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ORIGINAL ARTICLE

Protective roles of crude and fractions of *A. senegalensise* carpel against alloxan-induced hyperglycemia and hyperlipidemia in rats

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Abstract

Medicinal plants are increasingly been investigated for potentials to provides active, safe and cost-effective alternative to synthetic antidiabetics. In the present study, hypoglycemic and hypolipidemic activities of crude methanol, hexane and ethylacetate fractions of *Annona senegalensis* (*A. senegalensis*) in alloxan-induced diabetic rats were evaluated. The extract and fractions of *A. senegalensis* were administered to alloxan (120 mg/kg bw) induced diabetic rats at doses of 100, 300 and 600 mg/kg bw. Glibenclamide (5 mg/kg bw) was used as the reference drug. All treatments were administered daily for 14 days through oral route with the aid of esophageal cannula. Effect of the treatments on blood glucose levels, body weight, packed cell volume (PCV) and lipid profiles were monitored. The crude extract had significantly ($p < 0.05$) higher percentage glucose reduction range of 71.61 ± 2.34% and 75.59 ± 1.09% when compared with the metformin (69.15 ± 2.90%). Ethyl acetate and n-hexane fractions had reduction range of 60.17 ± 3.56 to 67.74 ± 2.67, and 55.63 ± 1.09% to 68.05 ± 2.98% respectively. The crude extract and fractions of *A. senegalensis* significantly ($p < 0.05$) decreases the serum concentrations of cholesterol, triglycerides, low-density lipoprotein-cholesterol and increase high-density lipoprotein-cholesterol when compared with diabetic untreated rats. The serum total cholesterol and triglyceride in rats treated with 100 and 300 mg/kg n-hexane and those treated with ethylacetate fractions were comparable ($p > 0.05$) with the normal control rats but significantly ($p < 0.05$) lower than those treated with 600 mg/kg bw of the fractions and crude extract (100, 300 and 600 mg/kg bw). *A. senegalensis* carpel contains significant amount of phytochemicals with hypoglycemic reputation. The crude extract, ethylacetate and hexane fractions exhibited dose-dependent hypoglycemic and hypolipidemic activity in alloxan-induced diabetic rats.

Keywords *Annona senegalensis* · Hypolipidemic · Hypoglycemic · Diabetics · Alloxan

Introduction

Diabetes mellitus is a chronic, non-communicable metabolic disorder characterized by high blood sugar level coupled with polyuria, polydipsia, polyphagia and other metabolic abnormalities (Omonije et al. 2019). Diabetes is a global health threat as it is the seventh leading cause of death incurring a reduced life expectancy and quality of life. As of 2014, the World Health Organization asserts that a global estimate of 171 million people are diabetic, and with rapid increase in this incidence it is estimated that this number will almost double by 2030 (WHO 2017).

Complications due to diabetes are so enormous ranging from abnormal lipid profile which thus predispose individual to increase risk of cardiovascular diseases and hepato-renal impairment (Omonije et al. 2019). At societal level, it has hindered economic growth, loss of productivity due to restricted activity, lost work days, permanent disability and mortality (Shewasinad et al. 2019).

Despite the increased use of synthetic medications such as metformin, biguanides, thiozolidinediones and sulfonylureas, there is limited therapeutic success in addition to undesirable and unbearable side effects, hence there may be need for an increased dependence on herbal

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drug by diabetic patients in order to manage diabetes mellitus, particularly in Nigeria were these herbal medicines are in abundance (Chedi et al. 2017).

Annona senegalensis (family; Annonaceae) is a medicinal plant that grows abundantly in Nigeria. It is commonly known as Gwandan daji, Ewe-aso and Dukuuhi in Hausa, Yoruba and Fulani respectively (Zimmet 2017). It is used as ingredient in making soup (soup hardner) and specifically prescribed to diabetic patients as a glucose-lowering agent (Mustapha 2013). Various researchers have justified the use of this plant on the basis of its biological activities ranging from antimalarial to antibacterial potentials (Samuel et al. 2016). Studies showing the pharmacological and toxicological evidences validating the safety and efficacy of several parts of *Annona senegalensis* can be found in literatures (Koli et al. 2010; Konaté et al. 2012; Chedi et al. 2017), but that on *Annona senegalensis* carpel are limited and not readily available; hence, this study was designed to evaluate the antidiabetic and hypolipidemic effect of *Annona senegalensis* carpel extracts in rats.

Materials and methods

Collection and identification of plant material

The carpels of *Annona senegalensis* were collected from Shebe village, in Kutigi, Lavun Local Government area, few kilometres away from Bida town Niger state, Nigeria in the month of September 2016. The plant was identified and authenticated in the herbarium and ethno-botany Unit of Medicinal Plant Research and Traditional Medicine, National Institute for Pharmaceutical Research and Development, Idu-Abuja, where specimen with voucher number (NIPRD/H/6768) was deposited.

Reagents and chemicals

Organic solvents (analytical grade) used for extraction of the plant material (methanol, ethylacetate and n-hexane) were products of Sigma Chemical Co St. Louis, MO (USA). Lipid profile kits for total cholesterol, triglyceride and high-density lipoproteins-cholesterol were product of Randox Liquizyme assay kits. All other chemicals used were also of analytical grade.

Experimental animals

Apparently healthy Swiss albino male rats with an average weight of 126.98 ± 6.90 g was obtained from the Department of Biochemistry, Benue state University Makurdi and transported to animal house, Department of Biochemistry Federal University of Technology, Minna, Nigeria. They were housed in clean cages with wood shavings as beddings under standard environmental conditions of temperature and relative humidity, 12 h day light/night cycle, with access to commercial feed pellets (growers) and water ad libitum. Animals were kept in compliance with internationally accepted principles for human handling and use of laboratory animals in the Canadian council on Animal Care Guidelines and Protocol Review (CCAC 1997).

Plant preparation and extraction of the crude extract

The *Annona senegalensis* carpels were rinsed under clean running water and air dried for 4 weeks in the laboratory (37 °C). The dried carpels were pulverized into coarse powder with mortar and pestle, milled into fine powder with an electric miller and stored in a clean container till ready for use. One hundred grams of powdered *Annona senegalensis* carpels was extracted with 400 ml of methanol using reflux extraction apparatus and the resulting extract was concentrated using rotary evaporator (9.88% brownish-coloured extract).

Fractionation of the crude extract

Thirty grams of methanol extract of *Annona senegalensis* carpels was fractionated with n-hexane using separating funnel. The n-hexane fraction was first eluted and the process was repeated with ethylacetate to obtained ethylacetate fraction. Both n-hexane and ethylacetate fractions were concentrated and dried in water bath. All fractions were kept at 4 °C in sterile containers prior to use; (52.30% and 33.60% respectively) of n-hexane and ethylacetate fractions respectively.

Antidiabetic study

Thirty-six Wistar albino rats were intra-peritoneally administered a freshly prepared solution of alloxan monohydrate (120 mg/kg) to overnight fasted rats. Diabetic state was confirmed by glucose level above 200 mg/kg bw (Etuk 2010). The animals were grouped as described below.

Group (NOR): positive control (normoglycemic)
Group B (STD): diabetic treated with 100 mg/kg bodyweight of metformin
Group C (DU): negative control (diabetic untreated)
Group D (CME-Crude methanol extract)

- Diabetic treated with 100 mg/bodyweight of methanol extract
- Diabetic treated with 300 mg/kg bodyweight of methanol extract

- Diabetic treated with 600 mg/kg bodyweight methanol extract

Group E (EAF-Ethylacetate fraction)

- Diabetic treated with 100 mg/kg bodyweight of ethylacetate extract
- Diabetic treated with 300 mg/kg bodyweight of ethylacetate extract
- Diabetic treated with 600 mg/kg bodyweight of ethylacetate extract

Group F (n-HF-n-hexane fraction)

- Diabetic treated with 100 mg/kg bodyweight of n-hexane extract
- Diabetic treated with 300 mg/kg bodyweight of n-hexane extract
- Diabetic treated with 600 mg/kg bodyweight of n-hexane extract

All treatments were administered daily for 14 days through oral route with the aid of esophageal cannula. The blood glucose level was checked and the weight taken after every 4 days (day 0, 1st, 5th, 10th, 14th). On the fifteenth day, animals in all group were euthanized under diethylether vapour and blood samples were collected and prepared to extract the serum according to the method described previous (Yusuf et al. 2018; Lawal et al. 2016).

Estimation of lipid profile

Serum concentrations of lipid profile including total cholesterol, triglycerides and high-density lipoprotein (HDL)-cholesterol were assayed by enzymatic colorimetric methods using commercially kits according to the manufacturer's instructions. VLDL-cholesterol was estimated as TG/5, and LDL-cholesterol was calculated using Friedewald formula (Friedewald et al. 1972) as follows:

$$\mathrm{LDL\ (mg/dl)} = \mathrm{TC} - (\mathrm{HDL} + \mathrm{VLDL})$$

Statistical analysis

Data were analysed using Statistical analysis system (SAS) and presented as means ± SEM. Comparisons between different groups were carried out by one-way analysis of variance (ANOVA) followed by Duncan's multiple range test (DMRT). The level of significance was set at $p < 0.05$.

Results

Phytochemical composition

Table 1 shows the qualitative phytochemical composition of methanol extract of *Annona senegalensis* carpel, revealing the presence of saponins, tannins, flavonoids, alkaloids and phenols. Quantitatively, saponin (286.50 ± 0.50 mg/g) was significantly ($p < 0.05$) the most abundant phytochemical in the crude extract while phenol was the least 2.24 ± 0.34 mg/g. Tannins, flavonoids and alkaloids recorded 52.92 ± 0.55 mg/g, 16.61 ± 1.43 mg/g and 9.82 ± 2.73 mg/g respectively (Table 2).

Hypoglycemic activity of extracts on diabetic rats

Figures 1, 2 and 3 show the blood glucose level of alloxan-induced diabetic rats administered 100, 300 and 600 mg/kg bodyweight of *Annona senegalensis* carpel extract and fractions. All extract and fractions-treated groups showed a significant ($p < 0.05$) decrease in the blood glucose level (Figs. 1, 2 and 3) when compared to the diabetic untreated group. The blood glucose of diabetic untreated rats continued to increase throughout the study period. The crude extract had significantly ($p < 0.05$) higher percentage glucose reduction of 71.61 ± 2.34%, 71.90 ± 2.93% and 75.59 ± 1.09% at 100, 300 and 600 mg/kg bw respectively when compared with the metformin (69.15 ± 2.90%). Ethyl acetate fraction had percentage glucose reduction range of 60.17 ± 3.56 to 67.74 ± 2.67 while n-hexane fraction had the least glucose reduction range of 55.63 ± 1.09% to 68.05 ± 2.98% (Table 2).

Bodyweight

Figures 4, 5 and 6 show the effect of *Annona senegalensis* carpel on bodyweight of rats. All rats in respective groups after induction demonstrated a significant ($p < 0.05$) weight reduction when compared to the normoglycemic rats that gained weight. However, compared to diabetic untreated group that incurred a significant weight loss, all extract treated

Table 1 Qualitative phytochemical compositions of methanol extract of *Annona senegalensis* carpel

Phytochemical	Inference	Quantitative (mg/g)
Saponins	+	286.50 ± 0.50^{e}
Tannins	+	52.92 ± 0.55^{d}
Flavonoids	+	16.61 ± 1.43^{c}
Alkaloids	+	9.82 ± 2.73^{b}
Phenols	+	2.24 ± 0.34^{a}

Data are Mean ± SEM of triplicate determination

Table 2 Percentage hypoglycemic effect of *A. senegalensis* carpel crude extract and fractions in diabetic rats

	Mean final glucose level (mg/Dl)	Percentage glucose reduction (%)
NOR	92.00 ± 2.00^{a}	–
DU	446.67 ± 33.65^{c}	–
CME 100 mg/kg bw	110.33 ± 21.61^{ab}	71.61 ± 2.34
CME 300 mg/kg bw	89.33 ± 9.28^{a}	71.90 ± 2.93
CME 600 mg/kg bw	102.33 ± 2.96^{a}	75.59 ± 1.09
EAF 100 mg/kg bw	178.67 ± 43.38^{b}	60.17 ± 3.56
EAF 300 mg/kg bw	110.00 ± 25.17^{a}	67.74 ± 2.67
EAF 600 mg/kg bw	120.33 ± 21.61^{b}	66.72 ± 3.32
n-HF 100 mg/kg bw	110.67 ± 19.88^{a}	63.57 ± 2.98
n-HF 300 mg/kg bw	100.67 ± 12.57^{a}	68.05 ± 2.98
n-HF 600 mg/kg bw	130.67 ± 17.94^{b}	55.63 ± 1.09
CME	132.00 ± 2.08^{ab}	69.15 ± 2.90

Data are Mean ± SEM of triplicate determination. Data followed by different superscript alphabet were significantly different ($p < 0.05$)

NOR normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

groups showed a significant ($p < 0.05$) weight gain except for n-hexane fraction that showed no significant ($p > 0.05$) weight gain at doses of 300 (Fig. 5) and 600 mg/kg bodyweight (Fig. 6).

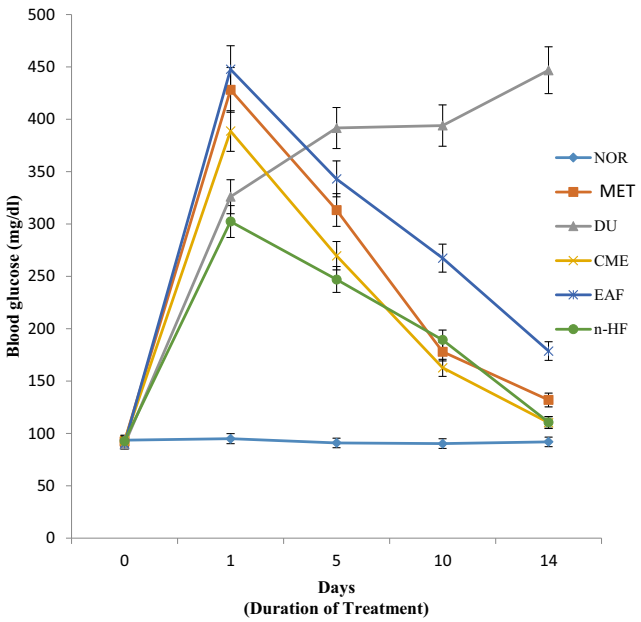

Fig. 1 Effect of *A. senegalensis* carpel extracts (100 mg/kg bodyweight) on blood glucose level of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

Packed cell volume

Figures 7, 8 and 9 show the packed cell volume (PCV) of rats administered 100, 300 and 600 mg/kg bodyweight of extracts of *Annona senegalensis* carpels. All rats in their respective groups showed significant ($p < 0.05$) increase in their PCV levels, while n-hexane fraction showed a decrease in PCV at a dose level of 600 mg/kg bodyweight.

Lipid profile

There were significant ($p < 0.05$) increases in the concentrations of serum total cholesterol, triglycerides, LDL-cholesterol and a significant decrease in HDL cholesterol in diabetic untreated rats when compared with the normal control and extract/fractions-treated groups (Figs. 10, 11, 12 and 13). The serum total cholesterol in rats treated with 100 and 300 mg/kg n-hexane and those treated with ethylacetate fractions at these concentrations were comparable ($p > 0.05$) with the normal control rats but significantly ($p < 0.05$) lower than those treated with 600 mg/kg bw of the fractions and crude extract (100, 300 and 600 mg/kg bw) (Fig. 10). Similarly, triglyceride concentrations in rats treated with 100 and 300 mg/kg bw of the fraction were comparable with the normal control but were lowered than those treated with crude extract and the fractions at 600 mg/kg bw (Fig. 11). High-density lipoprotein-cholesterol concentration in rats treated with 600 mg/kg bw ethylacetate and n-hexane fractions were not significantly different ($p > 0.05$) from the diabetic untreated group (Fig. 12). However, the concentrations of LDL-C were significantly lowered in all treated groups compared with diabetic untreated groups (Fig. 13).

Discussion

Diabetes is associated with hyperglycemia, hyperlipidemia and other metabolic disorders. The progressive increase in blood glucose levels of diabetic untreated rats could be attributed to destructive effect of alloxan on beta cells (Owolabi et al. 2014). As earlier reported by Bamidele et al. (2014), and correlating with this present study, the significant increase ($p < 0.05$) in blood glucose level was reduced by the *Annona senegalensis* carpel extracts when compared to the diabetic untreated group. The crude methanol extract at 600 mg/kg bodyweight showed the highest percentage reduction (75.6%) in blood glucose level. The variation in blood glucose reduction by 100, 300 and 600 mg/kg bodyweight of crude methanol extract and ethylacetate fraction may be due to the increase concentrations of the antidiabetic components with increase extract concentration. The

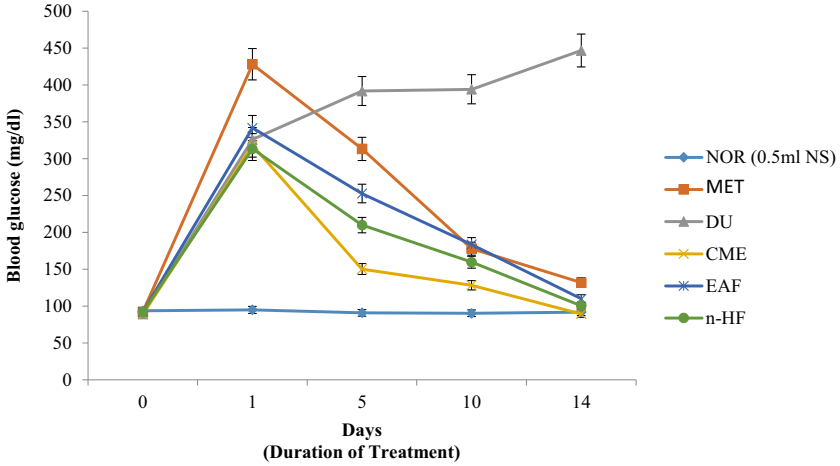

Fig. 2 Effect of *A. senegalensis* carpel extracts (300 mg/kg bodyweight) on blood glucose level of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

extract might have enhanced the secretion of insulin from β cells or exhibited insulin-like effects by stimulating glucose uptake and metabolism from muscle and adipose tissues (Daisy et al. 2010).

It is noteworthy to mention that the crude extract exhibited a better percentage glucose reduction than the metformin. This is an indication that the *Annona senegalensis* carpel could be as promising as metformin in the management of diabetes (Nisbet et al. 2004). Metformin is a biguanide oral antidiabetic drug that lowers the glucose levels by acting through numerous paths. This includes reducing hepatic glucose production, limiting glucose absorption in intestine and improving glucose uptake and utilization through enhancing insulin sensitivity (Klip and Leiter 1990). It is therefore possible that *Annona senegalensis* carpel exhibited its hypoglycemic effect via one of these mechanisms.

It is widely known that medicinal plants with hypoglycemic effect contain a variety of bioactive metabolites that is responsible for their activities (Sharma et al. 2008. Thus, phytochemical tests on *Annona senegalensis* carpel revealed that saponin (286.50 ± 0.50 mg/g) was significantly ($p < 0.05$) the most abundant phytochemical in the crude extract. Tannins, flavonoids and alkaloids recorded 52.92 ± 0.55 mg/g, 16.61 ± 1.43 mg/g and 9.82 ± 2.73 mg/g respectively. Flavonoids saponins and tannins have been reported for antioxidants properties (Lawal et al. 2017) and stimulatory effect on insulin secretion from pancreatic β cells (Rawi et al. 2011). The presence of significant amount of these phytochemicals in *A. senegalensis* is an indication that the above mechanism of

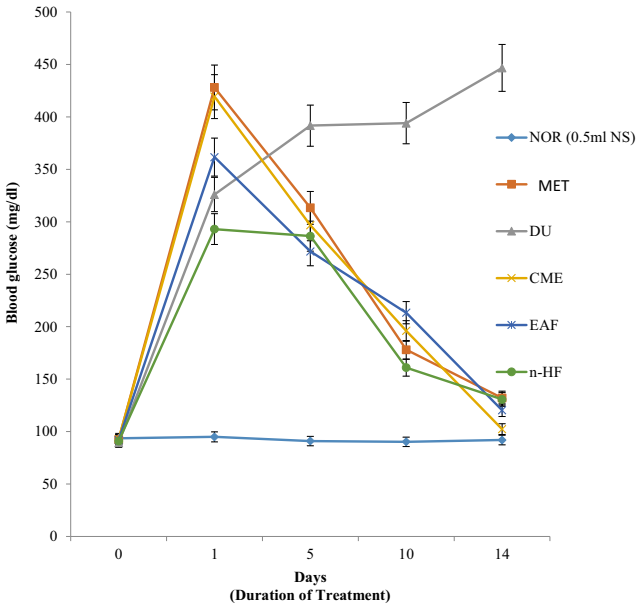

Fig. 3 Effect of *A. senegalensis* carpel extracts (600 mg/kg bodyweight) on blood glucose level of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

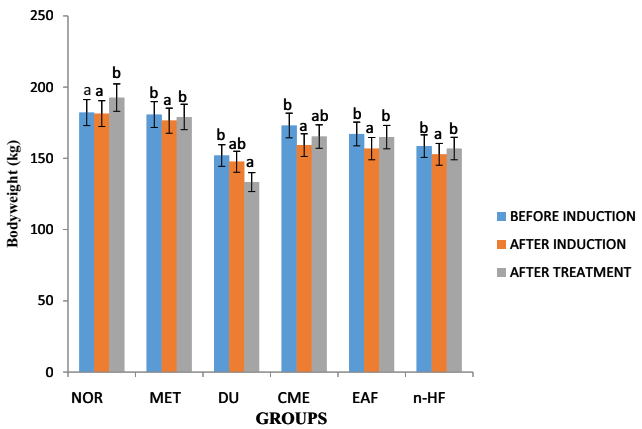

Fig. 4 Effect of *A. senegalensis* carpel extracts (100 mg/kg bodyweight) on bodyweight of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

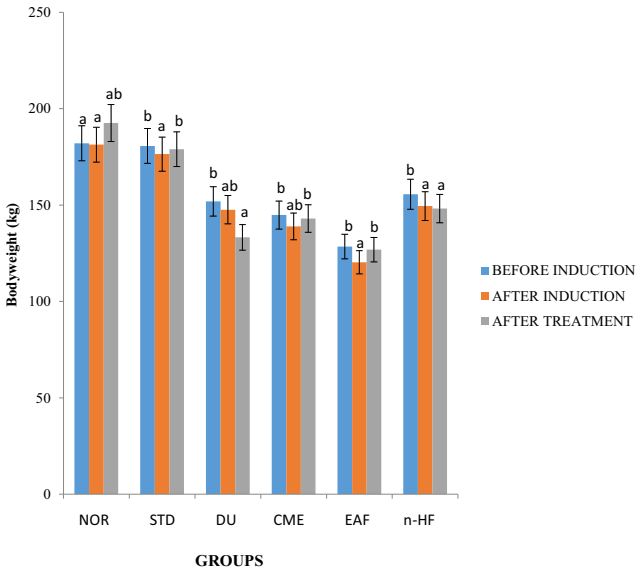

Fig. 5 Effect of *A. senegalensis* carpel extracts (300 mg/kg bodyweight) on bodyweight of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

action may be linked to the hypoglycemic activities of *A. senegalensis*. The presence of these phytochemicals therefore justified the hypoglycemic effect demonstrated by the plant and also indicated that this plant if properly screened could yield a drug of pharmacological significance.

Loss in bodyweight observed in the diabetic untreated rats is a characteristic of diabetic condition and correlates with the study of Freshet et al. (2017) who reported in line with Ravi et al. (2004) that weight loss could be due to increased protein wasting in a situation of unavailability of carbohydrate for utilization as an energy source (Jacobson et al. 2007). In line with the findings from this study, metformin has been reported for modulation of body weight and anti-hyperlipidemic properties in diabetic condition and hence is a drug of choice in diabetes associated with pathological condition (Robinson et al. 1998). In the same pattern with metformin, the crude methanol extract and ethylacetate fraction of *Annona senegalensis* carpel also caused improvement in body weights of test animals.

The improvement in the bodyweight of diabetic rats treated with crude methanol extract and ethylacetate fraction of *Annona senegalensis* carpel could be attributed to improved metabolic condition and improvement of glycemic and protein turnover control in all extract-treated groups (Daisy et al. 2010).

Anaemia is prevalent among diabetic patients and may also be significant in determining the outcome of heart failure and hypoxia-induced organ damage in patients with diabetes (Thomas et al. 2005). In this study, the low PCV in untreated rats is an indication of anaemia which is attributed to the fact that diabetes mellitus increase non-enzymatic glycosylation of RBC membrane proteins which correlates with hyperglycemia (Oyedemi et al. 2011). The

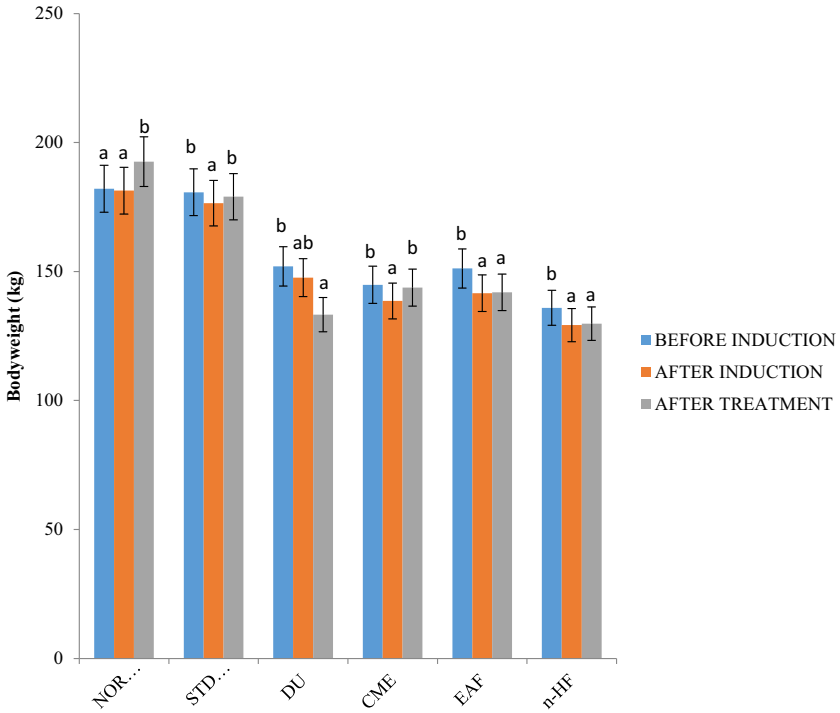

Fig. 6 Effect of *A. senegalensis* carpel extracts (600 mg/kg bodyweight) on bodyweight of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *STD* standard drug (100 mg/kg bw of metformin), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

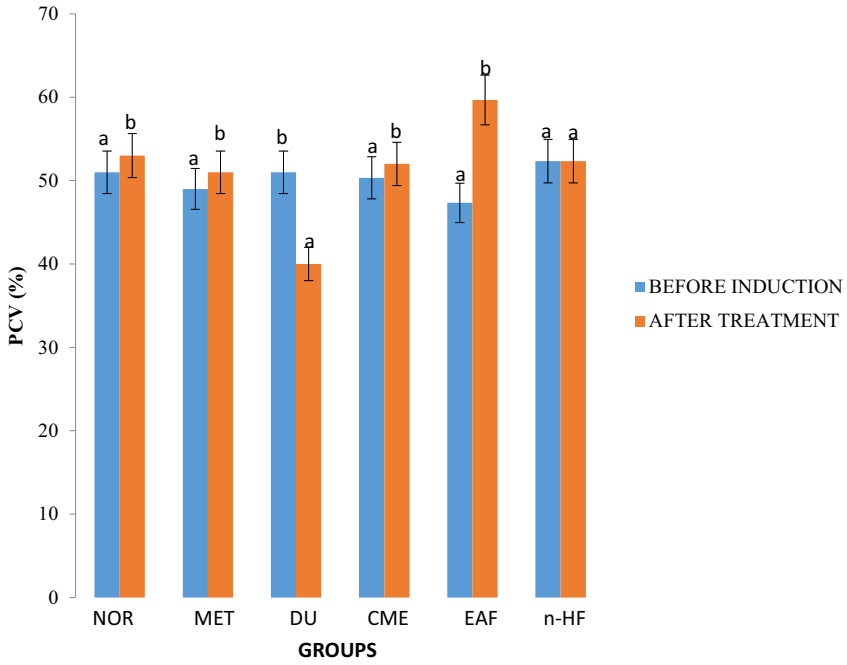

Fig. 7 Effect of *A. senegalensis* carpel extracts (100 mg/kg bodyweight) on packed cell volume of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

improvement in packed cell volume of treated rats could be attributed to the presence of flavonoids which stimulated the synthesis and releases of erythropoietin, which stimulates the production of more RBC in the bone marrow (Berinyuy et al. 2015; Lawal et al. 2015).

The higher levels of lipid profile in diabetic untreated rats were due to higher deployment of free fatty acids from peripheral storage and also due to hormonal-induced lipolysis (Rajaei et al. 2015). These abnormalities would predispose diabetic patient to increased risk for cardiovascular disease (Nagmoti et al. 2015). The decrease of cholesterol and LDL levels achieved by crude extract and fractions of *Annona senegalensis* carpel demonstrates a possible protection against hypercholesterolemia and the harm this condition brings about. The crude extract and fractions of *Annona senegalensis* carpel

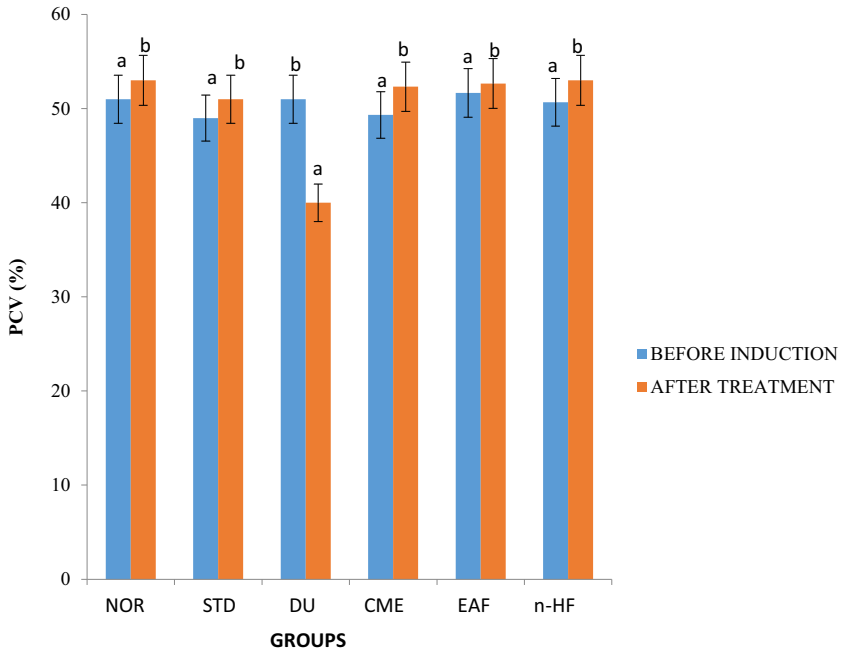

Fig. 8 Effect of *A. senegalensis* carpel extracts (300 mg/kg bodyweight) on packed cell volume of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

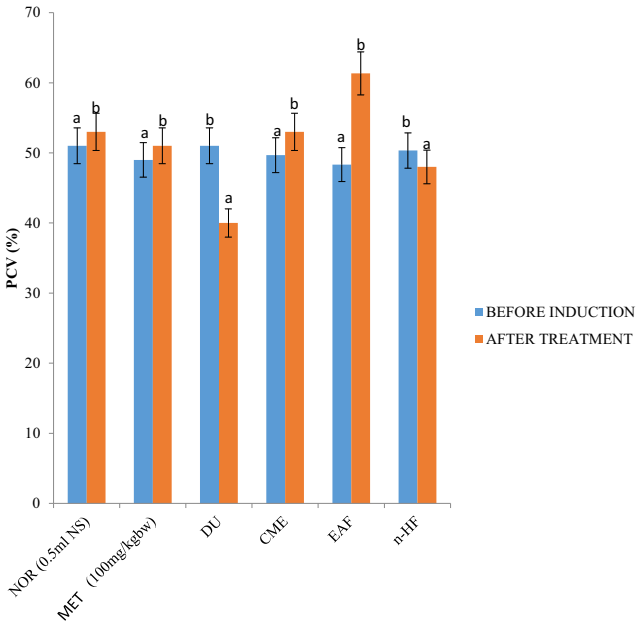

Fig. 9 Effect of *A. senegalensis* carpel extracts (600 mg/kg bodyweight) on packed cell volume of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

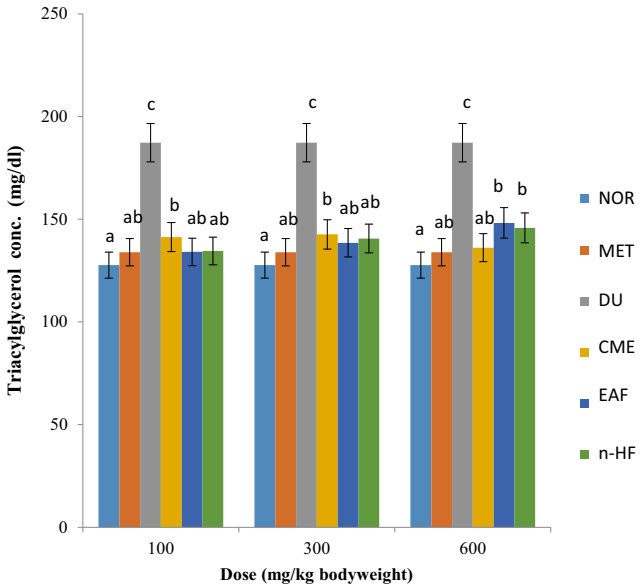

Fig. 11 Effect of *Annona senegalensis* carpel extracts on serum triacylglycerol levels of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

might have exhibited these effects through the b cells regeneration which inhibit lipid peroxidation and consequently control of lipolytic hormones. A number of medicinal plants have also been documented for hypoglycemic and hypolipidemic effect through these mechanisms, while other studies implicated saponins for

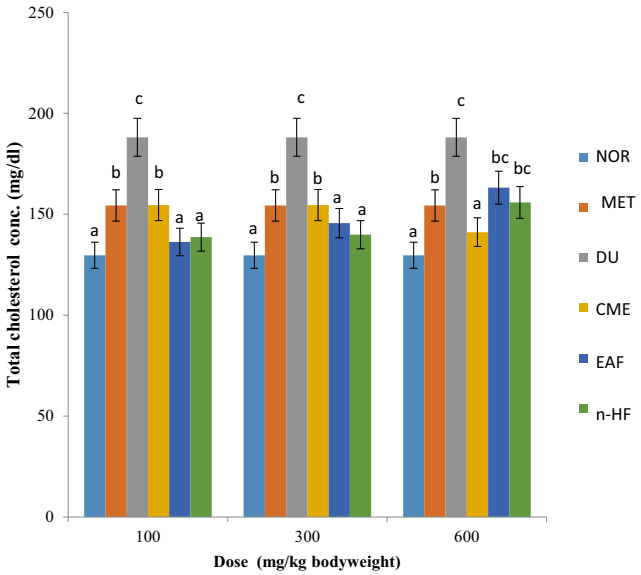

Fig. 10 Effect of *Annona senegalensis* carpel extracts on serum total cholesterol of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

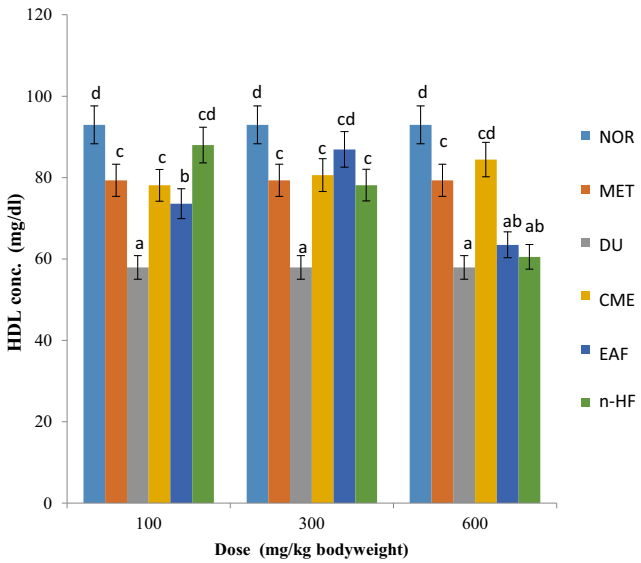

Fig. 12 Effect of *A. senegalensis* carpel extracts on high density lipoprotein levels of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

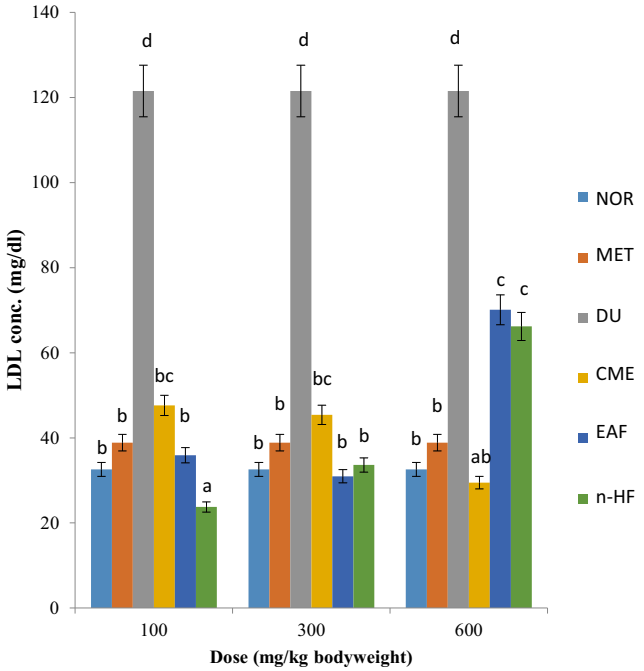

Fig. 13 Effect of *A. senegalensis* carpel extracts on low density lipoprotein levels of diabetic rats. Values are mean ± standard error of mean (SEM). Means with different superscripts differ significantly ($p < 0.05$). *NOR* normoglycemic (0.5 ml normal saline), *MET* metformin (100 mg/kg bw), *DU* diabetic untreated, *CME* crude methanol extract, *EAF* ethylacetate fraction, *n-HF* n-hexane fraction

hypolipidemic effect via the suppression of cholesterol luminal absorption and increase biliary excretion (Francis et al. 2002).

Conclusion

A. senegalensis carpel contains significant amount of phytochemicals with hypoglycemic reputation. The crude extract, ethylacetate and hexane fractions exhibited dose-dependent hypoglycemic activity in alloxan-induced diabetic rats. In addition, crude extract and ethylacetate fractions were found to be more effective in prevention of diabetic-induced hyperlipidemia.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All applicable international, national and/or institutional guidelines for the care and use of animals were followed.

References

Bamidele O, Arokoyo DS, Akinnuga AM, Oluwarole AO (2014) Anti-diabetic effect of aqueous extract of *Basella alba* leaves and metformin in alloxan induced diabetic albino rats. Afr J Biotechnol 13(24): 2455–2458

Berinyuy EB, Lawal B, Olalekan AA, Olalekan AA, Yusuf AA, Sakpe S, Ossai PC (2015) Hematological status and organs/body-weight parameters in Wister rats during chronic administration of Cassia occidentalis. Int Blood Res Rev 4(3):1–7

Canadian Council on Animal Care (1997) Guide to the Care and Use of Experimental Animals. Vol. 1, 2nd Edn., 212 pp. Ottawa ON: CCAC

Chedi BAZ, Abubakar JG, Adoum OA (2017) Acute toxicity and antihyperglycaemic effect of ethanol stem-bark extract of Annona senegalensis Pers. (Annonaceae) on alloxan induced diabetic rats. Afr. J Pharmacol Ther 6(3):155–160

Daisy P, Balasubramanian K, Rajalakshmi M, Eliza J, Selvaraj J (2010) Insulin mimetic impact of Catechin isolated from Cassia fistula on the glucose oxidation and molecular mechanisms of glucose uptake on Streptozotocin induced diabetic Wistar rats. Phytomed 17:28–36

Etuk EU (2010) Animals models for studying diabetes mellitus. Agric Biol J 1(2):130–134

Francis G, Kerem Z, Makkar HP, Becker K (2002) The biological action of saponins in animal systems: a review. Br J Nutr 88:587–605

Freshet A, Daniel S, Eyasu M (2017) Antihyperglycemic and antihyperlipidemic activities of ethanol extract of *Ajuga remota* Benth (Harmegusa) leaves in streptozotocin induced diabetic rats. Afr J Pharm Pharmacol 11(2):17–24

Friedewald WT, Levy RI, Fredrickson DS (1972) In: Tietz (ed) Determination of LDL cholesterol. Text Book of Clinical Biochemistry, New York

Jacobson TA, Miller M, Schaefer EJ (2007) Hypertriglyceridemia and cardiovascular risk reduction. Clin Ther 29(5):763–777

Klip A, Leiter LA (1990) Cellular mechanism of action of metformin. Diabetes Care 13(6):696–704

Koli CO, Onyeto CA, Akpa BP, Ezike AC, Akah PA, Okoye TC (2010) Neuropharmacological evaluation of Annona senegalensis leaves. Afr J Biotechnol 9(49):8435–8444

Konaté AWR, Sawadogo F, Dubruc O, Caillard M (2012) Ouedraogo, Guissou IP. Phytochemical and anticonvulsant properties of Annona senegalen-sis Pers. (Annonaceae), plant used in Burkina folk medicine to treat epilepsy and convulsions. Br J Pharmacol Toxicol 3(5): 245–250

Lawal B, Shittu OK, Abubakar AN, Haruna GM, Sani S, Ossai PC (2015) Haematopoetic effect of methanol extract of Nigerian honey bee (*Apis mellifera*) Propolis in mice. J Coast Life Med 3(8):648–651

Lawal B, Shittu OK, Oibiokpa FI, Berinyuy EB, Muhammed H (2017) African natural products with potential antioxidants and hepatoprotectives properties: a review. Clin Phytosci 2:23–66. https://doi.org/10.1186/s40816-016-0037-0

Lawal B, Shittu OK, Oibiokpa IF, Mohammed H, Umar SI, Haruna GM (2016) Antimicrobial evaluation, acute and sub-acute toxicity studies of *Allium sativum*. J Acute Dis 5(4):296–301

Mustapha A (2013) *Annona senegalensis* Persoon: a multipurpose shrub, its phytotherapic, phytopharmacological and phytomedicinal uses. Int J Sci Technol 2(12):862–865

Nagmoti DM, Kothavade PS, Bulani VD, Gawali NB, Juvekar AR (2015) Antidiabetic and antihyperlipidemic activity of *Pithecellobium dulce* (Roxb.) Benth seeds extract in streptozotocin-induced diabetic rats. Euro J Integ Med 7(3):263–273

Nisbet JC, Sturtevant JM, Prins JB (2004) Metformin and serious adverse effects. Med J Aust 180:53–54 20

Omonije OO, Saidu AN, Muhammad HL (2019) Anti-diabetic activities of *Chromolaena Odorata* methanol root extract and its attenuation effect on diabetic induced hepatorenal impairment in rats. Clinical Phytosci 5:23

Owolabi OJ, Inninh SO, Anaka ON, Iyamu OA (2014) Antidiabetic and hypolipidemic effects of methanol leaf extract of Napoleona vogelii(Lecythidaceae) Hook & Planch on alloxan-induced diabetes mellitus in rats. Trop J Pharm Res 13(11):1908

Oyedemi SO, Yakubu MT, Afolayan AJ (2011) Antidiabetic activities of aqueous leaves extract of *Leonotis leonurus* in streptozotocin induced diabetic rats. J Med Plant Res 5:119–125

Rajaei Z, Hadjzadeh MAR, Moradi R, Ghorbani A, Saghebi A (2015) Antihyperglycemic and antihyperlipidemic effects of hydroalcoholic extract of *Securigera securidaca* seeds in streptozotocin-induced diabetic rats. Adv Biomed Res 4:33. https://doi.org/10.4103/2277-9175.150427

Ravi K, Ramachandran B, Subramanian S (2004) Protective effect of *Eugenia jambolana* seed kernel on tissue antioxidants in streptozotocin-induced diabetic rats. Biol Pharm Bull 27:1212–1217

Rawi SM, Mourad IM, Sayed DA (2011) Biochemical changes in experimental diabetes before and after treatment with *Mangifera indica* and *Psidium guava* extracts. Int J Pharm Bio Sci 2:29–41

Robinson AC, Burke J, Robinson S, Johnston DG, Elkeles RS (1998) The effects of metformin on glycemic control and serum lipids in insulin-treated NIDDM patients with suboptimal metabolic control. Diabetes Care 21:701–705

Samuel EK, Edifofon A, Omolola TF, Kevwe BE, Oluyemisi FK (2016) *Annona senegalensis* Persoon (Annonaceae): a review of its ethnomedicinal uses, biological activities and phytocompounds. J Pharmacog Phytochem 5(2):211–219

Sharma B, Balomajumder C, Roy P (2008) Hypoglycemic and hypolipidemic effects of flavonoid rich extract from *Eugenia jambolana* seeds on streptozotocin induced diabetic rats. Food Chem Toxicol 46:2376–2383

Shewasinad A, Bhoumik D, Hishe HZ, Masresha B (2019) Antidiabetic activity of methanol extract and fractions of Thymus schimperi Ronniger leaves in normal and Streptozotocin induce diabetic mice. Iranian J Pharmacol Ther 16:1–8

Thomas MC, Walker MK, Emberson JR, Thomson AG, Lawlor DA, Ebrahim S, When PH (2005) Prevalence of undiagnosed type 2 diabetes and impaired fasting glucose in older British men and women. Diabet Med 22:789–793

WHO (2017). Monitoring health for the sustainable development goals (SDG) targets. https://www.who.int/gho/en/ Accessed 18 march, 2017

Yusuf AA, Lawal B, Yusuf MA, Omonije YO, Adejoke AA, Raji FH, Wenawo DL (2018) Free radical scavenging, antimicrobial activities and effect of sub-acute exposure to Nigerian *Xylopia Aethiopica* seed extract on liver and kidney functional indices of albino rat. Iran J Toxicol 12(3):51–58

Zimmet PZ (2017) Diabetes and its drivers: the largest epidemic in human history. Clin Diabetes Endocrinol 3(1):1–8