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RESEARCH ARTICLE

ANTIDIABETIC ACTIVITY OF THE AQUEOUS EXTRACTS OF *SARCOCEPHALUS POBEGUINII* (BARKS) *AND NAUCLEA DIDERICHII* (LEAVES AND BARKS) IN NORMAL AND STREPTOZOTOCIN INDUCED-HYPERGLYCEMIC RATS.

Mbot Elvis Jolinom[1], *Agnaniet Huguette[1], Ngueguim Tsofack Florence[2], Padzys Guy Stephane[3] and **DimoTheophile[2].

1. Laboratory of natural substances and organometallic synthesis, University of Science and Technique of Masuku, Faculty of Science BP. 943, Franceville, Gabon.
2. Department of Animal Biology and Physiology, Faculty of Science, University of Yaounde I, P.o. Box 812, Cameroon.
3. Department of Biology, University of Science and Technique of Masuku, Faculty of Science BP. 943, Franceville, Gabon.

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Abstract

Nauclea diderrichii (barks and leaves) and *Sarcocephalus pobeguinii* (barks) used in Gabonese traditional medicine for the management of diabetes have been shown to be potent inhibitor of α-glucosidase. The present study was aimed to evaluate the antidiabetic activity of the aqueous extract of these plants in normal and streptozotocin induced-diabetic rats. Effect of various doses (50-400 mg/kg) of extract was studied on their hypoglycemic activity. Two effective doses were selected to investigate their antidiabetic effect on streptozotocin induced-diabetic rats. Animals received substances at a unique daily dose for two weeks. Blood glucose levels were determined weekly. Several others parameters were evaluated: lipid profile, serum transaminases, total proteins, creatinin, total and direct bilirubin and uric acid. Some oxidative parameters were also measured. In normal rats, all extract reduced blood glucose levels with a marked effect at the dose of 200 mg/kg with *Nauclea diderrichii* bark. In diabetic rats, *Nauclea diderrichii* leaf extract (100 mg/kg) brought the blood glucose levels towards normal value and maintained it at the 2nd week. At the dose of 200 mg/kg, the glycaemia returned to the normal value after two weeks post-administration. The administration of streptozotocin induced abnormalities in lipid profile, transaminases, creatinemia and parameters of oxidative stress. Administration of plant extracts improved lipid profile, liver function and antioxidant status of rats. *Nauclea diderrichii* leaf extract was the most potent extract than *Sarcocephalus pobeguinii* and *Nauclea diderrichii* bark extracts. Thus it is concluded from this study that, *Nauclea diderrichii aqueous* leaves possess a marked potential-antidiabetic activity than other extracts.

Corresponding Author:-Agnaniet Huguette.
Address:-Laboratory of natural substances and organometallic synthesis, University of Sciences and Techniques of Masuku, Faculty of Sciences BP. 943, Franceville, Gabon.

Introduction:-

Diabetes mellitus is a chronic metabolic disorder of carbohydrate, protein and fat due to absolute or relative deficiency of insulin secretion with or without varying degree of insulin resistance (Sangeetha *et al*., 2014) characterized by high blood glucose. Besides hyperglycemia, several other factors, associated with diabetes, including dislipidemia or hyperlipidemia are involved in the incidence and progression of microvascular (diabetic retinopathy, and nephropathy) and macrovascular diseases (amputation, cardiovascular disease and mortality) that are difficult to manage (Menakshi *et al.,* 2011; Prinya *et al.,* 2012). These metabolic disorders constitute the main causes of morbidity and death in diabetic patients (Vishnu *et al.,* 2010). Diabetes mellitus is recognized as a global major health problem (IDF, 2013). Due to a higher incidence of the risk factors, the prevalence of diabetes is increasing worldwide, but more evidently in developing countries. The number of diabetic patients worldwide is projected to rise above 300 million before 2025 (Ganiyu et al., 2012). Current estimates indicate at 69% increase in the number of adults that would be affected by the disease between 2010 and 2030, compared to 20% for developed countries (Shaw et al., 2010). Despite considerable progress in the management of diabetes mellitus by synthetic drugs (insulin injection, oral antidiabetic drugs) and the modification of life style, the number of diabetic patients using medicinal plants for treatment continues to increase. This is due to the prominent side effects of drugs which fail to significantly alter the course of complications related to diabetes (Grover et al ., 2002).

Literature surveys summarize the benefit of several medicinal plants as anti-diabetic agents in the form of crude extracts and/or isolated pure compounds, which exhibit varying degrees of hypoglycemic or antihyperglycemic bioactivities. New drugs are continually being tested to prevent and treat diabetes. In our previously study, our team showed by *in vitro* study that, *Nauclea diderrichii* (barks and leaves) and *Sarcocephalus pobeguinii* (barks) are potent inhibitors of α-glucosidase. This result justifies their popular use for the treatment of diabetes (Agnaniet et al., 2016). There is a need to confirm the activity of these extract using *in vivo* study. Streptozotocin induced diabetes in rats is currently used **(**Hayashi et al, 2006; Takeshika et al 2006; Szkudelski et al, 2011) to demonstrate antidiabetic activity of plant extracts. Therefore the present study was undertaken to evaluate the effects of *Sarcocephalus pobeguinii* (barks), *Nauclea diderrichii* (barks and leaves) on some metabolic parameters in normal and STZ-induced diabetic rats.

Materials and Methods:-

Materials:-

Plant material:-

The samples of plants and extracts from *Nauclea diderrichii* and *Sarcocephalus pobeguinii* were collected and carried out as the procedures previously described by Agnaniet et al, 2016.

Chemicals:-

Streptozotocin was purchased from Sigma-Aldrich Co, USA. Glucose, Cholesterol, triglycerides, total proteins, creatinin, alanine amino-transferase (ALT), aspartate amino-transferase (AST), uric acid, total and direct bilirubin were assayed using commercial Kits from Fortress diagnostics and SGMitalia.

Animals:-

Adult male Wistar rats weighing 150 – 200 g, at the beginning of experiment were obtained from animal house of Faculty of Science, University of Yaounde I, (Cameroon). They were kept in cages at standard conditions: temperature room (25 ± 2 ^{0}C) with alternating 12h light/dark cycle, free access to standard food and water *ad libitum*. All procedures in this study followed the principles of laboratory animal use and care of the "European community" guidelines (EEC Directive 2010/63/EEC) and were approved by the "Animal Ethical Committee" of the Faculty of Science, University of Yaounde I.

Experiments:-

Effect of extracts on blood glucose levels on normal glycaemic rats:-

The hypoglycemic test was performed for 5h in overnight-fasted normoglycemic rats. The rats were divided into fourteen groups of five rats each. Group 1 served as normal control and received distilled water (1mL/100 g B.W). Group 2 positive control, received Glibenclamide 5 mg/kg. Group 3 to 14, received increasing doses of extracts (50, 100, 200 or 400 mg/kg B.W) of extracts from S. p. (E_{10}, groups 3 – 6), N. d. (E_{14}, group 7 – 10; E_{15}, group 11 – 14) suspended in distilled water.

Distilled water (1mL/100 g B.W), Glibenclamide (5 mg/kg) were respectively administered to the normal control (Group 1: NC) and positive control (Group 2: DC). The remaining groups (3-14) received increasing doses (50, 100, 200 or 400 mg/kg) of leaves (E_{14}, group 3-6) and barks (E_{15}, groups 7-10) aqueous extract of *N. diderrichii* and *S. pobeguinii* aqueous extract barks (E_{10}, groups 11-14) respectively. Blood samples were taken from the tail vein respectively before (0 h) and at 1, 2, 3, 4 and 5 h after extracts. The blood glucose levels were mesured using accu check glucometer. Only doses exhibiting hypoglycemic activity were used to screen the antihyperglycemic activity of these plant extracts.

Induction of diabetes Mellitus:-

The animals were acclimated during two weeks in laboratory conditions before experimental work. The healthy animals: albino Wistar rats were acclimated during two weeks in laboratory conditions before experimental work. Then they were fasted overnight for 12 hours. Diabetes mellitus was induced by subcutaneous injection of a single dose of Steptozotocin (55 mg/kg) freshly dissolved in ice citrate buffer (pH 4.5) glucometer and administered subcutaneously to fourty experimental rats. Non diabetic control rats received citrate buffer only, by the same route. Hyperglycemia was confirmed in the streptozotocin-treated rats by measuring (72 h post injection) blood glucose level withdrawn from the vein tail using a glucometer. Only rats in which hyperglycemia had been successfully induced (glucose levels above 250 mg/dL) were kept for 15 days post-injection before the beginning of the experiment to stabilize the hyperglycemic conditions. The rats with fasted blood glucose levels above 250 mg/dL, after this time of stabilisation, were considered to be diabetic and were used in the experiment (Dzeufiet *et al.*, 2006, Kesari et al 2006; Ngueguim *et al*, 2007).

Effects of extract on blood glucose of diabetic rats: The normal and the diabetic rats were each randomly separated into nine groups and each group consisted to five animals: Group 1 and 2 containing normal and diabetic rats respectively received distilled water (10 ml /kg). Group 3 containing diabetic rats, received Glibenclamide (5 mg/kg), representing the positive control. The diabetic others groups 4 to 9 were given 100 and 200 mg / kg of the extracts E_{10}, E_{14} and E_{15} respectively.

Baseline fasting blood glucose levels were initially determined in all the groups. The substances were given for 14 consecutive days. Glucose levels were determined at days 7 and 14. At the end of drugs and plant extracts administration. The rats were fasted for 12 h, sacrificed by decapitation after anesthesia with diethyl ether and blood sample collected in normal tubes. From the clotted blood at room temperature, serum was collected by centrifuging at 3000 g for 10 min to determine the glucose, cholesterol, triglyceride, total protein, creatinin, transaminases, total and direct bilirubin and uric acid levels. Organs such as aorta, heart, liver and kidney were dissected out and washed in ice saline solution to remove the blood., Homogenate (20 %) of each organ was prepared using Tris-HCl buffer 50 mM (pH 7.4). Mc Even solution was used for the aorta and heart homogenates. The mixture obtained was centrifuged at 3500 g for 25 min at 4^0C. The resulting supernatant were separated for the evaluation of some parameters of oxidative stress (superoxide dismutase, catalase activities; reduced glutathione and nitrite concentrations).

Statistical analysis: Results are expressed as the mean ± SEM. Statistical differences between control and treated group were tested by one way analysis of variance (ANOVA) followed by Tukey's test using GraphPad Prism, version 5.00 (Trial). *P* values less than 0.05 were considered to be significant.

Results:-

Effects of extract blood glucose levels of normal rats:-

Table 1 shows the results of blood glucose monitoring performed for five hours (5 hours). At the doses of 50 and 100 mg/kg, no diminution of blood glucose levels was observed. At dose 200 and 400 mg/kg, a significant decrease of blood sugar is observed respectively from 3and 4hours after administration of extracts until the end of experiment. Thus, 200 and 400 mg/kg are more active than others.

Effects of repeated administration of extracts on blood glucose levels on normal and STZ-induced diabetic rats:-

The variation of blood glucose levels in the experimental rats are given in table 2. After seven days of treatment, there is a significant reduction of blood glucose in some groups of diabetic rats receiving treatment. Among these groups, the extracts E_{14} at the doses 100 and 200 mg / kg and E_{15} at the dose 200 mg/kg have shown a fall of 78.71%, 73.22% and 65.34% of blood glucose respectively as compared to the initial value (early treatment). Whereas the Glibenclamide induced a non-significant decrease in blood glucose levels (7.67%). However after

fourteen days of administration extracts and Glibenclamide, the different groups of rats have shown a significant decrease of glycaemia by 53.95%, for E_{10} (100 mg/kg), 81.85%, 78.19% for E_{14} (100 and 200 mg/kg), 69.16% for E_{15} (200 mg/kg) and 71.31% for Gliben (5 mg/kg).

During the 7 and 14 days of treatment with 3 extracts (E_{10} at 100 mg/kg, E_{14} at 100 and 200 mg/kg and E_{15} 200 mg / kg), the diabetic rats had improvement in the normalization of the blood glucose levels. Irrespective of de sampling days, E_{14} (100 and 200 mg/kg) showed a better antidiabetic action, respectively by 81.85 and 78.19% than the Glibenclamide (71%). E_{15} at the dose of 200 mg/kg had the comparable reduction (69.16) with Glibenclamide (71.36). Whereas, E_{10} at the dose of 200 mg/kg and E_{15} at dose 100 mg/kg appeared weaker (22.90 and 20.05% respectively. After one to two weeks of treatment with the E_{10} (100 mg/kg), the E_{14} (100 and 200 mg / kg) and the E_{15} (200 mg / kg), the blood glucose levels returned to normal indicating that the hypoglycemic effect of the plant extracts, in the case of *N. diderrichii* (leaves), is achieved through repeated and not single administration.

Effects of the extracts on some biochemical parameters of normal an STZ-induced diabetic rats Lipid profile:-

Studies on lipid profile (Table 3) at the end of 14th days of the treatment with the aqueous extracts were compared with that of the diabetic control group. There was no significant change in total cholesterol and HDL-cholesterol in the diabetic rats. However significant increase was observed in triglycerides concentration as compared to normal control. When different extracts were administered, a significant decrease of triglycerides was observed with E_{10}at the doses of100 mg/kg ($p < 0.01$), 200 mg/kg ($p < 0.05$) and withE_{15}at the dose of100 mg/kg ($p < 0.05$). E_{14} failed to reduce triglycerides concentration at all doses. The administration of streptozotocin also provoked a significant increase in the LDL-cholesterol concentration. The extract E_{15} at the doses of 100 and 200 mg/kg significantly decreased ($p < 0.001$) LDL-cholesterol while E_{10} at the dose of 100 mg/kg and E 14 at the dose of 200 mg/kg). Thus,E_{10} and E_{15} were more active than $E_{14.}$ Glibenclamide used in the same conditions as plant extracts significantly reduced LDL-cholesterol but failed to change other parameters.

Change in total protein, creatinin, bilirubin, transaminases and uric acid:-

Table 4 shows the effects of different extracts on some parameters of liver and kidney functions. At the end of the experimental period, various plasmatic parameters were measured in all groups.There was a significant increase ($p < 0.001$) in ALT, AST activities and creatinin concentration as compared to normal control. However, the serum total proteins, total bilirubin, direct bilirubin and uric acid remain ($p > 0.05$) unchanged when compared to normal control rats. Streptozotocin injection induced about three times the levels of transaminases in diabetic group. After administration of different treatments, significant changes were observed: ALT activity was reduced by E_{10} ($p < 0.01$) at both doses, E14 reduced the ALT activity at doses of 100 ($p < 0.05$) and 200 mg/kg ($p < 0.01$) and E_{15} at the dose of 100 ($p < 0.001$) and 200 mg/kg ($p < 0.01$). Parallel, AST activity was reduced by E_{10} at both doses ($p < 0.05$); by E_{14} at the doses of 100 ($p < 0.01$), 200 mg/kg ($p < 0.05$) and by E_{15} at both doses ($p < 0.01$). E_{10} andE_{14} extracts also provoked a significant decrease ($p < 0.001$), in creatinin at both doses even E_{15} at the dose of 100 ($p < 0.05$) and 200 mg/kg ($p < 0.01$). Total Proteins and biluribin, direct biluribin and uric acid levels remained unchanged.

Effects of different plant extracts on some parameters of oxidative stress:-

Streptozotocin administration to animals induced variations in some parameters of oxidative stress (Fig1.) depending to the organ. In SOD activity (Fig. 1A) there was a significant increasein aorta ($p<0.05$) contrary to the heart, liver and kidney where SOD activity was no significant. The plant extract E_{14} at the dose of 200 mg/kg administered for two weeks, provoked a significant increase in the SOD activityin the aorta while the smallest dose significantly reduced this parameter in the heart. The extract E_{15} at all doses failed to reduce SOD activity in organs investigated. On other hand, diabetic rats showed a significant increase in the catalase concentration (Fig. 1B) only in the aorta. The extract E_{14} and E_{15} at all doses significantly reduced ($p<0.001$) catalase concentration in the aorta as compared to the diabetic control. These extract also reduced catalase concentration in other organs whenever non-significant. There was no variation in GSH concentration in diabetic rat's organs (Fig. 1C). At the dose of 200 mg/kg, only the extract E_{15}, induced a significant reduction in GSH concentration in the kidney as compared to the diabetic control. A unique dose of streptozotocin (55 mg/kg) was associated with an increase in nitrites ($p>0.05$) in aorta, heart and liver (Fig. 1D). The increase levels of nitrites were attenuated by two weeks administration of the extract E_{14} at the dose of 200 mg/kg and E_{15} by both doses. Glibenclamide (5 mg/kg) used as reference drug in the same conditions as the extracts, failed to reduced GSH and nitrites concentration in all organs but significantly reduced SOD activity and catalase concentration in the aorta.

Discussion:-

The activity of three plant extracts used in Gabonese traditional medicine to manage diabetes was investigated in the present study. The results indicated that *Sarcocephalus pobeguinii* aqueous bark (E_{10}) extract, *Nauclea diderrichii* aqueous leaf (E_{14}) and bark (E_{15}) extracts reduced the glucose levels in normal rats .E_{14} showed the lowest activity on blood sugar in normoglycemic rats. At equal dose (200 mg/kg), E_{15} extract was more potent than E_{10} extract because of the ability of the former to significantly reduce blood glucose levels 3hours post-dosing. However the effect of Glibenclamide used as reference drug was better than that of the extracts.The results also revealed that E_{15} (200 mg / kg) was more active than E_{15} (400 mg / kg), we can therefore say that the hypoglycemic effect of this extract is optimal at moderate doses. Moreover, these results allowed not only to know the more potent extract with hypoglycemic effect but, also to select the doses to use in the evaluation of anti-diabetic activity on streptozotocin-induced diabetic rats. Agnaniet et al., 2016 have shown that *Sarcocephalus pobeguinii* (barks) *Nauclea. Diderrichii* (leaves and barks) could be used to manage diabetes state due to their capacity to inhibit α-glucosidase activity. In this study the administration of this different extracts for two weeks to streptozotocin induced-diabetic rats have shown a decrease in blood glucose levels towards normal value at the dose of 100mg/kg with E_{14} extract one week post-administration. Parallel, E_{15} and E_{10} did not bring the glycaemia towards normal value even the treatment was continuing up to two weeks. These results suggest that, E_{14} extract is more potent that E_{10} and E_{15} in diabetic state. Since in acute treatment E_{15} was the most potent extract and E_{14} was the most potent extract in antidiabetic activity we can therefore say that, there is no correlation between hypoglycemic effect and antidiabetic activity. This allows us to suppose that the mode of action of the extracts is not the same.

Phenolic compounds have shown to possess a strong capacity to improve diabetic state. (Gandhi et., 2011; Yao et al., 2012). We can therefore attest that the hypoglycemic effect induced by E_{14} extract could be result to the presence of these secondary metabolites in the extract (Agnaniet et al., 2016). Alkaloids (Adeneye et al., 2012; Kwon et al, 2017) and saponins (Gao et al., 2016) also present in this extract are known for their hypoglycaemic activity. Taking together these observations, different secondary metabolites present in E_{14} extract act synergycally to induce the observed hypoglycemia activity. The hyperglycemia observed in diabetes conditions is accompanied by the lipid metabolism disorders characterized by an elevation in triglycerides, total cholesterol, LDL-cholesterol and a decrease in HDL-cholesterol. (Cam et al., 1993; Pari and Saravanan, 2002).The administration of plant extracts improved the lipid profile of diabetic rats probably due to their hypoglycemic effect. ALT and AST are key metabolic enzyme makers for liver function.The increase in these two parameters indicates hepatotoxicity which is related to glucose induce-oxidative stress (Poitout and Robertson, 2002). Infact, hyperglycemia induced autoxidation of glucose which in turn generates reative oxygen species, attacks cells and compromised membrane function thus caused leakage of these enzymes into the blood stream (Lery et al., 1999).The improvement of these enzymes by the extracts could be attributed to the presence in these extracts of triterpenes, flavonoids and phenols which are known to have an antioxidant activities (Montilla et al., 2003; Hennebele et al., 2004; Rodrigues et al, 2005). STZ induced-diabetic rats provoked a creatinemia suggesting the increase in muscular activity which was reversed by the plant extracts at all doses. In this study, permanent hyperglycemia provokes inbalance of antioxidant defence system characterized by an increase in SOD, catalase, GSH and NO mainly in the aorta. This increase attests the present of free radicals. However, the administration of the plant extract reduced these different parameters showing that E_{14} extract was the best extract to reduce oxidative stress.

In conclusion, *Sarcocephalus pobeguinii* (barks) and *Nauclea diderrichii* (barks and leaves) extracts could lower blood glucose levels in normal and diabetic rats. *Nauclea diderrichii* leaves (E_{14}) was the most potent extract than E_{10} and E_{15}. These extracts prevented the increase in serum ALT, AST, creatinin of diabetic rats; improved lipid profile, liver functions by decreasing ALT and AST levels. More studies still to be done to isolate the active principles and to determine clearly the action mechanisms of these extracts.

Table 1:-Effects of single administration of *Nauclea diderrichii* (E_{14} and E_{15}) and *Sarcocephalus pobeguinii*(E_{10}) on blood glucose levels in normal rats

Treatment	Doses (mg /kg)	Blood glucose levels (mg/dL)					
		0h	1h	2h	3h	4h	5h
DW	10	73.25 ± 1.29	84.25 ± 1.63	72.25 ± 2.27	72.5 ± 3.28	84.75 ± 3.83	79.5 ± 2.46
		73.50 ±	51.50 ±	37,5 ±	34.25 ±	34 ±	34 ± 1.27***

Gliben	5	1.67	6.86**	0.82***	1.13***	0.61***	
E_{10}	50	74.5 ± 2.30	81.25 ± 3.37	72.5 ± 1.43	78.25 ± 0.96	84.75 ± 3.32	82.75 ± 3.47
	100	72.25 ± 3.83	85 ± 5.35	84.75 ± 3.87*	88.25 ± 2.72**	90.25 ± 4.96	86.5 ± 3.32
	200	74.25 ± 7.84	80.5 ± 3.09	75.25 ± 1.55	65.5 ± 1.25	59.5 ± 0.90***	54.5 ± 0.81***
	400	70.25 ± 0.96	73.75 ± 2.96	61.5 ± 2.38	58.5 ± 0.43**	49.25 ± 1.9***	47.75 ± 2.10***
E_{14}	50	74.25 ± 1.88	76.75 ± 3.10	69.5 ± 2.83	72.5 ± 4.72	83 ± 2.26***	80.5 ± 0.55
	100	73.25 ± 3.20	76 ± 4.06	80.25 ± 1.63*	74 ± 1.45	82.75 ± 2.53	75.5 ± 2.61
	200	65.5 ± 2.51	70.5 ± 2.51	66.25 ± 1.70	74 ± 1.27	73.75 ± 0.81	73.25 ± 0.89
	400	67 ± 0.96	68.25 ± 1.98	68.5 ± 1.47	68 ± 0.61	62.5 ± 1.43***	47.75 ± 2.10***
E_{15}	50	73 ± 2,03	91 ± 3,90	85.75 ± 2.10*	83.25 ± 4.27	100.2 ± 4.57	82.75 ± 3,9
	100	72 ± 3,35	80.5 ± 2.41	72 ± 3.75	77 ± 7.35	85.75 ± 3.74	72.75 ± 6.57
	200	69.25 ± 5.45	64.5 ± 3.28	62.25 ± 3.64	50.5 ± 0.55*	47.5 ± 1.34***	45.25 ± 1.13***
	400	67.75± 2.19	69.25 ± 3.20	66.5 ± 1.29	52.50± 1.34*	54.75 ± 3.54***	53.00± 3.7**

Each value represents means ± SEM, n = 5, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$as compared with control at the same time;Gliben:glibenclamide; E_{10}: aqueous extract of *S. pobeguinii* (barks); E_{14}:aqueous extract of *N. diderrichii* (leaves);E_{15}: aqueous extract of *N. diderrichii* (barks); DW: distilled water

Table 2:- Effects of repeated administration of extracts on blood glucose levels in STZ-induced diabetic rats.

		Blood glucose levels (mg/dL)				
Treatment	Doses	Day 0 (D0)	Day 7 (D7)	% variation D7	Day 14 (D14)	% variation D14
N.C	10ml/kg	59.50 ± 0.28	59.75 ± 0,47	-0.42	58.25 ± 2.810	2.10
D.C	10 ml/kg	399.5 ± 37.05	442.3 ± 48,65	-10.71	348.3 ± 12,34	12.81
Gliben	5 mg/kg	354.5 ± 28.42	327.3 ± 52,28	7.67	101.5 ± 15.93***	71.36
E_{10}	100 mg/kg	337 ± 17.34	441 ± 28.00	-30.86	155.5± 38.54***	53.95
E_{14}	200 mg/kg	466.66 ± 44.77	436 ± 3.00	6.57	359.75± 14.63	22.90
	100 mg/kg	478 ± 16.00	101.75 ± 1.65***	78.71	86.75± 5.64***	81.85
	200 mg/kg	412.75 ± 20.81	110.5 ± 7.32***	73.22	90± 8.45***	78.19
E_{15}	100 mg/kg	400 ± 37.84	349.8 ± 18,38	12.55	299.8 ± 77.68	25.05
	200 mg/kg	393.3 ± 28.62	136.3 ± 24.63***	65.34	121.3 ± 7.718**	69.16

Each value represents means ± SEM, n = 5, $^{**}p < 0.01$, $^{***}p < 0.001$as compared with diabetic control. Distilled water: NC; Distilled water: D.C ; Glibenclamide :Gliben ;*S. pobeguinii* barks :E_{10} ; *N diderrichii* Leaves:E_{14};*N. diderrichii* barks :E_{15}

Table 3:- Effect of the tree extracts on lipid profile of normal and STZ-induced diabetic rats.

Treatment	Doses	Parameters			
		T. Chol (mg/dL)	**Triglycerides (mg/dL)**	**HDL-Chol (mg/dL)**	**LDL-Chol (mg/dL)**
N.C	10ml/1kg	35.13 ± 6.28	24.22 ± 1.49	19.44 ± 3.18	9.52 ± 6.22
D.C	10 ml/100g	37.58 ± 7.42	61.43 ± 1.28*	22.24 ± 2.57	31.48 ± 3.21***
Gliben	5 mg/kg	31.55 ± 4.87	52.02 ±22.74	17.35 ± 0.86	7.7815 ± 3.07***
E_{10}	100 mg/kg	30.69 ± 2.70	16.95 ± 0.73**	21.09 ± 0.56	6.20 ± 2.11***
	200 mg/kg	42.08 ± 0.95	22.71 ± 9.18*	16.41 ± 2.19	21.12 ± 1.39
E_{14}	100 mg/kg	64.18 ± 4.69**	61.06 ± 15.55	26.13 ± 2.21	25.84 ± 3.49#
	200 mg/kg	46.25 ± 2.41	47.65 ± 10.65	22.35 ± 0.80	14.36 ± 2.34*
E_{15}	100 mg/kg	26.01 ± 1.74	24.51 ± 4.41*	19.76± 2.48	7.13 ± 0.46***
	200 mg/kg	31.39 ± 1.35	30.78 ± 7.58	17.81 ± 0.58	7.30 ± 0.85***

Each value represents means ± SEM, n = 5, $^{*}p < 0.05$, $^{**}p < 0.01$compared with diabetic control. $^{\#}p < 0.05$ as compared with normal control.Distilled water:N.C;Distilled water:D.C ; Glibenclamide :Gliben ;*S. pobeguinii*barks :E_{10} ;*N diderrichii* Leaves:E_{14};*N. diderrichii* barks :E_{15}

Table 4:- Effect of the tree extracts on some parameters of kidney and liver functions of STZ-induced diabetic rats.

Treatment	Doses	Parameters						
		Proteins (mg/dL)	**Crea (mg/dL)**	**T. Bil (mg/dL)**	**D. Bil (mg/dL)**	**ALT (U/I)**	**AST (U/I)**	**Uric acid (mg/dL)**
N.C	10ml/1kg	12.74 ± 0.11	1.55 ± 0.71	0.90 ± 0.01	0.40 ± 0.12	46.89 ± 9.47	63 28± 10 72	1.02 ± 0.15
D.C	10 ml/100g	9.76 ± 0.45	7.14 ± 09###.	0.79 ± 0.01	0.40 ± 0.03	167.9 ± 26.28###	193.5 ± 2.63###	2.00 ± 0.21
Gliben	5 mg/kg	10.43 ± 0.18	1.47 ± 0.51***	1.17 ± 0.05	0.60 ± 0.11	59.41 ±29.76*	113.7 ± 13.74*##	1.75 ± 0.15
E_{10}	100 mg/kg	10.80 ± 0.49	2.64 ± 0.76***	0.75 ± 0.01	0.40 ± 0.14	57.81 ± 3.14**	120.0 ± 5.22*##	2.50 ± 0.38
	200 mg/kg	10.58 ± 0.10	1.91 ± 0.26***	0.99 ± 0.02	0.38 ± 0.05	81.95 ± 0.89**	146.5± 22.75*##	2.14 ± 0.41
E_{14}	100 mg/kg	13.61 ± 0.89	0.77 ± 0.07***	0.91 ± 0.03	0.21 ± 0.02	90.76 ± 28.60*	74.72 ± 10.20**	1.30 ± 0.08
	200 mg/kg	12.11 ± 1.71	1.97 ± 0.59***	1.00 ± 0.01	0.25 ± 0.01	75.59 ± 3.42**	128.4 ± 46.19*	1.22 ± 0.12
E_{15}	100 mg/kg	8.90 ± 0.35	3.96 ± 0.67*	0.85 ± 0.06	0.50 ± 0.07	32.59 ± 7.68***	76.78 ± 6.54**	0.97 ± 0.03
	200 mg/kg	10.26 ± 0.63	1.65 ± 0.59**	1.01 ± 0.02	0.61 ± 0.07	87.45 ± 33.94**	119.6 ± 2.16**	2.06 ± 0.30

Each value represents means ± SEM, n = 5, $^{*}p< 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$as compared with diabetic control. $^{\#\#}p < 0.01$,$^{\#\#\#}p < 0.001$as compared with normal control. Distilled water:NC; Distilled water: D.C ; Glibenclamide :Gliben ;*S. pobeguinii* barks :E_{10} ;*N diderrichii* Leaves:E_{14};*N. diderrichii* barks :E_{15}

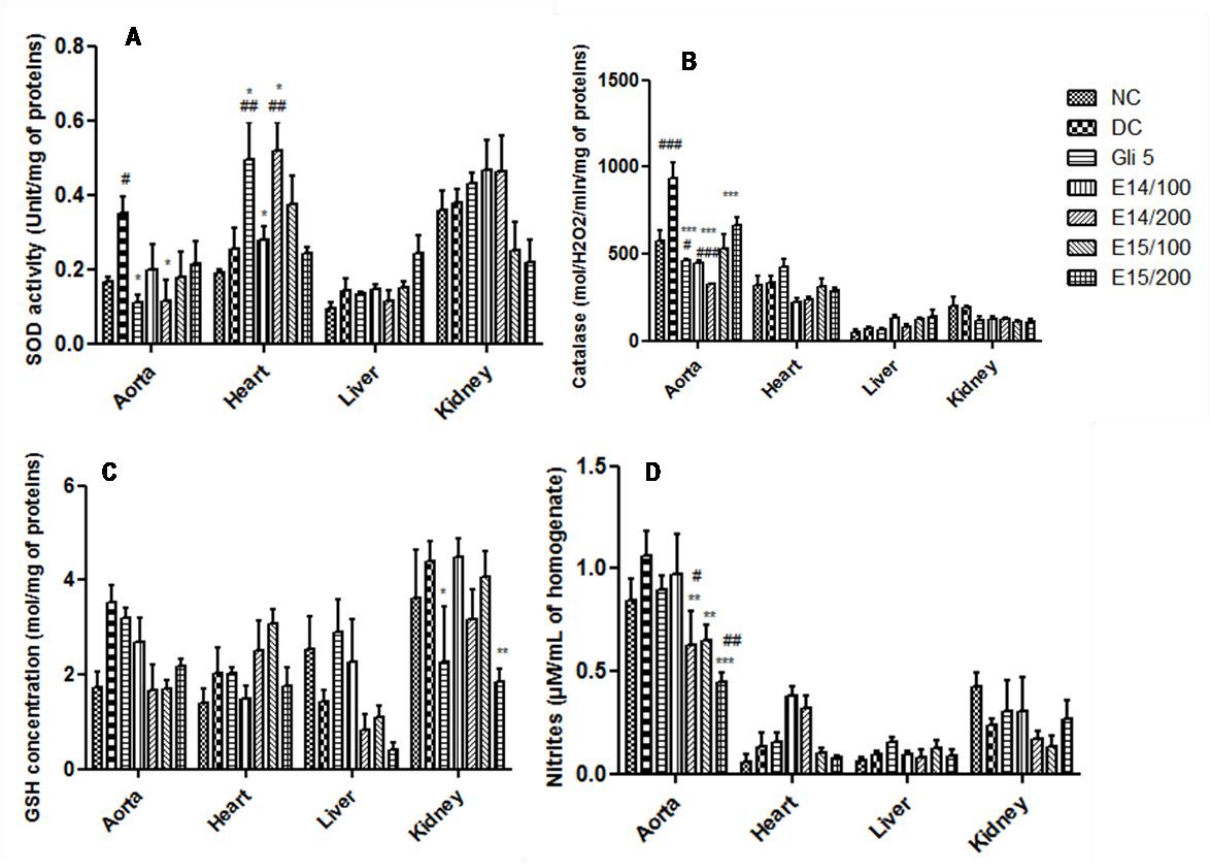

Figure 1:-Effects of the aqueous extract of *Sarcocephalus pobeguinii* and *Nauclea diderrichii* on SOD activity (A), catalase activity (B), reduced glutathione (C) and Nitrites (D) concentrations;
Each bar represents means ± SEM, n = 5, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$as compared with diabetic control. $^{\#}p < 0.05$, $^{\#\#}p < 0.01$ $^{\#\#\#}p < 0.001$as compared with normal control. E_{14}: *N diderrichii* Leaves (100 and 20 mg/kg); E_{15} *: N: diderrichii* barks (100 and 20 mg/kg) :

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