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ABSTRACT

Free radicals have been implicated in the pathogenesis of diabetes mellitus leading to various complications including atherosclerosis. Kigelia africana is highly used for ethnomedical purposes although there is paucity of scientific information on its uses. This study is designed to investigate the possible anti diabetic and anti oxidative effects of methanol extract of leaf and fruit of k. africana. Diabetes was induced with alloxan in a dose of 160mg b.wt. i. P. After 4 weeks of treatment, diabetic rats untreated (positive control) showed an apparent reduction in the body weight, significant increase in the blood glucose level, triacyglycerol (TG) total cholesterol and low density lipoprotein cholesterol (LDLC) with corresponding decrease in serum high density lipoprotein-cholesterol (HDLC) as compared to the normal control. In addition, there was significant deviation of lipid peroxide measured as malondialdehyle (MDA), with masked reduction in serum Glutathione Peroxidase activity, SOD, CAT and Vitamin C concentration. On the other hand, oral daily treatment of animal with K. africana in a dose of 200mg/kg bwt for the period of 4 weeks ameliorated alloxan-induced alterations in the animal body weight as well as blood glucose, MDA, lipid profile, activities of SOD, GPx and CAT. In conclusion, K. africana extract offers promising results mainly could be attributed to its potent antioxidant potential. Further studies will be required in future to determine which one (or more) of its active constituent has the main antidiabetic and antioxidative effects.

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ABSTRACT

Free radicals have been implicated in the pathogenesis of diabetes mellitus leading to various complications including atherosclerosis. Kigelia africana is highly used for ethnomedical purposes although there is paucity of scientific information on its uses. This study is designed to investigate the possible anti diabetic and anti oxidative effects of methanol extract of leaf and fruit of k. africana. Diabetes was induced with alloxan in a dose of 160mg b.wt. i. P. After 4 weeks of treatment, diabetic rats untreated (positive control) showed an apparent reduction in the body weight, significant increase in the blood glucose level, triacylglycerol (TG) total cholesterol and low density lipoprotein cholesterol (LDLC) with corresponding decrease in serum high density lipoprotein-cholesterol (HDLC) as compared to the normal control. In addition, there was significant deviation of lipid peroxide measured as malondialdehyde (MDA), with masked reduction in serum Glutathione Peroxidase activity, SOD, CAT and Vitamin C concentration. On the other hand, oral daily treatment of animal with K. africana in a dose of 200 mg/kg bwt for the period of 4 weeks ameliorated alloxan-induced alterations in the animal body weight as well as blood glucose, MDA, lipid profile, activities of SOD, GPx and CAT. In conclusion, K. africana extract offers promising results mainly could be attributed to its potent antioxidant potential. Further studies will be required in future to determine which one (or more) of its active constituent has the main antidiabetic and antioxidative effects.

Keywords: diabetes, alloxan, antioxidant, kigelia africana.

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I. INTRODUCTION

Diabetes mellitus is a metabolic disorder resulting from a defect in insulin secretion, insulin action or both. Insulin deficiency in turn leads to chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism [1]. During diabetes or insulin resistance, failure of insulin-stimulated glucose uptake by fat and muscle cause glucose concentration in the blood to remain high, consequently glucose uptake by insulin-independent tissue increases. Increased glucose flux both enhances oxidant production and impairs antioxidant defenses by multiple interacting non-enzymatic, enzymatic and mitochondrial pathways [2, 3]. These include activation of protein kinase C isoforms [4], increased hexosamine pathway [5], glucose autoxidation [6], increased methylglyoxal and advanced glycation end-product (AGEs) formation [7] and increased polyol pathway flux [8]. These seemingly different mechanisms are the results of a single process-that is, overproduction of

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superoxide by the mitochondrial electron transport system [9]. This hyperglyceamic-induced oxidative stress ultimately results in modification of intracellular proteins resulting in an altered function, DNA damage, activation of the cellular transcription (NF KB), causing abnormal changes in gene expression, decreased production of nitric oxide, and increased expression of cytokines, growth factors and procoagulant and proinflammatory molecules [10, 11, 2, 12].

Oxidative stress is responsible for molecular and cellular tissue damage in a wide spectrum of human diseases [13], amongst is diabetes mellitus. Diabetes produces disturbances of lipid profiles, especially an increased susceptibility to lipid peroxidation [14], which is responsible for increased incidence of atherosclerosis [15], a major complication of diabetes mellitus. An enhanced oxidative stress has been observed in these patients as indicated by increased free radical production, lipid peroxidation and diminished antioxidant status [16].

Globally, the estimated incidence of diabetes and projection for year 2030, as given by International Diabetes Federation is 350 million [17]. Currently available pharmacotherapies for the treatment of diabetes mellitus include oral hypoglycemic agents and insulin. However these drugs do not restore normal glucose homeostasis and they are not free from side effects [18]. In view of the adverse effects associated with the synthetic drugs and as plants are safer, affordable and effective, conventional antidiabetic plants can be explored [19]). Over 400 traditional plants have been reported for the treatment of diabetes [20]. Furthermore, following World Health Organization recommendations, investigation of hypoglycemic agents from medicinal plants has become more important [19].

Kigelia africana (Lam.) Benth (Family: Bignoniaceae) plant has many medicinal properties due to the presence of numerous secondary metabolites. Crude extracts of herbs and spices and other materials rich in phenolics are of increasing interest in the food industry because they retard oxidative degradation of lipids and thereby improve the quality and nutritional value of food. Flavonoids are groups of polyphenolic compounds with known properties, which include free radical scavenging, inhibition of hydrolytic and oxidative enzymes and anti-inflammatory action [21].

Due to paucity of scientific documentation on anti-diabetic properties of the plant, it is therefore the aim of the study to explore anti-diabetic and antioxidative potential of Methanol extracts the plant.

II. MATERIALS AND METHOD

Plant Materials: The leave and fruit of *Kigelia africana* were collected from Omor, Ahamelu Local Government Area, Anambra State, Nigeria. The plant was authenticated by the Department of plant Science and Biotechnology University of Nigeria Nsukka.

Chemicals: All the used chemicals were of the highest analytical grades commercially available.

Extraction of the Plant Material: The leaves and fruits of *K. africana* were air-dried at room temperature for after which it was grounded into powders. A quantity of 500mg each of the powdered leaves and fruits of *K. fricana* macerated in 2 litres of Methanol for 72h. The solution was filtered with whatman no 4 and concentrated using rotary evaporator.

Animals: Male Wistar Albino rats between 12 to 14 weeks of age, with average weight of 108±5 g were obtained from the Department of Zoology, University of Nigeria Nsukka. They were housed in the animal facilities of Department of Home Science and dietetics, University of Nigeria, Nsukka for one week before starting the experiment. The animals were allowed free access to standard diet, water and maintained under optimum conditions of temperature, relative humidity and light period. (12h light/12h dark).

Induction Of Diabetics: The rats were fasted (12h) prior to injection of alloxan dissolved in cold citrate buffer (pH. 45) in a dose of 160 mg/kg intraperitoneally. The baseline blood glucose level was determined before the induction. On the fourth day blood samples were taken from the tail vein to measure the blood glucose level using Accu-check glucose meter. Rat with blood glucose level of 200 mg/dl and above were considered diabetic and used for the study.

The treatment was for a period of 4 weeks in which the bloods obtained were used for parameters analysis.

Experimental Design: Thirty (30) male Wistar albino rats with average weight of 108±5g were classified into 6 groups (5 rats per group) and subjected to treatment as follows.

Group i: Normal control rats.

Group ii : Diabetics untreated rats.

Group iii: Diabetic rats treated 2.5mg/kg bwt glibenclamide

Group iv: Diabetics rats treated with 500 mg/kg btw methanol leaf extracts.

Group v: Diabetic rats treated with 500 mg/kg btw methanol fruit extracted.

Group vi: Diabetic rats treated with equal ratio of methanol leaf and fruit extracts.

At the end of the experiment, rats were starved for 12h and blood glucose levels were determined. Blood samples were received into clean dry centrifuge tubes and use for the analysis of the parameters.

Estimation of the Chosen Biochemical Parameters: All the chosen biochemical and oxidative parameters were estimated using bio-diagnostic kits and the procedures were strictly followed as outlined in the manual guide.

Statistical Analysis: Results were reported as mean± SEM, where appropriate. Both one-and two-way analysis of variance (ANOVA) were used to analyse the experimental data and Bucan multiple test rage was used to compare the group means obtained after each treatment with control measurement. Difference were considered significant where $p < 0.05$.

IV. RESULTS

4.1 Qualitative Phytochemical Composition of Methanol Leaf and Fruit Extracts of K. africana

Table1. Shows relative trace presence of saponin and terpenoids in all the extract samples. In the same vein, hydrogen cyanide and steroid were found to be present in trace concentrations. Relative moderate amount of soluble carbohydrates was found in all the extracts. Interestingly, flavonoid was found in high concentration in the extracts.

Table 1: Qualitative phytochemical composition of methanol leaf and fruit extracts of *Kigelia africana*

Extract	Soluble carbohydrate	Tannin	lAkaloid	Hydrogen cyanide	Saponin	Flavonoid	Reducing sugar	Steroid	Glycoside	Tepenoid
Methanol fruit	++	+++	++	+	+	+++	+++	+	++	+
Methanol leaf	++	+++	++	++	+	++	++	++	++	+

NB

\+ Present in trace concentration

++ Present in moderately high concentration

+++ Present in very high concentration

4.2 Quantitative Phytochemical Composition of Methanol Leaf and Fruit Extracts of Kigelia africana

Table 2 shows the quantitative composition of bioactive compounds present at various concentrations. Significant increase of flavonoid methanol compared with the leaf extracts. Trace concentration of hydrogen cyanides was found in the extracts. All the extracts contained moderate concentration of alkaloid. High tannin level was equally recorded.

Table 2: Quantitative Phytochemical Composition of Methanol Leaf and Fruit Extracts of *K. africana.*

Table 2: Quantitative Phytochemical Composition of Methanol Leaf and Fruit Extracts of *K. africana.*

Extract	Soluble carbohydrate (mg/100g)	Tannin (mg/100g)	Alkaloid mg/100g	Hydrogen cyanide mg/100g	Saponin mg/100g	Flavonoid mg/100g	Reducing sugar (mg/100g)
Methanol leaf	1.44±0.05	10.31±0.42	3.12±0.11	0.29±0.04	0.52±0.01	2.84±0.01	26.67±1.02
Methanol fruit	1.92±0.25	10.87±0.22	3.21±0.13	0.91±0.01	0.53±0.01	3.36±0.02	20.35±1.01

4.3 Percentage Proximate Composition of Leaf and Fruit Extracts of K .africana

The percentage proximate composition of *K. africana* was shown on the Table 3. *K. africana* leaf demonstrated high percentage protein concentration compared with the fruit. Relative percentage of fibre content was found. Carbohydrates concentration was high in fruit as against leaf

Table 3: Percentage Proximate Composition of Leaf and Fruit Extracts of *K. africana*

	Moisture (%)	Ash (%)	Fats (%)	Fibre (%)	Protein (%)	Carbohydrate (%)
Leaf	5.5	2.7	11.4	2.2	13.9	63.5
Fruit	5.1	1.8	3.7	1.3	10.4	77.5

4.4 Effects of Methanol Extracts of Leaf and Fruit of K. africana on Sugar Level of Diabetic Rats

The sugar levels of rats before the experiment in all groups were found to be non-significant ($p>0.05$) compared with the sugar level of group 2 rats (diabetic untreated) as shown in Table 4. At day 21, a significant increase ($p<0.05$) was also observed in the sugar level of rats in all groups compared with the sugar level of rats in group 2 (diabetic untreated). There was no significant ($p>0.05$) variation in the sugar level of rats in group 1 (normal control) at 72 hours after induction and day 21 after treatment compared with the sugar level before the induction. On the other hand, the sugar level of rats in group 4 significantly increased ($p<0.05$) at 72 hours after induction.

Table 4: Effect of Methanol Extracts of Leaf and Fruit of *K. africana* on sugar level of Diabetic Rats

Treatment Groups	Sugar Level (mg/dl)		
	Before Induction	72 Hours After Induction	After 21 Days Treatment
Group 1 (Normal Control)	76.20 ± 5.02^{ab}	78.80 ± 2.71^{ab}	75.40 ± 4.22^{ab}
Group 2 (Diabetic Untreated)	67.40 ± 3.50^{ab}	$558.40\pm14.01^{ac*}$	$405.40\pm15.96^{ac*}$
Group 3 (Standard Control)	66.40 ± 3.91^{ab}	$321.00\pm115.16^{ab*}$	$241.20\pm116.79^{ab*}$
Group 4 (Diabetic + Methanol Leaf Extract)	69.80 ± 10.37^{ab}	$393.00\pm150.16^{ab*}$	163.80 ± 68.81^{ab}
Group 5 (Diabetic + Methanol Fruit Extract)	64.00 ± 5.33^{ab}	$467.60\pm122.21^{ac*}$	$185.80\pm53.60^{ab*}$
Group 6 (Diabetic + Methanol Leaf and Fruit Extract)	66.60 ± 12.73^{ab}	$342.40\pm121.43^{ab*}$	$219.80\pm131.40^{ab*}$

Results are expressed in mean ± SD; n = 5

Mean values with different letters as superscripts across the column compared with group 2 (diabetic untreated) are considered significant ($p<0.05$) while mean values with asterisk (*) as superscripts across the row compared with the sugar level before the experiment are considered significant ($p>0.05$)

4.5 Body Weights of Diabetic Rats Treated with Methanol Extracts of Leaf and Fruit of K. africana before and after Experiment

Significant ($p<0.05$) increases in the body weight of group 1 rats (normal control) and diabetic rat in groups 4 and 5 treated with methanol leaf and methanol fruit extracts of *K. africana* respectively after experiment compared with that obtained before the experiment. Conversely, non-significant ($p>0.05$) decrease was observed in the body weights of the animals in other groups after the experiment compared with the body weights of the animals before the experiment (Table 5).

Table 5: Body weights of Diabetic Rats treated with Methanol Extracts of leaf and fruit of *K. africana* before and after experiment

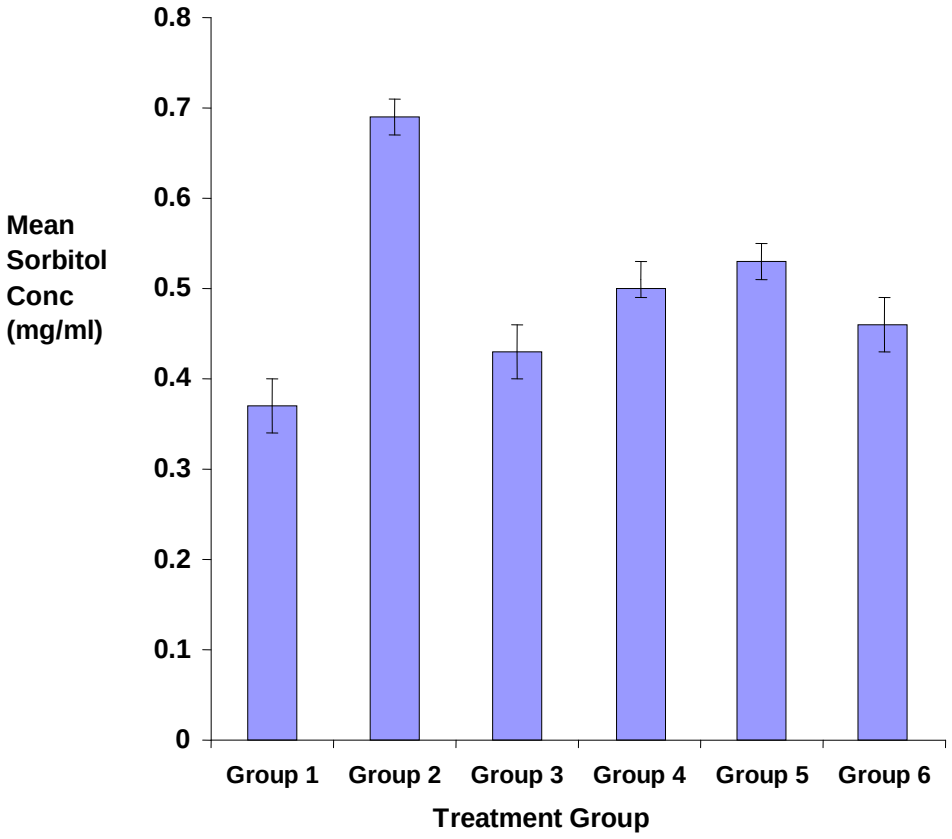
Treatment Groups	Body Weight (g)	
	Before Experiment	After Experiment
Group 1 (Normal Control)	92.59 ± 5.87^{ab}	130.36 ± 17.83^{ac}
Group 2 (Diabetic Untreated)	173.66 ± 12.24^{aa}	156.16 ± 13.14^{aa}
Group 3 (Standard Control)	94.58 ± 5.80^{aa}	107.34 ± 18.41^{aa}
Group 4(Diabetic + Methanol Leaf Extract)	81.40 ± 4.45^{ab}	112.44 ± 13.83^{ac}
Group 5 (Diabetic + Methanol Fruit Extract)	75.38 ± 605^{ab}	101.38 ± 17.57^{ac}
Group 6 (Diabetic + Methanol Leaf and Fruit Extract)	70.29 ± 4.42^{ab}	90.06 ± 18.75^{aa}

Results are expressed in mean ± SD; n = 5

Mean values with different letters as superscripts across the row are considered significant ($p<0.05$)

4.6 Effects of Methanol Leaf and Fruit Extracts of K. africana on Sorbitol Concentration in Alloxan-Induced Diabetic Rats

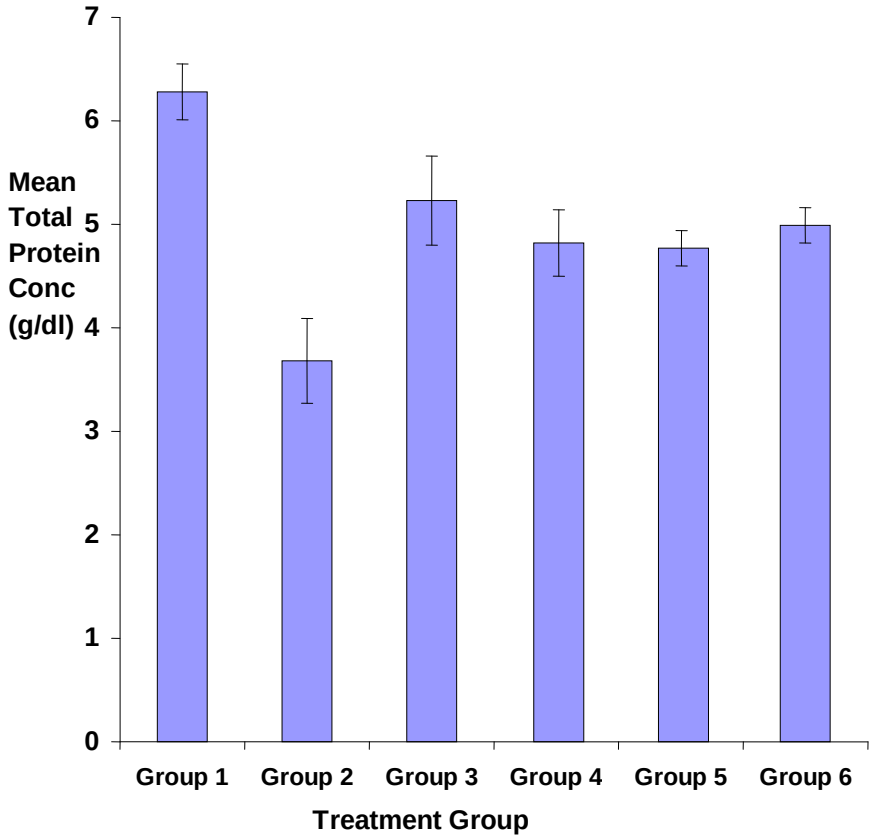
The sorbitol concentration in all the test groups decreased significantly ($p<0.05$) compared with the untreated diabetic animals (Group 2). A significant ($p<0.05$) reduction of sorbitol concentration was recorded in groups 6 treated with a combination of the leaf and fruit extracts of *K. africana* compared with the diabetic rats not treated. There was non- significant increase ($p>0.05$) of sorbitol concentration in all the test rats compared with the normal control rats (group 1) as depicted in Fig. 1 Similarly, non significant increase ($p>0.05$) of sorbitol concentration was recorded in group 6 (diabetic + methanol leaf and fruit extract) in comparison with group 3 treated with the reference drug, glibenclamide



Fi.g.1: Effects of methanol extracts of leaf and fruit of *Kigelia africana on* Sorbitol concentration in alloxan-induced diabetic rats

4.7 Effects of Methanol Leaf and Fruit Extract of K. africana on Total Protein Concentration in Alloxan-Induced Diabetic Rats

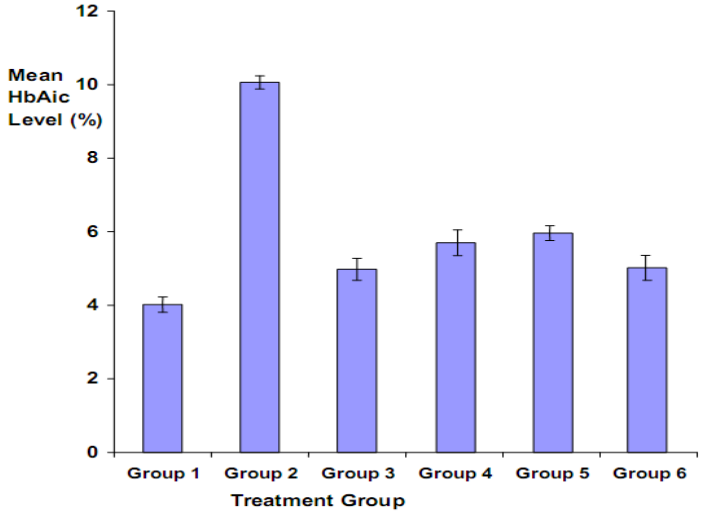
Fig. 2 reveals observable significant increased ($p>0.05$) of total protein was recorded in all test groups compared with the positive control rats (group 2). Total protein concentrations in group 6 orally fed with a combination of the leaf and fruit extracts showed significant increase ($p<0.05$) compared with test groups 4 and 5 administered methanol leaf and fruit extracts only. A non-significant increase ($p>0.05$) of total protein was noted across all test groups (groups 4-6) compared with the total protein concentration of group 3 rats fed with the standard drug.



Fi.g. 2: Effects of methanol extracts of leaf and fruit of *K. africana on* Total protein concentration in alloxan-induced diabetic rats

4.8 Effects of Methanol Leaf and Fruit Extract of K. africana on Glycosylated Haemoglobin Concentration in Alloxan- Induced Diabetic Rats

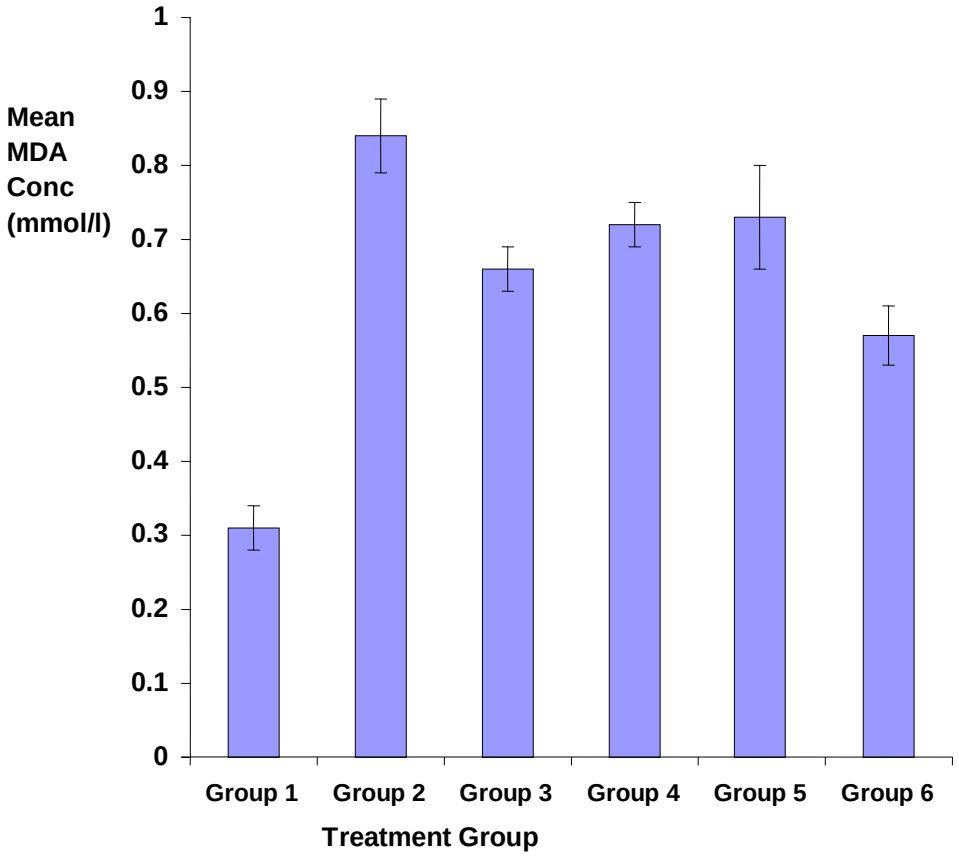
The mean HbA1c level decreased significantly ($p<0.05$) in all the test groups compared with the HbA1c level of untreated diabetics rats (group 2). Changes in HbA1c level was observed in group 6 rats treated with a combination of methanol leaf and fruit extracts in ratio of 1:1 compared with group 3 rats treated with the standard drug. A significant increase ($p<0.05$) HbA1c level was recorded in all the test groups against the normal control rats (negative control) Fig. 3.



Fi.g.3: Effects of methanol extracts of leaf and fruit of *K. africana* on Glycated Haemoglobin level in alloxan-induced diabetic rats

4.9 Effects of Methanol Extracts of Leaf and Fruit of K. africana on Malondialdehyde (MDA) Concentration in Alloxan-Induced Diabetic Rats

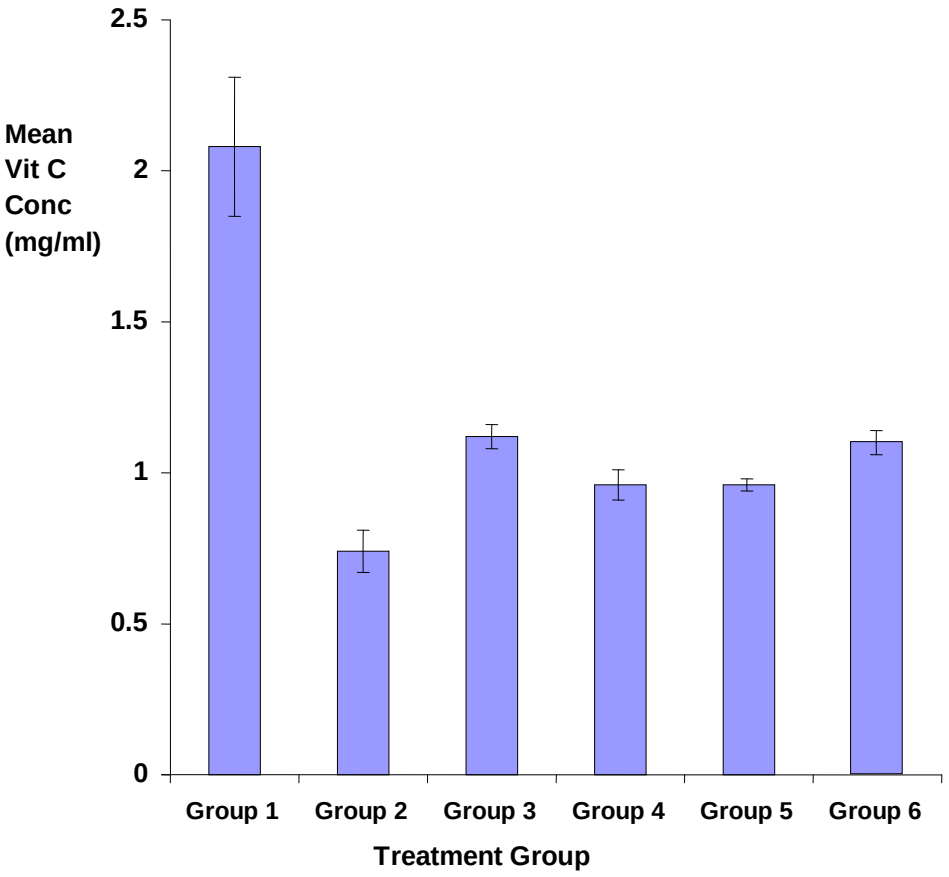
Lipid peroxidation measured as malondialdehyde (MDA) observed significantly increase ($p<0.5$) in all the test groups compared with untreated control as shown in Fig. 4. A significant decrease of MDA concentration was recorded in groups 6 treated with the combination of the plant extract compared with the groups administered with single extract (groups 4 & 5). Similarly, concentration of MDA in diabetic rat treated with methanol leaf and fruit extracts (group 6) significantly reduced ($p<0.05$) as against group 4 & 5.



Fi.g.4: Effects of methanol extracts of leaf and fruit of *K. africana* on Malondialdehyde concentration in alloxan-induced diabetic rats

4.10 Effects of Methanol Leaf and Fruit Extracts of K. africana on Vitamin C Concentration in Alloxan-Induced Diabetic Rats

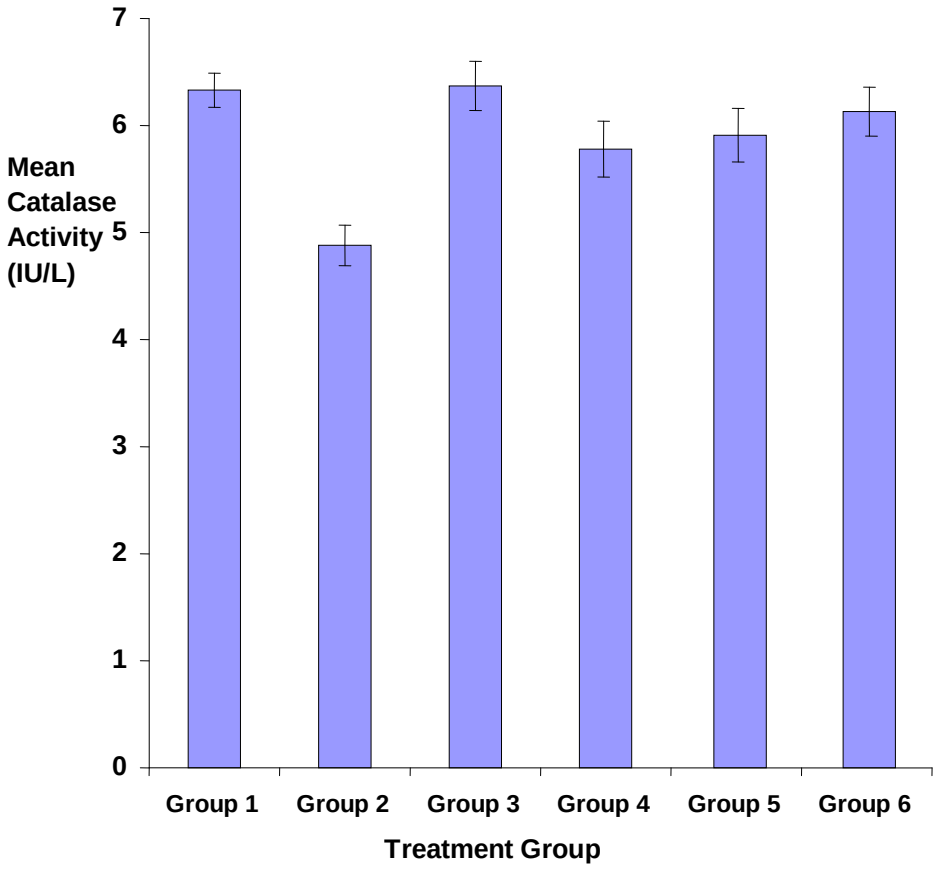
There was a general decrease in vitamin C concentration in all the test groups and the untreated diabetic group compared with the vitamin concentration of normal control rats (group 1). There was statistically significant increase ($p<0.05$) of vitamin C level in group 6 rats treated with a combination of methanol leaf and fruit extracts compared with other test groups 4 & 5. The diabetic rats administered 2.5 mg/kg of glibenclamide demonstrated an increased ($p<0.05$) vitamin c level compared with the vitamin C concentration of rats in group 2 (diabetic untreated rates), see Fig. 5.



Fi.g. 5: Effects of methanol extracts of leaf and fruit of *Kigelia africana on* Vitamin C concentration in alloxan-induced diabetic rats

4.11 Effects of Methanol Leaf and Fruit Extracts of K. africana on Catalase Activity in Alloxan-Induced Diabetic Rats

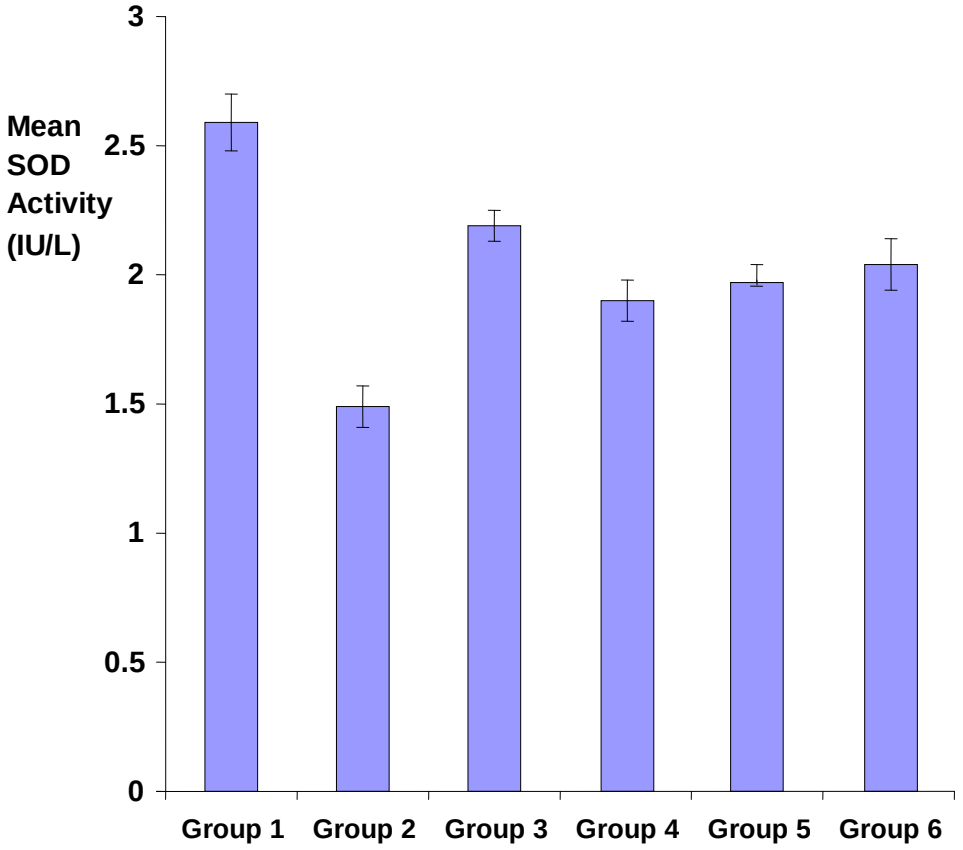
Across the test groups was recorded a statistically significant increase ($p<0.05$) of serum catalase activity (Fig. 6) compared with the untreated diabetic rats (positive control; group 2). Similarly, a significant increase ($p<0.05$) of catalase activity was observed in the diabetic rats treated with reference drug (glibenclamide) in comparison with the catalase activity of all the test groups. In the same pattern, groups 6 treated with equal ratio of methanol leaf & fruit extracts demonstrated a non significant increase ($p>0.05$) of catalase activity compared with other test groups (groups 4 to 5) administered with a single plant extract.



Fi.g. 6: Effects of methanol extracts of leaf and fruit of *K. africana* On Catalase activities in alloxan-induced diabetic rats

4.12 Effect of Methanol Leaf and Fruit Extracts of K. africana on Superoxide Dismutase (SOD) Activity in Alloxan-Induced Diabetic Rats

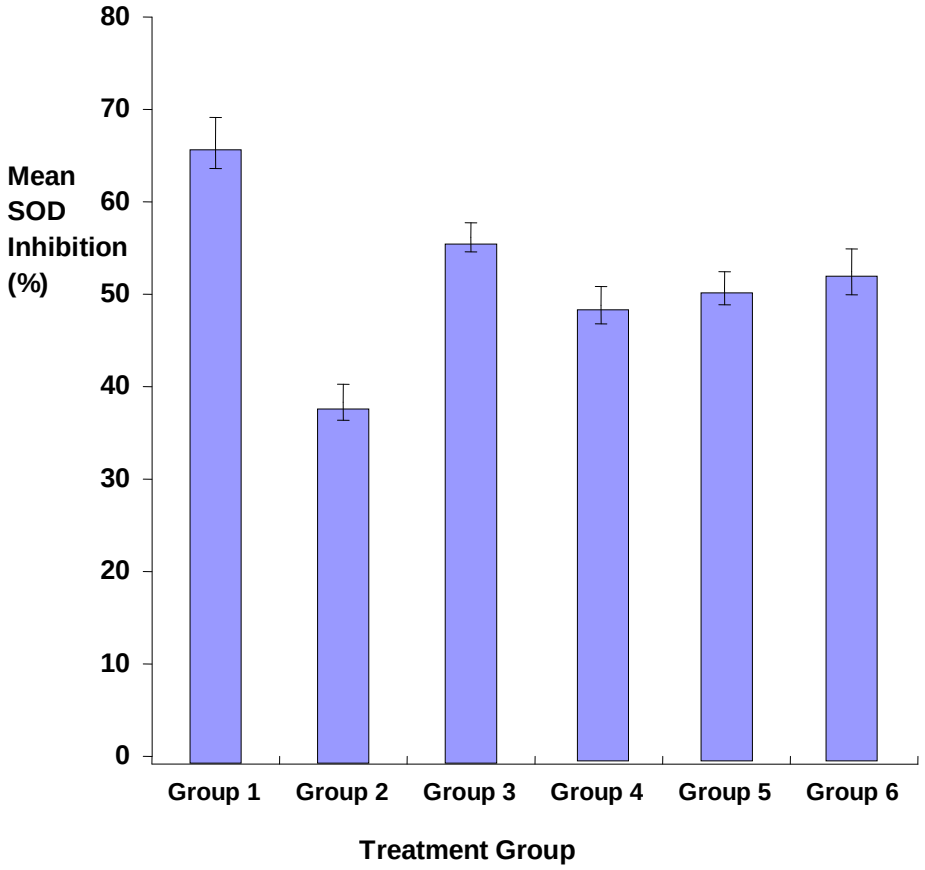
The activities of superoxide dismutase (SOD) reduced significantly ($p<0.05$) in all the test groups compared with the normal control (group 1).There were statistically significant ($p<0.05$) decreases in SOD activities of all test groups compared with the untreated diabetic rats (group 2) as shown in Fig. 7. Superoxide dismutase activities of the test group 6 administered with the combination of the extracts was significantly increased ($p<0.05$) compared with other test groups treated with the single extracts (groups 4 & 5). In the same vein, the activities of SOD in the diabetic rat administered with 2.5 mg /kg body weight of glibenclamide increased significantly ($p<0.05$) as against test groups.



Fi.g.7: Effects of methanol extracts of leaf and fruit of *K. Africana on* Superoxide dismutase activity in alloxan-induced diabetic rats

4.13 Effects of Methanol Leaf and Fruit Extracts of K. africana on Percentage Inhibition of SOD Activity in Alloxan-Induced Diabetic Rats

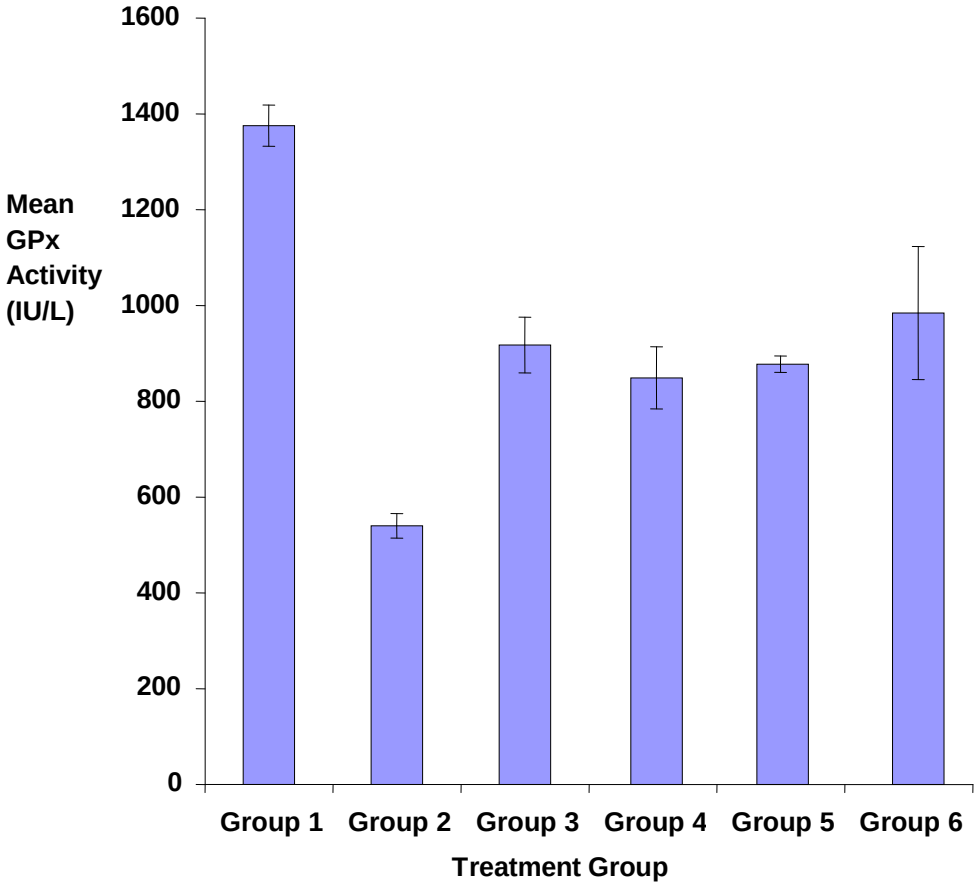
Fig.8 demonstrates statistically significant decrease ($p<0.05$) of percentage inhibition of SOD activity in the test groups compared with the normal control group. A significant reduction ($p<0.05$) of percentage inhibition of SOD activity occurred in the diabetic untreated rats (group 2) compared with the percentage inhibition of SOD activity in normal control. Diabetic rats in group 6 treated with a combination of leaf and fruit extracts recorded a non- significantly ($p>0.05$) increase of percentage inhibition of SOD activity compared with groups 4 & 5 administered monotherapically with leaf and fruit extracts of *K. africana*. Furthermore, non-significant reduction ($p>0.05$) of percentage inhibition was observed in groups 4 & 5 compared with the diabetic rats treated with 2.5 mg/kg body weight of glibenclamide (group 3)



Fi.g. 8: Effects of methanol extracts of leaf and fruit of *K. Africana on* Superoxide dismutase percentage inhibition in alloxan-induced diabetic rats

4.14 Effects of Methanol Leaf and Fruit Extract of K. africana on Glutathione Peroxidase Activity in Alloxan-Induced Diabetic Rats

Fig. 9 represents activity of glutathione peroxidase (GPx) which increased significantly ($p<0.05$) in all the test groups treated with both single and combination of the leaf and fruit of *K. africana* extract in comparison with the GPx activity of the rats in group 1 (normal control rats). The combination therapy in groups 6 demonstrated significant increase ($p<0.05$) of GPx activity compared with groups 4 & 5 of the test groups treated with a single plant extract (monotherapy).The test group 6 of diabetic rats treated with combined leaf and fruit extracts increased in GPx activity significantly relative to group 3 treated with the standard drug.



Fi.g. 9: Effects of methanol extracts of leaf and fruit of *K. Africana on* Glutathione peroxidase activities in alloxan-induced diabetic rats

4.15 Effects of Methanol Leaf and Fruit Extract of K. africana on Total Cholesterol Concentration in Alloxan-Induced Diabetic Rats

Fig. 10 shows relative increase in the total cholesterol concentration in diabetic rats treated in groups 5 & 6 compared with the total cholesterol concentration of normal control in group 1 however such increase was found to be non significant ($p>0.05$). A significant ($p<0.05$) decrease was noted in the diabetic rats administered with the standard drug compared with the untreated diabetic rats (group 2). Similar trend of result was observed in total cholesterol concentration of groups 6 treated with a combination of the extracts compared with the total cholesterol concentration in diabetic untreated rats. Furthermore, significant decrease ($p<0.05$) of total cholesterol concentration in group 3 was observed in comparison with diabetic untreated rats.

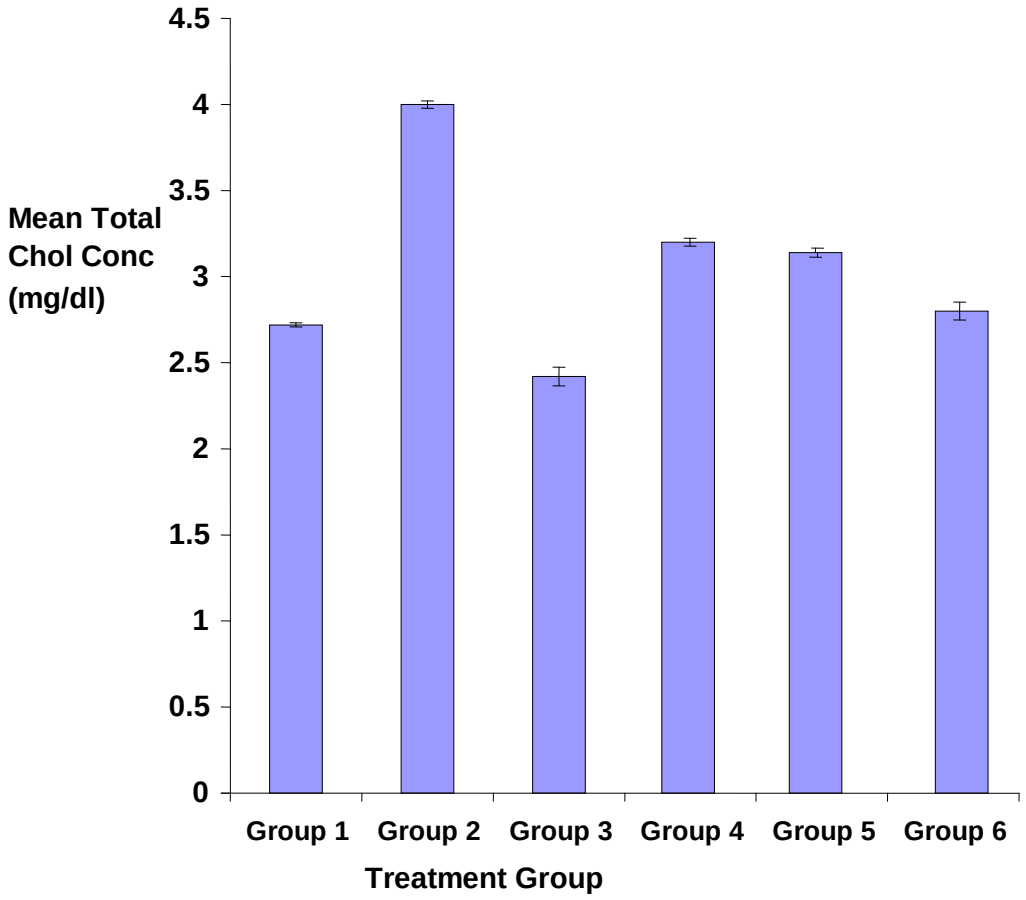


Fig. 10: Effects of methanol extracts of leaf and fruit *K. Africana on* Total Cholesterol concentration in alloxan-induced diabetic rats

V. DISCUSSION

In animals, diabetes induced experimentally has provided considerable approach on the physiologic and biochemical derangement of the diabetic state. Many of the derangement have been characterized in hyperglycemic animals. Significant changes in lipid metabolism and structure also occur in diabetes.

This study evaluated the antidiabetic and antioxidative properties of *K. africana* in alloxan-induced diabetic rats. From the results obtained; diabetic rats had much higher blood glucose level than that of the normal control. Changes in blood glucose levels reflect abnormalities in ß- cells structure and function. In this study, rats with blood sugar level of 500 mg/dl and greater were considered diabetic. Administration of *K. africana* leaf and fruit extracts restored glucose level in alloxan- induced diabetic rats near the normal level. Glibenclamide was used as a standard drug to compare the activity of *K. africana* extract in reference to blood glucose reduction. The results revealed that the extracts in a dose of 500 mg/kg body weight showed significant effect at 21st day indicating that the extracts possess extra pancreatic hypoglycemic activities. The comparable effect of the extract (500 mg/kg) with glibenclamide (2.5 mg/kg) may suggest similar mode of action, since the main mechanism of the action of glibenclamide is the stimulation of insulin release and the inhibition of glucagon secretion. The possible mechanism by which the plant extract brings about its hypoglycemic action may be by potentiating the insulin effect by increasing pancreatic secretion of insulin from ß-cells [22]. The findings also suggest that *K. africana* leaf and fruit extracts many generate ß-cells and have protective effect on ß- cells from glucose toxicity. Some plants have also been observed to exert hypoglycemic activity through insulin release stimulatory effect [23]. In general, there is little biological knowledge on the specific modes of action of plants in the treatment of diabetes, but most of the plants have been found to contain substances like glycosides, alkaloids, terpenoids, and flavonoid that are frequently implicated as having antidiabetic effect [24]. This

was also buttressed by the results of the phytochemistry of *K. africana* which revealed high percentage of flavonoid, glycoside, alkaloid, terpenoid among other constituents. These plant constituents can lower blood glucose level.

The alloxan-induced diabetic rats had a marked loss in body weight. Free radical generated under hyperglycemic condition could attack major biomolecules such as proteins, DNA and lipids and which could lead to the weight loss recorded in this work. Increased synthesis of ketone bodies coupled with increased lipolysis seen in diabetes leads to a severe body weight loss. However, the diabetic rats orally fed with *Kigelia* plant extracts had a remarkable gain in body weight compared with diabetic untreated rats. Significant increase ($p<0.05$) in body weight was recorded in the group administered a combination of the plant extracts in comparison with the group treated with a single extract. In addition, the observed decrease in body weight of diabetic animals agreed with Torres *et al.*, 1999, who also noticed a marked reduction in the body weight of animal with significant increase in serum triacylglycerol in STZ- induced diabetic rats

Sorbitol concentration significantly decreased ($P<0.05$) across all the test animals in reference to diabetic untreated rats. This reduction is probably due to the antioxidant contents of the plant extracts. Sorbitol is a product of polyol pathway and is a feature of diabetic complications. It could be suggested that some of the active constituents of *K. africana* extracts inhibit the activity of aldose reductase; the major enzyme in the polyol pathway. An increased flux of glucose via the polyol pathway leads to intracellular accumulation of sorbitol. Accumulation of this non-permeable sugar in cells especially the lenses and nerves results in osmotic stress, cellular edema, redox imbalance, depletion of water soluble antioxidants and susceptibility to oxidative insult [25]. This is implicated in the pathogenesis of long term complication in diabetes mellitus.

This study further revealed significant reduction ($P<0.05$) of sorbitol concentration in group 6 rats treated with the combination of leaf and fruit extracts relative to animals treated with the reference drug (2.5 mg of glibenclamide). This is in line with the fact that synthetic drugs do not restore normal glucose homeostasis and are not free from side effect [18] .

A significant ($p<0.05$) increase in glycosylated haemoglobin level in the diabetic rats untreated with reference to the normal control animals (group 1) was recorded in this study. The increase is in accord with the report of several other researchers [26, 27, 28]. The increased glycosylation may be as a result of diabetic complications caused by oxidative stress. Generally, decreased in glycosylated haemoglobin level was observed in diabetic rats treated with *K. africana* extracts as against diabetic rats not treated. Decrease in glycohemoglobin level could be attributed to the extracts' ability to reduce glucose level in the blood stream with corresponding decrease in glycated haemoglobin level.

A Significantly increase ($p<0.05$) in serum total protein was recorded in all the test groups treated with the plant extracts in comparison with the diabetic untreated rats. Decrease in serum total protein was observed in untreated diabetic rats with reference to test groups administered both single and combination of the plant extracts. This is in tandem with the proximate composition of the plant that revealed approximate 13% protein.

High concentration of MDA in diabetic untreated established oxidative stress status in the animals. In hyperglycemic condition, glucose is one of the major sources of free radicals. Malondialdehyde (MDA) significantly ($p<0.05$) decreased in all the test groups compared with diabetic rats untreated (group 2). Group 6 treated with a combination of leaf and fruit extracts showed significant ($p<0.05$) decrease in MDA concentration as against groups 4&5 treated with single extract. Reduction in the lipid peroxidation index in treatment groups indicates the ability of the extracts to stem down the oxidative stress by mopping up free radical that lead to lipid breakdown. The bioactive constituents of the extracts such as flavonoids, alkaloids could be implicated in free radical scavenging properties of the extracts.

This study revealed marked increase in serum total cholesterol level. Diabetes is associated with altered lipid levels. The most commonly observed lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia [29, 30] and these contribute to coronary artery disease. This lends credence to the significant ($P<0.05$) increase of total cholesterol in the diabetic rats used in this study. *K. africana* treated rats, showed a reduction in total cholesterol which buttressed the hypolipidemic effect of the plant. The hypolipidemic effect may be due to inhibition of fatty acid synthesis [1] . It could also be attributed to the increase in the reverse cholesterol transport pathway and decreased cholesterol concentration from the intestine due to α- glucosidase inhibition. In normal metabolism insulin activates the enzymes lipoprotein lipase and hydrolyses triacylglycerol. A deficiency in insulin results in inactivation of these enzymes thereby causing hypertriglyceridemia [31, 32]. Administration of a combination of leaf and fruit extracts of *K. africana* resulted in a significant ($p<0.05$) decrease in lipid parameter compared with the diabetic control animals (group-2). It can be further stated that *K. africana* plant extracts have the potential to correct the lipid abnormalities, thus delaying lipid peroxidation in diabetic condition.

In this study, significant ($P<0.05$) decreases in the activities of SOD, CAT and GPx were recorded in diabetic rats not treated compared with the normal control group. An observed significant ($p<0.05$) increases of these antioxidant enzymes were recorded in group 6 treated with a combination of two parts of *K.africana* extracts as against groups 4&5 with mono therapeutic administration of leaf and fruit extracts of the same. Reduction of the antioxidant enzymes was observed in diabetic rats not treated with reference to test rats treated with the standard drug. This is in line with the report that products of membrane lipid peroxidation and other oxidants like H_2O_2 may react with superoxide dismutase resulting in oxidative modification thereby causing loss of enzyme activity in diabetic condition [33]. The result, also concords with the reports that the relatively low expression of antioxidant enzymes such as catalase and superoxide dismutase, pancreatic ß-cells may be vulnerable to reactive oxygen species (ROS) attack when the system is under oxidative stress situation[34,35]. Similarly, elevated levels of free radicals, due to insufficiency of the antioxidant defense system, may lead to disruption of cellular functions, oxidative damages to protein, DNA, membranes and enhance their susceptibility to lipid peroxidation [16] under uncontrolled diabetic condition. Also hyperglycemia leads to glycation and inactivation of superoxide dismutase thus attributing to its decrease. In the study, the animals treated with *K. africana* extracts showed increase in the activity of antioxidant enzymes as against untreated diabetic rats (group 2) and this unveiled the extracts' potential in mopping up or scavenging free radicals generated under oxidative stress mediated diabetes. The bioactive compound, flavonoid may be implicated in the scavenging activity of the plant extracts in oxidative condition.

The fact that normal cells are protected against peroxidative damage *in vivo* can be attributed to efficient antioxidant mechanisms. This antioxidant protection is in part a function of the integrity of each cellular constituent, and in part a reflection of antioxidant system within the cell. In disease conditions, where oxidative stress plays causative and/or exacerbating roles, this mechanism is impaired. Antioxidant vitamins, such as vitamin C and E may be then low in such system. From the above premise, the low plasma vitamin C concentration obtained in group 2 of untreated diabetic rats compared with the control group 1 and the test rats (group 6) is a manifestation of oxidative stress.The fact that vitamin C protects against oxidative stress is now generally accepted [36,37]. Thus; decrease in vitamin C concentration in the present study of untreated diabetic rats is probably a consequence of its protective roles.

VI. CONCLUSION

From the results, it can be concluded that 500 mg of *K .africana* extracts possess antihyperglycemic

effect via α-glucosidase inhibition with corresponding increase in body weight of diabetic rats treated with the extracts. Significant reduction of glycohemoglobin level and sorbitol concentration was obtained in the all the diabetic treated groups in reference to positive control and therefore supporting sugar reduction ability of the extracts. The extracts were found to have lipid lowering effects through reduction of total cholesterol probably by increasing reverse cholesterol transport pathway. *K. africana* extracts exhibit antioxidant scavenging properties by reducing malondialdehyde concentration; hence retard lipid peroxidation. Antioxidative potential of the extracts was ascertained through increase in activities of antioxidant enzymes; CAT, SOD, GPx and antioxidant vitamin (Vitamin C) in test animals as against positive group. The increase in the antioxidant activities was due to the ability of the extracts to mop-up free radical generated under stress conditions. Total protein was improved in all the treatment groups. In general, the possible mechanisms by which *K. africana* brings about antidiabetic activities include: glycosidase (glucosidase) inhibitor mechanism, α-amylase inhibitor mechanism, inhibition of hepatic glucose metabolizing enzyme mechanism, antioxidant mechanism, inhibition of glycosylation of haemoglobin mechanism and modulation of glucose absorption from the gut. Therefore, management and prevention of diabetes complications can be achieved by use of *K. africana* extracts.

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