European Journal of Medicinal Plants

27(1): 1-8, 2019; Article no.EJMP.45970
ISSN: 2231-0894, NLM ID: 101583475

Anti-Hyperglycemic and Anti-Hyperlipidemic Potentials of Methanol Leaf Extracts of *Aframomum melegueta* and *Piper guineense*

Adetoun Elizabeth Morakinyo[1*], Temitope Adenike Oyedepo[1], Samuel Olufolarin Babarinde[1], Joy Motunrayo Adelowo[2], Ayodeji Emmanuel Adepoju[3] and Oluboade Oluokun Oyedapo[4]

[1]Department of Biochemistry, Adeleke University, Ede, Nigeria.
[2]Department of Basic Sciences, Adeleke University, Ede, Nigeria.
[3]Department of Pre-Clinical Sciences, University of Limpopo, Sovenga 0727, South Africa.
[4]Deparment of Biochemistry and Molecular Biology, Obafemi Awolowo University, Ile-Ife, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. Author AEM wrote the protocol and carry out the experimental work, author TAO designed the study, author SOB wrote the first part of the manuscripts. Author JMA carried some of the experimental work and wrote the second part of the manuscript. Author AEA carried out the statistical analysis. Author OOO designed the work and supplied the materials for the work. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/EJMP/2019/v27i130106
Editor(s):
(1) Daniela Rigano, Researcher, Department of Chemistry of Natural Compounds, University Federico II of Naples, via D. Montesano, Naples, Italy.
(2) Dr. Patrizia Diana, Section of Medicinal Chemistry and Biology, Department of Molecular and, Biomolecular Sciences and Technologies (STEMBIO), University of Palermo, Via Archirafi, Palermo, Italy.
(3) Prof. Marcello Iriti, Professor of Plant Biology and Pathology, Department of Agricultural and Environmental Sciences, Milan State University, Italy.
Reviewers:
(1) Leandro Freire dos Santos, The Midwestern State University (UNICENTRO), Brazil.
(2) R. Senthil Kumar, Swamy Vivekanandha College of Pharmacy, India.
(3) Mahendran Sekar, Universiti Kuala Lumpur, Malaysia.
Complete Peer review History: http://www.sdiarticle3.com/review-history/45970

Original Research Article

Received 23 November 2018
Accepted 09 March 2019
Published 30 March 2019

ABSTRACT

Aim: The study investigated the anti-hyperglycemic and anti-hyperlipidemic potentials of methanol extracts of *Piper guineense* and *Aframomum melegueta* leaves with a view to utilizing the plants in the treatment and management of cardiovascular disorders.
Methodology: Twenty-eight healthy albino rats were randomly divided into seven equal groups: Group I received normal saline (2 ml/kg bwt); Group II received a single dose of alloxan(150 mg/kg bwt) intraperitoneally; Group III received alloxan (150 mg/kg bwt) + glibenclamide (5 mg/kg

**Corresponding author: E-mail: adetounadejumobi05@gmail.com;*

bwt);Group IV received alloxan (150 mg/kg bwt) +PG (200 mg/kg bwt); Group V received alloxan (150 mg/kg bwt) + PG (400 mg/kg bwt); Group VI received alloxan (150 mg/kg bwt) + AM 200 (mg/kg bwt); Group VII received alloxan (150 mg/kg bwt) + AM (400 mg/kg bwt). The blood glucose level was determined before and after treatment with the extracts. The lipid: (total cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) were estimated using the Randox diagnostic kits.

Results: The results revealed that alloxan was able to induce hyperglycemia at 150 mg/kg bwt and post-treatment with *P. guineense* and *A. melegueta* at 200 mg/kg and 400 mg/ kg bwt were able to significantly lower the blood glucose level which was quite apparent in AM treated groups. Also, the extracts at 200 mg/kg and 400 mg/kg were able to bring a significant ($p < 0.05$) reduction in TC, TG and LDL concentrations when compared to the alloxan treated group with the highest reduction in AM treated groups.

Conclusion: These results revealed that the methanol extract of *P. guineense* and *A. melegueta* elicited anti-hyperglycemic and anti-hyperlipidemic potentials of the extracts with the highest effect observed in *A. melegueta* treated rats.

Keywords: Anti-hyperglycemic; anti-hyperlipidemic; Piper guineense and Aframomum melegueta.

1. INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder and is becoming a global health concern because of the increase in its prevalence. However, hyperglycemia and hyperlipidemia are some of the factors indicating this metabolic syndrome [1]. Hyperglycemia is a condition in which an excessive amount of glucose circulates in the blood plasma. Diabetic neuropathy may be a result of long-term hyperglycemia. Hyperlipidemia is characterized by abnormal elevation in plasma triglyceride, cholesterol and low density lipoprotein-cholesterol (LDL-c) and very low lipoprotein - cholesterol (VLDL-c) and has also been reported to be the most prevalent indicator for susceptibility to atherosclerotic heart disease [2]. Also, high blood glucose levels are associated with low level of high-density lipoprotein cholesterol (HDL-c) and increase of LDL-c cholesterol, thus increasing risk of coronary heart diseases. Therefore, it is vital to manage both diabetes and lipid levels [3].

The increase in demand for cheaper therapeutics with no/minimum side effects is stimulating interest in studying the use of natural products for the treatment and management of diseases [4]. The medicinal values of these plants are usually due to the presence of phytochemicals [5].

P. guineense belongs to the family Piperaceae commonly known as West African Black Pepper. It is a climbing plant climbing up to 12m high by its adventitious rootlets. It is known with different vernacular names in Nigeria which include 'Uziza' in Igbo, and 'Iyere' in Yoruba. The seeds are smooth and are prolate-elliptically shaped. The seeds, leaves and sometimes the stems are used in preparing soup. It imparts "heat" and a spicy pungent aroma to food. The plant is utilized for a variety of purposes which include human dietaries, preservative, bio-control agent as well as traditional medicine [6].

Previous phytochemical studies of *P. guineense* seed extract revealed the presence of various substances such as alkaloids, flavonoids, tannins triterpenoids, cardiac glycosides and saponins [7]. Pharmacological and physiological studies of *P. guineense* extract showed depolarizing neuromuscular blocking action, insecticidal properties, sexual behavioural effect and antifungal activity [8] and edema in gastrointestinal tract, urinary bladder and adrenal glands and immunotoxicological effects [9].

Aframomum melegueta K. Schum belongs to the ginger family (Zingiberaceae) and it is commonly known as grains of paradise or alligator pepper [10]. It is variously known locally as *oseoji* in Igbo, ataareinYoruba, and *cittáá* in Hausa of Nigeria. The seeds of *A. melegueta* have been variously reported to be rich in carbohydrates, crude fibre, and bulk minerals [11] suggesting it to be of good nutritional quality, and hence justifying its incorporation into diet. The report of [12,13], NMR and GC-MS analyses of the chloroform extract of the seeds and essential oils from various plant parts, respectively show the plant to be rich in secondary metabolites such as modified gingerols, paradols and shogaols. These metabolites account for some of peppery taste of the seeds [14]. The use of *A. melegueta* in traditional medicine in treating diabetes has

been age long. The essential oils, polyphenol profile and antioxidant activity of *Aframomum melegueta*, have been reported [15,16,17,18,19]. It is used medicinally to treat many diseases including measles, leprosy; tostop lactation and post-partum haemorrhage, as anti-diarrhea and anti-inflammatory activity which may be due to prostaglandin inhibition, and membrane stabilizing activity respectively [20].

Many studies have been carried out on the seeds of these plants but there is dearth of scientific information on the leaves of these plants. Hence, this study investigated the anti-hyperglycemia and the anti-hyperlipidemic effects of the leaf extracts of *A. melegueta* and *P. guineense.*

2. MATERIALS AND METHODS

2.1 Chemicals

All chemicals and drugs used were obtained commercially and of analytical grade.

2.1.1 Collection of plant materials

The leaves of *A. melegueta* and *P. Guineense* were collected in February, 2015 at Okuku, Odo-Otin local government, Osun State, Nigeria. It was identified and authenticated at IFE herbarium (17525), ObafemiAwolowo University, Ile- Ife.

The methanolic extracts of *A. melegueta* and *P. guineense* were separately prepared. The leaves were dried under shade and ground into powder. Typically, the powder (200g) was macerated in 2.5 L methanol (70%) at room temperature for 72h. It was then filtered using muslin cloth. The filtrates were allowed to settle, decanted and filtered using filtration assembly. The filtrates were evaporated using rotary evaporator and then freeze dried using lypholizer. The extracts were stored in air tight container in a refrigerator until used.

2.1.1.1 Acute toxicity study

The acute toxicity study was carried out using the Lorke's method [21]. The study was conducted using a total of twelve mice. The mice (12) weighing betwwen 30-34g were divided into 2 groups of 6 mice each. Groups 1 and 2 animals were given a single dose of 5000 mg/kg body weight (b.w.) of the *A. melegueta* and *P. guineense* extract respectively. The animals were observed for any toxic effect or mortality for 72 h after the treatment period.

2.2 Experimental Animals

Adult female and male albino rats (42) weighing between 120-150 g were obtained from the Animal House, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife. The rats were housed in polyethylene cages at the Animal House, Department of Biochemistry, Adeleke University, Ede and were kept under standard conditions; food and water were supplied *ad libitum*. They were allowed to acclaimatized for a period of 14 days.

2.3 Grouping and Treatment of Animals

The rats were randomly assigned into seven groups of six rats in each group as follows:

Group I : Control (Normal saline)
Group II : Alloxan Treated (150 mg/kg bwt)
Group III : Alloxan + Glibenclamide (5mg/kg bwt)
Group IV : Alloxan + PG (200 mg/kg bwt)
Group V : Alloxan + PG (400 mg/kg bwt)
Group VI : Alloxan + AM (200 mg/kg bwt)
Group VII : Alloxan + AM (400 mg/kg bwt)

The extracts and the reference drug (Glibenclamide) were administered orally.

2.4 Induction of *Diabetes* and Treatment with the Extracts

The animals were allowed to fast overnight and diabetes was induced by a single intra-peritoneal injection of alloxan monohydrate (150 mg/kg bwt). Increase glucose level was monitored 3 days after injection by measuring the tail vein blood glucose level using glucometer. The induced rats were orally treated with the extracts for 7 days.

2.5 Determination of Blood Glucose Levels

The level of blood glucose was determined according to the method described by [22] before and after treatment with the extract and standard drug by using a glucometer. The rats were subjected to fasting for 12-18 h with free access to water prior to the administration of the extract and the blood glucose level was measured. After

the last treatment with the extracts, the animals were fasted overnight and the blood samples were collected for the determination of the blood glucose concentration.

2.6 Sacrificing and Preparation of Blood Plasma

The rats were sacrificed under mild anesthesia with ether, 24 h after the last treatment (oral administration of extracts and drug). Blood was collected by cardiac puncture into bottles containing anticoagulant (trisodium citrate, 3.8% w/v) and mixed gently. Blood plasma was prepared using standard procedure as reported and modified by Bode and Oyedapo [23]. Blood sample was centrifuged on Bench Centrifuge Model 90-2 (Searchtech Instrument England, UK.) at3000 rpm for 10 min. The supernatant (plasma) was collected into sterile bottles, labeled and stored in freezer for biochemical analyses.

2.7 Estimation of Plasma Lipid Profiles

Plasma lipid profiles: triacylglycerol (TG), total cholesterol (TC), High density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), were estimated spectrophotometrically using Randox assay kits.

2.8 Statistical Analysis

The data were statistically analyzed using t-test and ANOVA with the aid of SARS software package. The level of statistical significance was also compared using Duncan's multiple range test $p < 0.05$.

3. RESULTS

3.1 Yield of the Extract

The methanol leaf extract obtained from 500g of powdered leaf weighed 5.6g which was 1.12% of the starting material.

The methanol leaf extract obtained from 500g of powdered leaf weighed 97.69g which was 19.5% of the starting material.

3.1.1 Acute toxicity

The acute toxic effect of methanolic extracts of *A. melegueta* and *P.guineense* was determined using the Lorke's method [21]. There was no related toxic symptom or mortality observed after oral administration of the tested plant extracts at a dose of 5000 mg/kg. The general behavioral of the extract treated mice was observed first for short period (4 h) followed by long period (72 h), did not display any drug related changes in behavior, breathing, skin effects, water consumption, impairment in food intake. Therefore, the extract seems to be safe at a dose level of 5000 mg/kg.

3.2 Blood Glucose Level

In Table 1 is the summary of the initial and final concentrations of blood glucose. After induction of hyperglycemia with alloxan monohydrate, there was a significant increase ($P<0.05$) in blood glucose level of other experimental groups when compared with the normal control group. After treatment the extracts at 200 mg/kg and 400 mg/kg, the blood glucose level was significantly reduced ($P<0.05$) when compared to the alloxan treated rats. This indicated the anti-hyperglycemic potentials of the extracts.

Table 1. Percentage change in the blood glucose concentration in the treatment groups

Treatment Group	Initial Blood Glucose (mg/dl)	Final Blood Glucose (mg/dl)
I	80.50 ± 2.02	75.75 ± 1.11
II	79.25 ± 0.85	199.00 ± 1.68^{a}
III	59.25 ± 0.48^{a,b}	95.75 ± 0.85^{a,b}
IV	68.25 ± 0.35^{a,b}	137.75 ± 2.66^{a,b,c}
V	75.50 ± 1.09^{c}	114.50 ± 3.07^{a,b,c}
VI	79.50 ± 0.87^{c}	65.50 ± 1.96^{a,b,c}
VII	74.25 ± 0.91^{c}	72.25 ± 1.58^{b,c}

Values are mean ± SEM of six determinations. (n=6), Superscripts a, b and c represent significant (p<0.05) differences between treatment groups (IV, V, VI, VI) and control (I), Alloxan (II) and Alloxan+ Glibeclamide (III) respectively, Key: I- control, II - Alloxan, III - Alloxan + Glibeclamide (5mg/kg), IV - Alloxan + PG (200mg/kg bwt), V - Alloxan+ PG (400mg/kg bwt), VI - Alloxan+ AM (200mg/kg bwt), VII - Alloxan + AM (400mg/kg bwt)

3.3 Lipid Profiles

Table 2 is the summary of the effect of the extracts on the plasma lipid profile of alloxan-induced hyperglycemia rats. There was significant increase in the concentrations of TC, TG and LDL-c but adecrease in HDL-c of the alloxan treated group when compared to the control group. However, treatment with the extracts at 200 and 400 mg/kg bwt caused a significant reduction in the concentrations of TC, TG and LDL-c but an increase in HDL-c.

Table 2. The effects of methanol leaf extract of *P. guineense* and *A. melegueta*on Lipid Profile (mmol/L) of Alloxan-induced hyperglycemic rats

Treatment group	TC (mmol/L)	TG (mmol/L)	HDL (mmol/L)	LDL (mmol/L)
I	5.99 ± 0.003	1.61 ±0.001	4.54 ± 0.001	0.714 ± 0.008
II	15.82 ± 0.019[a]	4.89 ± 0.002[a]	0.02 ± 0.001[a]	13.58 ± 0.019[a]
III	8.253 ± 0.019[b]	1.96 ± 0.310[b]	3.27 ± 0.019[b]	4.09 ± 0.014[a,b]
IV	9.448±0102[a,b]	3.862±0.021[a,c]	2.266±0.387[a,b]	5.426±0.061[a,b]
V	7.318±0.018[b]	2.008±0.003[b]	4.364±0.017[b]	5.426±0.061[a,b]
VI	9.35 ± 0.046 [a,b]	0.961 ± 0.032[b]	6.95 ± 0.04[a,b,c]	1.05 ± 0.10 [b,c]
VII	8.411 ± 0.062[b]	2.381 ± 0.02[b]	7.12± 0.002[a,b,c]	0.214 ± 0.07[b,c]

Values are mean ± SEM of six determinations. (n=6), Superscripts a,b and c represent significant (p<0.05) differences between treatment groups (IV, V, VI, VI) and control (I), Alloxan (II) and Alloxan+ Glibeclamide (III) respectively, Key: I- control, II - Alloxan, III - Alloxan + Glibeclamide (5mg/kg), IV - Alloxan + PG (200mg/kg bwt), V - Alloxan+ PG (400mg/kg bwt), VI - Alloxan+ AM (200mg/kg bwt), VII - Alloxan + AM (400mg/kg bwt)

4. DISCUSSION

The study evaluated anti-hyperglycemia and anti-hyperlipidemic effects of *A. melegueta* and *P. guineense* leaf extracts at 200 mg/kg bwt and 400 mg/kg bwt.The dose was chosen based on the reports of previous studies [24,25,26]. After the administration of alloxan monohydrate, there was significant increase ($p < 0.05$)in the blood glucose level of the alloxan-treatedgroup when compared to the normal control group(Table 2).Elevated value of fasting blood glucose concentration observed in alloxan treated rats may be due to the toxic effect of alloxan on islet beta cells of the pancreas through its ability to induce reactive oxygen species (ROS) formation, resulting in the necrosis of the pancreas and loss of capacity of the pancreas to secrete insulin resulting to hyperglycemia [27,28,29].

Chronic exposure to hyperglycemia is the primary casual factor in the pathogenesis of diabetic complications and cause changes in vascular tissue which promote atherosclerosis [30]. Our findings is in agreement with the report of earlier studies that administration of alloxan at the dose of 250mg/kg was able to increase to elevate the fasting blood sugar levels [31,32]. However, post-treatments with *P. guineense* and *A. melegueta* at 200 mg/kg and 400 mg/ kg bwt extracts were able to significantly lower the blood glucose respectively when compared to the alloxan treated group.

Both extracts compared favorably with the reference drug, Glibenclamide and the highest effect was observed in *A. melegueta* at 200 mg/kg bwt. The observed anti-hyperglycemia activity of these extracts may be attributed to the presence of phytochemicals such as: total phenols, flavonoids, alkaloids,tannins, terpenoids, and saponins in the plants that have been known to have anti-hyperglycemic activity [31]. The presence of these bioactive compounds was earlier reported by our previous studies [10,32]. Studies also reported that flavonoids have anti-hyperglycemic properties because they stimulate glucose uptake in peripheral tissues and attenuate oxidative stress during diabetic conditions [33,34]. Flavanoids have been reported to be actively involved in the restoration of pancreatic β-cell and insulin secretion. A large number of alkaloids have been isolated from numerous medicinal plants and investigated for their possible anti-hyperglycemic activity [35]. Saponins are known to be efficiently involved in the restoration of pancreatic β-cell and insulin secretion [33,36].

One of the associated metabolic disorders of diabetes is dyslipidemia which is one of the risk factors of diabetes [37]. Hypercholesterolemia and hypertriglyceridemia have been reported to occur in alloxan treated rats [38,39]. The elevated values for lipid profile: TC, TG, LDL-cholesterol, observed in the alloxan induced diabetic rats could be partly due to increased intestinal biosynthesis of cholesterol because diabetes shifted the major site of cholesterogenesis from the liver to the small intestine leading to hypercholesterolemia [40]. Severe diabetes mellitus due to insulin deficiency might be accompanied with a reduced LDL-receptor resulting to high concentration of serum LDL cholesterol in diabetic subjects [41].

The results of the extracts treated groups revealed a significant reduction in the levels of total cholesterol, triglyceride, LDL but an increase in HDL when compared to the alloxan-treated group. The anti-hyperlipidemic effect was more apparent in the *A. melegueta* treated group

at 200 and 400 mg/kg bwt. This revealed the anti-hyperlipidemic activity of the plant extracts. The ability of *A. melegueta* and *P. guineense* to ameliorate the lipid profile may be attributed to the presence of phytochemicals in the plants. Epidemiological studies have shown that bioactive compounds such as flavonoids intake are inversely related to mortality from coronary heart diseases and the incidence of heart attacks [42].

5. CONCLUSION

In conclusion, the results of this study revealed that the plant extracts elicited anti-hyperglycemic effect and normalized the lipid profile of diabetic rats. This study showed that these spices do not just impact flavour to foods, but may be sources of bioactive substances useful in the treatment and management of diabetes and related disorders.

CONSENT

It is not approval.

ETHICAL APPROVAL

As per international standard or university standard ethical approval has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. DeguchiY, Miyazaki K.Anti-hyperglycaemic and anti-hyperlipidemic effects of guava leaf extract. Nutrition and Metabolism. 2010;7:1-10.
2. Maruthapan V, Shree K. Antihyperlipidemic potential of a polyherbal drug (Geriforte) on atherogenic diet induced hyperlipidemia: A Comparison with Ayurslim. International Journal of Chemical and Analytical Science. 2010;3:37-39.
3. Sudasinghe HP, Peiris DC. Hypoglycemic and hypolipidemic activity of aqueous leaf extract of *Passiflora suberosa* L. Peer Journal. 2018;6:e4389. DOI:10.7717/peerj.4389
4. Dolui AK, Segupta R. Anti-hyperglycemic effect of different extracts of leaves of *Cajanus cajan* HPLC profile of the active extracts. Asian Journal of Pharmaceutical and Clinical Research. 2012;5:116–119.
5. Etim OE, Egbuna CF,Odo NM,Awah, FM.In vitro antioxidant and nitric oxide scavenging activities of *Piper guineense*. Global Journal of Research in Medical Plants and Indigenous Medicine. 2013;2: 485–494.
6. Martins AP, Salgueiro L, Vila R, Tomi F, Canigueral S, Casanova J, Proenca DA, Cunha A, Adzet T. Essential oils from four *Piper* Species. Phytochemistry. 1558;49: 2019-2023.
7. Fajobi OA, Fasakin OW, Oyedapo OO. Phytochemicals, antioxidant potentials, and 2, 2'- diphenyl-1-picrydrazyl (DPPH) Radical Scavenging Activity of *Piper guineense* (Schumach & Thonn.) Seed. African Journal of Plant Science. 2017;11: 99-104.
8. Adewoyin FB, Odaibo AB, Adewunmi CO. Mosquito repellent activity of *Piper guineense* and *Xylopia aethiopica* fruit oils. African Journal of Traditional Complementary Alternative Medicine. 2006;3(2):79-83.
9. DawareMB, Mujumdar AM, Ghaskadbi S. Reproductive toxicity of piperine in Swiss albino mice. Planta Medicine. 2000; 66:231-236.
10. Nwaehujor CO, Eban LK, Ode JO, Ejiofor CE, Igile GO. Hepatotoxicity of methanol seed extract of *Aframomum melegueta* [Roscoe] K. Schum(Grains of paradise) in Sprague-Dawley rats. American Journal of Biomedical Research. 2014;2:61–66.
11. Alaje DO, Owolabi KT, Olakunle TP, Oluoti OJ, Adetuberu IA. Nutritional, minerals and phytochemicals composition of *Garcinia cola* [Bitter cola] and *Aframomum melegueta* (Alligator pepper). IOSR Journal of Environmental Science, Toxicology and Food Technology. 2014;8: 86–91.
12. Owokotomo IA, Ekundayo O, Oguntuase BJ. Chemical constituents of the leaf, stem, root and seed essential oils of *Aframomum melegueta* (K. Schum) from South West Nigeria. International Research Journal of Pure and Applied Chemistry. 2013;4:395–401.
13. El-Halawany AM, El-Dine RS, El-SayedNS, Hattor IM. Protective effect of *Aframomum melegueta* phenolics against CCl4-inducedrat hepatocytes damage; role of apoptosis and pro-inflammatory

cytokines inhibition.Science Reports. 2014;30:5880.

14. Ajaiyeoba EO, Ekundayo O. Essential oil constituents of *Aframomum melegueta* (Roscoe) K. Schum seeds (alligator pepper) from Nigeria. Flavour and Fragrance Journal. 2009;14:109–111.
15. Iwu MM. Handbook of African Medicinal Plants. Second Edition, CRCPress, Taylor and Francis Group, Florida, USA.
16. Ajaiyeoba EO, Ekundayo O. Essential oil constituents of *Aframomum melegueta* (Roscoe) K. Schum seeds (alligator pepper) from Nigeria. Flavour Fragrance Journal. 1999;14:109–111.
17. Gabriel AO, Makinde O, Kolawole Falade O, Phyllis I, Peters U. Extraction and characterization of antioxidants from *Aframomum melegueta* and *Xylopia aethiopica*. European Food Research and Technology. 2003;216:526–528.
18. Jazet PM, Fekam BF, Sameza ML, Ndongson DB, Kwazou NL, Amvam PH, Menut C. Investigations on the essential oils of some *Aframomum* species (Zingiberaceae) from Cameroon as potential antioxidant and anti-inflammatory agents. International Journal of Essential Oil Therapeutics. 2008;2:149–155.
19. JulianiHR, Welch C, Asante-Dartey J, Acquaye D, Wang M, Simon JE. Chemistry, quality, and functional properties of grains of paradise (*Aframomum melegueta*), a rediscovered. Dietary Supplements. 2008;6:100–113.
20. Umukoro S, Ashorobi RB. Further evaluation of the anti-inflammatory activity of *Aframomum melegueta* seed extract and its possible mechanism of action. Nigerian Journal Health Biomedical Sciences. 2005;4:35–39.
21. Lorke D. A new approach to practical acute toxicity testing. Archives of Toxicology. 1983;53:275-287.
22. Mojekwu TO, Yama OE, Ojokuku SA, Oyebadejo SA. Hypoglyceamic effects of aqueous extract of *Aframomum melegueta* leaf on alloxan-induced diabetic male albino rats. Pacific Journal of Medical Sciences. 2011;8:28–36.
23. Bode SO, Oyedapo OO. Biological activities and phytoconstituents of the lower plant *Platycerium anglolense*, Welwex Hook. Journal of Medicinal Plants Research. 2011;5:1321-1329.
24. Ilic N, Schmidt BM, Poulev A, Raskin I. Toxicological evaluation of grains of paradise (*Aframomum melegueta*) [Roscoe] K. Schum. Journal of Ethnopharmacology. 2010;127:10–17. DOI:10.1016/j.jep.2009.10.031
25. Onoja SO, Ezeja MI, Omeh YN, Emeh EC. Phytochemical and hypolipidemic effects of methanolic extract of *Aframomum melegueta* seed. European Journal of Medicinal Plants. 2015;5(4):377-383.
26. Okoye CN, Obasi OL, Ezechukwu O.Effects of methanolic leaf extract of piper guineense on some reproductive parameters of male albino rats (Rattus Norvegicus). Animal Research International. 2016;13(3):2548–2553.
27. Ohno T, Horio F, Tanaka S, Terada M, Namikawa TA. Fatty liver and hyperlipidemia in IDDM (insulin dependent diabetes mellitus) of Streptozotocin treated shrews.Journal of Life Science. 2000; 66(2):125-131.
28. Lenzen S. Review: The mechanisms of alloxan- and streptozotocin-induced diabetes.Diabetologia. 2008;51:216–226.
29. Zafar M, Naeem-Ul H, Aaqvi A, Ahmed A. Altered liver morphology and enzymes in streptozotocin induced diabetic rats. International Journal of Morphology. 2009; 23:719-725.
30. Badin JK, Kole A, Stivers B, Progar V, Pareddy A, Alloosh M, Sturek M. Diabetes exacerbates coronary atherosclerosis in Ossabaw Miniature Swine with Metabolic Syndrome. Journal of Translational Med. 2018;16(1):58.
31. Middleton EJ, Kandaswami C, Theoharis CT. The effects of plant flavanoids on mammalian cells: Implications for inflammation, heart disease and cancer. Pharmacological Reviews. 2000;52:673-751.
32. Morakinyo AE, Oyedapo OO, Akinpelu BA, Fajobi AO, Fasakin WO, KomolafeIJ, Akinlalu AO. Evaluation of Antioxidant, Anti-inflammatory and Phytochemical Constituents of *Aframomum melegueta* Aqueous Leaf Extract. International Journal of Medicinal Plants. 2018;112:888-903.
33. Echo IA, Osuagwu AN,Agbor RB,Okaka EC, Ekanem BE. Phytochemical composition of *Afromomum melegueta* and *Piper guineense* seeds. World Journal of Applied Evironmental Chemistry. 2012; 2:17–21.

34. EidHM, Martineau LC, Saleem A, Muhammad A, Vallerand D. Benhaddou-Andaloussi, A. Stimulation of AMP-activated protein kinase and enhancement of basal glucose uptake in muscle cells by quercetin and quercetin glycosides, active principles of the anti-diabetic medicinal plant *Vaccinium vitis*-idaea. Molecular Nutrition and Food Research. 2010;54(7): 991-1003.
35. Rauter AP, Martins A, Borges C,Mota-Filipe H, Pinto R, Sepodes B. Anti-hyperglycaemic and protective effects of flavonoids on streptozotocin-induced diabetic rats. Phytotherapy Research. 2010;24:S133-138.
36. Aniszewski T. Alkaloids: Chemistry, biology, ecology, and applications. 2nd ed. Amsterdam: Elsevier. 2015;1–475.
37. Preuss HG, Bagchi D, Bagchi M, et al. Effects of a natural extract of (-)-hydroxycitric acid (HCA-SX) and a combination of HCA-SX plus niacin-bound chromium and *Gymnema sylvestre* extract on weight loss. Diabetes Obesity Metabolism. 2004;6:171–180.
38. Chehade JM, Gladysz M, Mooradian AD. Dyslipidemia in type 2 diabetes: Prevalence, pathophysiology, and management Drugs. 2013;73(4):327-339.
39. Wang L, Zhang XT, Zhang HY, Yao HY, Zhang H. Effect of *Vaccinium bracteatum* Thunb. leaves extract on blood glucose and plasma lipid levels in streptozotocin-induced diabetic mice.Journal of Ethnopharmacology. 2010;130(3):465-9.
40. Balamurugan R, Ignacimuthu, S. Antidiabetic and hypolipidemic effect of methanol extract of *Lippia nodiflora* L. in streptozotocin induced diabetic rats. Asian Pacific Journal of Tropical Biomedicine. 2011;1:S30-36.
41. Luka C, Tijjani H, Joel E, Ezejiofor U, Onwukike P. Hypoglycaemic properties of aqueous extracts of *Anacardium occidentale*, *Moringa oleifera*, *Vernonia amygdalina* and *Helianthus annuus*: A comparative study on some biochemical parameters in diabetic rats. International Journal of Pharmaceutical Science Invention. 2013;2:16-22.
42. Swami S, Sztalryd C, Kraemer FB. Effects of streptozotocin-induced diabetes on low density lipoprotein receptor expression inrat adipose tissue. Journal of Lipid Research. 1996;37:229-239.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle3.com/review-history/45970