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Effect of Extracts of Kigelia Africana Fruit and Sorghum Bicolor Stalk on the Biochemical Parameters of Alloxan-Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration among all authors. Authors NFO, CJO, OAO and SOO designed the study, performed the statistical analysis and wrote the protocol. Authors NFO and CJO wrote the first draft of the manuscript. Authors CJO, UC, EIO, SAY and ESG managed the analyses of the study and the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Diabetes and its complication continue to remain a concern in the world population despite the introduction of various hypoglycemic agents. Biochemical changes remain the major observable, clinical, and pathological factors as a derangement in the levels of these parameters increase the risk of developing complications. Although herbal extracts for the treatment of diabetes have been scientifically validated, the scientific interaction and alteration of the biochemical parameters due to

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the administration of this herbal product are not thoroughly investigated in this region. Therefore, this study aims to determine the effect of the extract of *Kigeliaafricana* and *Sorghum bicolor* stalk on the biochemical parameters of diabetic-induced rats. A total of eleven groups containing five rats per group of randomly selected Alloxan-induced Diabetes Healthy Wistar rats of both sexes were used in the study, with one serving as the control group, another serving as glibenclamide treated group, and the remaining nine, extract treated groups. After the overnight fast, the control group received a dose of 0.5 ml of 2% w/v acacia solution. Glibenclamide treated group received 600 µg/kg body weight (bwt) glibenclamide. In contrast, the other nine groups received specified doses (125, 250, and 500mg/kg bwt) of *Kigeliaafricana* and *Sorghum bicolor* extracts singly and in a mixture of ratio 1:1, respectively. After receiving the specified doses once a day orally for 30 days, the rats fasted overnight, and 5 ml of blood collected via cardiac puncture into heparinized and fluoride bottles. The samples were spun and separated for biochemical profiles (plasma glucose, lipid profile, liver function test, and electrolytes urea and creatinine) using a commercially prepared kit with outlined procedures. The result showed a significant decrease ($p < 0.05$) of plasma glucose level in the extract-treated rats, with a remarkable increase in untreated diabetic rats compared to the control. A significant reduction ($p < 0.01$) in the plasma levels of triglyceride and LDL-Chol was also observed in all treated groups at various doses of extracts compared to control with HDL-Chol values marginally increased in all extract-treated groups. Urea and creatinine showed a significant decrease ($p < 0.01$) in all treated doses except the lowest when compared to the control, while all the electrolytes parameters (Na+, K+, Cl- and HCO3-) show no significant difference ($p > 0.05$) across the groups when compared to the control. Liver function showed no significant differences in all parametersexcept for the noticeable decreasing effects on AST and ALT values compared to the control. The extracts and their mixture exhibited antidiabetic and hypolipidaemic activities and cardiovascular benefits due to their considerable lowering effects on total cholesterol, LDL-Chol, triglycerides, and increase in the HDL-Chol levels. The observed biological actions may be due to the presence of different phytocomponents present in the plant extracts. There is, therefore, a need to determine which of the active constituents has the main antidiabetic and hypolipidaemic effect for their optimal usage.

Keywords: Kigeliaafricana; Sorghum bicolor; glibenclamide; alloxan.

1. INTRODUCTION

Herbal medicine has received greater attention as an alternative to orthodox medicine in recent times, leading to a subsequent increase in herbal medicine preparations [1,2]. In rural communities, the exclusive use of herbal medicines prepared with single or combinations of different plant species parts and dispensed by herbalists without formal training to manage various diseases is still a widespread practice. Herbal medicines also have since the prehistoric era been recognized and acknowledged to be effective in treating both pathological and pathogenic diseases [3]. Their use in treating certain diseases where conventional drugs could only serve as palliatives is widespread now. Diabetes mellitus is a metabolic disorder characterized by multi groups of conditions that disturb the metabolism of carbohydrates, fat, and protein [4,5]. Its syndrome is characterized by the loss of glucose homeostasis, storage, and lack of insulin secretion [6,7]. Despite the introduction of various hypoglycemic agents, diabetes and its complication continue to be a significant problem in the world population [8]. The complication is mainly associated with a risk of atherosclerosis [9,10], coronary heart disease [10,11], stroke, and peripheral vascular diseases [12,13]. Biochemical changes are part of major observable clinical and pathological factors associated with Diabetes mellitus as a derangement in these parameters' levels increase the risk of complications. Some workers had observed persistent dyslipidaemia among people with diabetes with the characteristic features of high plasma triglyceride concentration, reduced HDL-Chol concentration, and increased concentration of LDL-Chol particles [10]. These changes are caused by increased free fatty acid flux secondary to insulin resistance and aggravated by increased inflammatory adipokines [14]. Herbal extracts as treatment of diabetes havebeen scientifically validated as they have been reported to provide symptomatic relief and help lower cholesterolamong diabetes [15]. Many of these plants and herbs have been associated with suitable antioxidant activities, acting through various cellular and metabolic mechanisms to

bring about their antidiabetic activities [16]. Different parts of African indigenous plants with potential medicinal properties like *K. africana* and *S. bicolor* have been used by herbal medicine practitioners in the treatment of various diseases in Nigeria [17]. The *K. africana* plant has many medicinal properties due to the presence of numerous secondary metabolites. It has been reported that the major plant constituents in *K. africana* include polysaccharides, polypeptides, glycopeptides, triterpenoids, steroids, xanthones, flavonoids, coumarins, phenols, iridoids, alkyl disulphides, inorganic ions, and guanidine [18]. Some of these products have been shown to exhibit antioxidant properties and as well as antidiabetic activities [19].

On the other hand, Sorghum, which is very important in the world's human diet, has been known to provide natural antioxidant and essential fatty acids that could fight cardiovascular-related diseases. The most abundant phytoconstituents in *S. bicolor* stalk include Erucic acid, Fatty acid ester, Omega 9 fatty acid, Ester compound, and Lauric acid [18]. Most of these compounds also exhibit antioxidant effects [20]. Their relevance in clinical practice has continued to increase over the years, with the Complementary and Alternative Medicine (CAM) applying the knowledge to the management of many people with diabetes in Nigeria [17]. However, there is poor understanding of the scientific interaction and alteration of the biochemical parameters due to the administration of these herbal products. Therefore, there is need to study the effect of the administration of the extracts of K. africana fruit and S. Bicolor stalk on the biochemical parameter of diabetes mellitus to ensure a better outcome; hence this study is aimed to determine the effect of the extract of *K. Africana* and *S. Bicolor* stalk on the biochemical parameters of diabetic induced rats.

2. METHODOLOGY

2.1 Plant Materials

The fresh fruits of *K. africana* (Lam.) Benth (Fam. Bignoniaceae) and *S. bicolor* stalks (L) Moench (Fam. Poaceae) were bought from the Mushin market in Lagos suburb, Nigeria. The fruits and stalks were identified and authenticated by a taxonomist at the Department of Botany, Faculty of Science, University of Lagos, Nigeria. The specimens were given voucher no LUH 6487 (*K. africana*) and no LUH 6488 (*S. bicolor*) respectively and were deposited in the Department's Herbarium. The plant materials were washed with a copious amount of clean tap water and spread to drain, then cut into small pieces and dried in an oven at a temperature of 45^{o}C for seven days.

2.2 Preparation of Extracts

The dried materials were pulverized to a coarse powder with an electric grinder. The powdered materials of *K. africana* fruits (3200 g) and *S. bicolor* stalks (3150 g) were macerated with 25 liters of hydroethanolic (2:8) respectively and allowed to stand for seven days, with regular stirring. The extracts were clarified by filtration using Whatman no.4 filter paper. They were then concentrated using a rotary evaporator then dried in a laboratory oven (450C) to a dry weight of 243.12 g (7.60 %w/w yield) for K. africana and 174.94 g (5.60 %w/w yield) for S. bicolor, respectively.

2.3 Animals

Male and female Wistar rats (150 ± 20 g) and Swiss albino mice (22.50 ± 2.50 g) obtained from the Laboratory Animal Centre of the College of Medicine, University of Lagos, Nigeria, were used. They were kept under standard environmental conditions (23-25°C, 12 h/12 h light/dark cycle), housed in plastic cages (5 rats/mice per cage), maintained on animal pellets (Livestock Feed PLC, Lagos, Nigeria), and allowed access to water ad libitum. The rodents were allowed to acclimatize for 7 days to laboratory conditions before any experiment. The rodents' use and care were in strict compliance with the National Research Council (NRC) Guidelines on the Care and Use of Laboratory Animals [21].

Diabetes was experimentally induced in the Healthy Wistar rats of both sexes after an overnight fast using 150 mg/kg bwt of Alloxan monohydrate dissolved in normal saline. The dissolved Alloxan was administered immediately through the intraperitoneal route (i.p). After 72 h, the blood glucose levels were monitored with a glucometer (Accu-Chek, Roche Diagnostics, Mannheim, Germany). The rats with plasma glucose ≥ 200 mg/dl were classified as diabetic were used in the study.

The rats used were weighed and randomly divided into eleven groups of five rats. The groups comprise one control group, another

serving as glibenclamide treated group, and the remaining groupsrecieved the extracts. After the overnight fast (withdrawal of feed), the control group received a dose of 0.5 ml of 2% w/v acacia solution. Then the *K. africana* and *S. bicolor* extracts treated group received doses of 125, 250, and 500mg/kg bwt, and then the mixture of (1:1) received 250 and 500 mg/kg bwt. The rats received the specified doses once a day through the oral route for 30 days in the following order.

Group I: Alloxan-induced diabetic rats treated with 125 mg/kg bwt *K. africana*
Group II: Alloxan-induced diabetic rats treated with 250 mg/kg bwt *K. africana*
Group III: Alloxan-induced diabetic rats treated with 500 mg/kg bwt *K. africana*
Group IV: Alloxan-induced diabetic rats treated with 125 mg/kg bwt *S. bicolor*
Group V: Alloxan-induced diabetic rats treated with 250 mg/kg bwt *S. bicolor*
Group VI: Alloxan-induced diabetic rats treated with 500 mg/kg bwt *S. bicolor*
Group VII Alloxan-induced diabetic rats treated with 250 mg/kg bwt of mixture (1:1)
Group VIII Alloxan-induced diabetic rats treated with 500 mg/kg bwt of the mixture (1:1)
Group IX: Alloxan-induced diabetic rats treated with glibenclamide 600 µg/kg bwt
Group X: Alloxan-induced diabetic rats treated with 2% acacia solution
Group XI Normal rats not induced with diabetes but received acacia 2% w/v solution.

On the 31st day, after an overnight fast, the animals were sacrificed, and blood was obtained via cardiac puncture into heparinized and fluoride containers, respectively, for biochemical analysis. The blood was centrifuged within 5 min of collection at 4000 rpm for 10 min to obtain plasma which was used for the following biochemical analysis.

1. Serum Aspartate Amino Transferase (AST) by Reitman and Frankel method [22]
2. Serum Alanine Amino Transferase (ALT) by Reitman and Frankel method [22]
3. Serum Alkaline Phosphatase (ALP) King-Armstrong modified by Kind and King [23]
4. Serum Bilirubin by Evelyn and Malloy method [24]
5. Serum Total Protein by Biuret method [25]
6. Serum albumin by BCG method Bartholomew and Delaney [26]
7. Plasma Urea using the Diacetyl Monoxide Method [27].
8. Plasma Creatinine plasma by the Jaffe reaction [28]
9. Sodium, Potassium, and Bicarbonate (electrolytes) by ISE method [29]
10. Plasma Total Cholesterol (TC) estimated using a modified Liebermann Burchard reaction described by Huang et al. [30]
11. Plasma Triglycerides (TRIG) enzymatic method of Bucolo and David [31]
12. Plasma HDL-Cholesterol (HDL-c) was estimated using the method for total cholesterol after precipitation by phosphotungstic acid [32]
13. Plasma LDL- Cholesterol (LDL-c) according to Friedwald et al. formula [33]
14. Fasting Plasma Glucose was estimated by Trinder's method [34]

Biochemical parameters were analyzed using a commercially prepared kit (COBAS, Mumbai, India) following outlined procedures.

3. RESULTS

The Effect of *K. africana* and glibenclamide, *S. bicolor* and glibenclamide, extracts mixture, and glibenclamide on glucose and lipid profile test values of the diabetic rats are shown in Tables 1, 2 and 3, respectively. Results showed a significant decrease ($p < 0.05$) of plasma glucose level in the extract-treated rats, with a remarkable increase in untreated diabetic rats compared to control. A significant reduction ($p < 0.01$) in the plasma levels of triglyceride and LDL-Chol was also observed in all treated groups at various doses of extracts compared to control with HDL-Chol values marginally increased in all extract-treated groups.

Tables 4, 5 and 6 also show the effect of *K. africana* and glibenclamide, *S. bicolor* and glibenclamide, as well as extracts mixture and glibenclamide on liver function test parameters with no significant difference in all parameters except for the noticeable decreasing effects on AST and ALT values when compared to the control.

Tables 7, 8 and 9 also shows the effect of *K. africana* and glibenclamide, *S. bicolor* and glibenclamide, as well as extracts mixture and glibenclamide on serum electrolytes, urea and creatinine levels of the diabetic rats with plasma Urea and creatinine showing a significant decrease ($p < 0.01$) in all treated doses except the lowest when compared to the control, while all the electrolytes parameters (Na^+, K^+, Cl^- and

HCO_3^-) show no significant difference ($p > 0.05$) across the groups when compared with the controls.

4. DISCUSSION

Alloxan was chosen to induce diabetes in the rat because Alloxan causes severe necrosis of pancreatic β-cells with consequent lack of insulin secretion, possibly through generating excessive reactive oxygen species [35]. In other words, Alloxan caused a massive reduction in insulin release by the destruction of beta cells of islets of Langerhans and thus induced hyperglycemia.

In this study, we observed that all the extract-treated groups had lowered blood glucose levels in both normal and diabetic treated rats, except for those treated with a lower concentration of *K. africana* with no significantly difference from the control. This agrees with other workers [36], who reported that hyperglycaemia is an independent risk factor in developing chronic diabetic complications. The management of Type 2 diabetes relies on the maintenance of blood glucose concentration at a normal or near-normal level. Since the extracts have demonstrated potent plasma glucose-lowering agents, they could also help control diabetes mellitus.

A statistical decrease ($p < 0.05$) in triglyceride and LDL-Chol levels were observed in the rats treated with the extracts and their mixture at the doses of 250 and 500 mg/kg bwt, respectively. Also observed was the ability of the extracts and their mixture to compete favorably with glibenclamide in increasing HDL-Chol. The observation that the extracts and their mixture could remarkably decrease the plasma lipids with an increase in HDL-Chol level had proved that they had reducing effects on the cardiovascular risk factors suggesting the extract had good anti-diabetic and antiatherogenic activities. These findings are in line with other workers [2,37], who have shown that Many anti-diabetic plants have beneficial effects on the cardiovascular system. Dada et al. [10,38], also explained that increased lipid abnormalities are a significant risk factor for cardiovascular complications in type 2 diabetes; hence Lowering LDL-Chol, triglyceride, and raising HDL-Chol has been shown to reduce microvascular disease and mortality in patients with type 2 diabetes. Additionally, According to Murali et al., and Juma et al. [10,39] significant control on serum lipids may present hypercholesterolemia's simultaneous coexistence hypertriglyceridemia and also reduce the cardiovascular risk factors.

The extracts and their mixture were observed to have noticeable decreasing effects on AST and ALT values when compared to the control.

The decrease in AST levels was more pronounced in the rats treated with higher concentrations of the extracts and their mixture (500 mg/kg bwt) and even better than that of the reference drug, glibenclamide. Similarly, the decreases in the extracts' ALT levels were noted to be significant ($p < 0.05$) compared to control. The reduction in the AST and ALT levels in the rats treated with the extracts and mixture had proved that neither the extracts nor mixtures had deleterious effects on the cardiac and hepatic tissues. However, ALP values showed a non-significant difference in all extracts and mixture treated groups compared to the control; hence the extracts did not tend to affect biliary functions. Total bilirubin showed a non-significant ($p > 0.05$) difference in all the extracts and mixture treated groups compared to control; hence the extracts and mixture did not have a deleterious effect on the liver. On the contrary, other workers [39] showed an elevation in the serum levels of AST and ALT in their work which are usually reliable indices of inflammatory changes in liver and heart organs.

The protein values result showed a significant decrease in total protein and albumin of untreated rats compared to non-glycaemic control groups and no significant difference in the rats treated with the mixture and glibenclamide.

Meanwhile, an increase in total protein level has been reported to have a hepato-protective effect [40]; since a significant ($p < 0.05$) decrease in plasma protein levels was observed in the untreated rats, this possibly showed that the ability of the liver to produce protein was affected.

In this study, a significant decrease ($p < 0.05$) in creatinine was observed in all rats treated with *K. africana*, *S. bicolor*, and their equal mixture compared to control. This suggests that the extracts and the mixture may have protective effect on the kidney, partly attributed to their antioxidant contents. There were no significant differences ($p > 0.05$) in all electrolyte's values observed in the extracts and mixture except in K+ level in extracts mixture. The extracts and their mixtures performed better than the reference drug glibenclamide.

Table 1. Effect of *K. africana*and glibenclamide on glucose and lipid profile test values in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPI	GPII	GPIII	F	P value
Gluc (m mol/L)	4.95±0.56	21.60±0.83**	3.53±0.40*	4.57±0.07	4.45±0.07	3.48±0.04*	1303	<0.0001
T.Chol (m mol/L)	1.56±0.47	2.78±0.83*	1.61±0.60	1.57±0.63	1.38±0.63	1.09±0.85	3.628	0.0138
Trig (m mol/L)	0.77±0.02	1.23±0.07**	0.81±0.02	0.52±0.04**	0.50±0.04**	0.36±0.07**	208.2	<0.0001
HDL-C (m mol/L)	0.58±0.02	0.31±0.02**	0.57±0.04	0.72±0.07*	0.62±0.09	0.65±0.04	36.44	<0.0001
LDL-C (m mol/L)	0.62±0.04	1.41±0.02**	0.44±0.07*	0.47±0.07*	0.42±0.02**	0.39±0.04**	330.8	<0.0001

*Mean ± SD (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs. control group.Control: Normal rats not induced with diabetes but received acacia 2% w/v solution. Diab. Untreat: Alloxan-induced diabetic rats treated with 2% acacia solution. Glib: Glibenclamide 600 µg/kg bwt: GPI: 125 mg/kg bwt of K. Africana; GPII: 250 mg/kg bwt of K. Africana; GPIII: 500 mg/kg bwt of K. africana*

Table 2. Effect of *S. bicolor* and glibenclamide on glucose and lipid profile test values in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPIV	GPV	GPVI	F	P value
Glu (m mol/L)	4.95±0.56	21.60±0.83**	3.53±0.40*	3.90±0.42*	3.86±0.16*	3.71±0.11*	1132	<0.0001
Chol (m mol/L)	1.56±0.27	2.78±0.83*	1.61±0.60	1.47±0.34	1.36±0.18	1.15±0.16	7.688	0.0002
Trig (m mol/L)	0.77±0.02	1.23±0.07**	0.81±0.02	0.75±0.07	0.63±0.02*	0.68±0.07*	72.35	<0.0001
HDL-Chol (m mol/L)	0.58±0.02	0.31±0.02**	0.57±0.04	0.64±0.13	0.76±0.09*	0.83±0.09*	23.7	<0.0001
LDL-Chol (m mol/L)	0.62±0.04	1.41±0.02**	0.44±0.07*	0.59±0.09	0.53±0.07*	0.42±0.07*	172.9	<0.0001

*Mean ± SD (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs. control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat: Diabetes untreated Glib: Glibenclamide 600 µg/kg bwt; GPIV: 125 mg/kg bwt of S. bicolor; GPV: 250 mg/kg bwt of S. bicolor; GPVI: 500 mg/kg bwt of S. bicolor*

Table 3. Effect of extracts mixtureand glibenclamide on glucose and lipid profile test values in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPX	GPXI	F	P value
Glu (m mol/L)	4.95±0.56	21.60±0.83**	3.53±0.40*	3.45±0.18*	3.28±0.13*	1281	< 0.0001
Chol (m mol/L)	1.56±0.27	2.78±0.83*	1.61±0.60	1.23±0.16	1.41±0.07	8.138	0.0005
Trig (m mol/L)	0.77±0.02	1.23±0.07**	0.81±0.02	0.51±0.07**	0.60±0.04**	160.8	< 0.0001
HDL-c (m mol/L)	0.58±0.02	0.31±0.02**	0.57±0.04	0.87±0.04**	0.78±0.07**	122.3	< 0.0001
LDL-c (m mol/L)	0.62±0.04	1.41±0.02**	0.44±0.07*	0.44±0.07*	0.46±0.09*	210.2	< 0.0001

*Mean ± SD (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs. control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat: Diabetes untreated Glib: Glibenclamide 600 µg/kg bwt; GPVII: 250 mg/kg bwt of extracts mixture; GPVIII: 500 mg/kg bwt of extracts mixture*

Table 4. Effect of *K. africana*and glibenclamide on liver function test parameters values in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPI	GPII	GPIII	F	P value
AST(U/L)	59.02±5.59	77.02±5.59**	52.52±5.59	62.20±3.91	59.02±6.04	50.01±4.92	15.99	<0.0001
ALT(U/L)	17.50±3.91	25.75±2.80*	15.05±3.40	12.25±3.91*	12.60±1.68*	10.50±4.70*	12.28	<0.0001
ALP(U/L)	67.01±6.15	98.01±8.39**	71.02±8.39	68.32±6.04	71.09±8.39	68.50±6.15	13.1	<0.0001
T. Bil(µ mol/L)	11.97±0.02	15.39±0.27*	10.26±0.04	13.68±0.11	11.97±0.11	8.55±0.02	61.11	0.001
Conj.Bil.(µ mol/L)	6.84±0.04	8.55±0.11*	6.84±0.07	6.84±0.09	6.84±0.04	5.13±0.02	4.068	0.0081
Unconj (µ mol/L)	5.13±0.02	6.84±0.04*	3.42±0.07	6.84±0.04	5.13±0.16	3.42±0.09	5.783	0.0012
TP (g/L)	8.71±0.02	6.82±1.68*	8.30±1.45	8.60±0.17	8.08±1.68	8.60±1.34	1.573	0.2057
ALB (g/L)	4.81±0.04	3.62±0.34*	4.40±0.11	4.51±0.16	4.62±0.04	4.22±1.68	1.742	0.1633

*Mean ± SD (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs. control group. Cont: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat. : Diabetes untreated; Glib. : Glibenclamide 600 µg/kgbwt; GPI: 125 mg/kg bwt of K. africana ; GPII: 250 mg/kg bwt of K. Africana; GPIII: 500 mg/kg bwt of K. africana*

Table 5. Effect of *S. bicolor* and glibenclamide on liver function test parameters values in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPIV	GPV	GPVI	F	P value
AST (U/L)	59.02±5.59	77.02±5.59**	52.52±5.59	62.20±3.91	59.01±6.04	50.02±4.58*	16.29	<0.0001
ALT (U/L)	17.50±3.91	25.75±2.80*	15.05±3.40	17.05±4.70	13.52±3.91	10.02±1.16*	11.43	<0.0001
ALP (U/L)	67.01±6.15	98.01±8.39**	71.02±8.39	61.40±6.04	62.05±7.20	68.20±7.67	17.05	<0.0001
T. Bil (µ mol/L)	11.97±0.02	15.39±0.27*	10.26±0.04	12.31±0.04	11.97±0.02	10.26±0.07	4.442	0.0053
Conj.Bil.(µ mol/L)	6.84±0.04	8.55±0.11*	6.84±0.07	6.16±0.11	6.84±0.04	5.99±0.04	2.38	0.0688
Unconj (µ mol/L)	5.13±0.02	6.84±0.04*	3.42±0.07	6.16±0.04	5.13±0.02	4.28±0.02	15.65	<0.0001
TP (g/L)	8.71±0.02	6.82±1.68*	8.30±1.45	8.30±1.68	8.52±2.35	8.73±0.34	1.151	0.3617
ALB (g/L)	4.81±0.04	3.62±0.34*	4.40±0.11	4.32±0.16	4.02±0.04	3.92±1.68	1.763	0.1587

*Mean (SD) ± (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs .control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat. : Diabetes untreated; Glib. : Glibenclamide 600 µg/kg bwt; GPIV: 125 mg/kg bwt of S. bicolor; GPV: 250 mg/kg bwt of S. bicolor; GPVI: 500 mg/kg bwt of S. bicolor*

Table 6. Effect of extracts mixtureand glibenclamide on liver function test parameters values in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPX	GPXI	F	P value
AST(U/L)	59.02±5.59	77.02±5.59*	52.52±5.59	62.20±3.91	52.02±6.04	17.76	<0.0001
ALT (U/L)	17.50±3.91	25.75±2.80*	15.05±3.40	13.20±5.86	16.15±4.47	6.627	0.0014
ALP (U/L)	67.01±6.15	98.01±8.39*	71.02±8.39	68.52±5.84	62.63±3.58	21.97	<0.0001
T. Bil (µ mol/L)	11.97±0.02	15.39±0.27*	10.26±0.04	12.48±0.07	10.60±0.13	3.66	0.0215
Conj.Bil.(µmol/L)	6.84±0.04	8.55±0.11*	6.84±0.07	7.35±0.04	5.30±0.07	4.578	0.0087
Unconj (µ mol/L)	5.13±0.02	6.84±0.04	3.42±0.07	5.13±0.11	5.47±0.04	5.907	0.0026
TP (g/L)	8.71±0.02	6.82±1.68*	8.30±1.45	8.71±0.13	8.82±0.16	3.514	0.025
ALB (g/L)	4.81±0.04	3.62±0.34*	4.40±0.11	4.61±0.45	4.54±0.04	15.96	<0.0001

*Mean (SD) ± (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat. : Diabetes untreated; Glib. : Glibenclamide 600 µg/kg bwt; GPVII: 250 mg/kg bwt of extracts mixture; GPVIII: 500 mg/kg bwt of extracts mixture*

Table 7. Effect of *K. africana*and glibenclamide on serum electrolytes, urea, and creatinine levels in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPI	GPII	GPIII	F	P value
Na^+ (mmol/L)	150.00±6.93	155.20±7.85	153.10±6.93	148.10±4.70	145.00±6.93	147.20±9.17	1.394	0.262
K^+ (mmol/L)	6.40±0.34	6.52±0.67	6.21±1.12	5.50±0.22	5.91±0.02	5.01±0.02*	8.186	0.0001
Cl^- (mmol/L)	115.80±6.98	112.10±4.74	110.60±5.37	110.10±5.14	107.90±5.81	109.00±4.70	1.271	0.3087
HCO_3^- (mmol/L)	26.02±5.64	27.02±4.07	27.31±6.08	25.06±4.79	24.40±2.55	25.02±5.01	0.2976	0.9094
Urea (mmol/L)	8.34±6.15	9.66±6.04	8.45±6.15	8.17±6.15	7.24±6.04	6.90±5.64*	6.778	0.0005
Creat (µmol/L)	177.68±0.04	199.10±0.11*	185.64±0.11*	150.28±0.11**	114.92±0.02**	106.08±0.07**	164.8	<0.0001

*Mean (SD) (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs .control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat. : Diabetes untreated; Glib. : Glibenclamide 600 µg/kg bwt; GPI: 125 mg/kg bwt of K. Africana; GPII: 250 mg/kg bwt of K. Africana; GPIII: 500 mg/kg bwt of K. africana*

Table 8. Effect of *S. bicolor* and glibenclamide on serum electrolytes, urea, and creatinine levels in the diabetes study

Parameters	GPI	Diab. Untreat.	Glib.	GPIV	GPV	GPVI	F	P value
Na^+ (m mol/L)	150.00±6.93	155.20±7.85	153.10±6.93	155.20±7.89	150.10±8.39	149.20±7.87	0.624	0.6829
K^+ (m mol/L)	6.40±0.34	6.52±0.67	6.21±1.12	6.30±0.27	5.52±0.11	5.42±0.56	3.01	0.0301
Cl^- (m mol/L)	115.80±6.98	112.10±4.74	110.60±5.37	111.30±6.98	109.10±5.59	110.20±4.79	0.8077	0.5556
HCO_3^- (m mol/L)	26.02±5.64	27.02±4.07	27.31±6.08	25.06±4.79	24.40±2.55	25.02±5.01	0.2976	0.9094
Urea (m mol/L)	8.34±6.15	9.66±6.04	8.45±6.15	8.36±5.66	4.33±2.80**	4.83±5.64**	34.16	<0.0001
Creat (µ mol/L)	177.68±0.04	199.10±0.11*	185.64±0.11*	116.52±0.07**	112.03±0.02**	106.08±0.07**	422.1	<0.0001

*Mean (SD) (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs .control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat. : Diabetes untreated; Glib. : Glibenclamide 600 µg/kg bwt; GPIV: 125 mg/kg bwt of S. bicolor ; GPV: 250 mg/kg bwt of S. bicolor; GPVI: 500 mg/kg bwt of S. bicolor*

Table 9. Effect of extracts mixtureand glibenclamide on serum electrolytes, urea, and creatinine levels in the diabetes study

Parameters	Cont.	Diab. Untreat.	Glib.	GPVII	GPVIII	F	P value
Na^+ (m mol/L)	150.00±6.93	155.20±7.85	153.10±6.93	144.10±7.49	143.00±3.91	3.171	0.0359
K^+ (m mol/L)	6.40±0.34	6.52±0.67	6.21±1.12	4.80±1.16*	4.93±0.04*	5.526	0.0037
Cl^- (m mol/L)	115.80±6.98	112.10±4.74	110.60±5.37	106.00±3.06	106.40±5.66	2.95	0.0456
HCO_3^- (m mol/L)	26.02±5.64	27.02±4.07	27.31±6.08	25.25±3.24	25.22±2.95	0.2268	0.9202
Urea (m mol/L)	8.34±6.15	9.66±6.04	8.45±6.15	8.01±3.40	6.41±3.69*	12.38	<0.0001
Creat. (µ mol/L)	177.68±0.04	199.10±0.11*	185.64±0.11*	132.45±0.12**	123.76±0.04**	158	<0.0001

*Mean ± SD (n = 5), *p<0.05, **p<0.01 (Significant difference at 95 and 99% confidence limit respectively) vs. control group. Cont.: Control (0.5 ml of acacia solution (2%w/v)). Diab. Untreat. : Diabetes untreated; Glib. : Glibenclamide 600 µg/kg bwt; GPVII: 250 mg/kg bwt of extracts mixture; GPVIII: 500 mg/kg bwt of extracts mixture*

5. CONCLUSION

The extracts and their mixture exhibited antidiabetic and hypolipidaemic activities and cardiovascular benefits due to their considerable lowering effects on total cholesterol, LDL-Chol, triglycerides, and increase in the HDL-Chol levels. The observed biological actions may be due to the presence of different phytocomponents present in the plant extracts. Further work is therefore needed to elucidate the actual mechanism of the constituents of the extracts and to determine which of the active constituents has the main antidiabetic and hypolipidaemic effect for their optimal usage.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend the useof these products to be an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

The College of Medicine, University of Lagos Health Research Ethics Committee approved the study (Ethical Approval No: CM/HREC/10/ 16/101).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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