ROSELLE HIBISCUS SABDARRIFA CALYCES EXTRACTS MODULATES CARDIOVASCULAR DISEASE RISK AND KIDNEY DYSFUNCTIONS IN DIABETIC RATS

Emmanuel O. Ajani 1,2, Fisayo A. Bamisaye 1,2, Tajudeen O. Amusa 1,3, Olubunmi Atolani 1,4, Adeola T. Kola-Mustapha 1,5, Ngaitad S. Njinga 1,6, Luqman A. Quadri 1,7, Moji T. Bakare-Odunola 1,6, Adenike T. Oladiji 1,7 and Learnmore Kambizi 1,8

1African Centre for Herbal Research, Ilorin (ACHRI), University of Ilorin, Nigeria
2Phytomedicine Toxicology and Drug Development Laboratory, Department of Biochemistry, Kwaara State University, Malete, Nigeria
3Department of Forest Research Management, University of Ilorin, Ilorin, Nigeria.
4Department of Chemistry, University of Ilorin, Ilorin, Nigeria.
5Department of Pharmaceutics and Industrial University of Ilorin, Ilorin, Nigeria.
6Department of Pharmaceutical and Medicinal Chemistry, University of Ilorin, Ilorin, Nigeria.
7Department of Biochemistry, University of Ilorin, Ilorin, Nigeria.
8Department of Hulticulture, Cape Peninsula University of Technology, South Africa

*Corresponding author address: Department of Pharmaceutical and Medicinal Chemistry, Faculty of Pharmaceutical Sciences, University of Ilorin, Ilorin, Nigeria.

ABSTRACT

Diabetes, an emerging major public health problem when untreated may lead to chronic complications. This study aimed to evaluate the *Hibiscus sabdariffa*, effects on renal dysfunction and cardiovascular disease risk associated with streptozocin induced diabetes. The study used 42 rats randomized to six groups: 2 diabetic groups (treated each with 200 and 500 mg/kg dose of the macerated aqueous extract); 2 diabetic groups (treated each with glibenclamide and metformin); 1 diabetic and 1 non diabetic group (treated with the vehicle). All treatments were carried out for 28 days. Fasting Serum Glucose (SG) was monitored at 4 days interval and the body weights were recorded each week. On the 28th day, rats were orally administered with 20 g/kg glucose and Oral Glucose Test (GTOT) was performed. Blood was then withdrawn and analysed. Treatment (500 mg/kg), revert SG level in the diabetic rats to normalcy after day 16. Percentage reduction in glycemia was highest with 500 mg/kg extract treatment. GTOT indicates that the same dose of glucose elevates SG level after 1 hour which then reduced to normalcy within 2 hours. The extract reduced atherogenic index, coronary risk index and LDL/HDL significantly. It also reduced serum creatinine, K+ and Cl-. Our results suggest that *Hibiscus sabdariffa* calyx contained components that may be efficacious in the management of diabetes and some risk factors associated with cardiovascular diseases.

Keywords: Blood glucose; Diabetes; Hypolipidemia; *Hibiscus sabdariffa*; Lipid profile

Introduction

Diabetes (DM) is justly recognized as an emerging global epidemic, representing one of the leading causes of morbidity and mortality worldwide (Vasim *et al.*, 2012). It is a disease of metabolic deregulation, most notably abnormal glucose metabolism, accompanied by characteristic long-term complications. Hyperglycemia, the common characteristic of both type 1 and type 2 diabetes mellitus (DM), has the potential to cause serious complications due to its insidious and chronic nature. Although, pathogeneses of some of the complications are clearly defined, the
mechanisms and cascade of biochemical events resulting in most of these complications are still poorly understood. These have complicated the overall approaches to the management of DM and still present it as one of the public health challenges till date.

The global incidence of DM revealed an estimated 171 million people as victims of the disease in 2000, and it has been projected that the prevalence will increase to 366 million by 2030 if no practicable and sustainable intervention is adopted (Wild et al., 2004). A report on its global prevalence has predicted an increase in this figure, pegging it at well above 438 million by 2030 (Colaguirri, 2010). In 2012, an estimated 1.5 million deaths were directly linked to DM and more than 80% of this occurred in developing countries including Nigeria (Vasim et al., 2012). In sub-Saharan Africa, DM is an important emerging disease presenting South Africa as the most affected with a prevalence of 8.3% and closely followed by Nigeria (4.5%) (IDF, 2014). This exponential increase in the prevalence of DM may be either due to changes in diet (highly refined diets), aging and lifestyle of the people (reduced physical activity, urbanization etc.) or ravaging effect of free radicals (Wild et al., 2004). While orthodox interventions have been embraced and have proved to be effective in the treatment of DM, affordability, sensitivity and inherent side effects have undermined their uses (Campbell et al., 1996). Interestingly, a considerable number of medicinal plants are being used as viable alternatives in the treatment of diabetes, particularly in the developing countries (Sabiu and Ashafa, 2016). Little wonder, the World Health Organization has specifically substantiated utilization of phytotherapies for the management and treatment of diabetes (Bailey, 2003), and in fact an ample proportion of the populace in some African countries including Nigeria now relies exclusively on plants as a source of medicine to augment the increasingly expensive orthodox medical services (Fasola and Egunyomi, 2005).

Roselle (Hibiscus sabdariffa L.) is grown in all parts of the world and has been used as a health drink in many countries. Fresh or dried calyces of H. sabdariffa are used in the preparation of herbal drinks, hot and cold beverages, fermented drinks, wine, jam, jelly confectionaries, ice cream, chocolates, flavouring agents, puddings and cakes (Ismail et al., 2008; Bako et al., 2009; Bolade et al., 2009). In Nigeria, the calyces are boiled with sugar to produce a drink known as “Karkade” or “Zoborodo” (Gibbon and Pain, 1985). In Traditional medical practices, roselle has been used for many years to reduce the risk of degenerative diseases. Studies have also shown that roselle was efficacious in lowering blood pressure (Onyenekwe et al., 1999; Ajani et al., 1999) and exhibits antioxidant properties (McKay et al., 2010). In the present study we investigated the efficacy of the aqueous extract of H. sabdariffa calyces in the management of some diabetic complications. At the end of the study some biochemical parameters which are indices of cardiovascular disease risk and kidney dysfunctions were evaluated.

Material and Methods

Assay kits, chemicals and drugs

The assay kits used were products of Randox Laboratories limited, United Kingdom. metformin and glibenclamide were obtained from Qianjin Pharm. Co. Ltd., China, and streptozotocin (STZ) was purchased from Sigma-Aldrich (St. Louis, MO, USA). The water used was glass-distilled and all other chemicals and reagents were of analytical grade.

Plant collection, authentication and extraction

Fresh calyces of roselle were collected in September 2016 from African Centre for Herbal Research (ACHRI) Farmland, University of Ilorin, Nigeria. They were authenticated at the University of Ilorin Herbarium, where a voucher specimen (no. UI/H38/16981) was prepared and deposited. The calyces were carefully rinsed under running water tap to remove contaminants. They were then air-dried to constant weight. Thereafter, the calyces were pulverized into coarse powder using an electric blender (model MS-223; Blender/Miller III, Taiwan, China). A portion of the powdered sample (250 g) was exhaustively extracted by cold maceration with continuous agitation in distilled water. The resulting infusion was filtered (Whatman no. 1 filter paper) and lyophilized using Virtis Bench Top lyophilizer (SP Scientific Series, USA). The yield was 22.3%.

Experimental Design

Experimental subject and animal care

The study was performed using forty two (42) Wistar rats of both sexes (7–8 weeks old). The rats were housed under a 12 h:12 h light-dark cycle at about 25 °C, room temperature. All animals have unlimited access to water and standard rat pellet as basal diet. Animal care and protocols was approved by the Departmental Ethical Committee (KWASU/IECCULA/003/04/022) and were in accordance with the National Institute of Health (NIH Publication, No. 85-23) for the Care and Use of Laboratory Animals and in accordance with good laboratory practices (NIH 1985; WHO, 1998; NRC, 2011).

Induction of diabetes mellitus

After one week acclimatization, 7 of the rats were randomly selected and designated as group A. They were rats administered with the vehicle (sodium citrate) and labelled as normal control. All other rats were injected intraperitoneally with a single dose of streptozotocin (STZ; 65 mg/kg of bodyweight) (Sulochana et al., 1998). STZ was dissolved in 0.1 M of sodium citrate buffer, with a pH of 4.5. Rats showing serum glucose (SG) level >300 mg/dl seven days after STZ administration were considered diabetic and included in the study (Shraddha and Goyal, 2015). Diabetic rats were then randomly assigned to five groups of 7 rats each (as indicated below) and used for further study.

Group B: DC (Diabetic negative Control); Vehicle alone

Group C: DT1 (Diabetic treatment 1); 200 mg/kg extract

Group D: DT2 (Diabetic treatment 2); 500 mg/kg extract

Group E: DTC1 (Glibenclamide treated); 10 mg/kg

Group F: DTC2 (Mertformin treated); 1.5 mg/kg

All treatments were carried out as a single dose orally every day using oral intubation.

Multiple dose 8 weeks study

Respective treatments were carried out for 8 weeks. Fasting blood glucose was measured at one week interval by the glucose oxidase method using a reflective glucometer.
was carried out using respective diagnostic kits (Sigma Chemical Company, UK). Colorimetric method as described by Bartels and Bohmer (1972) was used in assaying for plasma creatinine. VLDL-cholesterol (VLDL-c) and LDL-cholesterol (LDL-c) in serum were calculated as per Friedewald’s equation (Friedewald et al., 1972).

\[
\text{VLDL-c} = \text{Triglyceride} \\
\text{LDL-c} = \text{Total cholesterol} - \text{Triglyceride} - \text{HDLc}
\]

The markers of dyslipidemia such as TC/HDL-c (coronary index), LDL-c/HDL-c and LDL + VLDL/ HDL (atherogenic index), were also calculated.

**Results**

The result of the fasting blood glucose (Figure 1) showed an elevated glucose level of all the treated rats was not significantly different (p>0.05) from each other nor from the value obtained in the diabetic untreated group but that was significantly (p<0.05) higher than that of the normal control value on day zero. On the 4th day, the serum glucose level of the extract treated rats and the glibenclamide treated rats were significantly lower than that of the diabetic control group but were still higher than that of the normal control group. A similar trend was observed on day 8. On day 12, all the treated rats showed serum glucose level that were not significantly (p>0.05) different from each other but lowered than that of the diabetic control group. This same trend was maintained when the glucose level was determined on day 20 and on day 24.

The result of the percentage reduction in glycemia showed that the highest percentage reductions of glycemia in all the rats were obtained after day 16 (Figure 2). Metformin was seen to reduce glycemia by 77.8% on day 24 while 74.3% reduction was observed in glibenclamide treated rats. Treatment with the extract resulted in 71% reduction with 500mg/kg dose and 60.3% reduction with 200 mg/kg dose when determined on the same day. The diabetic control group and the normal control group showed glycemia reduction of 17.2% and 6.29% respectively.

**Fig. 1:** Effect of treatment on fasting blood glucose

- Vehicle= Sodium citrate, DR= diabetic rat.

Points on the graph are values expressed as mean of seven replicates ± SEM.
Roselle Hibiscus sabdarrifa calyces extracts modulates cardiovascular disease risk and kidney dysfunctions in diabetic rats

The result of the OGTT showed that highest increase in serum glucose in the normal control rats occurred after 60 minutes oral administration of glucose (Figure 3). Thereafter, the serum glucose level showed a reduction. The observed value after 120 minutes was not different from the baseline (68.7±7.5 mg/dL). Also at 60 minutes after oral glucose administration, diabetic control rats exhibited significant elevation in fasting serum glucose compared with the baseline. However, contrary to what was observed in the normal control group, the SG thereafter showed significant increase when determined after 120 and 240 minutes. When treated with H. sabdariffa (at both tested doses) and the standard drugs (metformin and glibenclamide) the diabetic rats in a similar manner also showed significant elevation in SG compared with the baseline (time zero). The serum glucose level of H. sabdariffa treated rats was also at this time observed to be significantly higher than the normal control group. After 240 minutes of oral glucose administration, Figure 3 showed a reduction in serum glucose level and the observed values in all the treatment groups were not significantly different from that of the normal control group (79.2 ± 99 mg/dL) but were significantly lower than that of the diabetic control group value (295.8 ± 8.5 mg/dL). The observed values after 240 minutes were also not different from the baseline values.

Fig. 2 : Percentage reduction in glycemia following treatment with the extract
- Vehicle= Sodium citrate, DR= diabetic rat.
Values are expressed as mean of seven replicates ± SEM.

Fig. 3 : Effect of treatment on oral glucose tolerance
- Vehicle= Sodium citrate, DR= diabetic rat.
Points on the graph are values expressed as mean of seven replicates ± SEM.
Result of the effect of treatment on serum lipid profile is shown in Figure 4. Following administration of STZ, there were significant alterations in the serum total cholesterol, VLDL-c, LDL-c and HDL-c value, but the triglyceride level was not significantly affected. Neither treatment with the extract nor treatment with the standard drugs significantly altered the serum triglyceride value. Administration of 200 mg/kg dose of the extract did not significantly changed the total cholesterol from the observed value of 175.70 ± 13.5 mg/dL in the diabetic control group. Administration of 500 mg/kg dose of the extract and of the standard drugs however reduced the total cholesterol level to that of the normal control value. Similarly, administration of the extract at the two tested doses and of the standard drugs also reduced the serum VLDL-c value below that of the diabetic control group. The observed value of 1.43 ± 0.02 mg/dL in the rats administered with 200 mg/kg dose of the extract was however significantly higher than that of the normal control value whereas the observed values in the rats treated with 500 mg/kg dose of the extract and that observed in the diabetic rats treated with the standard drugs were not significantly different from the normal control value. The result of the LDL-c followed a similar pattern to that of the VLDL-c. The result of the serum HDL-c showed that administration of STZ significantly lower the HDL-c level from that observed in the normal control group (6.75 ± 0.01 mg/dL). Treatment with the extracts at all the tested doses and with the standard drugs raised the serum HDL-c level above that of the diabetic control group (3.53 ± 0.02 mg/dL). The observed value of 5.75 ± 0.02 mg/dL in the rats administered with 200 mg/kg was however significantly lower than that of the normal control whereas the value was not different significantly in all other treatment groups from the normal control value.

When the markers of dyslipidemia were compared, results (Table 1) showed significant increase in coronary index, atherogenic index and LDL/HDL ratio with induction of diabetes. All these parameters were observed to be lowered in the diabetic groups treated with the extract and those treated with the standard drugs when compared with the untreated groups. The observed values in the treated groups were not significantly different from the normal control group.

**Table 1 :** Effect of treatment on dyslipidemia marker

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Coronary Index</th>
<th>Atherogenic Index</th>
<th>LDL/HDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Normal rats + 0.5 ml vehicle</td>
<td>16.90±2.10a</td>
<td>23.26±2.47a</td>
<td>9.18±0.09a</td>
</tr>
<tr>
<td>B</td>
<td>Diabetic rats + 0.5 ml vehicle</td>
<td>33.80±2.24b</td>
<td>49.77±3.86b</td>
<td>25.45±1.64b</td>
</tr>
<tr>
<td>C</td>
<td>Diabetic rats + 200 mg/kg extract</td>
<td>10.87±1.84a</td>
<td>17.27±2.42a</td>
<td>8.69±0.79a</td>
</tr>
<tr>
<td>D</td>
<td>Diabetic rats + 500 mg/kg extract</td>
<td>12.88±0.85a</td>
<td>24.08±2.75a</td>
<td>12.82±0.58a</td>
</tr>
<tr>
<td>E</td>
<td>Diabetic rats + 0.5 mg/kg glibenclamide</td>
<td>12.40±2.74a</td>
<td>27.21±2.68a</td>
<td>7.12±1.12a</td>
</tr>
<tr>
<td>F</td>
<td>Diabetic rats + 1.5 mg/kg metformin</td>
<td>22.96±2.86c</td>
<td>24.30±1.85a</td>
<td>5.22±1.13a</td>
</tr>
</tbody>
</table>

Note:  
- Results are mean±SEM; n=7;  
- All mean in the same column with similar superscripts are not significantly different from each other

Result of the changes in body weight (Figure 5) showed that no significant alterations were observed in the total body weights of all the rats throughout the treatment period.
Roselle *Hibiscus sabdariffa* calyces extracts modulates cardiovascular disease risk and kidney dysfunctions in diabetic rats

**Fig. 5:** Effect of treatment on body weight

- Vehicle = Sodium citrate, DR = diabetic rat.
Points on the graph are values expressed as mean of seven replicates ± SEM

Result of the kidney function test (Table 2) showed an elevation in creatinine, chloride ion and potassium ion when diabetes was induced by STZ administration. This treatment was however not observed to alter sodium ion concentration. Although treatment of the diabetic rats with the extract at 200 mg/kg reduced serum creatinine concentration significantly (p<0.05) below the untreated group, the observed concentration was higher than that of the normal control value of 0.500 ± 0.002 (mEq/L). Treatment with the extract at 500 mg/kg and with glibenclamide or metformin however raised the creatinine concentration to a value that was not significantly different from the normal control value. Similarly, the result of the chloride ion concentration showed that the observed values in all the treatment groups were not significantly different from the normal control value. Result of the serum potassium ion concentration showed that the potassium ion of the extract treated rats were not significantly different from that of the normal control group, however, the serum potassium ion of the rats treated with the standard drugs were significantly higher than the normal control group but not significantly different from that of the diabetic control group. No significant variation was observed in the sodium ion concentration of all the treatment groups when compared with that of the non treated groups.

**Table 2:** Effect of treatment on some kidney function biomarkers

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>Kidney function biomarkers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Creatinine (mg/dL)</td>
</tr>
<tr>
<td>A</td>
<td>Normal rats + 0.5 ml vehicle</td>
<td>0.500 ± 0.002</td>
</tr>
<tr>
<td>B</td>
<td>Diabetic rats + 0.5 ml vehicle</td>
<td>1.455 ± 0.001</td>
</tr>
<tr>
<td>C</td>
<td>Diabetic rats + 200 mg/kg extract</td>
<td>0.894 ± 0.003</td>
</tr>
<tr>
<td>D</td>
<td>Diabetic rats + 500 mg/kg extract</td>
<td>0.631 ± 0.003</td>
</tr>
<tr>
<td>E</td>
<td>Diabetic rats + 0.5 mg/kg glibenclamide</td>
<td>0.662 ± 0.002</td>
</tr>
<tr>
<td>F</td>
<td>Diabetic rats + 1.5 mg/kg metformin</td>
<td>0.203 ± 0.004</td>
</tr>
</tbody>
</table>

Note:
- Results are mean±SEM; n=7;
- All mean in the same column with similar superscripts are not significantly different from each other

**Discussion**

Diabetes, a well recognized metabolic disorder posses a major threat to national development as it causes high economic loss (Vasim et al., 2012; Sabiu and Ashafa, 2016). When uncontrolled, diabetes may leads to many secondary complications such as cataract, heart failure, and renal failure. It therefore becomes a major priority to research into new hypoglycaemic and potentially antidiabetic agents. Although there are many known anti diabetic medicines in the pharmaceutical market (Kavishakar et al., 2011), screening for new antidiabetic sources from natural plants is still of major interest as natural products are known to contain constituents that are efficacious and safe.

The result of the fasting blood glucose indicates that diabetes was induced in all the STZ treated rats. The process by which STZ induced diabetes has been previously reported (Kim et al., 2016). This is said to be by destruction of pancreatic β cells which thus impair insulin secretion. Streptozotocin is a chemical compound that provokes acute cytotoxic effects on cells and molecules, especially against
pancreatic β cell. Damaged pancreatic β cells lead to reduced insulin and causes hyperglycemia (Szkudelsk, 2001; Singh et al., 2002; Kim et al., 2006.). The mechanism by which STZ induced the destruction of the pancreatic β cells has been reported to be by generating free radicals such as superoxide radical O₂⁻, H₂O₂ and OH⁻ and nitric oxide. These reactive oxygen species (ROS) causes DNA damage. Hydroxyl group (OH⁻) is a very strong oxidizing compound that can react with DNA, proteins, lipids, amino acids and glucose. DNA damage causes the β cells of the pancreas unable to produce insulin so that blood glucose increases (Kohen and Nysta, 2002).

Serum glucose levels after oral administration of H. Sabdariffa extract to the diabetic rats at all the tested doses was seen in the study to normalize within two weeks of administration, thus confirming its hypoglycaemic properties. Glibenclamide and metformin at the doses administered produced similar effect. According to Valverde et al. (2012), glibenclamide lowers blood sugar through the mechanism of stimulation of insulin secretion and also by preventing glucagon secretion. It may be possible that H. Sabdariffa calyx extract achieved the same effect through similar mechanism. One possibility is that the pancreatic β cells of these rats get repaired within the period so that they were capable of producing insulin, thereby causing a lowering of the blood sugar.

The oral glucose tolerance test (OGTT) is performed to determine how the body responds to glucose. The test measures the body's ability to metabolize glucose (Islam et al., 2009). Oral administration of glucose (2 g/kg) did not produced significant change in SG level of normal control rats within the four (4) hours of study. The diabetic rats however, exhibited significant elevation in fasting SG (at time zero). In the diabetic untreated rats, no drop was observed in the glucose level within the treatment period showing significant impairment in glucose tolerance to exogenously administered glucose compared to normal rats. The result further indicates that although a significant elevation in serum glucose was seen in all the treated rats 30 minutes after oral glucose administration, a significant drop in serum glucose level was observed in the extract treated rats 2 hours after oral glucose administration and this was normalize in all the treated rats 4 hours after oral glucose administration. The effect seen with the extract was similar to what was observed in the glibenclamide treated rats. The result of this study suggests that exogenous administration of glucose stimulated the release of higher levels of insulin in normal control rats, whereas glucose load was ineffective in stimulating the release of insulin in diabetic rats. This study agrees with the study of Priyadarshini et al. (2016) where it was suggested that STZ induced diabetes resembled severe diabetic (type I) condition in which a maximum pancreatic damage occurred. Treatment with different doses of H. sabdariffa enhanced the glucose stimulated insulin release from pancreatic β-cells and this response was comparable with glibenclamide and metformin treated diabetic rats.

Report from some clinical studies has shown that dyslipidemia is one major risk factor for coronary disease (CHD) which is the leading cause of death worldwide (Kuriyan et al., 2010; Sabiu and Ashafa, 2016). Generally, dyslipidemia has been shown as low HDL-c among men and hypercholesterolaemia among women (Varady and Jones, 2005). The LDL-c/HDL-c ratio is a valuable and standard tool to evaluate CHD (Luz Fernandez, 2008). Some herbs have been thought to help reduce hyperlipidemia, abnormal tendency to form blood clots, impaired blood flow or other cardiovascular problems (Kuriyan et al., 2010). The present study suggests that H. sabdariffa calyx can effectively ameliorates hyperlipidemia effect induced by diabetes. This is in agreement with some previous studies (Farombi et al., 2007; Huang et al., 2015). These effects may arise from: Inhibition of cholesterol intestinal absorption; lipoproteins production interference; upregulation of hepatic LDL receptors with higher blood LDL removal; increased catabolism and degradation of cholesterol. These factors, alone or in combination, can reduce LDL and thus total cholesterol (Ochani and D’Mello, 2009). Individuals with a high total/HDL cholesterol or LDL/HDL cholesterol ratio and high atherogenic index have greater cardiovascular risk owing to the imbalance between the cholesterol carried by atherogenic and protective lipoproteins. This may be due to an increase in the atherogenic component contained in the numerator, a decrease in the anti-atherosclerotic trait of the denominator, or both (Jesus et al., 2009). In the present study, administration of H. sabdariffa calyx extract results in the reduction of TC, LDL-c and VLDL-c and an elevation of HDL-c. It also reduced LDL-c/HDL-c ratio, atherogenic risk index and coronary risk index but does not affect triglyceride level. Our observation in this study corroborates previous report of both animals and human studies (Chen et al., 2003, Chen et al., 2004, Rebecca et al., 2010). The report however, was contrary to the observation of Mohagheghi et al. (2011) who reported in a study that consumption of sour tea and black tea by hypertensive patients for 15 days, caused an upward trend in TC, HDL-c, LDL-c, and TGs in both groups. It may be noted that the response to administration of natural compounds could be heterogeneous depending on the concentration, form, and dosage of the compound, duration of treatment, and the elaboration and chemical composition of the extract, physiological conditions, sex, age, hormonal status, and dietary intakes. H. sabdariffa has been reported to be rich in polyphenols, anthocyanins, flavonoids (Ali et al., 2005; Lin et al., 2007; Ines et al., 2014) and this may justify its hypolipidemic effect observed in this study.

The result of the body weight variation showed that H. sabdariffa treatment did not significantly altered total body weight. This was contrary to the observation of Carvajal-Zarrabai et al. (2009) and Fakaye et al., (2008) both of who reported a drastic loss of weight among animals treated with various concentrations of H. sabdariffa extracts. The result however agrees with our earlier report (Ajani et al., 1999) and the report of Olatunji et al., (2005) where it was observed that there were no significant change in the body weight of rats that were chronically treated with H. sabdariffa extracts. This result indicates that H. Sabdariffa may not exercise anti obesity effect. Although while trying to provide explanation for observable weight loss during treatment with H. Sabdariffa, Carvajal-Zarrabal et al. (2009) suggest that such weight decreases might have been as a result of dietary palatability problem that may result when H. sabdariffa concentration is increased our observation in this study did not suggest that at the tested doses H. Sabdariffa treated rats suffered any dietary palatability problem.

The kidneys play a very important role in the regulation of electrolytes, intracellular fluid volume, the pH buffer system, endocrine processes such as RBC synthesis, Vitamin
the glomerular filtration rate. which may have caused increasing renal blood flow and thus the parameters measured in the study may be attributable to play a pivotal role in chronic kidney disease (CKD) perfusion and increases oxidative stress through et al. (2003) reported no changes in plasmatic and serum sodium levels when H. sabdariffa was administered (Prasongwatana et al., 2008; Wang et al., 2011). Results from the present study corroborate these reports. Reduction of serum potassium in healthy rats supplemented with aqueous extract of H. sabdariffa has also been reported (Wang et al., 2011). The observation made in the present study agrees with this report. This however is contrary to the observation of potassium elevation in healthy mice receiving H. sabdariffa reported by Emelike and Dapper, (2013) and the report by Allesandra et al., (2016) in which no change in plasma potassium ion concentration was reported. The mechanism for the alteration in serum potassium ion observed in the present study, may be due to the effect of the extract on the sodium pump that maintains the constancy of the extracellular concentration of potassium. Reports differ on the effect of administration of H. sabdariffa calyx extract on serum creatinine. Whereas, Whang et al., (2014) and Prasongwatana et al., (2008) reported no alteration in serum creatinine of obese patients placed on H. sabdariffa, other studies by Ukoha et al (2015) and Laikangbam, and Devi (2012) reported a reduction in creatinine in rats administered with H. sabdariffa. Report of the present study is in agreement with the later. Creatinine level in the serum is proportional to the rate at which it is excreted (Eteng et al., 2009). The nephroprotective effect of H. sabdariffa observed in this study may be attributable to the action of anthocyanins a phytochemical component that has been previously reported in H. sabdariffa (Ines et al., 2014), in increasing the GFR via inhibition of angiotensin II production (Nwachukwu et al., 2016). Angiotensin II adversely changes the renal perfusion and increases oxidative stress through inflammatory and thrombotic effects and it was considered to play a pivotal role in chronic kidney disease (CKD) progression (Wang et al., 2013). The increase clearance of the parameters measured in the study may be attributable to the vasodilatory action of the constituents of H. sabdariffa which may have caused increasing renal blood flow and thus the glomerular filtration rate.

**Conclusion**

The result of this study indicates that at 500 mg/kg Hibiscus sabdariffa calyces extract exhibits significant hypoglycaemic and specific lipid lowering effect. Data from the study suggest that the calyces extract lowers significantly atherogenic and cardiovascular disease risk and also lowers the risk of kidney dysfunction comparable to that of standard antidiabetic drugs; glibencamide and metformin. It however may not be efficacious as an agent that can lower the risk of obesity. The present study thus suggest that Hibiscus sabdariffa calyces contain specific phytochemicals that may serve as base for the development of agents that may lowers the risk of diabetes and its chronic complications.

**Conflict of Interest**

The authors declare that there is no competing interest.

**Acknowledgment**

The authors are grateful to the U6 consortium.

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Roselle Hibiscus sabdariffa calyces extracts modulates cardiovascular disease risk and kidney dysfunctions in diabetic rats


