Research Article

Ameliorative Effects of Methanol Leaf Extract of Ficus Sycomorus in Alloxan-induced Diabetic Rats

Abdullahi S Usman[1,2*], Ahmad Ali[1], Mudassir Lawal[1,3]
[1]Department of Biochemistry and Molecular Biology, Federal University Dutsin-ma, Nigeria.
[2]Department of Biochemistry, School of Basic and Applied Sciences, Career Point University Kota, Rajasthan, India.
[3]Department of Biochemistry, School of Bioengineering and Biosciences, Lovely Professional University, Punjab, India.
***Corresponding author's E-mail:** shehuman88@mail.com

Received: 19-04-2024; **Revised:** 28-06-2024; **Accepted:** 10-07-2024; **Published on:** 15-07-2024.

ABSTRACT

Diabetes mellitus has been linked to a number of complications, such as oxidative stress, liver damage, and excessive weight gain after a sustained elevation of blood glucose and cholesterol levels. Consequently, the goal of the current study is to investigate the antihyperglycemic, antioxidant, hypolipidemic and hepatoprotective potentials of *Ficus Sycomorus* leaf extract in induced diabetic albino rats. The Qualitative phytochemical analysis of *Ficus Sycomorus* extract was carried out using standard laboratory procedures. Albino rats were divided into four groups. Two groups were treated with Methanolic extract of *Ficus Sycomorus* at 200 mg/kg and 400 mg/kg body weight respectively, while the other groups served as the normal and positive control groups. The glucose concentrations were recorded, and on the fourteenth day of treatment, the animals were sacrificed. The blood samples collected were subjected to antioxidant, antihyperlipidemic and hepatoprotective assay. The phytoconstituents; flavonoids, steroids, terpenoid, cardiac glycoside, phenols and alkaloids were found to be present. The research data revealed that there was a significant ($p < 0.05$) decrease in glucose levels especially at dose of 400 mg/kg body weight. There was no significant ($P < 0.05$) difference in the level of sodium dismutase and catalase, while malondialdehyde level significantly decreases in animals treated at 200 mg/kg body weight. Also, no significant ($P < 0.05$) difference in triglycerides and cholesterol level in animals treated with 200 mg/kg body weight, however; HDL and LDL level were significantly increased. ALT and AST concentrations decrease significantly, but no significant ($P < 0.05$) difference was observed in ALP, TP and ALB as compared to the control groups. The findings had proven that the methanol leaf extract of *Ficus sycomorus* has antihyperglycemic, antioxidant and antihyperlipidemic activities and also improve liver function. Therefore, may be useful in the management of diabetes and its associated complications.

Keywords: Anti-hyperglycemic, antioxidant, anti-hyperlipidemic, diabetes mellitus, *Ficus Sycomorus*, hepatoprotective.

INTRODUCTION

Medicinal plants are used in almost all cultures particularly Asian and Western culture and play an important role in the discovery of more effective drug and extension of unidentified plant medicine sources [1]. Research indicates that 60% of people worldwide rely on herbal medicine, while in underdeveloped nations, 80% of people virtually exclusively depend on it for basic medical requirements. It is also thought that the majority of Nigerians still seek medical advice from traditional medicine practitioners and utilize medicinal plants [2]. However, there is a dearth of information on medicinal plants. Regrettably, as a result of human activities rapidly destroying some of these plants' native habitats, documentation of the therapeutic value of African species is becoming more and more crucial [3].

Medicinal plants with antioxidant potentials helps to restore the function of beta-cells in Diabetes mellitus. Oxidative stress is a major factor in the etiology of diabetes mellitus and its complications since free radicals are known to cause cell damage and mutation. Plants that possess antioxidant activity will thus be crucial in managing diabetes mellitus and its associated consequences by eliminating free radicals [4].

Ficus sycomorus (Moraceae) has more than a thousand different species, many of which have milky latex fluids. The family has roughly 40 genera. They are typically found in savannah regions next to streams. It is a 20-meter-tall tree with widely dispersed branches and a large crown [5]. Numerous pharmacological activities of the plant have been reported, these include antimycobacterial [6], antifungal [7], hepatoprotective [8], antidiarrheal [9], anti-inflammatory [10], aphrodisiac [11], and antioxidant activity [12]. The leaves are used as an antidote for snakebite and treatment of jaundice. The root is also useful as an anthelmintic and laxative. The stem back of the plant is used by herbalists in Kenya and Nigeria to treat infectious disorders and ameliorate the complications associated with the diabetes [13].

METHODOLOGY

Sample collection.

Ficus syocomorus fresh leaves were collected in Dutsinma, Katsina State, Nigeria and identified at the Biological Science Department of Federal University Dutsin-Ma, Katsina State.

Plant Extract Preparation

The *Ficus sycomorus* fresh leaves collected were rinsed with water and dried at room temperature for a period of

one week. It was then grinded to powder using an electric blender. The powdered sample (500 g) was soaked in 1500 ml of methanol for 72 hours, after which was prefiltered using a muslin cloth and then filtered using filter paper (Whatmann size no.1). The extract was Concentrated to a dry mass by evaporation under reduced pressure using rotary evaporator. The concentrated extract was then stored until required for use [14].

Phytochemical Analysis

The phytochemical screening of the methanol leaf extract of *Ficus sycomorus* was carried out using standard laboratory procedure by Yadav and Munin [15].

Induction of Experimental Rats

The experimental albino rats were housed in cages for seven days to allow for acclimatization, after which they were fasted overnight prior to induction and alloxan dissolved in normal saline was administered at the dose of 150 mg/kg body weight intraperitoneally. After 72 hours of alloxan administration, the albino rats with blood glucose levels greater than 200 mg/dl, were considered diabetic [16].

Grouping of Experimental Animals

Group I: Normal control (non-diabetic and not treated)

Group II: Positive control (diabetic + metformin with 100 mg/kg body weight)

Group III: Diabetic + extract (200 mg/kg body weight)

Group IV: Diabetic + extract (400 mg/kg body weight)

The blood obtained by a snip-cut of the tail was used to measure the blood glucose concentration using an Accu-Check Active glucometer [17].

Determination of Antioxidant, Antihyperlipidemic and Hepatoprotective Activities of the Plant Extract

After the 14 days treatment period, blood samples were collected using chloroform inhalation anesthesia. It was then centrifuge at 1000 rpm for 15 minutes and the resultant sera was introduced into plain sample bottles. The concentrations of the various biochemical parameters were determined. For antioxidant activity; catalase, superoxide dismutase and malondialdehyde, for antihyperlipidemic activity; triglyceride, low density lipoproteins, cholesterol and very low-density lipoproteins, while for hepatoprotective activity; alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total protein and albumin. All the parameters were determined using the Agappe Diagnostics Switzerland GmbH kits following the manufacturer's instructions.

Statistical Analysis

The data collected were analyzed for significance by one-way analysis of variance (ANOVA) and groups were compared by Duncan multiple comparism testing using Statistical Package for Social Science (SPSS) and p values are considered significant when $p < 0.05$.

RESULTS AND DISCUSSION

The phytochemical screening **(Table 1)** of *Ficus sycomorus* extract has shown the presence of phenols, alkaloids, steroids, flavonoids, cardiac glycoside and terpenoids. The blood glucose-lowering activities of plants with antidiabetic property is due to presence of various phytoconstituents. The molecular mechanism of managing hyperglycemia with plant derived agents could be due to inhibition of alpha amylase and alpha glucosidase, inhibition of DPP-4 enzyme, increased insulin secretion and sensitivity, reduction of glycated hemoglobin and glycated plasma protein concentration, enhancement of GLP-1 and also through regulation of GLUT-4 [18].

Table 1: Phytochemical Analysis

Phytochemicals	Observation
Phenols	+
Saponins	-
Alkaloids	+
Steroids	+
Flavonoid	+
Cardiac glycoside	+
Terpenoids	+
Tannins	-

Key: + present, - absent

The present study **(Table 2)** showed a significant decrease ($p<0.05$) in glucose concentration especially in the animals treated at dose of 400 mg/kg. This may be attributed to the presence of phytoconstituents exerting the effect through either of these mechanisms. Similar results were obtained from previously reported study on the antidiabetic activity of the same plant on alloxan-induced diabetic mice and showed a significant antidiabetic effect [19]. It was also reported that the aqueous extract also showed a significant reduction in glucose level in alloxan induced diabetic rats [20, 21]. Bioactive compounds in medicinal plants can ameliorate oxidative stress and repair the impaired beta cells in diabetics [22]. The body's natural defense against lipid peroxidation is the enzymatic antioxidant defense system. During oxidative stress, the most prevalent byproduct of lipid peroxidation is malondialdehyde and the scavengers of superoxide ion and hydrogen peroxide are Catalase and sodium dismutase[23].

The result obtained (**Table 3)** showed that there was no significant ($P < 0.05$) difference in the level of sodium dismutase and catalase, while malondialdehyde level significantly decreases in animals treated with extract at 200 mg/kg body weight as compared to the control groups. These suggest that the treatment of induced diabetic rats with *Ficus sycomorus* methanol extract increased the activity of enzymatic antioxidants that serve to prevent the excessive formation of free radicals and consequently

reduced lipid peroxidation. The plant stem bark showed an excellent antioxidant potential as reported by Daniel and Dluya [24]. The root and stem bark were also reported to show a potent DPPH radical scavenging activity [25]. Similar results were also obtained in a previously reported *in vitro* study on the fruit and leaf extract of the plant where they exhibited strong radical scavenging activities [26, 27].

Induced diabetes with streptozocin or alloxan leads to dyslipidemia, which is characterized by increases in LDL, triglycerides, and cholesterol and a decrease in HDL. This could be due to a rise in the activity of hormone-sensitive lipase, which increases the risk of developing cardiovascular illnesses by catalyzing the release of fatty acids from triacylglycerols stored in adipocytes [28].

In the present study **(Table 4)**, there was no significant ($P < 0.05$) difference in triglycerides and cholesterol level in the animals treated with 200 mg/kg body weight, however, HDL and LDL level were significantly increased in respect to the control groups. These suggest that the hyperlipidemia, that is as a result of alloxan induction is suppressed by the methanol leaf extract of *Ficus sycomorus* and may reduce diabetic complications. Increased level of these biomarkers was observed in a previously reported study on Streptozotocin-induced diabetic rats treated with *Ficus racemosa* stem bark [29]. Similar trend was also reported on the study of antidiabetic and antihyperlipidemic effects of a methanolic extract of *Mimosa pudica* in diabetic rats [30]

Table 2: Antihyperglycemic Effects of *Ficus sycomorus* Extract on Diabetic Treated Rats

GROUP	Before induction	After Induction	DAY 7	Day 14
Normal Control	52.60 ± 1.93^a	53.40 ± 3.23^a	59.80 ± 4.76^a	51.60 ± 2.80^a
Positive Control	42.20 ± 8.20^a	265.60 ± 18.14^b	173.60 ± 8.02^c	66.60 ± 8.82^d
Extract (200 mg/kg)	55.00 ± 6.50^a	276.60 ± 32.10^b	222.80 ± 23.54^c	141.00 ± 4.32^d
Extract (400 mg/kg)	48.20 ± 5.72a	215.20 ± 7.71^b	99.80 ± 7.75^c	43.20 ± 7.17^a

Values (mg/dl) are given as mean ± SEM and the different letters in the same row indicate a statistical difference (P <0.05).

Table 3: Antioxidant Effects of *Ficus sycomorus* Extract on Diabetic Treated Rats

GROUP	Sodium dismutase (mg/dl)	Catalase (mg/dl)	Malondialdehyde (mg/dl)
Normal control	9.20 ± 3.08^a	7.80 ± 2.48^a	115.26 ±15.21^a
Positive control	8.03 ± 1.32^a	4.60 ± 0.71^b	113.86 ± 21.6^a
Extract (200 mg/kg)	8.33 ± 7.41^a	6.53 ± 0.81^a	72.03 ± 1.74^b
Extract (400 mg/kg)	8.96 ± 1.15^a	4.86 ± 1.30^b	123.0 ± 2.00^c

Values are presented as mean ± SEM and the different letters in the same column indicate a statistical difference (P <0.05).

Table 4: Effects of *Ficus sycomorus* Extract on Lipid Profile of Diabetic Treated Rats

GROUP	Triglycerides	Cholesterol	HDL	LDL
N Control	35.73 ± 5.87^a	20.40 ± 3.93^a	3.17 ± 0.93^a	10.27 ± 2.04^a
P. Control	27.66 ± 3.66^a	18.43 ± 1.92^a	2.73 ± 0.19a	10.16 ± 1.48^a
E. 200 mg/kg	25.70 ± 4.00^a	12.96 ± 2.51^a	17.03 ± 1.88^b	17.80 ± 1.46^b
E. 400 mg/kg	40.33 ± 3.52^b	46.13 ± 11.05^b	56.30 ± 7.11^c	35.67 ± 0.69^c

Values (mg/dl) are presented as mean ± SEM and the different letters in the same column indicate a statistical difference (P <0.05).; High density lipoprotein (HDL) and Low-density lipoproteins (LDL)

Table 5: Effects of *Ficus sycomorus* Extract on Liver Function of Diabetic Treated Rats

GROUP	ALT (mmol/L)	AST (mmol/L)	ALP (mmol/L)	TP (mmol/L)	ALB (mmol/L)
N. Control	19.00±5.13^b	56.33±13.92^b	15.93±2.92^a	12.80±1.71^a	3.40±0.31^a
P. Control	24.67±5.89^b	54.67±25.33^b	15.73±2.56^a	14.83±2.14^a	3.47±0.19^a
E.200mg/kg	11.33±2.33^a	24.67±_5.67^a	20.57±7.42^a	19.90±6.83^a	4.170±0.44^a
E.400mg/k	13.33±_1.67^a	49.67±_9.26^a	18.90±8.12^a	14.23±1.01^a	3.33±0.32^a

Values are presented as mean ± SEM and the different letters in the same column indicate a statistical difference (P<0.05).
ALT: Alanine transaminase, AST: Aspartate transaminase, ALP: Alkaline phosphatase, TP: Total protein and ALB: Albumen

ALT, AST and ALP are liver enzymes that help the liver cells to convert proteins into energy. The enzymes concentrations tend to increase in the bloodstream when there is liver damage [31]. The synthesis of albumin in the liver is reduced in the end-staged of hepatic disease, hence; serum albumin concentration is considered a marker of

synthetic function of the liver [32]. The data obtained in this study **(Table 5)** showed that ALT and AST levels were found to decrease significantly (P< 0.05) but there was no significant (P< 0.05) difference in ALP, TP and ALB in respect to the control groups. These reflect the improving effects of the plant extract on the liver. Previous study on experimental rats showed hepatoprotective activity of the plant extract on induced hepatocarcinogenesis [7].

CONCLUSION

The methanol leaf extract of *Ficus sycomorus* showed antidiabetic, antioxidant, antihyperlipidemic and hepatoprotective activities; hence, might be an effective alternative in the management of diabetes and its complications.

Authors' Declaration: The authors hereby declare that this article is original and that any liability for claims relating to the content of this article will be borne by them.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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