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ANTIDIABETIC AND HYPOLIPIDEMIC EFFECTS OF *LAPORTEA OVALIFOLIA* (URTICACEAE) IN ALLOXAN INDUCED DIABETIC RATS.

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Abstract

*Laportea ovalifolia (*Scham and Thonn*)* is widly use in Cameroon for the treatment of diabetes mellitus. The present study was designed to evaluate the antidiabetic and hypolipidaemic effects of aqueous extract of *Laportea ovalifolia* aerial part in normal and alloxan diabetic rats. Diabetes was induced by intraperitoneal injection of alloxan (150 mg kg $^{-1}$ body weight). The treatment was given for 2 weeks. After the treatment a significant reduction was observed in fasting serum glucose levels in the treated diabetics rats. *L. ovalifolia* treatment showed considerable lowering of serum total cholesterol, triglycerides, LDL cholesterol, T.C/HDL.C and an increase in HDL cholesterol in the treated diabetic group. These results suggest that the *Laportea ovalifolia* aqueous extract of the aerial part possesses antidiabetic and hypolipideamic effects in alloxan-induced diabetic rats.

Keywords: *Laportea ovalifolia*, Alloxan, antidiabetic , hypolipidemic

Introduction

Diabetes is a disorder of carbohydrate, fat and protein attributed to a diminished production of insulin or mounting resistance to its action. Chronic hyperglycaemia during diabetes causes glycation of body proteins that in turn leads to secondary complications affecting eyes, kidneys, nerves and arteries (Kameswara, 1999). Along with hyperglycaemia and abnormalities in serum lipids (Virella and Virella, 2003; NCEP, 2002) diabetes is associated with microvascular and macravascular complications which are the majors causes of morbidity and death in diabetic subjects (Nagappa et al., 2003). It can be managed by exercise, diet and pharmaceutical drugs, which are either too expensive or have undesirable sides effects or contraindications (Serrano, 1990). The search for more effective and safer hypoglycemic agents therefore has continued to be an area of research of interest (Krishna et al., 2004; Pepato et al.,

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2003). The World Health Organisation has recommended and encouraged the use of alternative therapy especially in countries where access to the conventional treatment of diabetes is not adequate (WHO, 1980).

Laportea ovalifolia (*L. ovalifolia*) belongs to the family of Urticaceae. It is a tropical plant commonly found in swampy areas in Cameroon and other parts of the world in both dry and rainy seasons (Letouzey, 1968). Some people in Cameroon use the leaves as vegetable, which serves as a major component of their diet. The leaves of *Laportea ovalifolia* are used in traditional medicine for the remedy of bacterial infections, headaches, urinary infections, pneumonia, dysentery and epilepsy (Adjanohoun et al., 1996; Letouzey, 1968). Locally, the decoction of the aerial part is used as a cure for diabetes (personal information from users), and this has not previously been reported.

The present communication is to show the effect of aqueous extract of *Laportea ovalifolia* on alloxan-induced diabetic rats.

Materials and Methods

Collection of plant materials

The aerial part (leaves and stem) of *Laportea ovalifolia* were collected in October and November 2002, in Yaounde, Cameroon and identified at the National Herbarium, Yaounde Cameroon, where a voucher sample had been deposited under the number 50623/HNC.

Preparation of extract

The plant material was air-dried for 30 days at room temperature and ground into a powder. The plant powder (500g) was decocted in 4L of distilled water for 15min. This was repeated four times, until the resulting extract gave no further colouration. The extract was then filtered and evaporated to dryness in an oven at 40°C, to obtain 84g of crude residue (yield: 16.8%).

Experimental induction of diabetes in rats

Three month old male Wistar Albino rats weighing 180-240g were obtained from the animal house of the laboratory of Biochemistry, Department of Biochemistry, University of Yaounde I, Cameroon. All animals were kept in an environmentally controlled room with a 12h light/12h dark cycle .The animals had free access to water and standard rat diet. The study was approved by institutional animal ethical committee. The rats were injected alloxan monohydrate dissolved in sterile normal saline at a dose of 150 mg/kg body weight, intraperitoneally. Since alloxan is capable of producing fatal hypoglycaemia as a result of massive pancreatic insulin release, rats were treated with 20 % glucose solution intraperitoneally after 6h. The rats were then kept for the next 24h on 5 % glucose solution bottles in their cages to prevent hypoglycaemia (Dhandapani et al., 2002). After a fortnight, rats with marked hyperglycaemia were selected and used for the study.

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Experimental design

In the experiment a total of 25 rats (15 diabetic surviving rats, 10 normal rats) were used. Diabetes was induced in rats 2 weeks before starting the treatment. The rats were divided into five groups as follows after the induction of alloxan diabetes and each group comprised of 5 rats. Group I (untreated normal rats), Group II (treated normals rats given 200 mg/kg (dose which produces high hypoglycaemic activity in acute treatment after 5h) in distilled water daily using an intragastric gavage tube for 2 weeks), Group III (untreated diabetic rats), Group IV (treated diabetic given aqueous extract of *L.ovalifolia* at dose of 200 mg/kg daily using an intragastric gavage), Group V (Diabetic rats given Tolbutamide orally at 80mg/kg in distilled water daily for 2 weeks).

The animals were carefully monitored every day and weighed every week (2 weeks). No sign of toxicity was noticed on the behaviour and general health of the animals when exposed to extract. Animals described as fasted were deprived of food for at least 12 h but allowed free access to drinking water. Blood samples were drawn at weekly intervals till the end of study. Fasting blood glucose estimation, body weight, food and water intake measurement were done on day 0, 7 and 14 of the study.
On day 14, rats were sacrificed by cervical dislocation under ether anaesthesia. Blood was collected from overnight fasted rats and processed for the estimation of serum glucose and serum lipids profile.

Determination of Serum glucose

Fasting serum glucose was estimated by the oxidase method (Trinder, 1969). Determination of serum total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and total cholesterol/HDL cholesterol (T.C/HDL C.). Serum was separated and analysed for serum total cholesterol (Roeschlau et al.,1974), triglycerides (Buccolo et al., David, 1973), HDL cholesterol (Allain et al., 1974) and serum LDL (Friedewald et al., 1972).

Statistical analysis.

Data was expressed as means ± S.E.M. Statistical analysis was made by one-way ANOVA and post hoc Dunnet test, with $P < 0.05$ considered as significantly different.

Results.

Changes in body weight in untreated and treated rats are shown in Table 1. Significant ($P < 0.001$) weight loss was observed in untreated diabetic rats than untreated normal rats. Treatment with aqueous extract of *L. ovalifolia* or Tolbutamide improved the weight gain compared to untreated diabetic rats. Alteration in blood glucose on treatment of diabetic rats with *Laportea ovalifolia* and tolbutamide is given in Table 2. The blood glucose was increased significantly in untreated alloxan-diabetic rats as compared to untreated normal rats ($P < 0.001$). Administration of *L. ovalifolia* or

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Tolbutamide led to significant decrease in blood glucose levels in diabetics treated groups ($P < 0.001$), while no decrease in blood glucose levels was observed

Table 1: Effect of treatment with aqueous extract of *L ovalifolia* aerial part (200mg/kg. body weight) for 2 weeks on body weight.

Group of rats	Average body weight (g)		
	Day 0	Day 7	Day 14
I Untreated normal	192.80± 4.92	205.81 ±6.33	221.22± 5.92
II Treated normal	180.63 ±3.46	189.00± 4.13	208.02 ±5.81
III Untreated diabetic	206.40± 3.80	195.00 ±3.50	176.83± 2.22 #
IV Treated diabetic	217.20 ±2.70	222.40 ±3.70 *	231.61± 2.74 ***
V Diabetic+Tolbutamide	192.00 ±2.55	207.01± 5.19	222.80 ±6.61 ***

Values are expressed as mean ± S.E.M; (n=5).
# P<0.05 compared with untreated normal rats.
*P<0.05; *** P<0.001 compared with untreated diabetic rats.

Table 2: Effect of treatment with aqueous extract of *L ovalifolia* aerial part (200mg/kg. body weight) for 2 weeks on serum glucose concentration in normal and diabetic rats.

Group of rats	Average serum glucose (mg dl^{-1})		
	Day 0	Day 7	Day 14
I Untreated normal	83.20 ±3.99	89.44 ±5.68	88.85 ±2.35
II Treated normal	77.00±4.78	80.24±4.25	82.00±3.49
III Untreated diabetic	329.41 ±12.77#	340.11 ±6.78#	346.11 ±10.77#
IV Treated diabetic	333.81± 5.05	208.61 ±9.87***	124.26± 4.55***
V Diabetic+Tolbutamide	298.00 ±18.01	165.60 ±5.73***	76.46 ±4.41***

Values are expressed as mean ± S.E.M; (n=5).
# P<0.001 compared with untreated normal rats.
*** P<0.001 compared with untreated diabetic rats.

Table 3: Effect of treatment with aqueous extract of *L ovalifolia* aerial part (200mg/kg. body weight) for 2 weeks on food intake (g rat^{-1} day^{-1}).

Group of rats	Average food intake (g rat^{-1} day^{-1})		
	Day 0	Day 7	Day 14
I Untreated normal	13.51± 0.69	15.11±11	15.62± 1.41
II Treated normal	12.00 ±0.64	12.30 ±0.92	13.00± 1.02
III Untreated diabetic	25.03 ±1.41#	28.20 ±0.66 #	32.61 ±1.61#
IV Treated diabetic	27.00 ±1.04	31.40 ±1.16	25.60± 0.81 *
V Diabetic+Tolbutamide	26.61± 1.20	23.40± 1.12	19.20 ±0.84 *

Values are expressed as mean ± S.E.M; (n=5).
# P<0.05 compared with untreated normal rats.
*P<0.05 compared with untreated diabetic rats.

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in normal treated group.

The food and water intake (Tables 3 and 4) ($P < 0.05$) increased significantly in untreated diabetic rats compared to untreated normal rats. Significant reduction ($P < 0.05$) of food intake and water intake were noticed after the treatment with of *L. ovalifolia* and Tolbutamide. No effect of the extract was noticed in normal rats. Serum total cholesterol, triglycerides, LDL cholesterol and (T. C/HDL. C) were significantly elevated in untreated diabetic rats as compared to untreated normal rats ($P < 0.001$). All lipids parameters tested were improved after the treatment with aqueous extract of *L. ovalifolia* and Tolbutamide. No effect was observed in treated normal rats.

Discussion

Alloxan induces diabetes by damaging the insulin secreting cells of the pancreas leading to hyperglycaemia (Szuldelski, 2001). An observation in this study correlates with the previous research finding, in that the blood glucose levels significantly increased in alloxan untreated diabetic rats. In the present study, the continuous treatment with aqueous extract of *L. ovalifolia* for a period of 2 weeks caused a significant decrease in the blood glucose levels of treated diabetic rats but no effect was observed in normal treated rats. These results have confirmed the earlier results of our preliminary studies (not published). The possible mechanism by which aqueous extract of *L. ovalifolia* brings about its hypoglycaemic action may be, by potentiating the insulin effect, either by increasing the pancreatic secretion of insulin from the cells of islets of Langerhan's or its release from bound insulin (Pari, 2004). We have noticed a significant reduction in food and water intake and increased in the body weight in alloxan diabetic rats. This could be the result of improved glycaemic control produced by aqueous extract of *L. ovalifolia.*

Table 4: Effect of treatment with aqueous extract of *L ovalifolia* arial part (200mg/kg. body weight) for 2 weeks on water intake (ml rat $^{-1}$ day^{-1}).

Group of rats	Average water intake (ml rat $^{-1}$ day^{-1})		
	Day 0	Day 7	Day 14
I Untreated normal	18.62± 0.81	19.40± 1.09	16.42 ±0.91
II Treated normal	16.50 ±0.77	15.05± 0.98	16.08± 0.91
III Untreated diabetic	79.00± 3.19 #	88.62± 4.46 #	79.85 ±5.56 #
IV Treated diabetic	88.20 ±4.02	79.03± 8.42	49.06± 2.14 *
V Diabetic+Tolbutamide	82.22± 4.91	53.21 ±2.59 **	35.61±5.94 ***

Values are expressed as mean ± S.E.M; (n=5).
# $P<0.001$ compared with untreated normal rats.
*$P<0.05$; ** $P<0.01$; *** $P<0.001$ compared with untreated diabetic rats

We have noticed elevated serum lipids in alloxan-diabetic rats. Lipids play an important role in the pathogenesis of diabetes mellitus. The level of serum lipids is usually raised in diabetes and such an elevation represents a risk factor for coronary heart disease (Mironava et al., 2000). Lowering of serum lipids levels through dietary

Table 5: Effect of treatment with aqueous extract of *L ovalifolia* arial part (200mg/kg. body weight) for 2 weeks on serum total cholesterol, triglycerides, HDL cholesterol, LDL cholesterol and T.C/HDL.C (mg dl^{-1}).

Group of rats	Average serum lipids profil (mg dl^{-1})				
	Total cholesterol	Triglycerides	HDL cholesterol	LDL cholesterol	T.C/HDL.C
I Untreated normals	75.20 ±6.81	93.00 ±6.05	32.60± 3.72	24.00 ±3.00	2.35 ±0.25
II Treated normals	73.51± 3.13	112.00±4.20	28.80 ±5	21.80± 4.71	2.58 ±0.27
III Untreated diabetes	130.00 ±4.63 #	154.60 ±5.91#	22.80 ±1.71	74.40± 2.67#	5.69± 0.31#
IV Treated diabetes	100.60 ±3.37 *	93.00 ±2.70 **	33.01 ±1.22 *	55.48± 3.70 *	3.14± 0.11 *
V Diabetes +Tolbutamide	77.20 ±4.80 ***	66.41 ±3.53 ***	45.00 ±2.08***	19.52 ±2.80 ***	1.68 ±0.10 ***

Values are expressed as mean ± S.E.M; (n=5).

# P<0.001 compared with untreated normal rats.

*P<0.05; ** P<0.01; *** P<0.001 compared with untreated diabetic rats.

T.C/HDL.C (Total cholesterol/HDL cholesterol)

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or drugs therapy seems to be associated with a decrease in the risk of vascular disease (Scoot and Grundy, 1999). The abnormal high concentration of serum lipids in diabetes is mainly due to the increase in the mobilisation of fatty acids from the peripheral depots, since insulin inhibits the hormone sensitive lipase. On the other hand, glucagon, catecholamines and other hormones enhance lipolysis. The marked hyperlipidaemia that characterizes the diabetic state may therefore be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots (AL-Shamaony et al.,1994).

In our study, we have also observed an increase in the concentration of total cholesterol, triglycerides, LDL cholesterol and T.C/HDL.C in alloxan untreated diabetic rats. Hyperlipidaemia is a recognized consequence of diabetes mellitus (Pushparaj et al., 2000; Pepato et al., 2003; Sharma et al., 2003). Administration of aqueous extract of *L. ovalifolia* normalized serum lipids, secondary to the diabetic state. Diabetes-induced hyperlipidaemia is attributable to excess mobilization of fat from the adipose due to the under utilization of glucose (Krishnakumar et al., 2000). The ability of aqueous extract of *L. ovalifolia* to reduce the levels of plasma lipids in diabetic rats has never been studied before. The regression of the diabetic state due to aqueous extract of *L. ovalifolia* administration increased the utilization of glucose, thereby depressing the mobilization of fat.

Our findings indicate that an aqueous extract of *L. ovalifolia* can lower the blood glucose and serum lipids in alloxan diabetics rats. This is of interest, since elevated concentrations of both are risk factors in the development of arteriosclerosis in diabetes mellitus.

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