Anti-diabetic Activity of *Sanseviera liberica* Gerome and Labroy (Agavaceae) Root Extract and Fractions on Alloxan-induced Diabetic Rats

1Amao OS, 2Sofidiya MO, 1Olusanya AW, 1Ishola IO, 1Adeyemi OO
1Department of Pharmacology, Therapeutics, & Toxicology, Faculty of Basic Medical Sciences, College of Medicine, University of Lagos, Lagos, Nigeria.
2Department of Pharmacognosy, Faculty of Pharmacy, University of Lagos, Lagos, Nigeria.

**Corresponding Author**
OO Adeyemi
Department of Pharmacology, Therapeutics and Toxicology, Faculty of Basic Medical Sciences, College of Medicine, University of Lagos, Lagos, Nigeria.
Email address: ooadeyemi@cmul.edu.ng; Tel.: +2348034459618

**ABSTRACT**

**Background:** The root decoction of *Sanseviera liberica* Gerome and Labroy (Agavaceae) is used in traditional African medicine for the treatment of diabetes mellitus, convulsion, earache, and wounds.

**Objective:** This study sought to investigate the effect of *Sanseviera liberica* methanol root extract (SL) and its fractions - hexane (HF), chloroform (CF), ethylacetate (EF) and butanol (BF) on alloxan-induced hyperglycaemia in rats.

**Methods:** SL (100, 200 or 400 mg/kg, p.o.), and fractions (100 mg/kg, p.o.) or insulin (0.4 IU/kg, positive control) were respectively administered to rats which thereafter were subjected to glucose tolerance (2 g/kg, i.p.) or alloxan-induced hyperglycaemia (150 mg/kg, i.p.) tests for 21 consecutive days. Blood glucose level, glycosylated haemoglobin, liver glycogen, renal and liver functions were assayed.

**Results:** SL, CF and EF, as well as glibenclamide produced time course and significant reduction in blood glucose level in glucose tolerance test. Interestingly, alloxan administration increased blood glucose level, glycosylated haemoglobin, alkaline phosphatase (ALP), alanine aspartate transaminase (AST), and albumin which were attenuated by SL, CF, and EF administration. The preliminary phytochemical analysis revealed the presence of flavonoids, phenols, tannins, saponins, cardiac glycosides, terpenoids, anthraquinones and alkaloids.

**Conclusion:** Findings from this study established the antidiabetic activity of methanolic root extract of *S. liberica* and its fractions in rats. Thus, it could be a potential phytomedicine in the management of diabetes.

**Keywords:** Diabetes, *Sanseviera liberica*, glycosylated haemoglobin, hypoglycaemia.

**INTRODUCTION**

Diabetes Mellitus (DM) is a health problem that has been on the increase worldwide and its prevalence, according to the International Diabetes Federation (IDF) as at 2015 was about 415 million and is estimated to reach 642 million people by 2040 (1). It is characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin action and secretion which is due to loss of pancreatic beta-cell function (2). DM is associated with numerous health problems that ultimately reduces the quality of life and causes increased mortality (3). Type 1 diabetes is due to an autoimmune process or other mechanisms associated with beta cell destruction with consequent insulin deficiency. Type 2 diabetes is a spectrum ranging from predominant insulin resistance with relative insulin deficiency to a predominant secretory defect with insulin resistance (4).

It is well known that blood glucose levels are regulated not just by the absorption of dietary carbohydrate but also by the liver (5). Several studies have shown that the sub-acute administration of alloxan (a toxic glucose analogue), causes selective destruction of insulin producing cells in the pancreas, thus producing insulin-dependent Type 1-like diabetes syndrome (6).

The conventional treatment for Type 1 DM is the use of insulin analogues while that for Type 2 DM is oral antidiabetic agents and injectables like insulin and glucagon-like peptide-1 agonists (7). Although, these drugs are beneficial in achieving glycaemic control, they have been shown to have prominent side effects and do not modify the course of diabetic complications. Current trends in diabetes research is investigating potential replacement source for pancreatic beta-cell function with the aim of providing disease modifying therapy (8–12).

*Sanseviera liberica* Gerome and Labroy (Agavaceae) is a perennial plant with thick woody rhizomes widely distributed in the tropical, subtropical, and temperate zones of the world. The roots and leaves of the plant are used in African ethnomedicine for the treatment of diabetes, asthma, abdominal
and joint pains, colic, diarrhoea, eczema, gonorrhoea, haemorrhoids, and hypertension (13–14). Hence, this study sought to evaluate the antihyperglycaemic activity of the crude extract and various solvent fractions of Sanseviera liberica.

MATERIALS AND METHODS
Chemicals and Reagents
Alloxan monohydrate (Santa Cruz, Germany) dissolved in cold citrate buffer (pH=4.5), trichloroacetic acid, silver sulphate, methanol, n-hexane, chloroform, ethylacetate, butanol and all other chemicals and reagents used were procured from Sigma Aldrich, St. Louis MO, USA.

Plant Material Collection and Identification
The fresh roots of Sanseviera liberica were harvested from local horticulture garden in Odofin-Agbegi village, Ikire, Osun State, Nigeria. They were identified and confirmed by Dr. A.B. Kadiri of the Department of Botany, Faculty of Science, University of Lagos, Lagos, Nigeria. A voucher specimen number LUH-6303 was allotted for reference purpose.

Extraction and Fractionation
The plant roots were carefully washed with water, drained, sliced into pieces, and air dried for five days. The dried root was pulverised into powder (800 g) and extracted with 4 L of methanol using a Soxhlet apparatus. The resulting extract was evaporated to dryness to give 2.49% w/w of methanolic extract. The dried root was pulverised into powder (800 g) and extracted with 4 L of methanol using a Soxhlet apparatus. The resulting extract was evaporated to dryness to give 2.49% w/w of methanolic extract. The extract was subjected to successive partitioning with n-hexane, chloroform, ethylacetate and butanol. The extract and fractions were evaporated to dryness using a rotary evaporator, under reduced pressure at 40°C. The percentage yields are 24.90, 2.56, 3.80, 0.34, and 10.44% w/w for S. liberica extract, hexane, chloroform, ethylacetate, and butanol fractions, respectively.

Experimental Animals
Male albino rats (170–200 g, 12 weeks old) used in this study were obtained from the Laboratory Animal Centre, College of Medicine, University of Lagos, Ibi-Araba, Lagos. The experimental procedures adopted in this study was approved by the Health Research Ethics Committee of the College of Medicine, University of Lagos, Nigeria (CMUL/HREC/RH041/2019).

Qualitative Phytochemical Screening
The phytochemical screening of the methanolic root extract of S. liberica and its fractions were performed using standard methods (15–18).

Oral Glucose Tolerance Test
To evaluate the effect of SL and fractions on blood glucose level, animals were fasted overnight, and serum glucose levels determined using Accucheck® glucose kits, 30 min before (baseline glycaemia) oral glucose (2 g/kg) administration and postprandial serum glucose 30 min after oral glucose load (18). Glycaemic balanced animals were randomly divided into six groups of 6 animals each; Group 1: naive control (vehicle 10 ml/kg, p.a.); Group 2: vehicle + glucose 2 g/kg, p.a.; Groups 3–6: glibenclamide (5 mg/kg), HF, CF, EF and BF (100 mg/kg, p.o.), respectively. Time course serum glucose levels were recorded at 30, 60, 90 and 120 min post-glucose administration. Serum glucose area under curve (AUC) was determined.

Alloxan-induced Hyperglycaemia
Animals fasted overnight received alloxan monohydrate (150 mg/kg, i.p.) dissolved in cold citrate buffer. Blood glucose level was checked 3 days after alloxan injection (19). Rats with glucose level more than 200 mg/dl were considered diabetic, selected and were randomly divided into 11 groups (n=6). Group 1: vehicle control (10 ml/kg, normal rats); Group 2: diabetic rats + vehicle (10 ml/kg); Groups 3–5: diabetic rats + SL (100, 200 or 400 mg/kg, p.o.), respectively; Groups 6–9: HF, CF, EF or BF (100 mg/kg, p.o.), respectively; Group 10–11: GLIB (5 mg/kg, p.o.) or insulin (0.4 IU/kg, s.c.). Blood glucose level were checked weekly (days 7, 14 and 21) and percentage change in glucose level was determined.

Biochemical Assay
On day 21, animals were anaesthetized with chloralose, blood was collected for estimation of Hb, HbA1c level, aspartate aminotransferase (AST), alkaline phosphatase (ALP), alanine transaminase (ALT), bilirubin, albumin, creatinine and urea using automated analyser. Liver samples were dissected from rats, rinsed in phosphate buffer, and homogenized. The homogenate was diluted with distilled water for the estimation of liver glycogen using a spectrophotometer at wavelength of 520 nm (5).

Statistical Analysis
Results were expressed as mean ± SEM. The statistical level of significance were analysed by one or two way analysis of variance (ANOVA) followed by Tukey’s multiple comparison test using GraphPad Prism 6 software (GraphPad software, San Diego, CA, USA).

RESULTS
Qualitative Phytochemical Analysis
The preliminary qualitative phytochemical analysis of the crude extract and fractions of SL showed the presence of flavonoids, phenols, tannins, saponins, cardiac glycosides, terpenoids, anthraquinones and alkaloids.

Oral Glucose Tolerance Test (OGTT)
There was an increase in blood glucose levels 30 min. after glucose load. The peak in blood glucose levels was seen at 60 min. As depicted in Table 1, chloroform fraction (CF) and ethylacetate fraction (EF) caused significant reductions (p<0.001) in blood glucose of rats with peak effects at 90 and 120 min., respectively, when compared with the control group. Similarly, glibenclamide significantly reduced blood glucose which peaked at 90 min. post-glucose loading. In contrast, butanol and hexane fractions failed to reduce blood glucose level.
Effects of Treatment on Blood Glucose Level in Alloxan-induced Diabetes

As shown in Figures 1 and 2, alloxan caused a time course increase in blood glucose levels in comparison to control. However, SL (100, 200 and 400 mg/kg) and insulin administration significantly reduced blood glucose levels, respectively by 16.4, 48.1, 77.7 and 52.0%. In addition, CF and EF, as well as glibenclamide administration significantly reduced blood glucose levels by 76.80, 86.70 and 81.00% respectively.

Table 1: Oral Glucose Tolerance Test on Fractions of Methanolic Root Extract of *S. liberica* in Normal Fasted Rats after Oral Glucose Load

<table>
<thead>
<tr>
<th>Groups</th>
<th>0 min</th>
<th>30 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>81.1 ± 1.02</td>
<td>131.5 ± 2.06</td>
<td>153.0 ± 0.28</td>
<td>121.1 ± 2.09</td>
<td>102.3 ± 4.73</td>
</tr>
<tr>
<td>HF (100 mg/kg)</td>
<td>88.50 ± 15.67</td>
<td>127.00 ± 29.11</td>
<td>153.0 ± 15.27</td>
<td>108.75 ± 32.83</td>
<td>99.00 ± 28.46</td>
</tr>
<tr>
<td>CF (100 mg/kg)</td>
<td>67.40 ± 16.95</td>
<td>98.80 ± 16.79</td>
<td>100.20 ± 5.78</td>
<td>78.40 ± 4.63</td>
<td>65.40 ± 16.45</td>
</tr>
<tr>
<td>EF (100 mg/kg)</td>
<td>84.60 ± 9.29</td>
<td>104.60 ± 17.69</td>
<td>76.80 ± 5.78</td>
<td>73.80 ± 5.01</td>
<td>68.80 ± 12.82</td>
</tr>
<tr>
<td>BF (100 mg/kg)</td>
<td>56.00 ± 14.23</td>
<td>138.40 ± 44.82</td>
<td>117.60 ± 14.31</td>
<td>110.40 ± 4.57</td>
<td>110.40 ± 4.57</td>
</tr>
<tr>
<td>SL (400 mg/kg)</td>
<td>87.25 ± 5.25</td>
<td>116.75 ± 18.40</td>
<td>108.00 ± 11.67</td>
<td>79.50 ± 1.44</td>
<td>83.50 ± 8.57</td>
</tr>
<tr>
<td>Glibe (5 mg/kg)</td>
<td>66.25 ± 4.80</td>
<td>133.50 ± 7.85</td>
<td>95.00 ± 12.48</td>
<td>43.00 ± 7.91</td>
<td>64.25 ± 8.68</td>
</tr>
</tbody>
</table>

The values represent mean ± SEM; n=6. *p<0.05, †p<0.01, ‡p<0.001 compared with control; *p<0.05, †p<0.01, ‡p<0.001 compared with glibenclamide were considered significant. HF – hexane fraction; CF – chloroform fraction; EF – ethylacetate fraction; BF – butanol fraction; Glibe – glibenclamide; SL – *S. liberica* root extract.

Effects of Treatment on Body Weight in Alloxan-induced Diabetes

As shown in Figure 3, alloxan administration produced a time course and significant decrease (p<0.001) in body weights when compared to non-diabetic control. However, CF and glibenclamide reversed the decrease in body weights induced by alloxan.
Effects of Treatments on Haemoglobin, Glycosylated Haemoglobin (HbA1c) and Liver Glycogen Levels in Alloxan-induced Diabetes

Result in Table 2a–b show a significant increase in glycosylated haemoglobin in alloxan (diabetic control) group when compared with normal control group. However, administration of SL and fractions significantly reduced (p<0.01) the glycosylated haemoglobin levels compared with alloxan (diabetic control) group. The liver glycogen level of alloxan (diabetic control) group was significantly lower (p<0.01) when compared with the control group. However, insulin, SL (400 mg/kg), glibenclamide, CF and EF treated groups caused significant increase in liver glycogen level when compared with the alloxan (diabetic control) group.

**Table 2a: Effects of S. liberala on Haemoglobin (Hb), Glycosylated Haemoglobin (HbA1c) and Liver Glycogen Levels in Alloxan-induced Diabetes**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Haemoglobin (Hb; g/dl)</th>
<th>Glycosylated Haemoglobin (HbA1c) (g/dl)</th>
<th>Liver Glycogen (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>13.2±0.05</td>
<td>3.68±0.11</td>
<td>2.51±0.05</td>
</tr>
<tr>
<td>Alloxan</td>
<td>14.1±0.04</td>
<td>4.1±0.09</td>
<td>2.12±0.07</td>
</tr>
<tr>
<td>SL(100 mg/kg)</td>
<td>13.63±0.03&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.72±0.04&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.14±0.05&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>SL(200 mg/kg)</td>
<td>14.08±0.04&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5.18±0.09&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.25±0.03&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>SL(400 mg/kg)</td>
<td>14.66±0.01&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4.48±0.06</td>
<td>3.46±0.42&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Insulin (0.4 IU/kg)</td>
<td>12.44±0.00&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3.68±0.11</td>
<td>2.89±0.10</td>
</tr>
</tbody>
</table>

Results are represented as mean ± SEM (n=5). *p<0.05, †p<0.001 compared to control; ‡p<0.05, §p<0.001 compared to alloxan (one way ANOVA followed by Turkey’s multiple comparison test).

**Table 2b: Effects of Fractions of S. liberala on Haemoglobin (Hb), Glycosylated Haemoglobin (HbA1c) and Liver Glycogen Levels after Treatment**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Haemoglobin (Hb; g/dl)</th>
<th>Glycosylated Haemoglobin (HbA1c) (g/dl)</th>
<th>Liver Glycogen (g/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>13.56 ± 0.29</td>
<td>3.73 ± 0.14</td>
<td>6.09 ± 0.5</td>
</tr>
<tr>
<td>Alloxan</td>
<td>9.16 ± 0.16</td>
<td>7.13 ± 0.08</td>
<td>2.6 ± 0.26</td>
</tr>
<tr>
<td>HF (100 mg/kg)</td>
<td>10.73 ± 0.14&lt;sup&gt;c&lt;/sup&gt;</td>
<td>6.43 ± 0.70&lt;sup&gt;c&lt;/sup&gt;</td>
<td>3.64 ± 0.1&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>CF (100 mg/kg)</td>
<td>12.03 ± 0.54&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.66 ± 0.08&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4.37 ± 0.22&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>EF (100 mg/kg)</td>
<td>11.03 ± 0.54&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5.93 ± 0.26&lt;sup&gt;c&lt;/sup&gt;</td>
<td>4.08 ± 0.2&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>BF (100 mg/kg)</td>
<td>9.73 ± 0.14&lt;sup&gt;d&lt;/sup&gt;</td>
<td>6.56 ± 0.72&lt;sup&gt;d&lt;/sup&gt;</td>
<td>2.91 ± 0.12&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>SL (400 mg/kg)</td>
<td>10.93 ± 0.23&lt;sup&gt;d&lt;/sup&gt;</td>
<td>6.36 ± 0.64&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3.69 ± 0.16&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Glibe (100 mg/kg)</td>
<td>11.00 ± 0.12&lt;sup&gt;d&lt;/sup&gt;</td>
<td>5.86 ± 0.04&lt;sup&gt;d&lt;/sup&gt;</td>
<td>4.08 ± 0.13&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Results are represented as mean ± SEM (n=5). *p<0.01 compared to control; †p<0.001 compared to alloxan (two way ANOVA followed by Turkey’s multiple comparison test).

**Table 4: Effects of Fractions of S. liberala on Liver Enzymes and Kidney Functions in Alloxan-induced Diabetes**

<table>
<thead>
<tr>
<th>Groups</th>
<th>AST (mg/dl)</th>
<th>ALT (mg/dl)</th>
<th>ALP (mg/dl)</th>
<th>BIL (mg/dl)</th>
<th>ALB (%/dl)</th>
<th>Urea (mg/dl)</th>
<th>Cr (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>52.0±5.18</td>
<td>36.8±3.28</td>
<td>113.6±5.12</td>
<td>1.3±0.14</td>
<td>33.8±1.35</td>
<td>30±0.71</td>
<td>42.8±1.51</td>
</tr>
<tr>
<td>Alloxan</td>
<td>48.5±1.50</td>
<td>43.5±2.50</td>
<td>115.5±1.50</td>
<td>1.4±0.15</td>
<td>39.8±2.35</td>
<td>43.5±1.5</td>
<td>56.8±1.45</td>
</tr>
<tr>
<td>HF (100 mg/kg)</td>
<td>53.4±2.23</td>
<td>27.4±1.60&lt;sup&gt;c&lt;/sup&gt;</td>
<td>104.4±1.63</td>
<td>1.7±0.13</td>
<td>31.5±1.62&lt;sup&gt;c&lt;/sup&gt;</td>
<td>38.2±1.39</td>
<td>45.2±1.7</td>
</tr>
<tr>
<td>CF (100 mg/kg)</td>
<td>59.0±2.45</td>
<td>39.0±3.11</td>
<td>102.8±5.25</td>
<td>1.0±0.10</td>
<td>30.8±1.38</td>
<td>35.5±8.06</td>
<td>46.7±4.75</td>
</tr>
<tr>
<td>EF (100 mg/kg)</td>
<td>47.0±2.08</td>
<td>38.0±2.08</td>
<td>102.0±0.58&lt;sup&gt;c&lt;/sup&gt;</td>
<td>1.8±0.12</td>
<td>37.1±1.21</td>
<td>38.0±5.8</td>
<td>45.2±0.42</td>
</tr>
<tr>
<td>BF (100 mg/kg)</td>
<td>51.4±0.23</td>
<td>31.0±0.41&lt;sup&gt;c&lt;/sup&gt;</td>
<td>109.8±0.48</td>
<td>2.9±0.05&lt;sup&gt;b&lt;/sup&gt;</td>
<td>29.0±0.44&lt;sup&gt;c&lt;/sup&gt;</td>
<td>42.6±0.48</td>
<td>47.8±0.11&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>SL (400 mg/kg)</td>
<td>53.8±1.93</td>
<td>37.3±0.85</td>
<td>103.8±1.55</td>
<td>2.0±0.17&lt;sup&gt;b&lt;/sup&gt;</td>
<td>24.7±0.9&lt;sup&gt;b&lt;/sup&gt;</td>
<td>32.5±1.19</td>
<td>31.7±0.67</td>
</tr>
<tr>
<td>Glibe (5 mg/kg)</td>
<td>58.3±1.23</td>
<td>37.1±1.50</td>
<td>107.5±0.43</td>
<td>2.0±0.11&lt;sup&gt;b&lt;/sup&gt;</td>
<td>33.3±2.62</td>
<td>38.1±1.19</td>
<td>45.1±1.7</td>
</tr>
</tbody>
</table>

Results represent mean ± SEM (n=5). *p<0.05 compared to control; †p<0.001 compared to diabetic control (two way ANOVA followed by Turkey’s multiple comparison test).

**DISCUSSION**

This study demonstrated the beneficial effect of oral administration of the methanolic root extract of *S. liberala* and its fractions on body weight and blood glucose in alloxan model of Type 1 diabetes. More so, the blood glucose-lowering effect of *S. liberala* is dose-dependent at 400 mg/kg, with a better activity when compared with the 100 and 200 mg/kg doses. Moreover, phytochemical analysis revealed the presence of flavonoid, phenols, tannins, saponins, cardiac glycosides, terpenoids, anthraquinones, and alkaloids. These components have been shown to possess glucose lowering properties (21) and this may account for the anti-hyperglycaemic activity of the extract.

Insulin is an anabolic hormone and its deficiency is associated with increased loss and degradation of structural protein (22). This may manifest as weight loss and a failure to gain weight in growing animals. In agreement with previous studies, alloxan-treated rats showed no appreciable gain in weight during the period of the study, in contrast to the non-diabetic control that gained weight (22, 23). Rats administered fractions of *S. liberala* had moderate weight gain which was not significantly different from the non-diabetic control and rats treated with glibenclamide. A previous study had also shown moderate weight gain which was not significantly different from the non-diabetic control and rats treated with glibenclamide. However, insulin, SL (400 mg/kg), and the fractions of *S. liberala* caused significant increase in liver glycogen level when compared with the alloxan (diabetic control) group.
demonstrated the benefit of plant extract on weight changes in DM (23).

The oral glucose tolerance test (OGTT) is used to measure tissue response to the presence of high glucose load. A high glucose load is expected to cause an increase in phase two insulin secretion and consequently an increase in glucose uptake, a deficiency in any of this leads to hyperglycaemia or impaired glucose levels (24). The results of OGTT showed that the chloroform and ethylacetate fractions treated normoglycaemic rats produced a significant decrease in the blood glucose levels when compared with vehicle treated, which was similar to the effect of glibenclamide. However, the butanol and n-hexane fractions failed to reverse the increase in blood glucose. This indicates that the chloroform and ethylacetate-fractions of *S. liberica* improved glucose tolerance and aided glucose uptake in diabetic rats.

Hypoglycaemia is one of the most common adverse effects of antidiabetic drugs, especially with first generation sulphonylurea such as glibenclamide (25). The group administered glibenclamide had a trough of 43 mg/dl which supports its potential to cause hypoglycaemia. This was not seen in any other treatment group, suggesting that the fractions of *S. liberica* had lower potentials to cause hypoglycaemia. This makes *S. liberica* an attractive alternative to glibenclamide. Further studies comparing it with other antidiabetic drugs are required to confirm our findings.

*S. liberica* and its fractions demonstrated anti-hyperglycaemic effect by causing a significant decrease in the blood glucose levels after 21 days of administration compared to baseline measurements. The highest anti-hyperglycaemic activity was observed in the chloroform and ethylacetate fractions. This suggests that the active component of the plant extract may be present in large amount in the chloroform and ethylacetate fractions.

In poorly controlled diabetes, there is an increased glycosylation of a number of proteins including haemoglobin. Glycosylated haemoglobin is used to assess long term glycaemic control usually over a period of 2 to 3 months in humans. It is also used as a diagnostic parameter in DM (26). Glycosylated haemoglobin is less subject to variations when compared with fasting or random blood glucose measurement and oral glucose tolerance test, but may not be the best method for assaying glycaemic control over a short period of time and also in conditions associated with reduced life span of haemoglobin (27). The diabetic groups had significantly higher levels of glycosylated haemoglobin compared to the control group. Although levels were slightly lower in the treated group, this was not significant, but a trend towards lower levels was obtained in the chloroform and ethylacetate fractions, which was similar to that obtained with glibenclamide. The result obtained confirms the poor discriminatory effect of glycosylated haemoglobin when used to assay treatment effect over a short period of time (28–29).

Evaluation of the nephrotoxic and hepatotoxic potentials of *S. liberica* and its fractions suggests that the extract is relatively safe. The liver enzymes were not significantly higher compared to the control group. However, bilirubin was found to be significantly higher in butanol fractions treated rats compared to control and alloxan group. Glibenclamide also increased bilirubin level contrary to known effects. The significance of this finding is uncertain but increased levels of bilirubin is a non-specific marker of liver injury since it is found in association with other pathological states (30). However, further studies are needed to confirm this. Albumin was also significantly lower in the butanol fraction of *S. liberica* group compared with control. Albumin is a marker of synthetic capacity of the liver and nutritional status; reduced levels in liver diseases are seen in chronic liver damage such as in cirrhosis and more severe liver damage (31). The reduced levels in this study may not be associated with liver disease because of the duration of use in this study and the absence of markers of severe liver damage like increased ALT which is a more specific marker of liver damage (32). The results from this study show a non-significant increase in the level of plasma urea and creatinine in the diabetic (alloxan) group compared to control. Albumin is also a marker of liver damage (32). The results from this study show a non-significant increase in the level of plasma urea and creatinine in the diabetic (alloxan) group compared to control level which may be associated with dehydration resulting from hyperglycaemia. The fractions of *S. liberica* did not appear to have nephrotoxic potential.

This present study also showed an increased glycogen content after 21-day treatment with fractions of methanolic root extract of *S. liberica*. The lower liver glycogen level in diabetic rats is related to reduced glycogen synthesis and increased glycogenolysis resulting from insulin deficiency (33). Reduced insulin levels seen in fasting state is also permissive for increased gluconecogen release which favours glucoseogenesis, further depleting glycogen stores (33). The increased glycogen levels in the treated group suggest that the extract may increase insulin secretion; however, further studies are needed to confirm this.

CONCLUSION

Our data suggests that the methanolic root extract of *S. liberica* and its fractions (chloroform and ethylacetate) produced potential anti-hyperglycaemic activity. In addition to decreasing the blood glucose, *S. liberica* and its fractions also improved the weight and liver glycogen in alloxan-diabetic rats. Thus, could be a potential phytomedicine in the management of diabetes mellitus.

ACKNOWLEDGEMENT

The authors wish to acknowledge the efforts of Mr. Chijioke Micah of the Department of Pharmacology, Therapeutics, and Toxicology, Faculty of Basic Medical Sciences, College of Medicine, University of Lagos. This work was fully supported by Tertiary Education Trust Fund (TETFund; TETF 2010/2011).

Conflict of Interest

The authors declare that there is no conflict of interest in this study.

REFERENCES

Anti-diabetic Activity of Sansevieria liberica


