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Antihyperglycaemic and antioxidant activities of *Sansevierialiberica* as justification for its antidiabetic claims

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Diabetes has become a global emergency because of its high prevalence, morbidity and mortality while the available hypoglycaemic drugs possess various adverse effects and are expensive. This has necessitated a continuous search for cheaper antidiabetic agents of plant origin with fewer or no side effects. The study evaluated the antihyperglycaemic activities of the methanol extract of *Sansevieria liberica* Gerome and Labroy (Agavaceae) rhizome. Both the partitioned and column fractions were tested on glucose-induced hyperglycaemic rats while their *in vitro* antioxidant effects studied using 1,1-diphenyl-2-dipicrylhydrazyl radical scavenging (DPPH), ferric reducing antioxidant power (FRAP), total antioxidant capacity (TAC), hydroxyl radical scavenging activity (HRSA) as well as the total phenolic content (TPC) and total flavonoid content (TFC) assays. Glibenclamide (5 mg/kg) and appropriate anti-oxidant standard drugs were used as positive controls. The estimated median lethal dose (LD_{50}) of the methanol extract was 3,808.0 mg/kg; at 100, 200 and 400 mg/kg, it gave comparable ($p>0.05$) antihyperglycaemic activity to glibenclamide at 5 mg/kg. Its ethyl acetate fraction at 200 and 400 mg/kg gave the highest antihyperglycaemic activities of 49.5 and 53.9%, respectively, the highest antioxidant activities in all the models used. The highest antihyperglycaemic and antioxidant values were observed in the column fractions, C_3, C_4 and C_7 of the ethylacetate partitioned fraction. The comparable antihyperglycaemic activity to glibenclamide of the methanol extract of *S. liberica*rhizome in this study has justified its ethnomedical claims as antidiabetic agent. The consistently high antihyperglycaemic and antioxidant activities of the extract and its partitioned and column fractions would suggest a direct relationship between the two biological activities investigated.

Key words: Diabetes mellitus, *Sansevierialiberica*, anti-hyperglycaemic activity, antioxidant activity.

INTRODUCTION

Diabetes mellitus is defined as a group of metabolic disorders that could be identified by a significant increase in the level of glucose in the blood (hyperglycaemia) and reduced production or action of insulin secreted by the

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pancreas inthe body (Maritim et al*.,* 2003; Adebajo et al*.,* 2013a,b; ADA, 2014). Globally, about 415 million individuals were affected with diabetes in 2015 and this has been projected to increase to 629 million by 2045 (IDF, 2017). The high costsand adverse effects of insulin and the available oral hypoglycaemic agents have necessitated increased investigations on medicinal plants used ethnomedically for the management of diabetes (Adebajo et al*.,* 2013a,b, Ayoola et al*.,* 2017a,b).

Reactive oxygen species (ROS) are natural by-products of various metabolic processes that are produced at low levels during normal metabolism in the body and they are known to cause damage to cellsat higher physiological levels than normal(Ma et al*.,*2013;Gbadamosi and Emi, 2017).Several diseases such as diabetes, artherosclerosis, hypertension, cancer and neurodegenerative diseases have been linked to the damaging effects of ROS including, superoxide ($O_2^{\bullet-}$), hydroxyl (OH), peroxyl (RO_2) and hydroperoxyl (HO_2) radicals (Aslan et al*.,* 2010; Dix and Legg, 2017; Ayoola et al., 2017a,b). Antioxidants which arescavengers of ROS have been found to be effective in preventing experimental diabetes in animal models as well as reduction in severity of Types I and II diabetic complications (Jeanette, 2005).

Plant-derived antioxidants have been reported to possess physiological effects such as antidiabetic, antitumor and anti-inflammatory activities (Adebajo et al*.,* 2009; Andre de Souza et al*.,* 2011). *Sansevieria liberica* Gerome and Labroy (Agavaceae) is a tropical, West African perennial, rhizomatous plant and an erect herb with several stiffed-edged, elliptic leaf, arising from the rhizome and 1-3 or more leaves in a clump (Eze et al., 2011). It is traditionally used for the treatment of asthma, diabetes, abdominal pains, hypertension, menorrhagia, piles, sexual weakness, snake bites and wounds of the foot (Gill, 1992; Osabohien and Egboh, 2008). Its antihypertensive (Ikewuchi et al., 2012); anticancer (Abidemi et al., 2015); diuretic and antioxidant (Omodamiro and Jimoh, 2017); hepatoprotective (Ikewuchi et al., 2011); antimicrobial (Eze et al., 2011) and hypoglycaemic activities (Amao, 2015) have been reported.Some isolated compounds from *S. liberica* include, pavetannin, aplysamine-2, abscisic acid, α-conidendinin and quercetin-3-O-α-L-arabinofuranoside (Eze et al., 2017).Thepresent study was designed to investigate the antihyperglycaemic and antioxidant activities of the plant with a view to justifying its antidiabetic folkloric claim and also examine any possible correlation between the two biological activities.

MATERIALS AND METHODS

Chemicals, equipment and instrumentation

UV Spectrophotometer (Model M107, SpectronicCamspec Ltd, U.K.), Vortex Genie rotamixer (K-550-GE model, Vortex-Genie accessories, U.S.A.), CareSensTMN Glucometer (model PGA 1E3028 REV3, i- SENS, Inc., Korea) with CareSensTM test strips (i- SENS, Inc., Korea), ammonium molybdate, ascorbic acid, sodium acetate, 2,4,6-tripyridyl-s-triazine (TPTZ), trolox, and 1,1,-diphenyl-1-picrylhydrazyl radical (Sigma-Aldrich Co. LLC, U.S.A.), column chromatographic (dimension: 60 × 4 cm, silica gel mesh 70–230) apparatuses were used. Others were aluminium plated thin-layer chromatographic (silica gel 60 F254, 0.25 mm) and glass plated preparative thin-layer chromatographic (silica gel 60 F254, 0.25, 0.5, 1, 2 mm, Whatman Inc., U.S.A.), silica gel (70-230 mesh, Merck & Co., Inc., U.S.A.). All solvents used were of analytical grade.

Animals

Albino Wistarrats (150–270 g) of both sexes bred under standard conditions (27 ± 3 °C, relative humidity 65%) in the animal house, Department of Pharmacology, Faculty of Pharmacy, O.A.U., Ile-Ife, Nigeria were used for the study. They were fed on a standard commercial rat pellet diet (Bendel Feeds, Nigeria) and water was given *ad libitum.* Rats were handled according to the suggestedNational Ethical Guidelines for the care of laboratory animals by theAnimal Ethics Committee(Committee for the update of the guide for the care and use of laboratory animals).

Plant material

*S.liberica*Gerome and Labroy (Agavaceae) rhizome was collected from the medicinal plant garden, Department of Pharmacognosy, Faculty of Pharmacy, ObafemiAwolowo University (OAU), Ile-Ife, Nigeria. It was identified andauthenticated by Mr. I. I. Ogunlowo,and a voucher specimen(FPI 2176) was deposited at the Pharmacy Herbarium, Department of Pharmacognosy, Faculty of Pharmacy, OAU, Ile-Ife, Nigeria. The rhizomewas washed with water, chopped into small pieces, oven-dried at 60 °Cand powdered; 4 kg of the powdered plant was extracted with methanol at room temperaturefor four days and concentrated using rotary evaporator at 50^0C to give 11.0% w/w yield(coded A).The extract (A) was suspended in water and solvent partitioned with n-hexane and ethyl acetate, concentrated *in vacuo* to obtain their corresponding n-hexane, ethyl acetate and aqueous partitioned fractions, coded B_1, $B_2$and B_3, respectively.

Acute toxicity study of the extract

Themethanol extract (A) of *S. liberica*at doses ranging from 10 to 5000 mg/kg was orally administered to 24 h fasted rats weighing between 150-270 g in two phases. The Phase 1 of the test consisted of nine (9) rats,divided into 3 groups of 3 rats each and administeredwith A using doses of 10, 100 and 1000mg/kg. The animals were then observed for mortality and/ or toxicity within each group over a 24-h period. From the results obtained in the Phase 1, the phase 2 test was carried out using eight (8) rats that were divided into 4 groups of 2 rats each. Each group was given 1000, 1600, 2900 and 5000 mg/kg of A, respectively. The animals were also observed for mortality and/or toxicity for 24h. The LD_{50} was calculated as the geometric mean of the dose that resulted in 100% lethality and that which caused no lethality at all (Lorke, 1983).

Antihyperglycaemiceffect of the extract and fractions

Glucose (10g/kg) was orally administered to normal rats that were fasted for 24 h and those that were hyperglycaemic with blood glucose level ≥ 7.0 mmol/L (126 mg/dL) after 0.5 h (T_0) were selected and divided into groups of five rats. Each group of rats was

separately orally administered with extract (A) at 100, 200 and 400 mg/kg,with1% Tween 80 in normal saline as negative control and glibenclamide at 5 mg/kg aspositivecontrol. A drop of blood was taken fromthe tip of the tail of each rat at 0.0, 0.5, 1.0, 2.0 and 4.0 h and the glucose level was measured usinga glucometer and strip. The blood glucose levels at 0.0 h (T_0)were recorded as 100%while the others were expressed as percentage of theT_0 values (Adebajo et al.,2009., 2013a,b;Akinwunmi and Ayoola, 2018).The partitioned and bulked column fractions of the extract were similarly tested for anti-hyperglycaemic activity using this procedure.

Antioxidant assay

1,1-Diphenyl-2-dipicrylhydrazyl (DPPH) radical scavenging assay

The DPPH Radical Scavenging Activity was determined using the standard method earlier reported with*l*-ascorbic acid as reference standard (Brand-Williams et al., 1995;Adebajo et al., 2013a;Akinwunmi and Ayoola, 2018).

Ferric reducing antioxidant power (FRAP) assay

FRAP assay was carried out according to the method described by Benzie and Strain (1999).

Total antioxidant capacity(TAC) assay

This was done following the prescribed method of Prieto(1999) and the results were expressed as ascorbic acid equivalents (AAE) (µmoL/g).

Hydroxyl radical scavenging activity (HRSA) assay

The HRSA of the test extract was evaluated by modification of a described method ofFerrer-Sueta and Radi(2009).

Total flavonoid content

The estimation of the total flavonoid content of the extracts was based on the aluminium chloride colorimetric method according to the method of Zhilenet al. *(*1999)as described by Miliauskaset al.(2004).

Total phenolic content

The total phenol content of the extract was determined byFolin-Ciocalteu's method of Singleton et al. *(*1999)as described by Gulcinet al.(2003).

Statistical analysis

Data were expressed as the mean ± SEM for the number (N) of the animals in the group. Analysis of variance (ANOVA) was first used, followed by Bonferroni t-test comparisons to determine the source of significant differences for all determinations, and $p<0.05$ was considered to be statistically significant. Primer version 3.01 Inc. (McGraw-Hill, USA, 1992) and Graph Pad Instant Software Inc. version 5.0 (San Diego, USA) were used.

RESULTS AND DISCUSSION

Safety profile of *S. liberica*

Using the Lorke's method, no death nor anychanges inthe breathing of the rats was observed. Also, there were no effects on the skin, gastrointestinal, sensory and nervous systems of the rats when given 10, 100, 1000, 1600 and 2900 mg/kg of *S. liberica* rhizome extract. However, death of the two rats was observed at 5000 mg/kg of methanolextract, giving the median lethal dose (LD_{50}) of *S. liberica* rhizome extract in this study as 3,808.0 mg/kg. Hence, the extract was tolerably safe and possessed a low risk of toxicity within the dose range used in these experiments; while also the doses at 100, 200 and 400 mg/kg used in the test model for the antihyperglycaemic activity of the crude methanol extract were experimentally safe. However, the LD_{50} of the aqueous leaf extract of the same *S. liberica* rhizome had previously been shown to be 4570mg/kg (Achi and Ohaeri, 2012), thus slightly safer than the methanol extract in the present investigation.

Antihyperglycaemic effects of the extract

Verspohl (2002) and Adebajo et al. (2013a,b) have reported that the results of glucose-loaded rat model in the hyperglycaemia-lowering experiments of medicinal plants or modern drugs could be extrapolated on theType II diabetic state in humans (especially when glibenclamide and other insulin stimulatory drugs are used as reference standards). Furthermore, the use of glibenclamide in antidiabetic experiments as the standard drug (Luzi and Pozza, 1997) could be used to determine the early extra-pancreatic and late insulin stimulating effects in terms of the mechanisms of action of the extract being investigated (Murray et al., 2006; Adebajo et al., 2013a,b).

Antihyperglycaemic activities of *S. Liberica* methanol extract

There was asignificant ($p < 0.05$) blood glucose level reduction from 0.5 to 4 h in the glucose- induced hyperglycaemic rats administered with 1% Tween 80 in normal saline (negative control). This was due to homeostasisand confirmed that the pancreas of the rats used was functioning well (Kar et al., 1999;Adebajoet al., 2009, 2013a; Ayoola et al., 2017a,b). Similarly, the glucose- induced hyperglycaemic rats that were administered with glibenclamide at 5 mg/kg(the positive control)showed a time-dependent reduction of their blood glucose levels, up to the fourth hour, confirming its early minor extra pancreatic and late major insulin stimulating activities (Luzi and Pozza, 1997). The extract (A) at 100

Table 1. Antihyperglycaemic activities of *S. liberica* methanol extract in glucose loaded rats.

Extract/drug (Dose mg/kg)	Blood glucose levels as percentages of T_0 (% reduction in blood glucose relative to negative control at T_0)				
	0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100.0	83.79±3.81[a]	85.89±0.50 [b]	76.45±1.71[b]	74.18±1.97[b]
A (100)	100.0	69.17±7.63[a] (17.44%)	57.54±3.75 [a] (33.01%)	58.17±4.41 [a] (23.99%)	44.17±2.73 [a] (40.46%)
A (200)	100.0	75.04±2.58[a] (10.44%)	65.48±2.09[a, b] (23.76%)	59.24±4.19 [a] (22.51%)	36.74±1.23 [a] (50.47%)
A (400)	100.0	74.54±1.95[a] (11.04%)	67.30±7.29[a, b] (21.64%)	59.14±3.64 [a] (22.64%)	42.80±3.64 [a] (42.30%)
GLI (5)	100.0	75.64±6.73[a] (9.72%)	70.68±6.86[a, b] (17.71%)	58.32±6.44 [a] (23.71%)	45.27±6.88 [a] (38.97%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentages of levels at 0h (To), n=5. Values in parentheses represent the percentage reductions in blood glucose levels relative to negative control for each time point. Values with different superscripts within columns are significantly different ($p > 0.05$, one-way analysis of variance followed by the Bonferroni t-test). **GLU** (negative control); **A**: Extract of *S. liberica*rhizome; **GLI**: Glibenclamide (positive control).

and 200 mg/kg lacked a time-dependent antihyperglycaemic activity while its effect at 400 mg/kg was time-dependent. The comparable ($p>0.05$) antihyperglycaemic activity of the extract (A) with glibenclamide (5 mg/kg) at all doses and at each time pointsuggested similar early extrapancreatic and late insulinotropic mechanisms of action of glibenclamide as seen in Table 1 (Luzi and Pozza, 1997). However, increasing the dose has not significantly increased the activity. These results are in agreement with the reported hypoglycaemic activity of the aqueous extract of the rhizome of the same plant in alloxan-induced diabetic rats (Ikewuchi and Ikewuchi, 2011).

Antihyperglycaemic effects of partitioned fractions of *S. liberica*

At 200 mg/kg, only B_1 and B_2 gave a time dependent blood glucose level reduction activity with glibenclamide suggesting early extrapancreatic and late insulin stimulating mechanisms of action of these fractions (Table 2) (Luzi and Pozza 1997). Fraction B_2 with significantly higher effect than glibenclamide at 2 h indicated better extrapancreatic effect of this fraction. None of the partitioned fractions (B_1-B_3) had better antihyperglycaemic activity than the extract indicating synergism in the activity of the constituents of the extract at this dose (Table 2). At 400 mg/kg, B_1-B_3gave the same profile of activity with glibenclamide suggesting similar mechanisms of action. Similar to B_2 (200 mg/kg), its 400 mg/kg also elicited a significantly higher effect than glibenclamide at 2 h showing additional extrapancreatic effect (Table 2). At 400 mg/kg also, there was the evidence of synergism in the activity of the plant constituents. Generally, at 200 and 400 mg/kg, the ethylacetate fraction (B_2), was the most promising fraction with additional extra pancreatic effect and it was subjected to further work in this study.

Antihyperglycaemic effects of column fractions of *S. liberica*

Seven bulked column fractions (C_1- C_7) of *S. liberica* were obtained when the ethylacetate fraction of the extract was subjected to column chromatography. Column fractions (C_2- C_7) were tested for antihyperglycaemic activity while C_1 could not be tested due to its low weight. From the result obtained, C_2, $C_5$and C_6 lacked antihyperglycaemic activities at 0.5-4 h while C_3, $C_4$and C_7showed moderate insulin stimulating effects at 4 h that was significantly lower than those of the extract, ethyl acetate fraction and glibenclamide (Table 3). This further confirmed that partitioning the extract did not improve the activity of the extract and the antihyperglycaemic constituents of the plant are working synergistically (Table 3). Similar synergistic effect of partitioned and column fractions has been reported for *Eugenia uniflora* leaf (Adebajo et al*.,* 2013a).

Antioxidant activities of *S. liberica*

The DPPH test provides the basic information on the free radical scavenging ability of natural compounds (Nenadis and Tsimidou, 2002). Other antioxidant assay protocols, HRSA, FRAP and TAC were also employed in this study to further confirm the result of DPPH assay (Adebajo et al*.,* 2013a). In the DPPH assay, partitioning the extract caused a reduction in $IC_{50}$of the resulting fractions indicating an improvement in its antioxidant properties. The ethylacetate fraction, (B_2) with the least IC_{50} value of 0.136 possessed the highest antioxidant activity (Table

Table 2. Antihyperglycaemic effects of the partitioned fractions of *S. liberica*rhizome methanol extract.

Extract/Fractions/Drug (Dose mg/kg)	Blood glucose levels as percentages of T_0 (% reduction in blood glucose relative to negative control at T_0)				
	0 h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100.0	83.79±3.81^{a}	85.89±0.50^{c}	76.45±1.71^{c}	74.18±1.97^{c}
A (200)	100.0	75.04±2.5^{a} (10.44%)	65.48±2.09^{a} (23.76%)	59.24±4.19^{b} (22.51%)	36.74±1.23^{a} (50.47%)
B_1 (200)	100.0	89.71±2.25^{b} (-7.07%)	76.28±1.73^{b} (11.19%)	58.48±6.61^{b} (23.51%)	49.88±5.47^{a,b} (32.76%)
B_2 (200)	100.0	80.83±2.82^{a,b} (3.53%)	58.55±4.62^{a} (31.83%)	51.36±5.23^{a} (32.82%)	37.40±2.93^{a} (49.52%)
B_3 (200)	100.0	61.19±8.97^{a} (26.97%)	59.97±8.83^{a} (30.18%)	57.12±5.92^{b} (25.28%)	56.68±3.07^{b} (23.59%)
Glib (5)	100.0	75.64±6.73^{a} (9.72%)	70.68±6.86^{a,b} (17.71%)	58.32±6.44^{b} (23.71%)	45.27±6.88^{a,b} (38.97%)
GLU (10 g/kg)	100.0	83.79±3.81^{a}	85.89±0.50^{c}	76.45±1.71^{c}	74.18±1.97^{b}
A (400)	100.0	75.04±2.5^{a} (10.44%)	65.48±2.09^{a,b} (23.76%)	59.24±4.19^{b} (22.51%)	36.74±1.23^{a} (50.47%)
B_1 (400)	100.0	77.36±3.93^{a} (7.67%)	61.11±6.71^{a,b} (28.85%)	46.79±4.83^{a,b} (38.79%)	39.99±1.61^{a} (46.09%)
B_2 (400)	100.0	85.44±6.39^{a} (-1.97%)	57.86±2.03^{a} (32.63%)	37.54±4.35^{a} (50.89%)	34.23±4.39^{a} (53.86%)
B_3 (400)	100.0	79.18 ±3.25^{a} (5.50%)	58.09±2.69^{a} (32.37%)	51.54±1.46^{b} (32.58%)	36.35±2.76^{a} (50.99%)
Gli (5)	100.0	75.64±6.73^{a} (9.72%)	70.68±6.86^{b} (17.71%)	58.32±6.44^{b} (23.71%)	45.27±6.88^{a,b} (38.97%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentage of levels at 0 h (T_0), n = 5. Values with different superscripts within columns are significantly different ($p<0.05$), while values with similar superscript are comparable ($p<0.05$): **GLU** (10 g/kg): glucose with normal saline (negative control); **A:** *S. liberica* extract **B_1**: *n*-Hexane fraction; **B_2**: Ethyl acetate fraction; **B_3**: Aqueous fraction; **GLI**: Glibenclamide (positive control).

Table 3. Antihyperglycaemic effects of the column fractions of *S. liberica*rhizome.

Extract/Drug (Dose mg/kg)	Blood glucose levels as percentages of T_0 (% reduction in blood glucose relative to negative control at T_0)				
	0h	0.5 h	1 h	2 h	4 h
GLU (10 g/kg)	100.0	83.79±3.81^{a}	85.89±0.50^{b}	76.45±1.71^{c}	74.18±1.97^{c}
A (200)	100.0	75.04±2.58^{a} (10.44%)	65.48±2.09^{a} (23.76%)	59.24±4.19^{b} (22.51%)	36.74±1.23^{a} (50.47%)
B_2 (400)	100.0	85.44±6.39^{a,b} (-1.97%)	57.86±2.03^{a} (32.63%)	37.54±4.35^{a} (50.89%)	34.23±4.39^{a} (53.86%)
C_2 (400)	100.00	91.46±2.40^{a,b} (-9.15%)	88.53±3.18^{b} (-3.07%)	82.32±2.51^{c} (-7.13%)	73.97±3.92^{c} (0.28%)
C_3 (400)	100.00	94.78±1.09^{b} (-13.12%)	86.67±1.87^{b} (-0.91%)	74.21±2.59^{b,c} (2.93%)	62.39± 2.56^{b} (15.89%)
C_4 (400)	100.00	95.60±2.07^{b} (-14.09%)	88.28±3.01^{b} (-2.78%)	83.21±3.49^{c} (-8.84%)	63.69±0.82^{b} (14.14%)
C_5 (400)	100.00	91.54±1.10^{b} (-9.14%)	83.65±0.94^{b} (2.61%)	78.99±0.43^{c} (-3.32%)	74.12±1.65^{c} (0.08%)
C_6 (400)	100.00	92.53±2.99^{b} (-10.43%)	87.76±3.76^{b} (-2.18%)	80.50±2.07^{c} (-5.29%)	70.66±1.97^{c} (4.75%)

Table 3. Cont'd.

C_7 (400)	100.00	83.89±3.81[a] (-0.12%)	78.24±2.59[b] (8.91%)	72.61±2.46[b,c] (5.02%)	64.80±1.55[b] (12.65%)
GLI (5)	100.0	75.64±6.73[a] (9.72%)	70.68±6.86[a,b] (17.71%)	58.32±6.44[b] (23.71%)	45.27±6.88[a] (38.97%)

Data show the mean ± SEM blood glucose levels at the different time points expressed as percentage of levels at 0 h (T_0), n = 5. Values with different superscripts within columns are significantly different (p<0.05), while values with similar superscript are comparable (p<0.05): **GLU** (10 g/kg): glucose with normal saline (negative control); **A:** *S. liberica* extract; **B_2**: Ethyl acetate fraction; **C_2 – C_7**: Bulked column fractions; **GLI**: Glibenclamide (positive control).

Table 4. Antioxidant activities of methanol extract, partitioned and column fractions of *S. liberica*.

Extract/ Drug	IC_{50} (mg/ml)	(µgAAEq/ml)				IC_{50} (mg/ml)
	DPPH	**TPC**	**TFC**	**TAC**	**FRAP**	**HRSA**
SLE	0.170	0.632 ±0.083[a]	0.348 ±0.025[a]	3.888 ±0.070[c]	0.236 ±0.083[e]	0.677
B_1	0.149	0.988 ± 0.030[b]	0.537 ± 0.013[b]	5.712 ± 0.014[d,e]	0.436 ± 0.029[e]	0.068
B_2	0.136	1.628 ± 0.058[c]	0.866 ± 0.037[c]	9.504 ± 0.143[f]	0.826 ± 0.013[f]	0.018
B_3	0.142	0.897 ± 0.018[b]	0.462 ± 0.007[a,b]	4.632 ± 0.029[c]	0.372 ± 0.007[e]	0.235
C_2	0.126	0.913 ± 0.01[b]	0.785 ± 0.02[c]	6.055 ± 0.07[e]	0.017 ± 0.001[a]	0.160
C_3	0.034	1.983 ± 0.01[d]	1.996 ± 0.07[d]	5.470 ± 0.21[d]	0.081 ± 0.005[c,e]	0.085
C_4	0.044	0.940 ± 0.01[b]	0.482 ± 0.03[b]	3.266 ± 0.08[b]	0.069 ± 0.005[c]	0.082
C_5	0.119	0.670 ± 0.003[a]	0.395 ± 0.11[a,b]	2.574 ± 0.19[a]	0.042 ± 0.004[b]	0.081
C_6	0.061	0.940 ± 0.01[b]	0.759 ± 0.05[c]	4.008 ± 0.33[c]	0.106 ± 0.014[d]	0.055
C_7	0.026	0.981 ± 0.004[c]	1.274 ±0.23[c]	4.056 ± 0.13[c]	0.040 ± 0.003[b]	0.082
Vit. C	0.037	NA	NA	NA	NA	0.060

Data show the mean ± SEM (*n* = 6). IC_{50}: Concentration needed to give 50% activity; µgAAEq/ml: µg Ascorbic acid equivalent per mL; **DPPH**: 1,1-diphenyl-2-picryhydrazyl assay; **FRAP**: Ferric reducing antioxidant power assay; **TAC**: Total antioxidant capacity; **HRSA**: Hydroxyl radical scavenging assay; **TPC:** Total phenolic content; **TFC**: Total flavonoid content. **SLE:** *S. liberica* extract, **B_1**: *n*-Hexane fraction; **B_2**: Ethyl acetate fraction; **B_3**: Aqueous fraction; **C_2-C_7**: Column fractions.

4). Smaller IC_{50} value has been reported to correspond to higher and stronger antioxidant activity (Maisuthiasakul et al*.,* 2008).

Similar to DPPH assay, $B_2$with the leastIC_{50} value of 0.018 in HRSA assay with better activity than the extract was also the most active antioxidant fraction. In the TAC and FRAP assays, the antioxidant properties of B_2 were consistent with those observed in DPPH and HRSA assays with B_2 giving the highest values of 9.5 and 0.8 µgAAEq/mL, respectively that were significantly higher (p<0.05) than those of extract and other partitioned fractions (Table 4). The highest antihyperglycaemic effect that was elicited by B_2 (Table 3) and its best antioxidant properties in the four antioxidant assays (Table 4) suggested a strong link between the two biological activities. Similar effects have been reported for *Entandrophragma cylindricum* and *Eugenia uniflora* leaf (Adebajo et al*.,* 2013a; Ayoola et al*.,* 2017a). High values of total phenolic content (TPC) and total flavonoid content (TFC) elicited byB_2 (Table 4) indicated that this fraction was richer in phenolic compounds than all other fractions and were possibly responsible for the observed effects. *Carica papaya* and *Citrillus lanatus* seeds have similarly been reportedfor their antihyperglycaemic and antioxidant activities and have been found to be rich in total phenolic and total flavonoid content (Akinwunmi and Ayoola, 2018).

The antioxidant activities of the bulked column fractions of B_2 showed that in DPPH assay, C_3, C_4 and C_7, which were the most active antihyperglycaemic bulked column fractions, gave a highradical scavenging activity that was comparable to the positive control (Table 4). In HRSA assay, C_3, C_4 and C_7 similarly demonstrated good antioxidant effects with low IC_{50} values. Furthermore, in TAC and FRAP assays, C_3, C_4 and C_7gave significant free radical scavenging activities with C_3 showing better effect than C_4 (Table 4). High TPC and TFC values, especially for $C_3$and C_7 showed high concentration of phenolic constituents in these fractions and implicated them in their observed antihyperglycaemic and antioxidant activities (Table 4). It was evident from the results of this work that purification of the extract

improved its antioxidant activities while its antihyperglycaemic effect was further reduced (Tables 1 to 4). Therefore, further fractionation of the fractions for the isolation of their antihyperglycaemic constituents may not be worthwhile.

Lower antihyperglycaemic activities of the fractions of*S. liberica* rhizome in this study suggested that the plant is more effective as an extract in the management of diabetes and should be used as such. Also, the high antioxidant activities of the bulked column fractions may be linked to the other activities of the plant such as anticancer (Abidemi et al*.,* 2015) and hepatoprotective (Ikewuchi et al*.,* 2011);

Conclusion

The results of this study confirmed that *S. liberica* is safe for use, has a significant anti-hyperglycaemic activity that justified its antidiabetic ethno-medicinal claims. It also has additional anti-oxidant effects.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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