	Sodium(mmol/l)	Urea (mmol/l)	Creatinine (µmol/l)	Chloride (mmol/l)
1	NC n=5	25.60±1.67[a]	3.58±0.08[ac]	115.20±4.09[ac]	6.12±1.11[ac]	110.40±10.62[ac]	56.20±2.16[ac]
2	PC n=5	27.60±1.67[a]	4.20±0.479[acd]	131.60±15.11[acd]	10.90±2.16[a]	170.40±28.11[acd]	63.80±0.84[acdi]
3	SD n=5	24.00±2.45[ac]	3.26±0.17[adi]	104.60±2.88[adi]	8.10±1.12[a]	127.80±18.44[ad]	54.60±1.67[adi]
4	FC 500 n = 5	26.80±0.84[a]	3.60±0.12[ad]	114.00±4.90[ad]	7.36±0.17[a]	117.60±2.88[adi]	55.00±1.22[ad]
5	FC 200 n=5	2360±1.67[a]	3.14±0.13[ad]	104.60±2.41[ade]	9.06±0.98[a]	140.60±13.48[a]	53.20±1.64[ad]

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 3 and 4 shows the mean ±SEM of renal parameters in albino rats after 14 and 28 days of treatment. The positive control (PC) shows a significant increase in all the renal parameters at P<0.05 but upon treatment, there was a significant reduction in concentration of the renal parameters as compared with the positive control but no significant difference at P<0.05 when compared with the negative control (NC). It is important to note that FC_{500} had much reduction in the elevated concentration of the renal parameters after 14 days of treatment than FC_{200} while FC_{200} has much reduction in the elevated renal parameters after 28 days of treatment than FC_{500}. We may recall that, the Kidney removes metabolic wastes such as urea and creatinine, the concentration of which are usually required to assess the normal functioning of different parts of the nephron [11] and even the basic electrolyte such as Cl, K, Na and Biocarbonate. Their concentrations in serum are widely interpreted as measures of the glomerular filtration rate (GFR) and are used as indices for renal function in clinical practices [8]. The concentration of these metabolites increase in blood during renal damage associated with uncontrollable diabetes mellitus [14]. As contained in Table 3 and 4, the diabetics rats has an increase in the concentration of these metabolites. On the contrary those treated with extract and standard drug have a decreased effect. Decreased in them indicating ameliorative effect of the plant extract on kidney function parameters in diabetic rats. This may suggest that the damage caused on renal function indices by the diabetic condition had been restored by the plant extract, thus the proper function of the nephrons at the tubular and glomerular level [8].

Table 5 and 6 shows the mean ±SEM of hepatic parameters in alloxan-induced diabetic rats. There was elevation of hepatic enzymes concentration and other liver biomarkers in the serum of alloxan-induced diabetic rats as shown in the positive control group (PC) when compared with the normal control. However, after 14 and 28 days of treatment with the extract at different doses, there was a significant reduction in the elevated liver biomarkers at P<0.05 as compared with the positive control. However, there was enzyme induction while using the standard drug (Co-Mepriyl) for treatment after 14 days but that was not the case after 28days of treatment. It is important to note that FC_{500} has much reduction in the elevated concentration of the hepatic biomarkers after 14 days of treatment than FC_{200} while FC_{200} has much reduction after

28 days than FC_{500}. However, the high concentration of serum levels of the hepatic markers is a sign of hepatic cellular damage as a result of the diabetic induction which is one of the characteristic changes in diabetes [15].

The release of these liver biomarkers into the serum is as a result of tissue injury or changes in the permeability of liver membrane, hence the concentration may increase with acute damage to liver cells [12].

However, the treated groups showed a significant reduction in the levels of these liver biomarkers when compared with the diabetic untreated control, thus an indication of the protective effect of the extract over Alloxan-induced liver damage [15].

Table 7 and 8 shows the mean ± SEM of serum lipid profile of alloxan-induced diabetic rats after 14 and 28 days of treatments. There was elevation in the concentration of TC, TG, LDL, Non-HDL and VLDL but a fall in the concentration of HDL of the diabetic rats as compared with the negative control. However, upon treatment with the extract at different doses, there was a significant reduction in the elevated concentration level when compared with the positive control at P<0.05 after 14 and 28 days of treatment except in the case of HDL which has a significant increase at P<0.05. Hence, the pathogenesis of diabetic mellitus is associated with disturbance in carbohydrate, fat and protein metabolism under normal circumstances, insulin activities, the enzyme lipoprotein lipase, which hydrolyses TGs. However, in diabetic state, lipoprotein lipase is not activated because of insulin deficiency, resulting in hyperglyceamia owing to metabolic abnormalities [2,7]. The dyslipidaemia is characterized by increase in total cholesterol (TC), low density lipoprotein (LDL), very low-density lipoproteins (VLDLS), total triglycerides (TGs) and a fall in high density lipoprotein (HDL). In this study the levels of TC and total TG were markedly increased following induction of diabetes with alloxan confirming dyslipidaemia associated with diabetes mellitus and these alteration in the levels of major lipids such as cholesterol and TGs can give useful information on lipid metabolism as well as an indicated predisposition of animals to cardiovascular risk [14]. The altered serum lipid profile in this study was, however, reversed significantly (P<0.05) following treatment with *Ficus capreifolia* extract after 14 and 28 days respectively. This is in agreement with the study by Pari and Uma [11].

Table 5. Mean ± SEM of Hepatic Parameters in albino rats after 14 days of treatment

S/N	Groups	AST (U/L)	ALT (U/L)	ALP (U/L)	Total Protein (g/l)	Albumin (g/l)	Total Birilubin (mmol/l)	Conjugated Bi (mmol/l)
1	NC n=5	53.60±5.37[ac]	30.00±2.45[ac]	27.20±2.86[ace]	67.60±5.37[ac]	39.40±2.51[a]	11.08±0.62[a]	7.10±1.23[ac]
2	PC n=5	61.00±4.85[ab]	30.00±4.58[ad]	43.80±2.68[acd]	80.80±0.84[ac]	45.00±1.22[a]	11.74±1.33[ac]	8.80±2.32[ad]
3	SD n=5	62.80±7.79[ad]	24.00±1.22[a]	31.40±1.34[acdi]	73.60±5.37[a]	42.20±2.16[a]	12.44±1.81[ad]	8.46±1.58[ae]
4	FC 500 n = 5	62.40±9.69[ac]	27.60±2.57[ae]	36.00±1.22[ae]	70.80±3.29[ac]	40.80±3.27[a]	12.46±2.27[ai]	8.20±1.52[ai]
5	FC 200 n=5	50.20±6.06[ai]	28.40±7.33[ai]	28.40±2.51[ai]	76.20±2.86[a]	42.00±1.87[a]	9.04±1.88[a]	5.42±0.50[adi]

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 6. Mean ± SEM of Hepatic Parameters in albino rats after 28 days of treatment

S/N	Groups	AST (U/L)	ALT (U/L)	ALP (U/L)	Total Protein (g/l)	Albumin (g/l)	Total Birilibin (mmol/l)	Conjugated Bi (mmol/l)
1	NC N=5	53.60±5.37[ac]	30.00±2.45[ac]	27.20±2.86ac	67.60±ac 5.37	39.40±a 2.50	11.08±a 0.62	7.10±ac 1.23
2	PC N=5	88.60±8.85[acd]	35.80±0.84[ad]	44.60±1.67[acd]	77.60±ac 2.40	41.80±acdi 2.05	17.78±acd 2.21	13.44±acd 0.86
3	SD N=5	62.80±7.79[ad]	24.00±1.22[adi]	43.80±2.68[aah]	70.80±ad 3.27	40.80±acdi 3.27	12.44±ad 1.81	8.46±ad 1.58
4	FC 500 N = 5	51.80±8.73[ad]	26.60±1.67[ad]	36.80±10.52[ai]	7.60±ac 1.67	43.40±acdi 1.34	10.64±ad 1.89	6.84±ad 2.62
5	FC 200 N=5	43.80±0.84[ad]	34.00±3.40[aih]	29.40±2.07[adh]	73.60±a 2.57	44.20±ac 1.64	9.24±ad 0.25	4.78±ad 0.08

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 7. Mean ±SEM of serum lipid profile of albino rats after 14 Days of Treatment

S/N	Group	TC (mmol/l)	TG (mmol/l)	HDL (mmol/l)	LDL (mmol/l)	Non-HDL (mmol/l)	VLDL (mmol/l)
1.	NC n = 5	1.98 ± 0.08^{a}	1.34 ± 0.24^{a}	1.26 ± 0.12^{a}	1.30 ± 0.10^{a}	0.69 ± 0.07^{a}	0.61 ± 0.10^{a}
2.	PC n = 5	2.24 ± 0.33^{ab}	1.39 ± 0.15^{a}	1.16 ± 0.12^{a}	1.74 ± 0.41^{a}	1.08 ± 0.49^{a}	0.63 ± 0.07^{a}
3.	SD n = 5	2.44 ± 0.44^{ab}	1.28 ± 0.25^{a}	1.10 ± 0.13^{a}	1.91 ± 0.51^{a}	1.30 ± 0.58^{a}	0.55 ± 0.10^{a}
4.	FC_{500} n = 5	2.14 ± 0.19^{a}	1.60 ± 0.10^{a}	1.05 ± 0.08^{ab}	1.86 ± 0.23^{a}	1.13 ± 0.19^{a}	0.73 ± 0.05^{ab}
5.	FC_{200} n= 5	2.14 ± 0.11^{a}	1.08 ± 0.42^{abc}	1.09 ± 0.27^{a}	1.47 ± 0.08^{a}	0.98 ± 0.23^{a}	0.49 ± 0.20^{abc}

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 8. Mean ±SEM of serum lipid profile of albino rats after 28 days of treatment

S/N	Group	TC (mmol/l)	TG (mmol/l)	HDL (mmol/l)	LDL (mmol/l)	Non-HDL (mmol/l)	VLDL (mmol/l)
1.	NC n = 5	2.06 ± 0.25^{a}	1.33 ± 0.23^{a}	1.32 ± 0.15^{ac}	1.30 ± 0.10^{ac}	0.69 ± 0.06^{aci}	0.61 ± 0.10^{a}
2.	PC n = 5	2.14 ± 0.27^{a}	1.51 ± 0.15^{ac}	1.23 ± 0.19^{ae}	1.60 ± 0.14^{ai}	0.87 ± 0.11^{ai}	0.70 ± 0.07^{ac}
3.	SD n = 5	2.44 ± 0.27^{aci}	1.20 ± 0.20^{a}	1.10 ± 0.13^{aid}	1.91 ± 0.51^{aci}	1.30 ± 0.58^{aci}	0.55 ± 0.10^{ae}
4.	FC_{500} n = 5	1.72 ± 0.08^{acd}	1.25 ± 0.08^{a}	0.78 ± 0.08^{aced}	1.35 ± 0.14^{ai}	0.92 ± 0.16^{a}	0.55 ± 0.01^{ai}
5.	FC_{200} n = 5	1.92 ± 0.08^{ai}	1.42 ± 0.02^{a}	1.11 ± 0.15^{ad}	1.30 ± 0.10^{ai}	0.72 ± 0.16^{a}	0.65 ± 0.01^{a}

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 9. Mean ±SEM of atherogenic indices of normal and alloxan-induced diabetic rats after 14 days of treatments

S/N	Group	Cardiac Risk Ratio (CRR)	Atherogenic Coefficient (AC)	Altherogenic index of Plasma (AIP)
1.	NC n = 5	1.53 ± 0.11^a	0.60 ± 0.20^a	0.03 ± 0.05^a
2.	PC n = 5	2.00 ± 0.41^a	0.94 ± 0.50^a	0.03 ± 0.10^a
3.	SD n = 5	2.20 ± 0.66^a	1.20 ± 0.66^a	0.05 ± 0.02^a
4.	FC$_{500}$ n = 5	2.05 ± 0.20^a	1.04 ± 0.21^a	0.17 ± 0.05^a
5.	FC$_{200}$ n = 5	1.90 ± 0.42^{ai}	0.88 ± 0.42^a	0.01 ± 0.07^a

Table 10. Mean ±SEM of the atherogenic indices of normal and alloxan-induced diabetic rats after 28 days of treatments

S/N	Group	Cardiac Risk Ratio (CRR)	Atherogenic Coefficient (AC)	Altherogenic index of Plasma (AIP)
1.	NC n = 5	1.54 ± 0.11^a	0.60 ± 0.20^{ac}	0.03 ± 0.05^a
2.	PC n = 5	1.69 ± 0.72^a	0.70 ± 0.07^a	0.08 ± 0.03^{ai}
3.	SD n = 5	2.20 ± 0.66^a	1.19 ± 0.66^{aci}	0.05 ± 0.02^{ad}
4.	FC$_{500}$ n = 5	2.06 ± 0.27^a	1.05 ± 0.27^a	0.17 ± 0.05^{aicdeh}
5.	FC$_{200}$ n = 5	1.65 ± 0.22^a	0.65 ± 0.22^a	0.09 ± 0.05^{ac}

Values are presented in mean ± SEM. Values with (a) superscript as compared with NC (normal control) are not significantly different at P<0.05. Values with the same superscripts other than (a) superscript are significantly different at (P<0.05) from each other

Table 9 and 10 shows the mean ± SEM of atherogenic indices of normal and alloxan-induced diabetic rats after 14 and 28 days of treatment. There were elevated level of CRR, AC and AIP in the concentration of the diabetic rats as compared with the negative control which was an indication of cardiovascular disease. However, after 14 and 28 days of treatment, there was a reduction in the elevated atherogenic indices concentration when compared with the positive control at P<0.05. Recall that atherogenic indices are powerful indicators of heart disease. The higher the value, the higher the risk of developing cardiovascular disease and vice versal [10,16]. Low athrogenic indices are protective against coronary heart disease [17]. Thus, the low atherogenic indices especially in FC$_{200}$ of *Ficus capreifolia* extract indicates the plant extract ability to protect against cardiovascular complications in the diabetic rats. Thus, the extract showed a protective effect against coronary heart disease.

4. CONCLUSION

The results shows that the extract of *Ficus capreifolia* exhibited anti-diabetic potential by reduction in elevated glucose level. It also has the ability to stabilize the liver biomarkers thereby showing it's protective potential on hepatocyte and renal function, ameorilate dyslipidaemia and showed protective effect against coronary heart disease. This action is in agreement with other medicinal plants extracts that is known as anti-diabetic agent [9]. Therefore, the extract can be used for the management of diabetes and other metabolic disorder that may arise.

DISCLAIMER

The plant used for this research are commonly and predominantly used plant in our area of research and country. There is absolutely no conflict of interest between the authors because we do not intend to use these as an avenue for

any litigation but for the advancement of knowledge. Also, the research was funded by personal efforts of the authors.

ETHICAL APPROVAL

All authors hereby declare that principles of laboratory animal care were followed as well as specific national laws where applicable. All experiments have been examined and approved by the appropriate ethics committee.

NOTE

The study highlights the efficacy of "traditional medicine" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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