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Evaluation of The Antidiabetic Properties of The Aqueous And Methanol Extracts of *FICUS MUCUSO* (Wild Figs)

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***Abstract*— The vital nature of diabetes mellitus (DM) and the need for continuous search for a possible cure were the motivation for this research work. Wistar strain of albino rats weighing between 100-246g were used and diabetes mellitus was induced via the intraperitoneal injection of 55mg/kg body weight of streptozotocin. The rats were treated with 100mg/kg, 200mg/kg and 400mg/kg body weight of the aqueous and methanol leaf extracts of Ficus mucuso while 100mg/kg body weight of Metformin was used as reference drug. At the concentrations given, the extract significantly ($p<0.05$) reduced glucose concentration from 23.47±1.24 5.95±0.09 and 24.02±0.92 to 5.95±0.09 and 6.02±0.35mmol/L in the treated groups for aqueous and methanol extracts respectively. Liver function markers and lipid profile that were affected in the diabetic control group were improved in many of the treated groups. The extracts also caused marked improvement in the activities of superoxide dismutase (SOD) and reduced glutathione (GSH) and a reduction in malondialdehyde (MDA), creatinine and urea. The results obtained from this study indicates that the aqueous and methanol leaf extracts of F. mucuso have antidiabetic characteristics and can be harnessed in alternative medicine in the management of diabetes mellitus.**

***Index Terms*— Diabetes mellitus, Ficus mucuso, aqueous and methanol extract..**

I. INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder which manifest because of protracted high blood sugar levels. When this condition occurs, the affected body is usually not able to put the level of glucose in blood under control. It is better to describe diabetes mellitus not as a disease, but a syndrome or disorder with the special feature of a persistently increased blood glucose concentration usually above normal level, which over a long time causes glucose to be eliminated in urine. The uninterrupted increase in blood glucose level is caused by a direct or comparativelack of insulin (a hormone primarily made in the pancreas which responsible for the control glucose metabolism), deficiency of the body's cells toacknowledge and replyproperly to the action of insulin or as a result of a person's way of life. In this condition, glucose level rise progressively but glucose is not able to gain access into the body cells and they become deprived of energy. The body reacts to this development by putting extra effort to remove excess glucose from the blood and by using protein and fatobtained from muscles as substitute sources of energy. This has the attendant effect of disruption of the normal metabolic procedure in the body and gives rise to most of the symptoms and complications linked to diabetes mellitus (Walker and Rodgers, 2010).

The symbol of diabetes mellitus, is hyperglycaemia (high blood glucose), withpolydipsia(increased thirst), polyuria (frequent urination), polyphagia (increased hunger) and glucosuria (presence of high glucose levels in urine) as basic features and can degenerate to acute long-term complications ranging from chronic kidney failure, foot ulcers, diabetic ketoacidosisto coma and even death in the long run(William, 1985).The impact of diabetes mellitus is felt on all organs of the body and alters the general quality of life in ways that leads todurableimpairments (Nathan et al., 2005).The major impairments in body function in diabetes mellitus arise because of blood vessel damage (Sarwar et al., 2010), with impacts which could be deadly. Conditions such as age, genetics, gender and the type of diabetes are common risk factors and it can be made worse by the presence of underlying disease conditions ranging from obesity, high blood pressure, hypercholesterolemia, to inappropriate life style like lack of exercise, drinking and smoking (Diabetic Control and Complications Trial Research Group, 1995).Managing peoplewith diabetes mellitus is a difficult taskbecause of the challenges involved in attaining good and normal blood glucose level control. Monitoring the level of glucose is a component part of the routine daily care for the diabetic as this provides insighton how well the blood glucose level is being controlled.

*Ficus mucuso*is a rare tall plant that grows up to 30m in height. It is a member of the Moracae family of thegenus ficus comprising up to 150 different species of plants widely spread in various parts of the world. Its leaves are evergreen and rough with a chordate base having a ring of short stable brown hairs at each node and it grows favourably in secondary forests with its major habitat being the grassland. The fruits produced by this tree is called figs which are ovoid in shape and dark orange in appearance (Berg, 1990). The common names for *Ficus mucuso* includewild figs or forest sycamore fig (Djemgou *et al*, 2009).Locally it is called Odan-afomo, Obobo (Tolu, 2008) and Ogum in Epie language. The plant is believed to be an oxygen producing plant as its evergreen leaves permits photosynthesis.The plant is found in West Africa from Angola, Guinea, Ethiopia, Mozambique, Tanzania to Uganda and Nigeria and was named after an Angolan community called Mucuso where it was discovered for first time. Research work by Djemgou *et al*. (2009)

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reported the presence of terpenes, alkaloids and flavonoids as chemical constituents in *Ficusmucuso*. A number of species in the genus ficus have been reported to possessvital pharmacological characteristicslike; antimicrobial, anti-cancer, anti-anaemic and anti-diabetic.
Although the fruits from this plant serves as a major source of food for birds and chimpanzees, the leaves of this plant are locally known as a blood buster and it is boiled and the extract given for this purpose.

II. MATERIALS AND METHODS

This study received ethical approval from the University of Port-Harcourt Research Management and Development Ethics Committee. A total of 63 wistar strain of albino rats were used. Diabetes mellitus was induced via the intraperitoneal injection of 55mg/kg body weight of streptozotocin (STZ) liquified in citrate buffer at pH 4.5. The rats were treated with 100, 200 and 400mg/kg body weight the extracts, while 100mg/kg body weight of metformin was used as a reference treatment. The parameters evaluated were glucose concentration, triglycerides (TG), cholesterol, HDL cholesterol, oxidative stress markers, urea and creatinine. The standard Randox enzymatic method(Randox kits, Randox laboratories Limited, United Kingdom) was used in the estimation of glucose concentration, TG and cholesterol. Urea was estimated using the modified Bertholot's method, while creatine was measured using the Direct End-Point Method.

III. RESULTS AND DISCUSSION

The results of this study are presented in the tables below;

Table 1: Effect of the treatments on plasma glucose concentrations (mmol/L) of streptozotocin-induced diabetic rats

Day	Normal control	Diabetic control	Metformin	DTR on 100mg/kg AE of *F. mucuso*	DRT on 200mg/kg AE of *F. mucuso*	DRT on 400mg/kg AE of *F. mucuso*	DRT on 100mg/kg ME of *F. mucuso*	DRT on 200mg/kg ME of *F. mucuso*	DRT on 400mg/kg ME of *F. mucuso*
0	4.62±0.91 [a]	5.22±0.25 [a]	4.90±0.26 [a]	4.80±0.42 [a]	4.97±0.13 [a]	4.55±0.30 [a]	5.37±0.36 [a]	4.77±0.17 [a]	4.12±0.23 [a]
3	487±0.66 [b]	18.20±2.27 [b]	15.20±2.44	14.12±2.61 [b]	19.37±0.89 [b]	23.47±1.24 [b]	18.17±2.32 [b]	22.70±2.50 [b]	24.02±0.92 [b]
21	4.90±0.21 [c]	22.45±1.04 [c]	5.57±0.11 [c]	6.75±0.72 [c]	5.97±0.23 [c]	5.97±0.09 [c]	6.40±0.03 [c]	6.80±1.03 [c]	6.02±0.35 [c]

Values in the table are Mean ± S.D, n = 5 animals per group.
Values with different superscript letters on the same column differ significantly at $p<0.05$.

Table 2: Effect of treatment with the extracts on the plasma lipid profiles of streptozotocin-induced diabetic rats

Groups	Parameters				
	Total cholesterol (mmol/L)	**Triglycerides (mmol/L)**	**High density lipoprotein cholesterol (mmol/L)**	**Low density lipoprotein cholesterol (mmol/L)**	**Very low density lipoprotein cholesterol (mmol/L)**
Normal control	4.40±0.37[a]	1.40±0.18 [a]	1.01+0.12 [a]	2.40±0.29 [a]	0.98±0.49 [a]
Diabetic control	6.50±0.40[b]	2.01±0.62 [b]	0.91±0.14 [b]	3.60±0.44	1.76±0.08 [b]
Metformin	4.25±0.64[c]	1.13±0.29 [c]	1.08±007 [c]	1.41±0.44 [c]	1.67±0.38 [c]
DTR on 100mg/kg AE of *F. mucuso*	4.37±0.61[c]	1.16±0.47 [d]	1.03±0.11 [d]	2.11±0.39 [d]	1.21±0.91 [d]
DTR on 200mg/kg AE of *F. mucuso*	4.55±0.66[d]	0.90+0 20 [e]	1.07±0.04 [e]	1.38±0.61 [e]	1.87±0.96 [e]
DTR on 400mg/kg AE of *F. mucuso*	3.05±0.45[e]	1.10±00.18 [f]	1.00±0.08 [f]	1.52±0.69 [f]	0.84±0.50 [f]
DTR on 100mg/kg ME of *F. mucuso*	4.35±0.58[f]	1.12±0.23 [g]	1.12±0.04 [g]	2.08±0.77 [g]	1.66±1.00 [g]
DTR on 200mg/kg ME of *F. mucuso*	4.50±0.16[f]	1.21±0.49 [h]	1.06±0.08 [h]	1.36±0.22 [h]	2.20±0.25 [h]
DTR on 400mg/kg ME of *F. mucuso*	3.75±.91[g]	1.11±037 [i]	1.05±0.08 [i]	2.04±0.53 [i]	0.65±0.51 [i]

Values in the table are Mean ± S.D, n = 5 animals per group.
Values with different superscript letters on the same column differ significantly at p<0.05.

Table 3: Effect of treatment with the extracts on plasma oxidative stress markers and enzymes in streptozotocin-induced diabetic rats

Groups		
	Reduced glutathione (µg/mL)	**Glutathione peroxidase (U/mL)**
Normal control	0.95±0.10 [a]	0.06±0.00 [a]
Diabetic control	0.52±0.04 [b]	0.05±0.00 [b]
Metformin	1.36±0.03 [c]	0.06±0.00 [c]
DTR on 100mg/kg AE of *F. mucuso*	0.74±0.15 [d]	0.03±0.00 [d]
DTR on 200mg/kg AE of *F. mucuso*	1.23±0.30 [e]	0.05±0.00 [e]
DTR on 400mg/kg AE of *F. mucuso*	1.27±0.53 [f]	0.07±0.00 [f]
DTR on 100mg/kg ME of *F. mucuso*	0.85±0.33 [g]	0.03±0.00 [g]
DTR on 200mg/kg ME of *F. mucuso*	0.98±0.35 [h]	0.58±0.00 [h]
DTR on 400mg/kg ME of *F. mucuso*	1.01±0.17 [i]	0.05±0.00 [i]

Values in the table are mean ± S.D, n = 5 animals per group.
Values with different superscript letters on the same column differ significantly at p<0.05.

Table 4: Effect of treatment with the extracts on plasma electrolytes, urea and creatinine concentrations of streptozotocin-induced diabetic rats

Groups	Parameters						
	Potassium ion (mmol/L)	**Calcium ion (mmol/L)**	**Sodium ion (mmol/L)**	**Chloride ion (mmol/L)**	**Bicarbonate ion (mmol/L)**	**Urea (mmol/L)**	**Creatnine (mmol/L)**
Normal control	3.82±0.97[a]	2.39±0.02[a]	139.50±43.37[a]	139.50+43.37[a]	26.00±1.63[a]	4.67±0.17[a]	71.75±6.34[a]
Diabetic control	5.57±0.54[b]	2.41±0.02[b]	116.75±10.27[b]	116.75+10.27[b]	21.50±1.29[b]	8.70±0.21[b]	146.00±13.06[b]
Metformin	3.85±0.42[c]	2.37±0.08[b]	135.50±7.76[c]	135.50±7.76[c]	26.50±3.41[c]	4.5±0.35[c]	107.50±2.08[c]
DTR on 100mg/kg AE of *F. mucuso*	4.65±0.12[d]	2.38±0.00[b]	139.00±22.73[d]	139.00±22.73[d]	26.50±1.91[c]	4.85±0.20[c]	114.75±2.06[d]
DTR on 200mg/kg AE of *F. mucuso*	4.15±0.12[d]	2.36±0.01[c]	132.50±4.50e	132.50±4.50[e]	28.25±1.70[d]	4.86±0.14[c]	109.50±4.20[e]
DTR on 400mg/kg AE of *F. mucuso*	3.95±0.12[e]	2.38±0.00[d]	139.75±7.50[f]	139.75±7.50[f]	28.75±1.89[e]	4.32±0.26[d]	111.50±7.72[e]
DTR on 100mg/kg ME of *F. mucuso*	5.30±0.16[f]	2.33±0.05[e]	136.25±3.68[h]	136.25+3.68[g]	27.25±2.50[f]	4.75±0.28[e]	112.25±3.30[f]
DTR on 200mg/kg ME of *F. mucuso*	4.32±0.36[g]	2.37±0.04[f]	140.75±29.84[g]	140.75±29.54[h]	28.00±1.63[g]	4.60±1.88[f]	119.00±3.30[g]
DTR on 400mg/kg ME of *F. mucuso*	4.12±0.30[g]	2.41±0.02[g]	136.25±1.25[i]	136.25±1.25[i]	28.00±1.63[i]	4.77±0.29[f]	113.00±4.08[g]

Values in the table are Mean ± S.D, n = 5 animals per group.
Values with different superscript letters on the same column differ significantly at $p<0.05$.

The challenges and disturbances that the diabetes mellitus condition presents makes it mandatory for both the affected and non-affected individuals to be alarmed, and the truth that a permanent cure is yet to be arrived at has imposed on researchers all over the world the need to continuously develop methods of care for the condition which can manage the accompanying complications. From the results of this study, glucose concentration that was markedly raised following the induction of diabetes mellituswas significantly reduced in all the groups on treatment with the extracts. This reduction in glucose concentration shows normal glucose response and can be associated with the presence of the phytochemicals present in the plant, which must have acted in concert to advance the secretion and release of insulin, the ability of the cells to recognize and respond to the action of insulin in taking cells up glucose and inhibition of enzymes, all climaxing to the reduction of glucose concentration in the treated groups.

Dyslipidaemia induced by the diabetic state as seen in the significant reduction in HDL cholesterol and increase in, LDL, VLDL and TG in the diabetic control group clearly depicteda possible development of cardiovascular complexities. This agrees with the works of Danielle et al. (2012), Hao et al. (2015), and Nandini et al. (2019) where the induction of experimental diabetes caused diverse levels of alterations in lipid profile. The raised level of TG can be associated to the increased action of hormone-sensitive lipase; the major enzyme that stimulates the breakdown of fatty acids originally stored as TG in the adipose tissue which give rise to the reassembling of more of the fatty acids returning to the liver to form TG and very low-density lipoprotein (VLDL) (Cullen et al., 1999). Treatment with the extracts showed a positive impact on lipid profile as depicted in the significant increase in HLD and reduction in total cholesterol, LDL, VLDL and TG. The analysis of reduced glutathione (GSH), glutathione peroxidase (GPX), catalase (CAT), superoxide dismutase (SOD) and malondialdehyde (MDA) showed clear indication that the diabetic animals were exposed to oxidative stress following the induction of diabetes leading to lipid peroxidation likely mediated by free radicals. Marked improvement in the antioxidant status was seen as there was significant ($P< 0.05$) rise in the activities of SOD and GSH; two relevant antioxidants that primarily functions to track down and free the system of free radicals and prevent elements in the cells from oxidation (Raphael,

1976). The activities of CAT and GPX were also markedlyenhance. The extracts reduced the concentration of MDA; a highly harmful by-product released by free radicals.The concentration of urea and creatinine were also reduced, indicating a possible positive impact on the kidney.

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