



GLUCOSE LEVEL, HAEMATOLOGICAL PARAMETERS AND LIPID PROFILE IN *FICUS SUR* TREATED DIABETIC RATS.

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This work was designed to study the effects of ethanol extract of *Ficus sur* leaves on glucose level, haematological parameters and lipid profile of Alloxan induced diabetic rats. Acute and sub-acute studies on blood glucose level revealed that 150 and 300 mg/kg of *Ficus sur* ethanolic leaf extract significantly ($P<0.05$) lowered blood glucose level in diabetic rats and compared favourably with effect of Glibenclamide (5mg/kg), a standard hypoglycaemic drug. The diabetic rats showed marked reduction in Packed cell volume, Haemoglobin content, Red blood cells count, Mean corpuscular haemoglobin, Mean corpuscular volume, Mean corpuscular haemoglobin concentration and platelets with increased White blood cells counts. These anomalies were all restored to about normal values after 21 days of treatment with *Ficus sur* leaf extract. The extract significantly ($P<0.05$) decreased the levels of triglycerides, low density lipoprotein cholesterol, very low density lipoprotein cholesterol and total cholesterol but increased the levels of high density lipoprotein cholesterol in diabetic rats. These results suggest that *Ficus sur* leaves contain potent hypoglycaemic and hypolipidemic agents capable of reversing hyperglycaemia and haematological abnormalities associated with the pathophysiology of diabetes mellitus.

KEY WORDS: *Ficus sur*, Haematological, Diabetes mellitus, Glucose, Hypolipidemic, Cholesterol.

INTRODUCTION

The increasing interest in herbal medicine is not surprising. This may be attributed to the upsurge in cases of drug resistance, cost and several side effects associated with most orthodox medicines. The use of plant materials as spices, condiments and for medicinal purposes has therefore become more popular and as such more wild plants are being exploited. There is therefore no doubt that orthodox medicine itself appears to be strongly anchored on traditional medicine (Nweze, 2009). The fact that the tropics into which majority of Africa lies is host to about 2/3 of the world's flora and fauna means that a lot of medicinal plants can be found here for both curative and management of diseases (Sofowora, 1993).

Diabetes Mellitus (DM) is a common disorder associated with increased morbidity and mortality and can be defined as a group of metabolic diseases characterized by chronic hyperglycemia due to defective

insulin secretion, insulin action, or both, resulting in impaired carbohydrate, lipid, and protein metabolism (Akah, et al., 2009). Pharmacological treatment of Diabetes mellitus is based on oral hypoglycaemic agents and insulin which have so many side effects. In diabetes, the causes and sites of intervention in biochemical process are divers and high serum total triglyceride level has been implicated. Differences in the lipid profile of diabetic and non-diabetic individuals are now apparent and lipid abnormalities are common in patients with diabetes mellitus (Akah, et al., 2009). The use of *Ficus sur* in the treatment of Diabetes mellitus is not common, however there is claim by traditional medicine users that the plants leaves have haemopoietic properties (Wisdom, et al., 2011).

Ficus sur commonly called wild fig is a medium sized tree of 6-9 meters high with large alternate and spirally arranged leaves with regularly serrated margins. The leaves have found relevance in traditional medicine in the treatment of diarrhea, anaemia, wounds, stomach problems, infertility, peptic ulcer and gonorrhoea. This study was designed to evaluate the effects of *Ficus sur* on blood glucose levels, haematological parameters and lipid profile of Alloxan induced diabetic rats.

MATERIALS AND METHODS

1. Collection and Preparation of Plant Materials

Fresh leaves of *Ficus sur* were collected from a farm settlement in Ozuitem, Bende Local Government Area of Abia State and were identified by Dr. M.C. Dike of the forestry Department, Michael Okpara University of Agriculture Umudike, Abia State, Nigeria. The leaves were air dried in the laboratory for 7 days after which they were ground to powder using an electric blender. Soxhlet extraction was done on 35g of the powdered materials for 48 hours using ethanol and maintained at a temperature of 70°C. At the end of the period, the extract was dried in a laboratory oven at 40°C to obtain dried extract weighing 10.8g which represented a yield of 30.9%.

1.1 Animals

Adult albino rats of both sex (120-160g) obtained from the Animal house of the University of Nigeria, Nsukka were used. They were fed with standard rat feed, with water ad libitum but starved for 12hr prior to the commencement of experiment. All animal experiments were conducted in compliance with NIH guidelines for care and use of laboratory animals, as expressed by Akah et al., (2009). The study was conducted partly at the Physiology Laboratory, Abia State University, Uturu, and partly at the Physiology Laboratory, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria.

1.2 Induction of Diabetes

Diabetes was induced in rats by a single intraperitoneal (I.P) injection of freshly prepared solution of Alloxan-monohydrate (160 mg/kg). Eight days later rats with blood glucose concentrations above 190 mg/dL were considered diabetic and 35 of such rats were used for the study.

1.3 Blood Glucose, Haematological and Lipid Profile Studies

28 Diabetic rats were divided randomly into 4 groups of 7 rats per group (groups 2 to 5), while 7 normal rats in Group 1 served as the normal control and received 0.2 ml normal saline. Group 2 served as the diabetic control (untreated). Group 3 received 5mg/kg Glibenclamide (a standard drug), while Groups 4 and 5 received 150 and 300 mg/kg respectively of ethanol leaf extract of *Ficus sur*. A total of 35 rats were used for the study. All treatments were done daily via the oral route using gavage and lasted for 21 days.

1.4 Acute and sub-acute effect of *Ficus sur* on Blood Glucose

This was done on the first day of treatment. Blood was obtained from the tail of each rat in all groups (1-5) prior to and at 2 and 5 hours following treatment and glucose levels determined using Glucose meter following standard procedures prescribed by the producer, Roche diagnostic company, Germany. For the sub-acute studies, the test was repeated on day 7, 14 and 21.

1.5 Haematological Studies

On day 22 the rats were sacrificed and blood was collected by cardiac puncture into EDTA bottles for determination of parameters including: Red blood cell (RBC), packed cell volume (PCV), Haemoglobin (Hb), white blood cell (WBC), white blood cell, differential counts, platelets, mean corpuscular haemoglobin (MCH) and mean corpuscular Haemoglobin concentration (MCHC). These parameters were obtained at once for each blood sample using an Automated Haematology Analyser (Mindray BC-2800).

1.6 Lipid Profile Studies

A portion of each blood sample was centrifuged to collect plasma which was used to estimate total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), very low density lipoprotein cholesterol (VLDL-C) and triglycerides (TG) using commercial kits obtained from Randox Laboratories, UK.

1.7 Statistical Analysis

Results were expressed as mean +SEM. Statistical analysis was performed by one-way analysis of variance (ANOVA), students t-test at 95% level of significance was used to establish differences between control and treated groups.

RESULTS

2.1 Acute Effect of *Ficus sur* on Blood Glucose

Ethanol extract of *Ficus sur* significantly ($P < 0.05$) decreased blood glucose level in treated diabetic rats. 150mg/kg decreased blood sugar from 234.8 + 30.4mg/dl in diabetic rats to 203.6 + 5.57 and 169.7 + 18.9 mg/dl while 300 mg/kg lowered same from 341.6 + 8.18 g/dl in diabetic rats to 197.4+ 6.95 and 152.2 + 7.50mg/dl after 2 and 5 hours respectively. The results compared favourably with that of glibenclamide, a standard drug (Table 1).

Table 1: Acute effect of *F. Sur* on blood glucose level

Group	Treatment	0 Hour	2 Hours	5 Hours
		Mean blood sugar ± SEM(mg/dl)	Mean blood sugar ± SEM (mg/dl)	Mean blood sugar ± SEM (mg/dl)
1	Normal control	110.4 ± 7.10	107.8± 4.52	101.4 ± 3.90
2	Diabetic control	311.8 ± 37.10	307.8 ± 34.3	311.6 ± 51.40
3	Glibenclamide(5mg/kg)	288.2 ± 37.50	206 ± 37.00	150.6 ± 10.50
4	<i>F.sur</i> (150mg/kg)	234.8 ± 30.40	203.6 ± 5.57	169.7 ± 18.90
5	<i>F. sur</i> (300 mg/kg)	341.6 ± 8.18	197.4 ± 6.95	152.2 ± 7.50

$P < 0.05$ versus control

2.2 Sub-acute Effect of *Ficus sur* on Blood Glucose

All doses of *Ficus sur* successfully returned the blood glucose level in diabetic treated rats to about normal values at the end of the 21 days of treatment during the period of sub-acute study with 150mg/kg lowering blood sugar level to 105.8 + 3.11mg/dl while 300mg/kg lowered same to 98.7 + 4.8mg/dl (Table 2).

Table 2: Sub-acute effect of *F.sur* on blood glucose level in diabetic rats

Group	Treatment	day 7	day 14	day 21
		Mean blood sugar±SEM(mg/dl)	Mean blood sugar± SEM (mg/dl)	Mean blood sugar± SEM (mg/dl)
1	Normal control	98.4 ± 4.69	102 ± 3.27	101 ± 4.21
2	Diabetic control	377.4 ± 56.30	323.2 ± 27.87	318 ± 2.92
3	Glibenclamide(5mg/kg)	104.4 ± 6.34	80.8 ± 5.21	83.3 ± 4.90
4	<i>F. sur</i> 150 (mg/kg)	124.8 ± 1.66	108.2 ± 2.27	105.8 ± 3.71
5	<i>F.sur</i> 300 (mg/kg)	120.0 ± 4.30	99.4 ± 4.20	98.7 ± 4.80

P<0.05 versus control

2.3 Effects of *Ficus sur* on Haematological Parameters

150 and 300mg/kg of *F.Sur* significantly raised RBC, PCV and Hb values in diabetic treated rats (Table 3). MCV, MCH and MCHC were not significantly affected. Diabetic rats had elevated WBC and lymphocytes counts. All doses of *F.sur* however significantly (P<0.05) lowered the elevated WBC count. Lymphocytes and basophils were not significantly affected (Table 4) 150 and 300mg/kg of the extract significantly (P<0.05) raised the lowered platelets counts in diabetic control group to 8.30 + 30.7 x 10⁹ and 694.3 + 160.9 x 10⁹ per liter respectively in treated rats (Table 4).

Table 3: Effect of *F. Sur* on RBC, PCV, Hb, MCV, MCH and MCHC in diabetic rats

Group	Treatment	RBC x 10 ¹² per liter	PCV %	Hb g/dL	MCV fL	MCH Pg	MCHC g/dL
1	Normal control	6.80±0.26	40.97±2.43	12.4 ± 0.53	60.23 ± 3.67	18.23 ± 0.29	30.5 ± 1.71
2	Diabetic control	4.77 ± 0.17	30.1 ± 1.18	10.03 ± 0.31	63.4 ± 3.96	21.03 ± 1.14	33.5 ± 2.20
3	Glibenclamide(5mg/kg)	5.10 ± 0.25	30.97 ± 1.61	10.30±0.26	60.73 ± 4.32	20.20 ± 0.18	33.26 ± 1.05
4	<i>F. sur</i> (150 mg/kg)	6.87 ± 0.55	39.9 ± 2.95	11.73 ± 0.81	11.73 ± 0.81	17.13 ± 4.56	29.8 ± 1.47
5	<i>F.sur</i> (300 mg/kg)	6.59 ± 0.28	42.27 ± 0.59	12.53 ± 0.35	12.53 ± 0.35	18.0 ± 0.59	28.03 ± 0.98

P<0.05 versus control

Table 4: Effects of *F. sur* on platelets counts, WBC and WBC Differential counts

Group	Treatment	Platelets $\times 10^9/L$	WBC $\times 10^9/L$	Lymphocytes %	Neutrophils %	Midcells (eosinophils, basophils and monocytes) %
1	Normal control	909 \pm 227.50	9.76 \pm 2.97	46.57 \pm 5.93	33.87 \pm 7.98	19.7 \pm 1.63
2	Diabetic C	611.80 \pm 102.80	29.63 \pm 2.29	51.31 \pm 0.57	27.43 \pm 2.06	21.57 \pm 2.03
3	Glibenclamide(mg/kg)	571.40 \pm 103.80	17.7 \pm 0.44	46.97 \pm 1.88	29.77 \pm 0.24	23.2 \pm 1.68
4	<i>F. sur</i> 150 mg/kg	830 \pm 30.70	11.52 \pm 2.75	43.7 \pm 7.30	37.77 \pm +8.10	18.53 \pm 1.39
5	<i>F. sur</i> 300mg/kg	694.30 \pm 160.90	10.53 \pm 1.29	49.5 \pm 6.98	28.0 \pm 4.37	22.5 \pm 2.68

P<0.05 versus control

2.4 Effect of *Ficus sur* on Lipid Profile of Diabetic Rats

All doses of *F. sur* significantly (P<0.05) decreased the elevated levels of TG, LDL-C, VLDL-C and increased HDL-C levels in the diabetic rats (Table 5). These parameters were significantly (P<0.05) different in the diabetic treated rats when compared to the diabetic control group.

Table 5: Effects of *F. Sur* on lipid profile in diabetic rats

Group	Treatment	Total cholesterol(mg/dL)	TGL (mg/dL)	HDL-C (mg/dL)	LDL-C (mg/dL)	VLDL-C (mg/dL)
1	Normal control	81.29 \pm 0.32	37.97 \pm 0.64	40.26 \pm 0.73	33.44 \pm 0.84	7.59 \pm 0.13
2	Diabetic Control	158.10 \pm 3.27	70.83 \pm 0.82	17.05 \pm 0.53	126.9 \pm 3.43	14,17 \pm 0.16
3	Glibenclamide (5mg/kg)	52.10 \pm 1.69	41.64 \pm 0.42	35.32 \pm 0.51	8.44 \pm 1.97	8.44 \pm 1.97
4	<i>F. sur</i> 150 mg/kg	71.23 \pm 0.33	28.26 \pm 0.50	43.95 \pm 1.37	21.63 \pm 1.36	5.65 \pm 0.10
5	<i>F. sur</i> 300(mg/kg)	59.33 \pm 0.32	32.82 \pm 0.94	22.29 \pm 0.97	30.48 \pm 0.94	6.56 \pm 0.19

P<0.05 versus control

DISCUSSION

This study was carried out to investigate the effects of *Ficus sur* ethanol leaf extract on blood glucose level, haematological parameters and lipid profile of diabetic rats. From results obtained, Alloxan monohydrate selectively destroyed the pancreatic beta cells of the rats used causing marked degeneration of the islets of langerhans which lowered insulin secretion with reduction in the rate of conversion of glucose to glycogen. The result of which is the marked increase of sugar level (hyperglycaemia) in the diabetic rats. The result agrees with already existing literature that Alloxan induces diabetes mellitus by selectively destroying the beta cells of the pancreas which are involved in the synthesis of, storage and release of insulin, the peptide hormone regulating carbohydrate, protein and lipid metabolism (Adeneye, 2008, Malaisse, 1982), leading to marked increase in blood glucose concentration observed in the rats after administration and confirms the development of diabetes mellitus (Akindele et al., 2012).

Results obtained from the acute and sub-acute studies show that all doses of *Ficus sur* leaf extract significantly ($P < 0.05$) lowered blood glucose levels within the 5 hours of acute study and 21 days of sub-acute study. The action of *Ficus sur* on blood glucose in diabetic rats is similar to that of Glibenclamide (5mg/kg), a potent hypoglycaemic agent, and suggested that *F. sur* leaf extract contain active principles with potent hypoglycaemic property. The extract may have achieved this hypoglycaemic property via increased insulin secretion, increased peripheral utilization of glucose, inhibition of endogenous, glucose production or by inhibition of intestinal glucose absorption as reported in existing literatures (Adeneye, et al., 2008; Eddouks., et al., 2003; Bakirel, et al., 2007). The extract may also have potentiated pancreatic secretion of insulin from existing residual Beta cells of islets of langerhans.

In the haematological studies, the diabetic control showed marked reduction in RBC, PCV, Hb, MCH, and MCHC, agreeing with existing literature that anaemia is a common pathophysiology associated with diabetes mellitus (Akindele, et al., 2012). Colak, (2012), also reported that diabetes mellitus causes the development of hypochromic anaemia due to a fall in the iron content of the body resulting from oxidative stress associated with the condition. *Ficus sur* however elevated these parameters including the platelets which suggest that the extract has anti-anaemic property which may be due to its high iron content (Saliu, et al., 2012) and the ability to improve bone marrow functions, a major site for erythropoiesis (Orhue, et al., 2008).

The diabetic control rats had elevated mean total cholesterol, triglycerides (TG), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) with decreased high density lipoprotein cholesterol (HDL-C) (Table 5). The results agreed with Akah, et al., (2009), who reported that high levels of triglycerides, LDL-C, VLDL-C have been associated with heart disease, insulin resistance and diabetes mellitus and that the rise in blood sugar was accompanied by marked increase in cholesterol, triglycerides, LDL-C, VLDL-C and reduction in HDL-C. All doses of *Ficus sur* and glibenclamide significantly ($P < 0.05$) reduced cholesterol, Triglycerides, LDL-C, VLDL-C and significantly increased the HDL-C level in the diabetic treated rats. Ethanol extract of *Ficus sur* therefore has shown hypolipidemic effect in diabetic rats.

In conclusion, results obtained from the studies reveal the hypoglycaemic and hypolipidemic property of *Ficus sur* and suggest that the extract is a safe and potent agent capable of bringing to normal, glucose, haematological and lipid abnormalities associated with diabetes mellitus and as such could be used in the management of the disease.

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