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Antihyperglycaemic Effect of Methanol Leaf Extract of Alchornea laxiflora (Benth) Pax and Hoffman in Diabetic Rats

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Abstract
The administration of the methanol leaf extract of *Alchornea laxiflora* (Benth) Pax and Hoffman regulates blood sugar levels in alloxan-induced diabetic rats. *A. laxiflora* therapy also caused significant reductions in hitherto raised levels of plasma cholesterol, urea and creatinine and reversed the decreases in concentration of plasma total protein and albumin following alloxan injection ($p<0.05$). The significant increases in activity ($p<0.05$) elicited in plasma liver enzymes studied: aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase, in the diabetic rats were gradually restored to normal values ($p<0.05$). No significant changes ($p>0.05$) were observed in the normal rats administered with the extract. Thus *A. laxiflora* is an antihyperglycaemic agent and not hypoglycaemic and appears to correct the metabolic derangements indicative of diabetes mellitus.
Keywords: *Alchornea laxiflora* (Benth) Pax and Hoffman, antihyperglycaemic, diabetic rats, methanol, leaf, extract.

1. INTRODUCTION

The use of medicinal plants as antidiabetic agents is common place in developing countries. In view of this, the WHO expert committee on diabetes mellitus (WHO, 1980) recommended that it is important to investigate the effect of agents of plant origin used in traditional medicine.

Diabetes mellitus refers to the group of diseases that leads to high blood glucose levels due to defects in either insulin secretion or insulin action (Rother, 2007). Most cases of diabetes mellitus fall into one of two broad categories: type 1 and type 2. The principal treatment of type 1 diabetes even in its earliest stages is the delivery of artificial insulin via injection. Type 2 diabetes is usually first treated by increasing physical activity, decreasing carbohydrate intake and losing weight, and in later stages, if necessary, treatment with oral medication to improve insulin production (e.g. sulphonylureas), to regulate inappropriate release of glucose by the liver and attenuate insulin resistance to some extent (e.g. metformin) and to substantially attenuate insulin resistance e.g. thiazolidinediones) (UK Prospective Diabetes Study Group, 1998). Long term complications include retinal damage, nerve damage, microvascular disease, cardiovascular disease, liver damage, renal failure etc if the disease is not adequately controlled.

Diabetes epidemic is spreading in the developing world and the number of people with diabetes will increase by 150% by 2030 with an increasing proportion of affected people in younger age groups (WHO, 2003; Ingrid and Matthias, 2006). In spite of the variety of drugs used for diabetic treatment, a perfect glycemic control is rarely achieved, thus making it imperative for new alternatives to be investigated.

Alchornea laxiflora (Benth) Pax and Hoffman (Family: Euphorbiaceae), commonly called “pepe” in Southwest Nigeria, is a tree which grows to about 6 m. It is also found in the Cameroon and it is widespread in the Central and Southern tropical Africa. The leaves play important role in the preservation of kolanuts widely eaten in Nigeria. The stems and branches are also used in Nigeria as chewing stick. Deconctions of the leaves are used in the treatment and management of inflammatory and infectious diseases (Adewole, 1993; Ogundipe *et al*., 2001). The methanolic extract of *Alchornea laxiflora* (the leaves and root) possess antioxidant activities (Farombi *et al*., 2003).

This study reports the effects of the methanolic leaf extract of *Alchornea laxiflora* (Benth) Pax and Hoffman on biochemical indices such as glycaemic control, lipid profile, liver and renal dysfunction markers in alloxan-induced diabetic rats.

2. MATERIALS AND METHODS

2.1 Chemicals/Reagents

Alloxan monohydrate was purchased from Sigma Chemical Company, MO, USA.
Assay kits for biochemical analysis were purchased from Randox Laboratory Ltd, UK.
All other reagents were of analytical grade.

2.2 Animals

24 albino rats of wistar strain (males and females) weighing between 150 – 250 g bred in the animal house of Pharmacology Department, University of Benin, Benin City were used. Animals were housed in clean metal cages at a temperature of 25 ± 2 ^{0}C with 12 hours light/dark cycles. They were acclimatized for one week and

received a pellet diet (Bendel Feed Mill, Ewu, Edo State, Nigeria) and water *ad libitum*.

Animals were handled in accordance with internationally accepted principles for laboratory animal use and care (NIH Publication 85 – 193, revised 1985).

2.3 Induction of Diabetes

Animals received a freshly prepared solution of 100 mg of alloxan monohydrate (dissolved in distilled water) per kg body weight, intraperitonially for two consecutive days. Two days was allowed for stabilization of the injected alloxan, and rats showing mild diabetes with hyperglycaemia (blood glucose concentrations of 140 – 150 mg/dl) were used for the experiment. Rats were initially fasted overnight (14 h) and blood drained from tail vein of conscious rats for base line values of fasting blood glucose (FBG) and other biochemical parameters. Thereafter, rats were fasted on alternate days.

2.4 Experimental Design

The rats were randomly divided into 4 groups with 6 animals each. 500 mg/kg body weight of *Alchornea laxiflora* (Benth) Pax and Hoffman methanol leaf extract was administered to Groups 2 and 4 rats orally by gavage twice daily.

Group 1: Normal rats received water (Normal control).
Group 2: Normal rats received *A. laxiflora* (500 mg/kg body weight) in solution.
Group 3: Diabetic rats received water (Diabetic control).
Group 4: Diabetic rats received *A. laxiflora* (500 mg/kg body weight) in solution.

2.5 Plant Material and Extraction

Alchornea laxiflora plant was collected from a cocoa plantation at Alade, Idanre town, Ondo State, Nigeria. The plant was identified and authenticated at the Plant Biology and Biotechnology Department Herbarium, University of Benin, Benin City, Nigeria. The leaves were subsequently sun-dried for a week, after which they were blended into powder.

100 g of the powdered sample was soaked in 500 ml of methanol for 60 h. The resultant mixture was sieved and the filtrate concentrated by evaporation in a water bath (Gallenkamp, UK) at 80 ^{0}C giving a semi-solid extract. 20 g of the extract was reconstituted to 100 ml with distilled water and refrigerated at 4 ^{0}C until required.

2.6 Blood Collection

Blood samples were withdrawn from conscious rats by tail vein puncture 3 days after alloxan induction, Day 20 (pre-treatment) and afterwards on days 22, 24 and 26 (post-treatment). Blood samples were collected into vials containing sodium fluoride and EDTA for the determination of blood glucose and other blood parameters respectively. The samples collected were immediately placed on ice and centrifuged (Gallenkamp, UK) at 3500 r.p.m. for 10 min to obtain the plasma.

2.7 Biochemical Analysis

Assay kits from Randox Laboratory Limited, UK were used for estimation of concentrations of glucose, cholesterol, total protein, albumin, urea and creatinine.

Serum glucose concentration was estimated using enzymatic colorimetric kits (Randox Laboratory, UK) in which the glucose oxidase/peroxidase/4-aminophenazone method of Trinder (1969) was adopted. Plasma cholesterol was estimated by the method described in the Randox cholesterol kit where the indicator quinoneimine is formed from hydrogen peroxide and 4-amino antipyrene in the presence of phenol and peroxidase. Absorbance of the sample and standard were read against the reagent blank within 60 min at 546 nm. The protein concentration in the plasma was determined using the biuret method for detecting the presence of peptide bonds as described in the Randox Total Protein kit (Tietz, 1995). The albumin concentration in the plasma was determined as described by Doumas *et al*. (1971), based on the quantitative binding of the albumin to the indicator bromocresol green (BCG). The albumin-BCG complex absorbs maximally at 578 nm. Plasma urea concentration was determined by photometrically measuring the ammonia liberated by the urea in plasma in the presence of urease (Berthlot's reaction). Absorbance was read at 546 nm (Weatherburn, 1967). Creatinine concentration in the plasma was determined as described in the Randox creatinine kit.

2.8 Liver Enzyme Assays

The activities in plasma of alanine aminotransferase (ALT), aspartate aminotransferase (ASP) and alkaline phosphatase (ALP) were assayed by the methods described in the Randox kits and values expressed in IU/L.

2.9 Statistical Analysis

Data were analyzed using Analysis of Variance (ANOVA) by employing the method of Steel and Torrie (1960).

Significant difference between the treatment means was determined at 95% confidence level using Dancan's Multiple Range Test (Duncan, 1955).

3. RESULTS

The results of blood glucose concentration in experimental animals are presented in Table 1. Alloxan-induction cased a significant increase ($p<0.05$) in blood glucose concentrations (Groups 3 and 4) when compared with normal rats (Group 1). Administration of methanol leaf extract of *A. laxiflora* to normal rats (Group 2) did not cause any significant changes ($p>0.05$). However, administration of the extract resulted in significant decreases ($p<0.05$) in blood glucose concentration of the diabetic treated rats (Group 4) compared to diabetic control rats (Group 3).

Table 1: Effect of *A. laxiflora* extract on fasting plasma glucose concentration of normal and diabetic rats (mg/dl)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	56.80 ± 10.01^{a}	57.68 ± 5.11^{a}	56.95 ± 3.28^{a}	58.00 ± 5.01^{a}	57.98 ± 6.77^{a}
2	63.60 ± 6.18^{a}	61.40 ± 6.63^{a}	62.62 ± 6.53^{a}	63.84 ± 1.92^{a}	62.76 ± 1.12^{a}
	Pre-Alloxan		Post-Alloxan		
3	58.15 ± 10.57^{a}	144.85 ± 11.18^{b}	158.42 ± 3.13^{b}	165.48 ± 5.84^{b}	177.17 ± 9.40^{b}
4	57.27 ± 5.25^{a}	146.12 ± 12.90^{b}	102.21 ± 15.66^{c}	92.19 ± 2.09^{c}	87.66 ± 5.93^{c}

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different ($P \leq 0.05$).

Table 2 shows alloxan induction caused significant increases ($p<0.05$) in plasma cholesterol concentration of rats in Groups 3 and 4 while significant ($p<0.05$) decreases were observed in the diabetic rats administered with the extract compared to diabetic untreated rats (Group 3). No such changes ($p>0.05$) occurred with the normal treated rats (Group 2).

Table 2: Effect of *A. laxiflora* extract on plasma cholesterol concentration of normal and diabetic rats (mg/dl)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	64.47 ± 16.78^{a}	66.84 ± 16.53^{a}	68.28 ± 3.79^{a}	64.50 ± 0.51^{a}	65.55 ± 15.05^{a}
2	63.19 ± 6.53^{a}	66.24 ± 5.09^{a}	65.00 ± 10.26^{a}	65.90 ± 2.80^{a}	65.50 ± 2.70^{a}
	Pre-Alloxan		Post-Alloxan		
3	64.84 ± 7.53^{a}	79.28 ± 6.08^{b}	86.42 ± 4.51^{b}	97.13 ± 4.36^{b}	105.98 ± 5.00^{b}
4	63.71 ± 5.77^{a}	76.80 ± 3.45^{b}	71.96 ± 7.09^{a}	67.87 ± 8.50^{a}	63.25 ± 3.72^{a}

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different ($P \leq 0.05$).

Alloxan induction caused decreases in plasma total protein concentration in diabetic rats (Groups 3 and 4) but these were not statistically different ($p>0.05$) on Day 20 (Table 3). However, the diabetic control rats (Group 3) continued to have decreased protein concentrations which were significant ($p<0.05$) compared to other groups. Though administration of *A. laxiflora* methanol leaf extract did not cause any significant changes ($p>0.05$) to the normal treated rats (Group 2), it restored protein levels back to normal in treated diabetic rats (Group 4).

Table 3: Effect of *A. laxiflora* extract on plasma total protein concentration of normal and diabetic rats (g/dl)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	5.76 ± 0.14^{a}	4.25 ± 0.84^{a}	6.99 ± 0.18^{a}	5.45 ± 0.10^{a}	5.62 ± 0.70^{a}
2	5.45 ± 0.18^{a}	5.04 ± 0.28^{a}	5.53 ± 0.76^{a}	5.81 ± 0.08^{a}	5.95 ± 0.48^{a}
	Pre-Alloxan		Post-Alloxan		
3	5.35 ± 0.39^{a}	4.35 ± 0.54^{a}	3.68 ± 0.12^{b}	2.83 ± 0.15^{b}	2.24 ± 0.43^{b}
4	5.78 ± 0.14^{a}	3.83 ± 0.47^{a}	6.05 ± 0.68^{a}	4.97 ± 0.36^{a}	5.22 ± 0.36^{a}

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different ($P \leq 0.05$).

Results of the concentrations of albumin in experimental rats are presented in Table 4. Alloxan induction caused significant decreases ($p<0.05$) in the diabetic rats compared to normal rats. While albumin levels in the diabetic control rats continue to decrease ($p<0.05$), administration of the extract brought the plasma albumin levels in Group 4 rats back to normal. Administration of the extract to normal rats (Group 2) did not cause any statistically ($p>0.05$) different changes in the level of albumin.

Table 4: Effect of *A. laxiflora* extract on plasma albumin concentration of normal and diabetic rats (g/dl)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	4.50 ± 0.04^{a}	4.28 ± 0.25^{a}	4.50 ± 0.10^{a}	4.93 ± 0.47^{a}	4.74 ± 0.58^{a}
2	4.71 ± 0.10^{a}	4.26 ± 0.15^{a}	4.43 ± 0.13^{a}	4.70 ± 0.13^{a}	4.01 ± 0.25^{a}
	Pre-Alloxan		Post-Alloxan		
3	4.29 ± 0.20^{a}	4.07 ± 0.10^{bc}	3.77 ± 0.27^{b}	3.55 ± 0.32^{b}	2.77 ± 0.45^{b}
4	4.62 ± 0.11^{a}	3.52 ± 0.15^{c}	3.55 ± 0.25^{b}	3.98 ± 0.54^{ab}	4.33 ± 0.13^{a}

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different (P≤0.05).

Alloxan induction caused significant increases ($p<0.05$) in urea concentration in the rats in Groups 3 and 4, compared to the normal rats (Group 1) (Table 5). While administration of the extract caused a lowering ($p<0.05$) of urea concentration in the diabetic treated rats, changes observed in normal rats treated with the extract were non-significant ($p>0.05$).

Table 5: Effect of *A. laxiflora* extract on plasma urea concentration of normal and diabetic rats (mg/dl)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	27.29 ± 1.70^{a}	28.76 ± 5.99^{a}	29.64 ± 3.26^{a}	29.08 ± 3.69^{a}	28.64 ± 4.08^{a}
2	26.58 ± 6.00^{a}	29.23 ± 5.76^{a}	27.42 ± 5.73^{a}	30.24 ± 2.35^{a}	28.29 ± 0.90^{a}
	Pre-Alloxan		Post-Alloxan		
3	27.75 ± 1.50^{a}	60.83 ± 11.75^{b}	66.71 ± 2.37^{b}	67.75 ± 4.38^{b}	67.22 ± 3.00^{b}
4	28.29 ± 1.41^{a}	60.63 ± 13.22^{b}	52.12 ± 15.57^{c}	45.08 ± 9.01^{c}	33.45 ± 5.38^{a}

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different (P≤0.05).

Table 6 shows plasma concentrations of creatinine in experimental rats. Following the induction of diabetes, plasma creatinine levels were significantly ($p<0.05$) raised in Groups 3 and 4 rats. Administration of the extract elicited a significant ($p<0.05$) lowering of hitherto raised levels of creatinine. The extract had no significant ($p>0.05$) effect on normal rats (Group 2).

Table 6: Effect of *A. laxiflora* extract on plasma creatinine concentration of normal and diabetic rats (mg/dl)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	0.96 ± 0.06^{a}	1.01 ± 0.21^{a}	1.04 ± 0.11^{a}	1.02 ± 0.13^{a}	1.00 ± 0.14^{a}
2	0.93 ± 0.21^{a}	1.02 ± 0.20^{a}	0.96 ± 0.20^{a}	1.06 ± 0.08^{a}	0.99 ± 0.03^{a}
	Pre-Alloxan		Post-Alloxan		
3	0.97 ± 0.05^{a}	2.13 ± 0.41^{b}	2.33 ± 0.08^{b}	2.37 ± 0.15^{b}	2.35 ± 0.38^{b}
4	0.99 ± 0.05^{a}	2.12 ± 0.46^{b}	1.47 ± 0.54^{a}	1.23 ± 0.32^{a}	1.00 ± 0.19^{a}

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different (P≤0.05).

Results of the liver enzyme assays in plasma are shown in Tables 7, 8 and 9. Alloxan induction caused a statistically significant ($p<0.05$) increase in plasma aspartate aminotransferase (ASP) activities in Group 3 and 4 rats (Table 7). While the activities continued to increase in the diabetic control rats (Group 3), administration of the extract caused a lowering of the activities of ASP in plasma of Group 4 rats. Administration of the extract to normal rats (Group 2) did not cause any statistically significant ($p>0.05$) changes.

Alloxan induction caused significant increases ($p<0.05$) in alanine aminotransferase activities in plasma of the diabetic rats (Group 3 and 4) (Table 8). While the activities of ALT continued to increase in the diabetic control rats, there was a gradual lowering of the ALT activities in the plasma of the diabetic rats administered with the extract ($p<0.05$). No significant changes were observed in the normal rats treated with the extract (Group 2) compared to the untreated normal rats (Group 1).

As observed in Table 9, alloxan-induced rats had increased alkaline phosphatase (ALP) activities in plasma. Administration of the methanol leaf extract of *A. laxiflora* caused a statistically significant lowering ($p<0.05$) of the ALP activities. The extract did not elicit any significant differences ($p>0.05$) in plasma ALP activities on administration to normal rats (Group 2).

Table 7: Effect of *A. laxiflora* extract on plasma activities of aspartate aminotransferase (ASP) in normal and diabetic rats (IU/L)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	23.40 ± 2.38[a]	23.80 ± 7.66[a]	23.50 ± 7.38[a]	23.90 ± 7.23[a]	23.60 ± 2.80[a]
2	23.00 ± 3.33[a]	23.80 ± 2.13[a]	23.20 ± 1.91[a]	26.80 ± 4.05[a]	24.70 ± 3.75[a]
	Pre-Alloxan		Post-Alloxan		
3	23.83 ± 2.15[a]	35.17 ± 6.61[a]	46.83 ± 3.32[b]	55.67 ± 2.39[b]	60.33 ± 3.02[b]
4	23.50 ± 2.32[a]	40.33 ± 7.41[b]	39.17 ± 6.00[c]	35.73 ± 3.36[a]	31.50 ± 2.84[a]

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different (P≤0.05).

Table 8: Effect of *A. laxiflora* extract on plasma activities of alanine aminotransferase (ALT) in normal and diabetic rats (IU/L)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	24.60 ± 2.04[a]	22.80 ± 1.46[a]	26.20 ± 3.79[a]	24.20 ± 4.29[a]	24.60 ± 4.76[a]
2	24.60 ± 6.55[a]	29.80 ± 4.07[a]	26.40 ± 3.52[a]	24.80 ± 0.73[a]	24.70 ± 3.36[a]
	Pre-Alloxan		Post-Alloxan		
3	24.50 ± 7.91[a]	43.83 ± 2.40[b]	49.17 ± 1.70[bc]	49.83 ± 3.07[bc]	52.83 ± 4.57[b]
4	24.17 ± 10.98[a]	36.33 ± 7.97[b]	37.17 ± 7.18[c]	35.33 ± 2.82[c]	32.33 ± 7.97[a]

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different (P≤0.05).

Table 9: Effect of *A. laxiflora* extract on plasma activities of alkaline phosphatase (ALP) in normal and diabetic rats (IU/L)

Group	Basal	Treatment Began		Post-Treatment	
	Day 15	Day 20	Day 22	Day 24	Day 26
1	23.58 ± 3.47[a]	25.79 ± 0.91[a]	26.28 ± 2.77[a]	25.30 ± 0.34[a]	26.51 ± 1.06[a]
2	23.22 ± 0.92[a]	25.80 ± 0.63[a]	23.94 ± 1.35[a]	26.03 ± 1.66[a]	26.04 ± 0.87[a]
	Pre-Alloxan		Post-Alloxan		
3	23.18 ± 2.14[a]	38.61 ± 1.15[b]	40.87 ± 2.03[b]	45.49 ± 1.14[b]	46.58 ± 3.81[b]
4	23.39 ± 1.85[a]	37.20 ± 2.11[b]	35.22 ± 2.34[c]	29.31 ± 0.38[a]	28.83 ± 1.21[a]

Data are means ± SEM of 6 determinations. Values in the same column carrying different superscripts are significantly different (P≤0.05).

4. DISCUSSION

Vegetable substances often in the form of powders or teas have long been used as popular remedies for diabetes mellitus. The present study investigated the effects of *Alchornea laxiflora* (Benth) Pax and Hoffman methanol leaf extract on some biochemical indices in albino rats with the aim of scientifically establishing its ethnomedicinal use as an antidiabetic agent.

Alloxan induction of rats caused an increases in blood glucose from 57.27 ± 5.25 mg/dl to 146.12 ± 12.90 mg/dl in Group 4 rats. Hyperglycaemia is an important factor in the development and progression of the complications of diabetes mellitus. Effective blood glucose control is the key for preventing or reversing diabetic complications (Marx, 2002). This study has clearly demonstrated the glucose lowering effect of *A. laxiflora* in the diabetic state. The significant reductions in glucose levels of diabetic rats administered the methanol extract of *A. laxiflora* may be due to the presence of antihyperglycaemic principles such as tannins saponins, alkaloids and glycosides reported to be present in the plant (Adegoke *et al*., 1968). The plant did not exhibit hypoglycaemic properties as no significant changes ensured when normal rats were treated with the methanol extract of the leaf. Other workers have also reported antihyperglycaemic properties in some medicinal plants (Nimenibo-Uadia and Osagie, 1999; Adeyemi *et al*., 2015).

Cholesterol and other lipids are raised in the diabetic state. Elevation of plasma cholesterol has been well documented in diabetes (Chase and Glasgow, 1976). The gradual reduction in cholesterol level on administration of the extract to diabetic rats shows *A. laxiflora* has antihypercholesterolaemic effects. Some medicinal plants have been reported to lower high concentrations of lipids in diabetic rats (Sharma *et al*., 2003; Adeyemi *et al*., 2015). However, its non-significant effect in normal rats suggests *A. laxiflora* cannot be employed in treating non-diabetes related lipid diseases.

Both protein and albumin concentrations in the diabetic control rats continued to fall (decreases of 58.13% for protein and 35.43% for albumin by Day 26). Alloxan may have damaged the liver thus impairing protein

(including albumin) synthesis. Albumin is the most abundant serum protein representing 55 – 65% of the total protein. Hypoalbuminaemia is associated with impaired albumin synthesis in the liver, liver disease, malnutrition or malabsorption. In diabetes, there is a decreased synthesis of proteins and hence less albumin is synthesized by the liver because of the need of amino acids for gluconeogenesis (William, 1989). Protein metabolism is also affected in diabetes. There is increased catabolism of proteins and the less protein synthesis, leads to debilitating protein deficiency, depletion and wasting (William, 1989). The fact that the methanol extract of *A. laxiflora* leaf was able to restore protein and albumin levels in the diabetic rats (Group 4) confirms *A. laxiflora* is able to ameliorate the derangement in metabolism associated with diabetes mellitus.

Urea and creatinine are markers of renal dysfunction (El-Demeradash *et al*., 2005). In the present study, urea and creatinine were significantly increased in the diabetic rats. In diabetes, amino acid breakdown in the liver and muscle tissues of diabetic animals results in an increased production of urea and creatinine, as observed in the diabetic animals (William, 1989). Furthermore, since its rate of production is constant, elevation of plasma creatinine is indicative of under-excretion, suggesting kidney impairment (Kumar and Clark, 2000). The reduction in urea and creatinine levels on administration of the extract suggests *A. laxiflora* may have reversed the impairment in the kidneys with proper glycaemic control in the diabetic rats.

The activities of the aminotransferases in blood are useful indicators of liver damage/disease. The statistically significant increases in plasma activities of the liver marker enzymes aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase in the diabetic rats suggest damage to the liver. Many researchers have reported increase in aminotransferase activities in the liver and serum (Shanmugasundaram *et al*., 1983). The gradual restoration back to normal values on administration of the extract suggests *A. laxiflora* was able to restore the architecture of the liver hitherto damaged.

5. CONCLUSION

The observations in this study have shown that the methanol extract of *A. laxiflora* leaf is able to ameliorate the biochemical defects indicative of diabetes mellitus. Since it had no significant effects on normal rats, its mechanism of action may be similar to that of biguanides (metformin) which rather than increase insulin secretion, reduce gluconeogenesis thus suppressing hepatic glucose output thereby producing antihyperglycaemic effect and not hypoglycaemic effect (Knowler *et al*., 2002).

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