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ANTIHYPERGLYCEMIC AND RENAL PROTECTIVE ACTIVITIES OF *ANACARDIUM OCCIDENTALE* (ANACARDIACEAE) LEAVES IN STREPTOZOTOCIN INDUCED DIABETIC RATS.

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Abstract

Earlier studies from our laboratory have indicated hypoglycaemic action of *Anacardium occidentale* (AO) leaves in experimental type 1 diabetes. Streptozotocin-induced diabetes in rats had been shown to be associated with functional and/or morphological changes in the kidney. Therefore, in the present investigation, we carried out studies on streptozotocin (STZ)-induced type 1 diabetes in rats chronically treated with *Anacardium occidentale* on the functional and histological alterations of kidneys. Albino rats were divided into 7 groups (n = 5) receiving graded doses of hexane extract of *Anacardium occidentale* leaf by gavage, (150 and 300 mg/kg/day) and insulin (5 IU/kg). Renal ultrastructure was studied by measuring: diameter of Bowman's capsule, distribution and total area occupied by glomerular capillaries, PAS positive structures. AO at the dose of 300 mg/kg/day, showed significant reduction ($P < 0.05$) of blood glucose level, total protein excreted, glycosuria and urea in diabetic rats. *Anacardium* treatment, initiated 3 days after diabetes induction, reduced destruction of renal structure and other metabolic disturbances more than when treatment was initiated two weeks after. Histopathological study showed that *A. occidentale* significantly reduced accumulation of mucopolysaccharides in the kidneys of diabetic animals. The extract of AO at the dose of 300 mg/kg had no nephrotoxic potential in normal rats. The present study demonstrates the efficacy of *Anacardium occidentale* (hexane extract) in reducing diabetes-induced functional and histological alterations in the kidneys.

Key words: *Anacardium occidentale*, Hexane extract, Diabetes mellitus. Rats, Nephropathy.

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Introduction

Insulin-dependant diabetes mellitus (IDDM), also called type 1 diabetes is defined as a chronic disease, characterised by a clinical disorder of sugar, fat and proteins metabolism, caused by absence of insulin to promote sufficient glucose output from the liver (Sanchez et al., 2000). Patients depend on insulin for management of IDDM. Without insulin, they develop degenerative complications such as microangiopathy, nephropathy and retinopathy. Diabetic nephropathy is the most important cause of death in type 1 diabetic patients, of whom, 30- 40% eventually develop end-stage renal failure (Giorgino et al. 2004). Studies have shown that good metabolic control is beneficial in slowing the progression of nephropathy in diabetes, and if the duration of diabetes is prolonged before reinstitution of normoglycaemia, nephropathy is not easily reversed (Renu et al., 2004; Floretto et al., 1998). Experimental type 1 diabetes induced with streptozotocin in rats display many of the features seen in human subjects with uncontrolled diabetes mellitus (Chattopadhyay et al., 1997).The development of new therapies that are able to improve glycaemia management and even to cure diabetes is of great interest. *Anacardium occidentale* L. (Anacardiaceae), plant originated from Brazil is used as folk medicine in south of Cameroon and other African countries for the treatment of diabetes mellitus, diarrhoea and hypertension (Paris et al., 1977).

In our laboratory, hypoglycaemic and protective role of this plant has been reported (Kamtchouing et al., 1998; Sokeng et al., 2001). Moreover, a preliminary test has revealed that hexane fraction of *Anacardium* is more potent in lowering blood glucose than methanol, ethyl acetate and methylene chloride fractions.

Based on our previous findings, the current study was aimed at identifying biochemical and renal histopathological abnormalities that occur with the evolution of streptozotocin-induced diabetes in rats and to appreciate their possible reversal after the establishment of good metabolic control with the hexane extract of *Anacardium occidentale*.

Materials and methods

Plant

Leaves from *Anacardium occidentale* were collected in the month of January 2003 and were authenticated by comparison with national herbarium (Yaounde-Cameroon) file, voucher specimen (N° 41935 /HNC). The plant leaves were dried in the laboratory at room temperature and powdered in a mixer grinder. 3 kg of powder-dried was macerated in 8 L of methanol at room temperature. After filtration, the solution was concentrated under reduced pressure. The resulting extract (262 g) was eluted in hexane (1 L) and concentrated to dryness to obtain a mass of hexane extract (35.7 g) with the extraction yield of 1.2%. 1.5 g of this extract was dissolved in 3 ml of dimethyl sulfoxide (DMSO) and solution adjusted to 97 ml with distilled water to obtain a solution of 100 ml.

Analysis of hexane extract of *A. occidentale*

Hexane extract was tested for the presence of alkaloids, saponins and polyphenols following standard methods (Harborne, 1973).

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Animals

The study was carried out with the approval of the Institutional Animal Ethical Committee. Male Wistar rats weighing 150-230 g from the animal house of the Faculty of Science, University of Yaounde I, were used. The animals were fed with standard laboratory diet, and given water *ad libitum*. After randomisation into various groups, the rats were acclimatized for a period of 6-7 days in another environment before the initiation of experiment. Animals described as fasted were deprived of food for at least 12 h, but had free access to water. The study was approved by the Institution's Ethical Committee.

Streptozotocin-induced diabetic rats

Thirty five fasted Wistar rats (200-250 g) were intravenously injected with 55 mg/kg of streptozotocin (Sigma chemical Co (St Louis, Mo, USA), freshly dissolved in physiological saline, while non-diabetic rats were injected with saline by the same route. 72 h following these injections, the blood glucose, levels were monitored weekly, using glucometer Accutrend GC (Boeringer Mannheim, Germany). Fasted animals with plasma glucose levels higher than 200 mg/dL were selected for the study.

Administration of plant extract

Using 25 diabetic and 10 normal rats, they were divided into 7 groups of 5 rats each. Group 1-Non-diabetic control rats (NDCR) received distilled water; Group 2-Non-diabetic treated control rats (NDTCR) received 300 mg/kg/day of extract; Group 3-diabetic control rats of 8 weeks (DCR-8W) received distilled water; Group 4-diabetic rats which received AO, 300 mg/kg/day, immediately after diagnosis of diabetes (AO was given in this group 3 days after induction of diabetes) for three weeks; Group 5-Two weeks diabetic rats which received AO. 150 mg/kg/day for 5 weeks. Group 6-Two week's diabetic rats which received AO 300 mg/kg/day for 5 weeks. Group 7-Two weeks diabetic rats received insulin. The route of administration was oral except insulin which was treated once a day (7AM) by subcutaneous injection of 1 unit of insulin (Insulatard HM, 100 UI/ml, Novo Nordisk, AIS, 2880 Bagsvaerd, Danemark). Treatment with extracts of plants was given for 4 weeks after which rats were monitored for the 5^{th} and 6^{th} week. Insulin treatment continues over the 6 weeks.

Determination of glycemia and other biochemical parameters.

To determine the blood glucose level, all animals had overnight fasting (Except of insulin group). Blood was obtained from the tail vein and glycaemia monitored once per week as described above. At the end of the treatment, all the rats were sacrificed; blood samples and organs were collected for further analysis. Blood was centrifuged at 4°C for 10 min and the serum was separated and analysed. Total protein excreted was measured using Bio-Direct Kit N°1257-01; urinary albumin was quantified using Bio-Direct Kit RC 1203-01; glycosuria was analysed using Randox Kit, Laboratories Ltd, United Kingdom, Ref 2326; urinary urea levels were estimated using Bio-Direct Kit, RC 1262-01. All these parameters were quantified by reading the absorbance of the standard and sample, using spectrophotometer Secoman CE (Type Basic 70VBO 358, France).

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Renal histological assessment

Nephropathy was assessed after treatment by measurements of 24 h total protein excreted, urinary albumin, glycosuria and urea. For urinary collection, rats were housed in metabolic cages for 24 h. Several drops of toluene were added to the urine collection beaker to inhibit microbial growth (Alderson et al., 2004). At the end of treatment, rats were sacrificed; kidneys were removed and weighed, fixed in 10% buffered formalin, dehydrated in gradual ethanol (80-100‰), cleared in xylene, and embedded in paraffin. Section (3 μm thick) were prepared and then stained with hematoxylin-eosin and PAS dye for photomicroscopic observations. Renal ultrastructure was studied by measuring: diameter of Bowman's capsule, distribution and total area occupied by glomerular capillaries, PAS positive structures (related in to the intensity of reaction resulting from the different amount of mucopolysaccharides). Structures of kidneys were submitted to morphometric analysis of images, using Quantimet 500 image Analyser (Leica- Qwin, Germany) equipped with specific software.

Statistical analysis

All values are expressed as means ± SEM. Statistical differences between the means of various groups were evaluated, using one-way analysis of variance (ANOVA) followed by Kruskal-Willis test. A p value of less than 5% was considered statistically significant ($P < 0.05$).

Results

Effect of *Anacardium occidentale* (hexane extract) on body weight

Phytochemical analysis revealed the presence of alkaloïds, saponins and polyphenols.

Diabetic rats grew poorly and had significantly ($P < 0.05$) lower body weight compared to normal control rats (Table 1). At the same time, diabetic rats treated with *A.occidentale* (300mg/kg/day), immediately after diagnosis of diabetes and 2 weeks later as well as insulin treated rats had their body weight comparable to non-diabetic control groups. The body weight of 2 weeks diabetic rats treated with *A. occidentale* at a dose of 150 mg/kg/day was not different from that of diabetic control rats. There was no increment in relative percentages of kidneys between control and treated groups.

Effect of *Anacardium occidentale* (hexane extract) on plasma glucose.

The anti-hyperglycaemic effect of the extracts on the fasting blood sugar levels of diabetic rats is shown in Figure1. The plasma glucose levels of diabetic-induced rats significantly increased 72 h following the induction. Thus, the initial blood glucose level of the diabetic rats ranged from 208 to 440 mg/dL compared to basal glycemic of non diabetic control animals (89 mg/dL). At the entry of treatment (two weeks after diabetic state), the mean plasma glucose of diabetic untreated rats significantly increased and was in range of 438 and 445 mg/dL and 2/11 rats died during this period. There after 4/9 animals died in the second period of experiment and the mean glucose levels on the last days of treatment in 5 animals, which survived was 432 mg/dL.

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Hexane extract at a dose of 300 mg/kg/day, administered to diabetic rats, immediately after diagnosis of diabetes (D-0W+AO300), produced a significant decrease in glucose level ($P < 0.05$) compared with diabetic controls from the 1st and 2nd week of treatment. This tendency got more prominent and the plasma glucose concentration appeared to be normal at 4-weeks treatment (112.5±4.2 mg/dL) and these were maintained throughout the experiment (6 weeks). Five weeks of daily treatment with two doses of *A. occidentale* (DR-2W+AO150 and DR-2W+AO300) led to a dose dependant-fall in blood sugar levels by 43% and 71% compared to diabetic groups. Considering the dose of 150 mg/kg/day used in the study, effect seems to reach maximum after 2 weeks of treatment (220.0±4.5 mg/dL) and remains constant in the third, fourth and fifth week. The higher dose (300 mg/kg/day) administered for the same condition, had shown that *A. occidentale* (DR-2W+ AO300) decreased gradually and normalised glycaemia at the fifth week of treatment (114±2.0 mg/dL).
Phytochemical analysis revealed the presence of alkaloids, saponins and polyphenols in hexane extract of our plant.

Effect of *Anacardium occidentale* (hexane extract) on kidney function

Figure 2 show data for total protein excreted, albuminuria, urinary glucose and urinary urea levels for healthy and diabetic rats. Total urinary protein levels were significantly ($P < 0.01$) increased in DCR of 8 weeks by 94% compared to NDCR (Fig. 2A). At the end of 5 weeks treatment, *A. occidentale* at a dose of 300 mg/kg/day, given immediately after diagnosis of diabetes, significantly ($P < 0.05$) reduced the urinary protein excretion by 46% compared to diabetic control rats. AO at 300 mg/kg/day and insulin (5 IU/kg/day), given 2 weeks after diagnosis of diabetes significantly decreased total protein excretion by 39 and 53%, respectively. There was no significant difference in the ability of lower dose (150 mg/kg/day) to prevent the increase and total protein excreted in diabetic control group. Parallel diabetic rats of 8 weeks were associated with significant ($p<0.05$) rise in albuminuria compared with non-diabetic control rats (Figure 3B). Over the treatment period, *A. occidentale* and insulin treatment significantly ($P < 0.05$) retarded the increase of albuminuria levels in all groups compared to the untreated diabetic group. As shown by data from healthy and diabetic rats (Figure 2C), the dose of STZ administered produced in animals a marked increase ($P < 0.01$) in urinary glucose excretion in non-treated diabetic rats compared to normal control rats. AO at 150, 300 mg/kg/day and insulin, given 2 weeks after diagnosis of diabetes, significantly lowered ($P < 0.05$, $P < 0.05$ and $P < 0.01$) glycosuria by 27, 46 and 75%, respectively compared to DCR of 8 weeks. Urinary urea levels in healthy and diabetic rats are shown in Figure 3D. We did not observe any significant change between NDCR and NDCTR+AO300 mg/kg. Diabetic rats of 8 weeks showed a marked increase ($P < 0.01$) of urea compared to normal control rats. The beneficial effect of *A. occidentale* on urea level appeared with AO at a dose of 300 mg/kg/day, given immediately after diagnosis of diabetes which decreases urinary urea by 46% comparable to that of insulin (53%). Treatment with AO, at doses of 150 and 300 mg/kg/day, initiated 2 weeks after diagnosis of diabetes did not influence urinary urea levels.

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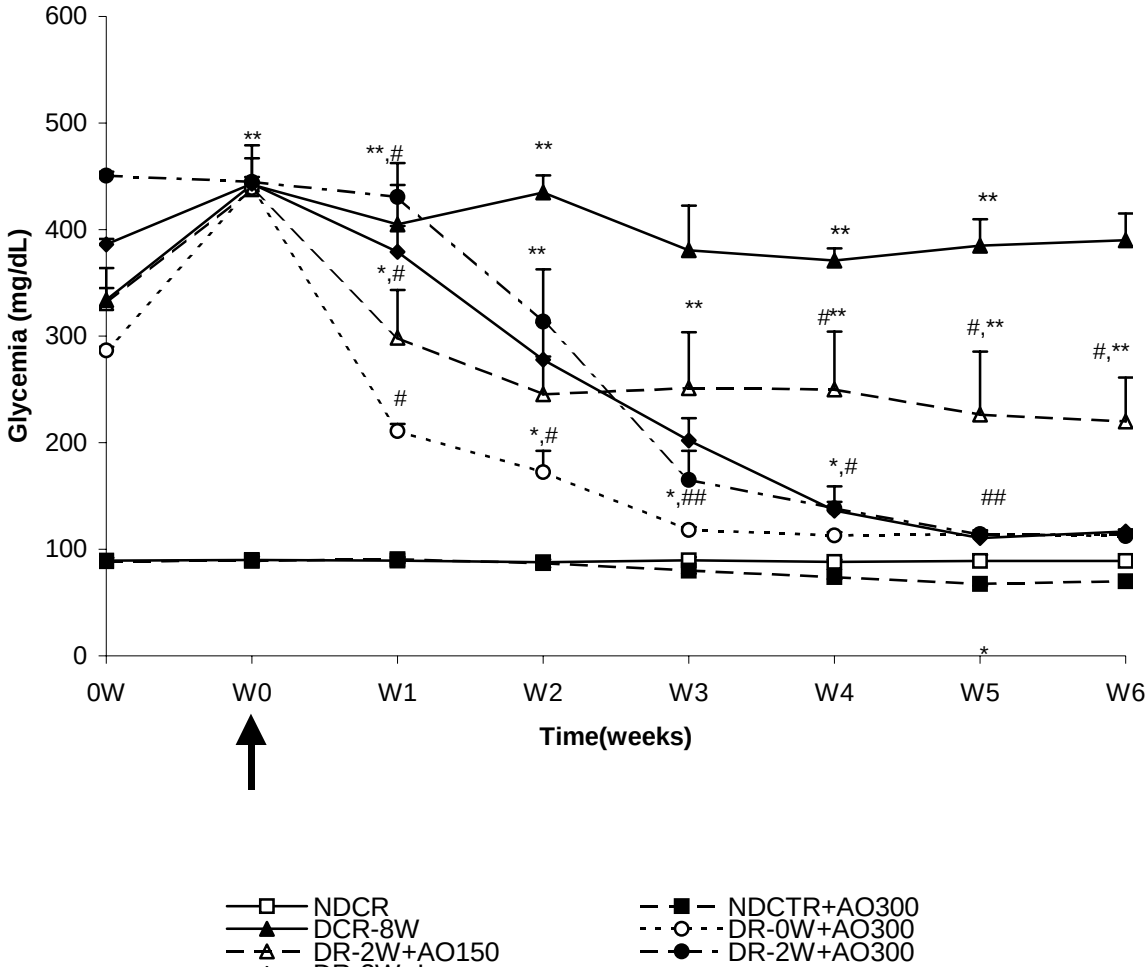

Figure 1: Effect of *Anacardium occidentale* (Anacardiaceae) leaves hexane extract on glycemia glycemia in normal and streptozotocin fasted diabetic rats

Non diabetic control rats (NDCR-8W), (white squares); Non diabetic control treated rats (NDCTR), with AO-300 mg/kg/day, (black squares); Diabetes control rats (DCR), (black triangles); Diabetes rats of 2 weeks, given AO-150 mg/kg/day (white triangles), AO-300 mg/kg/day (black circles) or insulin (5 IU/kg/day, Black diamond); Diabetic rats given AO-300 mg/kg, immediately after diagnosis of diabetes (white circle). Diabetic control rats of 8 weeks duration showed a marked increase of blood glucose level compared with non-diabetic control rats. n=5 rats. 0W: Glycemia values after diagnosis of diabetes; W0: the arrow indicates the beginning of *Anacardium* administration. Values are shown as means ± SEM. **p< 0.01, ***p< 0.001; *p<0.05 (compared control normal groups); # p<0.05; ## p<0.01 (compared to diabetic control rats).

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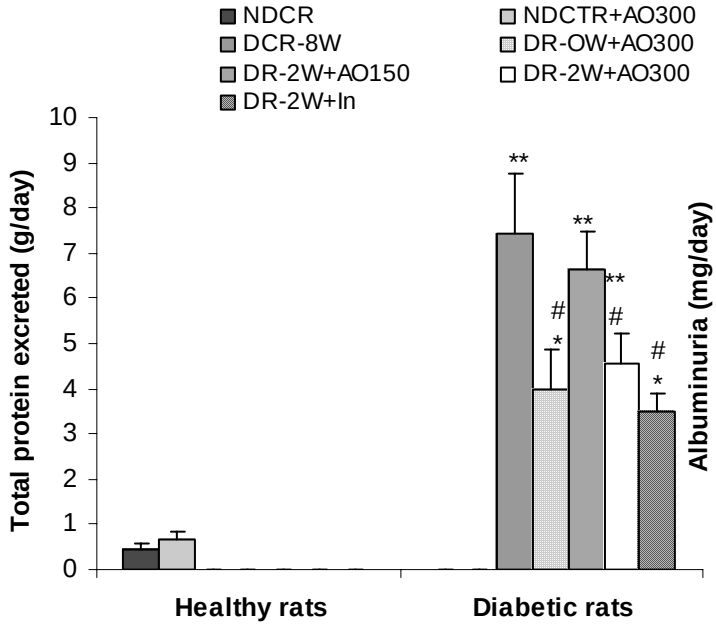

Fig. 2A

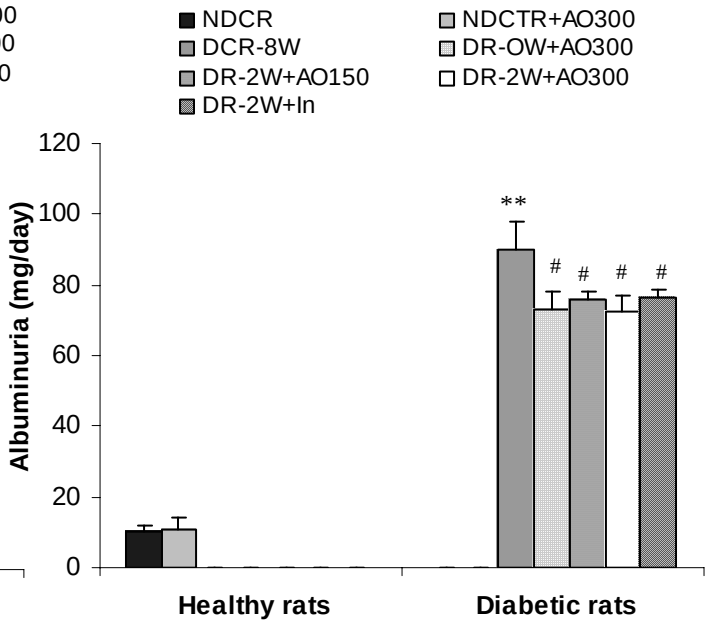

Fig. 2B

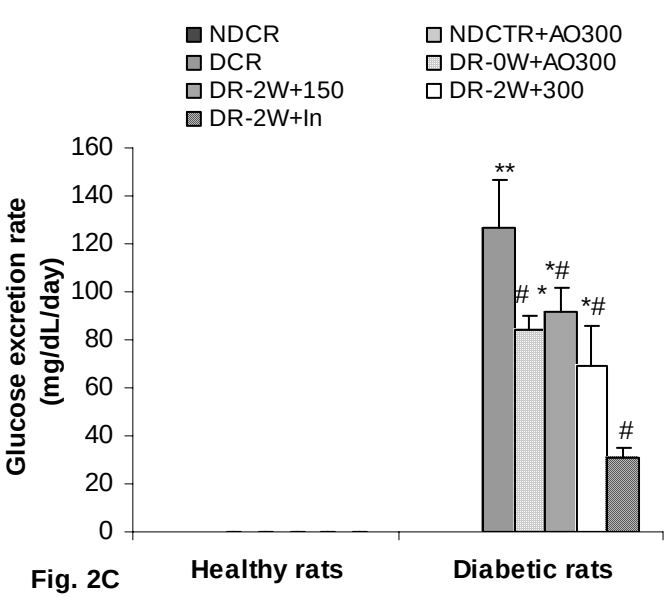

Fig. 2C

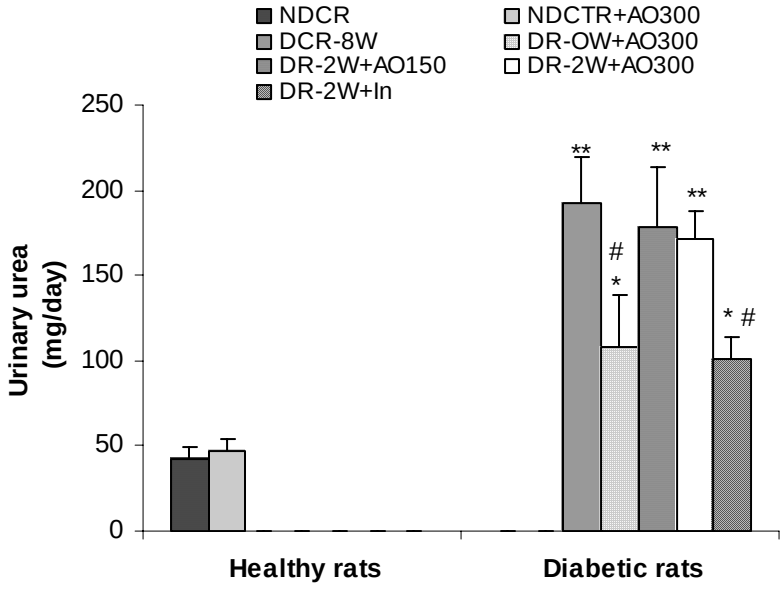

Fig. 2D

Figure 2: Effect of *Anacardium occidentale* on urinary metabolic parameters of healthy and STZ-diabetic rats. A: Total protein excreted; B: Albuminuria; C: Glucose excretion rate; D: Urea. Diabetic control rats of 8 weeks duration (DCR-8W), showed a marked increase in all metabolic parameters compared with non-diabetic control rats (NDCR). NDCTR: Non diabetic control treated rats with AO, 300 mg/kg/day; D-0W+AO300: Diabetic rats given AO, 300 mg/kg/day immediately after diagnosis of diabetes; DR-2W+ AO150 and DR-2W+AO300: 2 weeks diabetic rats, given AO at doses of 150 and 300 mg/kg/day, respectively; D-2W+In: 2 weeks diabetic rats, administered insulin, 5 IU/kg/day. Each experiment was performed on 5 rats. Values are shown as means ± SEM. **p< 0.01; *p<0.05 (compared to normal control groups); # p<0.05; ## p<0.01 (compared to diabetic control groups).

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Kidney histopathology and morphometric studies

Histological examination of the sections of kidneys from normal control rat is shown in Figure 3A. The two circular areas observed on this photograph are renal glomeruli. Each is composed of glomerulus surrounded by Bowman's capsule. Numerous tubules (proximal and distal) lie in the area adjacent to glomeruli. Kidneys section of STZ-diabetic control rats showed marked microscopic changes like multifocal clarifications and vacuolations (Figure 3B1) compared to kidney of non diabetic control rat. Periodic acid Schiff (PAS) staining revealed that mucopolysaccharide were abundant in diabetic rats' kidneys (Figure 3B2). The incidence and intensity of tubular vacuolations as well as other degenerative structures were much lower in STZ-diabetic rats treated with *A. occidentale* at a dose of 300 mg/kg/day (administered in the two experimental conditions, Figures 3C and 3D, compared to diabetic control kidneys. In the morphometric studies, we observed an atrophy of glomerular capillaries with Bowman's space dilated in STZ-untreated diabetic rats (Table 1). Diabetic untreated-rats of 8 weeks duration, exhibited a significant ($P < 0.05$) atrophy of total area occupied by glomerular capillaries (3.5 μm^2 versus 6.4 μm^2). These structures tended to be normal in *Anacardium*-treated animals with a dose of 300 mg/kg/day. Kidney sections of healthy rats treated with *A. occidentale* showed no pathological changes and were comparable to those of control rats.

Discussion

The main function of the kidneys is to excrete the waste products of metabolism and to regulate the body concentration of water and salt. The morphological changes in STZ diabetic rats in the present investigation is associated with significant increased of total protein excreted, albuminuria, glycosuria, and urinary urea levels, indicating impaired renal function of diabetic rats. STZ-induced diabetes in rats had been shown to be associated with functional and/or morphological changes in the kidney (Alderson et al., 2004). In our study, treatment of STZ-diabetic rats either with insulin or *Anacardium occidentale*, induced a fall in the level of all these metabolic parameters. However, the improvement in urinary protein, albumin, glucose and urea excretion with *A. occidentale* extract were not sufficient to reach the levels observed in the non-diabetic rats; moreover *A. occidentale* did not alter any biochemical kidney function variables in non diabetic rats. Similar results were obtained with diabetic rabbits treated with *Eugenia jambolana* (Kedar and chakrabarti, 1983) and non-diabetic rats treated with *Bauhinia forficata* (Pepato *et al*, 2002). Albumin measurements are required, as measurements of urinary total protein are insufficiently sensitive (Harycy, 2002). Microalbuminuria and proteinuria typically reflect the presence of moderate and advanced lesions, respectively, in kidney disease (Roy, 2004; Van den Born et al., 1995). However, the development of diabetic nephropathy is characterised by a progressive increase in urinary protein particularly albumin and a late decline in glomerular filtration rate, leading eventually to end-stage renal failure (Salah et al., 2004). Histologically, the kidneys section of STZ-diabetic control rats showed marked multifocal clarifications, vacuolations and abundance of mucopolysaccharide in diabetic rats' kidneys. Moreover, it has been reported that streptozotocin does not possess any significant nephrotoxic potential (Floretto et al., 1998). All structural changes in kidneys resulting from STZ administration in rats can thus be attributed to altered metabolism in diabetes (Rasch, 1980). Normoglycaemia with *A. occidentale* treatment could ameliorate the glomerular and tubular lesions that characterise diabetic nephropathy.

Table 1: Effect of *Anacardium occidentale* leaf (hexane extract) on kidneys physical parameters of fasted non diabetic and STZ-diabetic rats after 35 days of treatment.

	NDCR	NDCTR-AO300	DCR-8W	DR-0W+AO300	D2W+AO150	D2W+AO300	D-2W+In 5 IU/kg
Mean variation of BW (FBW-IBW) (g)	+34.2	+49.75	-46.82*	+17.67$^{\#}$	-24.38	+18.67$^{\#}$	16.5$^{\#}$
Kidney weight (g)	0.88±2.33	0.92±1.24	0.65±3.04*	0.79±1.64	0.74±4.20	0.79±2.61	0.81±2.11
Relative percentage of the kidneys weight	0.38	0.37	0.38	0.38	0.44	0.37	0.35
UER (ml/24h)	3.58±1.02	8.62±0.52	62.83±4.68*	18.75±1.11$^{\#}$	45.82±8.41*	30.79±0.78*	20.00±1.13$^{\#}$
Total surface of glomeruli n=5 (μm^2)	8.71±0.33	8.51±1.04	5.78±1.21*	7.05±0.14$^{\#}$	6.59±0.38	7.63±1.06$^{\#}$	7.17±0.49
Total area occupied by glomerular capillaries n=5 (μm^2)	6.38±0.13	6.44±1.02	3.50±0.77*	4.85±0.31$^{\#}$	5.10±0.43$^{\#}$	4.37±0.73$^{\#}$	5.22±0.39$^{\#}$

Values are shown as means ± SEM. *p<0.05 significant different as compared to, control normal groups; # p<0,05 as compared to diabetic control rats. Each experiment was performed on 5 rats. NDCTR: Non diabetic control treated rats with AO, 300mg/kg/day; D-0W+AO300: Diabetic rats given AO, 300 mg/kg/day immediately after diagnosis of diabetes; DR-2W+ AO150 and DR-2W+AO300 mg/kg: 2 weeks diabetic rats, given AO at doses of 150 and 300 mg/kg, respectively; DCR-8W: Diabetic control rats of 8 weeks D-2W+In: 2 weeks diabetic rats, administered insulin, 5 IU/kg. UER: Urinary Excretion Rate. n: number of glomeruli measured. IBW: Initial body weight. FBW: Final body weight.

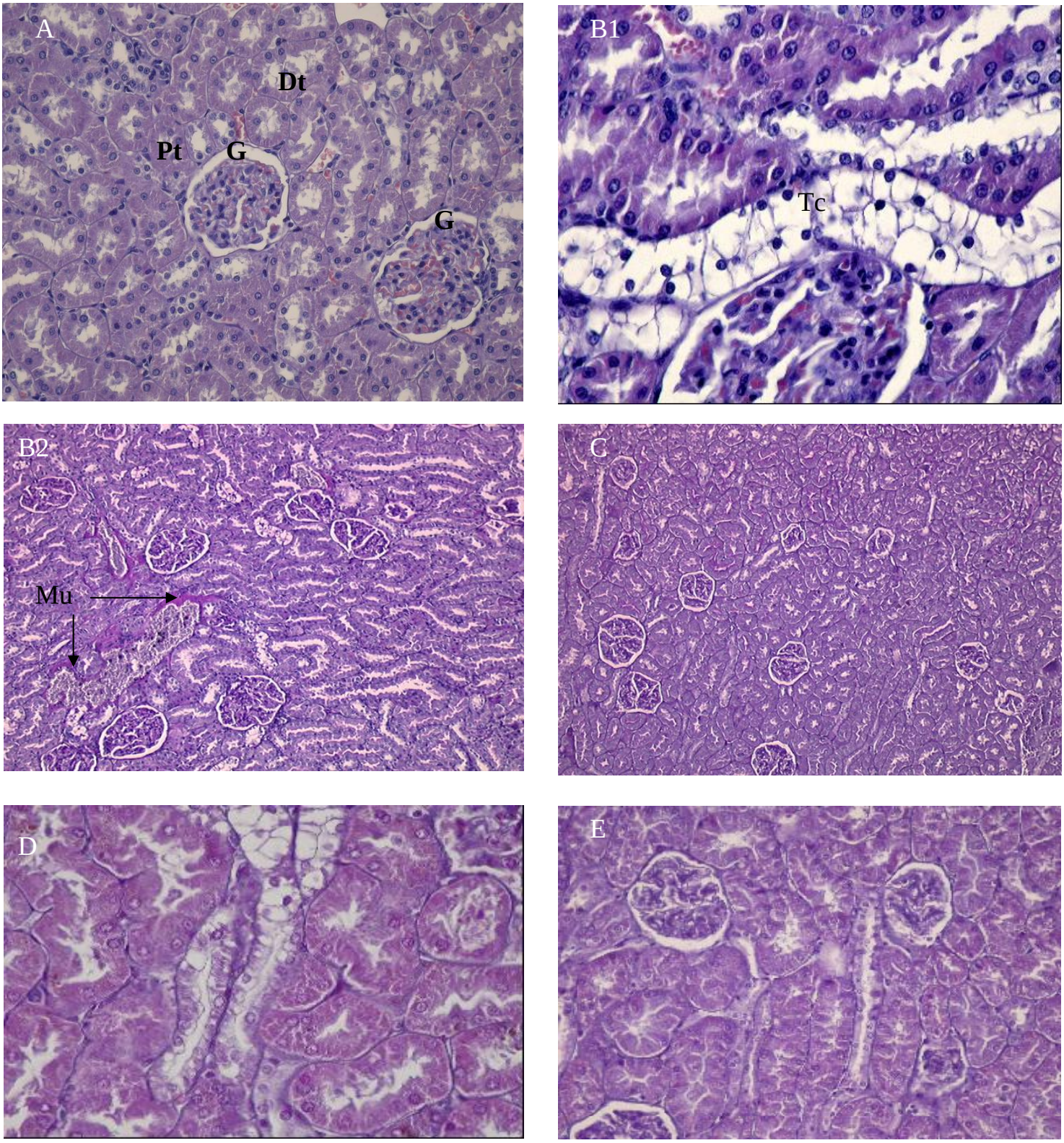

Figure 3: Effect of *Anacardium occidentale* hexane extract (300 mg/kg/day) 35 days treatment on kidneys structures of rats with streptozotocin-induced diabetes.

A: Non diabetic control rats (NDCR) rat (HE, x200). **B**: Diabetic control rat (DCR) of 8 weeks showing, tubules clarification (**Tc**), (**B1,** HE, x200) and positive structures from the different amount of mucopolysaccharides (**Mu**) (**B2,** PAS, x100); **C**: Diabetic rat, given AO 300 mg/kg/day, immediately after diagnosis of diabetes (PAS, x100). **D**: Diabetic rat of 2 weeks, given AO-300 mg/kg/day. **E**: Diabetic rat on 2 weeks, given insulin, 5 IU/kg/day (HE, x200). **G**: glomerulus; **Pt**: proximal tubules; **Dt:** distal tubules.

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The improvement of renal morphology and function associated with STZ-induced diabetes and *A. occidentale* treatment in the present investigation could be attributed to its antidiabetic action resulting in alleviation of altered metabolic status in animals. However, the excellent recovery of renal function expected with treatment of AO can be explained by the regenerative capability of the renal tubules (Kissane, 1985). The action by which the extract lowered the blood glucose is not well known; it may increase glycogen level in liver by an increase in glycogenesis and/or a decrease in glycogenolysis. Since *A. occidentale* did not significantly reduce glycaemia in non-diabetic animals, it is possible that its mechanism of action is similar to that of glibenclamide and insulin. Similar results have been observed with the treatment of STZ-induced diabetic rats with *Cassia kleinii* leaf extract and glibenclamide (Babu et al., 2003). In another hand, the chemical substances therapeutic properties could be mediated by the stimulation of regeneration process and revitalisation of remaining β cells (Diatewa et al., 2004). 2 weeks after diagnosis of diabetes, the insulin group treated once daily by subcutaneous injection of a unit of Insulatard, HM, led to a gradual fall in blood glucose over 5 weeks of treatment. These results are in line with those of Paz and Homonnai. (1979) who noted that insulin Protamine-Zinc, Nordisk, administered(2 IU/day/rat) subcutaneously normalized the glycaemic status of STZ-diabetic rats after 5 weeks of treatment. Previously published work (Pepato et al., 2002) showed that 8 days diabetic rats, treated with insulin (NPH, 3 IUx2/day), normalized glycemia after 38 days of treatment. However, to maintain glycaemia nearer the normal value, Sanchez et al. (2000) administered insulin Monotard, MC, 3-4 IU twice daily in diabetic rats. All these results suggest that normalization of glycaemia depend of the type of insulin and the dose used. The phytochemical analysis had revealed the presence of alkaloids, polyphenols and saponins in the plant extract. Based on the increasing number of reports on blood glucose reduction associated with some saponins (Diatewa, 2004) and alkaloids (Bolkent et al., 2000) isolated from other medicinal plants, it is likely that the active principle (s) could be present in one or the two families of chemical substances. Accelerated chemical modification of proteins by glycosidation and accumulation of AGE (Advanced Glycation End-products) are implicated in diabetic nephropathy and Hennebele et al. (2004) suggested that these molecules can be inhibited with polyphenols. Standard antidiabetic drugs such as insulin and sulfonylureas cause hypoglycaemia when taken in excessive doses and hypoglycaemia is the most worrisome effect of these drugs. *Anacardium occidentale* did not cause any hypoglycaemia, therefore, it could be an effective treatment for early renal disease and possibly other diabetic complications.

Conclusion

The goal of these studies was to evaluate the effect of *Anacardium occidentale* (hexane extract) on development of renal complications in streptozotocin-induced diabetic rats. Our data show that, the hexane fraction of *Anacardium occidentale* was found to effectively improve the renal function and reduce lesions associated with diabetic state in streptozotocin-diabetic rats.

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