DOI: https://doi.org/10.4314/njbmb.v40i1.11 NJBMB (2025) 40(1) 83-89

e-ISSN: 2659-0042

Nigerian Journal of Biochemistry and Molecular Biology

The Official Publication of the Nigerian Society of Biochemistry & Molecular Biology (NSBMB). Journal homepage: https://www.nsbmb.org.ng/journals/

Research Article

Hypolipidemic Impact of 'Aju Mbaise' Herbal Mixture in Type II Diabetic Female Rats

Chinonso U. Nnadiukwu[1], Tochukwu A. Nnadiukwu[2,*]

[1]*Africa Centre of Excellence in Public Health and Toxicological Research (PUTOR), University of Port Harcourt, Port Harcourt, Nigeria.*
[2]*Department of Biochemistry/Chemistry Technology, School of Science Laboratory Technology, University of Port Harcourt, Port Harcourt, Nigeria.*

OPEN ACCESS

****CORRESPONDENCE***
Nnadiukwu, T. A.
tochu.nnadiukwu@uniport.edu.ng

ARTICLE HISTORY
Received: 21/07/2024
Reviewed: 22/10/2024
Revised: 22/12/2024
Accepted: 20/05/2025
Published: 31/10/2025

CITATION
Nnadiukwu C. U. and Nnadiukwu T. A. (2025). Hypolipidemic impact of 'aju mbaise' herbal mixture in type ii diabetic female rats. *Nigerian Journal of Biochemistry and Molecular Biology.* 40(1), 83-89 https://doi.org/10.4314/njbmb.v40i1.11

ABSTRACT

This study was conducted to evaluate the hypolipidemic potential of the combined multiple plant extract (CMPE) of *Sphenocentrum jollynum, Cnestis ferruginea, Xylopia aethiopica, Uvaria chamae, Palisota hirsuta, Scleria sp., Napoleona sp., Dialium guineense, Combretum racemosun*, and *Heterotis rotundifolia* commonly referred to as 'Aju Mbaise' in South Eastern Nigeria. The study involved fifty-four (54) rats grouped into 6 with 9 rats per group. The groups include the normal control (NC), diabetic control (DC), metformin treated group, and three diabetic treated groups that received different concentrations (500 $mgkg^{-1}$, 250 $mgkg^{-1}$, and 100 $mgkg^{-1}$) of the CMPE correspondingly. Diabetes was ascertained after high fat diet (HFD) and streptozotocin (STZ) administration. Total cholesterol (TC), triglyceride, high-density lipoprotein (HDL) and low-density lipoproteins (LDL) were assayed accordingly at interval of four weeks and results obtained revealed significant reduction in concentrations of total cholesterol (1.49±0.33 mmol/l), triglyceride (0.95±0.18 mmol/l), LDL (1.34±0.57 mmol/l), as well as increased HDL (1.38±0.22 mmol/l) at week 12, in the diabetic animals treated with 250mg/kg body weight of the CMPE. This study revealed a positive hypolipidemic effect of the multiple plants extracts. Thus, it could be employed as a potential therapy for managing the risks associated with cardiovascular diseases.

Keywords: *Aju Mbaise, Cholesterol, Combined Multiple Plant Extract, Diabetes, Hypolipidemia*

INTRODUCTION

Hyperlipidemia is a condition associated with several disorders generally indicated by high concentration of lipids in the bloodstream (Shattat, 2015). According to Pulipati et al. (2022), it is often associated with significant upsurge of low-density lipoprotein (LDL), triglycerides (TRG), and omega-6 free fatty acids (FFA). The serum lipid upsurge are associated to increased hepatic TRG synthesis and/or declined TRG clearance. Hyperlipidemic effect on insulin secretion and synthesis of some pro-inflammatory cytokines such as tumour necrosis factor alpha (TNF-α) and interleukin-1 beta (IL-1β) contributes significantly to the pathogenesis of diabetes (Boarescu et al., 2022). As per Li et al. (2020), increased levels of FFA, LDL, and TRG are linked to diabetes. Meanwhile, high secretion of IL-1β and TNF- α is associated with hyperlipidemia. Increased lipids and/or pro-inflammatory cytokines lead to insulin resistance by obstructing insulin signalling or obliteration of pancreatic beta cells, and escalate the risk of diabetes. According to Zhou et al. (2015), high blood glucose is often accompanied by hyperlipidemia in both types of diabetes, though some studies have reported increased total cholesterol, TRG, LDL, and decreased HDL in diabetic patients. In diabetics, the translation of omega-6 polyunsaturated fatty acids to active metabolites is suppressed as a result of inhibition of delta-6-desaturase (D6D) enzyme activity induced by insulin deficiency. Zhou et al. (2015), also stated that hyperlipidemia is also responsible for the emergence of some complications attributed to diabetes.

The possible control or treatment of hyperlipidemia linked to type 1 diabetes mellitus (DM) has been established, whereas it's seen to persist in type 2 DM treatment. Considering the fact that the remedy and decline in the effects of these conditions are key in the prevention of cardiovascular diseases, this study adopted combined multiple plants extract (CMPE) as a regimen in the management and/or control of hyperlipidemia in diabetics. Application of CMPE was considered due to its wide range of bioactivity that is dependent on the characteristic activity of the individual plant constituent.

The CMPE adopted in this study constitutes *Sphenocentrum jollynum, Cnestis ferruginea, Xylopia aethiopica, Uvaria chamae, Palisota hirsuta, Scleria sp., Napoleona sp., Dialium guineense, Combretum racemosun,* and *Heterotis rotundifolia* and are commonly referred to as 'Aju Mbaise' by the Igbo ethnic group in Nigeria (Nnadiukwu et al., 2020). The therapeutic actions of these individual plants as reported by Nnadiukwu et al. (2024) are attributed to their individual bioactive compounds. Thus, the collective bioactive compounds of these plants will have a potential broad therapeutic effect.

According to Otieno et al. (2008), multi-plant extracts demonstrated more action and effectiveness against single plant extracts (SPE) and could be developed into more potent therapeutics. Thus, led to an advocacy for the preference of mixed extracts in management of infections. The use of MPE regimens increase the confidence level that most pathogens may be controlled or eliminated with any one of the mixture's constituents. Considering the prediction by Artasensi et al. (2020), for the adoption of combination therapy of multiple antidiabetic agents, and the intensifying awareness in the adoption of plants and their products for therapeutic purpose, this study investigated the impact of this cocktail of multiple plants on the lipid function assay in diabetic female Wistar rats.

MATERIALS AND METHODS

Reagents

All biochemical reagents and materials applied in this study were of standard analytical grade. Streptozotocin (STZ) was acquired from Sigma Chemicals Co. St. Louis, MO, USA; Metformin was from Merck Serono, Milano, Italy, while the lipid function test kits are products of Randox Laboratories Ltd.

Collection and identification of plant samples

Fresh leaves samples of the individual plants *Cnestis ferruginea, Xylopia aethiopica, Uvaria chamae, Palisota hirsuta, Scleria sp., Napoleona imperialis, Dialium guineense, Combretum racemosun*, and *Heterotis rotundifolia* were collected at Obodo Ujichi, Ahiazu and Amuzi, Ahiara Towns, in Ahiazu Mbaise L.G.A, of Imo State, Nigeria. The plant samples were identified at the Department of Plant Science and Biotechnology, University of Port Harcourt, Rivers State, Nigeria. The fresh plants parts after collection were air dried, cut into pieces and pulverised before extraction using maceration method (Farooq et al., 2022).

Experimental animals

Fifty-four female Wistar rats were used for this research. This gender was desired as they mostly consume this herbal cocktail. The rats were procured from the Department of Veterinary Medicine, University of Nigeria, Nsukka, Nigeria. At the time of procurement, the rats weighed between 40 – 50 g. They were housed in the animal house of the Department of Pharmacology, University of Port Harcourt, Rivers State, Nigeria, and were left for seven days to adapt to the experimental conditions during which they were given normal chow and clean water. The animal handling in this study was conducted in line with the global practice for the care and use of animals for scientific purposes as approved by the Research Ethics Committee of the UNIVERSITY OF PORT HARCOURT with authorization number: UPH/CEREMAD/ REC/MM64/003.

Induction of type 2 diabetes mellitus(T2DM)

T2DM was induced in the experimental rats (Groups II - VI) with a single dose intraperitoneal injection of 35 $mgkg^{-1}$ body weight (b.w) of STZ prepared with normal saline according to the method described by Gheibi et al. (2017), after 5 weeks of high fat diet (HFD) administration. The HFD was constituted in accordance with the method of Liu (2018), using standard laboratory chow (Top feed) growers mash, lard and sucrose at the ratio of 3:1:1. Fasting blood glucose (FBG) was checked to ascertain diabetes mellitus (DM) after 7 days of STZ administration.

Experimental design

The experimental animals were gathered into six groups of nine animals each. The diabetic animals in group II remained untreated while those in groups III to VI were treated with metformin 7.2 $mgkg^{-1}$ b.w, and three different doses of the cocktail extract respectively, as shown below.

Group I: Normal control rats
Group II: Diabetic induced rats without treatment
Group III: Diabetic induced rats + metformin (7.2 mgkg-1 b.w)
Group IV: Diabetic induced rats + CMPE (500 mgkg-1 b.w).

Group V: Diabetic induced rats + CMPE (250 mgkg-1 b.w)
Group VI: Diabetic induced rats + CMPE (100 mgkg-1 b.w)
Following the oral treatment with metformin and the extracts; which was done daily according to their grouping for a period of twelve (12) weeks, at four weeks intervals, three animals from each group were fasted overnight, anaesthetized, sacrificed, and blood samples collected for lipid function assay.

Determination of lipid contents

The lipid content such as TC, TRG, and HDL were determined with their appropriate Randox assays kits, following the established protocol, and absorbance read with Advanced Microprocessor UV-VIS Spectrophotometer (Single Beam -295), while LDL was calculated using the equation described by Friedewald et al. (1972).

Statistical analysis

Values were presented as Mean ± standard error of mean (SEM), while Tukey Test of oneway ANOVA was applied to test for significant differences between treatment groups using the Statistical Package for the Social Sciences (SPSS) (version 25.0). The results were considered significant at $p<0.05$.

RESULTS

Effect of the combined multiple plants extract (CMPE) on liquid profile in type II diabetic wistar rats

From the result presented in Table 1, TC concentration of the diabetic control (DC) group was significantly higher ($p<0.05$) than that of the rest of experimental groups all through the experimental period. Meanwhile, the normal control (NC), the group treated with 500 mgkg-1 b.w CMPE and the metformin treated group recorded the least TC concentration in weeks 4, 8, and 12 respectively.

Reduction in TC concentration was recorded among the groups in week 12 with respect to weeks 4 and 8. Also, the metformin treated group recorded lower TC than the groups administered the CMPEs in weeks 4 and 12. From the result shown in Table 2, the DC group recorded a significantly higher ($p<0.05$) triglyceride (TG) concentration than the other experimental groups except the group that received the 250 mgkg-1 b.w CMPE in weeks 8 and 12.

There was also a decline in TG concentration in the diabetic treated groups in weeks 8 and 12 when compared to week 4. Meanwhile, within the weeks, the metformin treated group recorded the lowest TG concentration when compared to the CMPE administered groups, except in week 12 when the group that received 500 mgkg-1 b.w CMPE recorded a lower TG concentration. From the result shown in Table 3, there was no significant difference in the HDL concentration among the groups in weeks 4 and 12. Meanwhile, the 500 mgkg-1 b.w and 250 mgkg-1 b.w CMPE administered groups recorded an increase in HDL concentration at weeks 8 and 12 when compared to week 4. The metformin treated group recorded a higher HDL concentration than the CMPE treated groups in weeks 4 and 8. At the twelfth week, the group treated with 500 mgkg-1 b.w CMPE recorded the highest HDL concentration when compared with the other treated groups. From the result shown in Table 4, no significant difference was recorded for low density lipoprotein (LDL) concentration among the groups in weeks 4 and 12. Meanwhile, the DC group recorded the highest LDL concentration all through the experimental period, while the metformin treated group recorded the least LDL concentration in weeks 4 and 12.

Table 1. Table 1: Effect of the CMPE on Total Cholesterol (TC) Level of HFD/STZ-induced Diabetic Wistar Rats

Groups	Total Cholesterol (mmol/l)		
	Week 4	Week 8	Week 12
NC	1.77 ± 0.32^a	1.70 ± 0.26^a	1.60 ± 0.35^{ab}
DC	3.60 ± 0.69^b	3.87 ± 0.48^b	3.40 ± 0.64^b
Metformin	1.80 ± 0.12^a	1.67 ± 0.18^a	1.29 ± 0.38^a
500mg Extract	1.83 ± 0.20^a	1.57 ± 0.12^a	1.67 ± 0.09^{ab}
250mg Extract	2.13 ± 0.19^{ab}	2.20 ± 0.15^a	1.49 ± 0.33^{ab}
100mg Extract	1.87 ± 0.29^a	2.07 ± 0.27^a	1.61 ± 0.52^{ab}

Groups with varied superscript(s) down the week are significantly different at $p<0.05$, while groups with similar superscript(s) are not.

NC= Normal control; DC= Diabetic control; Metformin= Treated with metformin; 500 mg Extract = administered 500 mgkg-1 b. w. of the CMPE; 250 mg Extract = administered 250 mgkg-1 b. w. of the CMPE; 100 mg Extract = administered 100 mgkg-1 b. w. of the CMPE.

Table 2. Effect of the CMPE on Triglyceride (TG) Level of HFD/STZ-induced Diabetic Wistar Rats

Groups	Triglyceride (mmol/l)		
	Week 4	Week 8	Week 12
NC	0.78 ± 0.19[a]	0.76 ± 0.18[a]	0.74 ± 0.10[a]
DC	2.46 ± 0.73[b]	2.53 ± 0.67[b]	2.03 ± 0.50[b]
Metformin	1.01 ± 0.15[ab]	0.90 ± 0.04[a]	0.82 ± 0.02[a]
500mg Extract	1.09 ± 0.22[ab]	0.99 ± 0.16[a]	0.69 ± 0.02[a]
250mg Extract	1.35 ± 0.05[ab]	1.29 ± 0.04[ab]	0.95 ± 0.18[ab]
100mg Extract	1.24 ± 0.04[ab]	1.29 ± 0.04[ab]	0.84 ± 0.20[a]

Groups with varied superscript(s) down the week are significantly different at p<0.05, while groups with similar superscript(s) are not.

NC= Normal control; DC= Diabetic control; Metformin= Treated with metformin; 500 mg Extract = administered 500 mgkg-1 b. w. of the CMPE; 250 mg Extract = administered 250 mgkg-1 b. w. of the CMPE; 100 mg Extract = administered 100 mgkg-1 b. w. of the CMPE.

Table 3. Effect of the CMPE on HDL-C Concentration of HFD/STZ-induced Diabetic Wistar Rats

Groups	HDL (mmol/l)		
	Week 4	Week 8	Week 12
NC	1.76 ± 0.38[a]	1.89 ± 0.27[b]	1.61 ± 0.26[a]
DC	0.93 ± 0.05[a]	0.99 ± 0.11[a]	0.65 ± 0.05[a]
Metformin	1.32 ± 0.33[a]	1.57 ± 0.13[ab]	1.40 ± 0.36[a]
500mg Extract	1.12 ± 0.21[a]	1.28 ± 0.06[ab]	1.59 ± 0.45[a]
250mg Extract	1.22 ± 0.21[a]	1.34 ± 0.16[ab]	1.38 ± 0.22[a]
100mg Extract	1.21 ± 0.14[a]	1.11 ± 0.04[a]	1.42 ± 0.20[a]

Groups with varied superscript(s) down the week are significantly different at p<0.05, while groups with similar superscript(s) are not.

NC= Normal control; DC= Diabetic control; Metformin= Treated with metformin; 500 mg Extract = administered 500 mgkg-1 b. w. of the CMPE; 250 mg Extract = administered 250 mgkg-1 b. w. of the CMPE; 100 mg Extract = administered 100 mgkg-1 b. w. of the CMPE.

Table 4. Effect of the CMPE on LDL-C Concentration of HFD/STZ-induced Diabetic Wistar Rats

Groups	LDL (mmol/l)		
	Week 4	Week 8	Week 12
NC	1.53 ± 0.16[a]	1.45 ± 0.20[ab]	1.25 ± 0.09[a]
DC	2.82 ± 0.38[a]	2.95 ± 0.26[b]	2.76 ± 0.33[a]
Metformin	1.19 ± 0.12[a]	1.24 ± 0.10[a]	1.25 ± 0.10[a]
500mg Extract	1.64 ± 0.47[a]	1.19 ± 0.35[a]	1.49 ± 0.39[a]
250mg Extract	1.85 ± 0.83[a]	1.43 ± 0.64[ab]	1.34 ± 0.57[a]
100mg Extract	1.41 ± 0.47[a]	1.14 ± 0.32[a]	1.67 ± 0.61[a]

Groups with varied superscript(s) down the week are significantly different at p<0.05, while groups with similar superscript(s) are not.

Key: NC= Normal control; DC= Diabetic control; Metformin= Treated with metformin; 500 mg Extract = administered 500 mgkg-1 b. w. of the CMPE; 250 mg Extract = administered 250 mgkg-1 b. w. of the CMPE; 100 mg Extract = administered 100 mgkg-1 b. w. of the CMPE.

DISCUSSION

The use of combination therapy of multiple plants extracts for medicinal purpose especially in traditional healing systems is a global practice aimed at achieving desired therapeutic goal. According to Vaou et al. (2022), a precise approach does not constantly enrich its particular pharmacological effect; thus, combinations comprising two or more components can afford additive, synergistic, or antagonistic effects. The current study evaluated the synergistic impact of combined multiple plants extract (CMPE) comprising of *S. jollynum, C. ferruginea, X. aethiopica, U. chamae, P. hirsuta, Scleria sp., Napoleona sp., D. guineense, C. racemosun*, and *H. rotundifolia* on lipid profile of female diabetic rats. These plants contain many bioactive compounds such as phytochemicals, proximate nutrients, vitamins and minerals (Nnadiukwu et al., 2024). According to Mason and Routledge (2005), combination therapy has been applied in traditional herbal medicines since the emergence of therapeutics. The high concentration of TRG, TC and LDL as well as low concentration of HDL observed in the DC animals when compared with the NC and the treated animals in this study is in line with the report of Nnadiukwu et al. (2016) ascertaining that ascent in glucose level influences the aforementioned lipid biomarkers. According to Asuquo et al. (2010), hyperlipidemia, a typical risk factor for cardiovascular diseases is a recognized diabetic complications characterized by extremely high levels of cholesterol, TRG, LDL, phospholipids and other lipoproteins.

The most frequently dyslipidemia observed in type 2 diabetes is characterized by increased TRG levels and decreased HDL-cholesterol levels (Sunil and Ashraf, 2020). Saponaro et al. (2015), additionally stated that increased serum lipid levels in diabetic conditions is attributed to the increased mobilization of FFAs from peripheral fat deposits, since insulin inhibits the lipase enzyme. The excess FAs synthesized are converted into phospholipids and cholesterol, which together with excess triglycerols formed at the same time in the liver are emptied into the blood in form of lipoprotein cholesterol concentrations.

According to Tomkin and Owens (2017), insulin effects on the liver, apoprotein synthesis, peripheral actions of insulin on other tissues such as adipose, as well as alterations in regulation of enzymes responsible for maintaining adequate levels of lipoproteins in the blood especially decreased lipoprotein lipase function that results to hypertriglyceridemia are the common probable mechanisms that influence dyslipidemia. The hypertriglyceridemia subsequently leads to an increase in LDL and decrease in HDL, further predisposing a patient to coronary artery disease.

This study recorded a progressive decline in TC, TRG and LDL in the diabetic treated animals as treatment with metformin and the CMPE progresses. As indicated by Burci et al. (2015) decrease in lipid concentrations was ascribed to the activities of fiber, alkaloids, saponins, flavonoids and polyphenols present in the plant samples. Likewise, the elevated plasma HDL produced by administration of the CMPE indicates its synergistic potential against cardiovascular risk or complication. As per Ouimet et al. (2019), high HDL provides a protective effect by minimizing the rate of entry of cholesterol into the cell and increasing the rate of cholesterol discharge from the cell. From this study, the HDL of the normal control and the diabetic treated animals are significantly ($p<0.05$) higher than that of the diabetic control animals.

As indicated by Ikewuchi et al. (2011), increase in serum HDL-cholesterol concentration is linked to vitamin supplementation. Thus, the increased serum HDL-cholesterol concentration recorded in this study post CMPE administration could be attributed to the high vitamin content of 'Aju Mbaise'. The increase in HDL-cholesterol is desirable, as it mitigates atherosclerosis incidence. Moreover, the lipoprotein lowering potential of the CMPE might be linked to the collective phytochemicals present in the individual plants that constitute the multi-plant combination. Nnadiukwu et al. (2019), reported that the CMPE of 'Aju Mbaise' is rich in phytochemicals such as phenols, flavonoids, tannins, alkaloids, saponins, steroids, glycoside, and terpenoids.

The antidiabetic potential of this CMPE commonly referred to as 'Aju Mbaise' was also reported by Nnadiukwu et al. (2023). According to Nnadiukwu et al. (2020), CMPE of 'Aju Mbaise' contains appreciable amount of minerals (arsenic, aluminum, cadmium, calcium, cobalt, copper, iron, lead, magnesium, manganese, mercury, molybdenum, nickel, potassium, selenium, silver, sodium, and zinc), vitamins (A, B1, B2, B3, B6, B12, C, D, and K), and nutritional components like carbohydrate, protein, moisture and fat; with negligible amount of crude fibre and ash. The impact of combination therapy of multiple plants cannot be overemphasized. Donkor et al. (2023), posited that synergy might result from affecting of multiple pathways such as substrates, enzymes, metabolites, ion channels, ribosomes, and signal cascades.

CONCLUSION

This study revealed that type-2 diabetes mellitus can trigger dyslipidemia characterized by significant alteration in the lipid profile. From the study, elevated concentrations of TRG, TC, and LDL as well as declined concentration of HDL was recorded after diabetes induction with high fat diet (HFD) and streptozotocin (STZ). The result of the study revealed the effectiveness of the combined multiple plant extracts (CMPE) of 'Aju Mbaise' in regulating the assayed lipid profile shown by decreased concentrations of TG, TC and LDL as well as increased HDL concentration. The synergistic features demonstrated by the CMPE in this work could be ascribed to the diverse bioactive composites in the individual plants. This potential might be associated to the targeting of multiple pathways. Application of CMPE has indicated to have a broad therapeutic model, considering its multiple targets, links, and approaches. Thus, could be applied for the development of effective hypolipidemic therapeutics.

AUTHORS' CONTRIBUTIONS

The research was conceptualized by TAN. TAN and CUN carried out the laboratory analysis as well as the data analysis. TAN and CUN participated in the literature searches, writing of the original draft of the manuscript and the subsequent editing. All authors have read and agreed to the published version of the manuscript.

FUNDING STATEMENT

This research did not receive any funding.

Institutional review board

The animal handling in this study was conducted in line with the global practice for the care and use of animals for scientific purposes. The Research work was approved by the Research Ethics Committee of the UNIVERSITY OF PORT HARCOURT with authorization number: UPH/CEREMAD/REC/MM64/003.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this paper

ACKNOWLEDGEMENT

The authors are grateful to the staff at Primary Health Centers in Calabar, Cross River State, Nigeria for their technical assistance throughout the study duration.

REFERENCES

Artasensi, A., Pedretti, A., Vistoli, G., and Fumagalli, L. (2020). Type 2 diabetes mellitus: A review of multi-target drugs. *Molecules*, 25(8), 1987. https://doi.org/10.3390/molecules25081987

Asuquo, O. R., Igiri, A. O., Akpan, J. E., and Akpaso, M. I. (2010). Cardioprotective potential of Vernonia amygdalina and Ocimum gratissimum against streptozotocin (STZ)-induced diabetes in Wistar rats. *The Internet Journal of Tropical Medicine, 7(1).* 1-8.

Boarescu, P. M., Boarescu, I., Pop, R. M., Roşian, Ş. H., Bocşan, I. C., Rus, V., Mada, R.O., Popa, I. D., Neagu, N., Bulboacă, A. E., and Bolboacă, S. D. (2022). Evaluation of oxidative stress biomarkers, pro-inflammatory cytokines, and histological changes in experimental hypertension, dyslipidemia, and type 1 diabetes mellitus. *International Journal of Molecular Sciences*, 23(3), 1438. https://doi.org/10.3390/ijms23031438

Burci, L. I. M., da Silva, C. B., de Oliveira, M., Dalarmi, L., Zanin, S. M. W., Miguel, O. U. G., and Miguel, M. D. (2015). Determination of antioxidant, radical scavenging activity and total phenolic compounds of Artocarpus heterophyllus (Jackfuit) seeds extracts. *Journal of Medicinal Plants Research*, 9(40), 1013-1020. https://doi.org/10.5897/JMPR2015.5926

Donkor, M. N., Donkor, A. M., and Mosobil, R. (2023). Combination therapy: Synergism among three plant extracts against selected pathogens. *BMC Research Notes*, 16(1), 83. https://doi.org/10.1186/s13104-023-06354-7

Farooq, S., Mir, S. A., Shah, M. A., and Manickavasagan, A. (2022). Extraction techniques. In Plant extracts: Applications in the food industry (pp. 23-37). *Academic Press*.

Friedewald, W. T., Levy, R. I., and Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clinical Chemistry*, 18(6), 499- 502. https://doi.org/10.1093/clinchem/18.6.499

Gheibi, S., Kashfi, K., and Ghasemi, A. (2017). A practical guide for induction of type-2 diabetes in rat: Incorporating a high-fat diet and streptozotocin. *Biomedicine and Pharmacotherapy*, 95, 605-613. https://doi.org/10.1016/j.biopha.2017.08.098

Ikewuchi, J. C., Onyeike, E. N., Uwakwe, A. A., and Ikewuchi, C. C. (2011). Effect of aqueous extract of the leaves of Acalypha wilkesiana 'Godseffiana'Muell Arg (Euphorbiaceae) on the hematology, plasma biochemistry and ocular indices of oxidative stress in alloxaninduced diabetic rats. *Journal of Ethnopharmacology*, 137(3), 1415-1424. https://doi.org/10.1016/j.jep.2011.08.015

Li, N., Qiu, Y., Wu, Y., Zhang, M., Lai, Z., Wang, Q., Du, Y., Guo, L., Liu, S., and Li, Z. (2020). Association of serum total fatty acids with type 2 diabetes. *Clinica Chimica Acta*, 500, 59-68. https://doi.org/10.1016/j.cca.2019.09.018

Liu, G., Bei, J., Liang, L., Yu, G., Li, L., and Li, Q. (2018). Stachyose improves inflammation through modulating gut microbiota of high-fat diet/streptozotocin-induced type 2 diabetes in rats. *Molecular Nutrition and Food Research*, 62(6), 1700954. https://doi.org/10.1002/mnfr.201700954

Mason, E., and Routledge, P. A. (2005). Combination therapy of diseases: General concepts (pp. 3-15). Cambridge University Press: Cambridge, London, UK.

Nnadiukwu, A. T., Monago-Ighorodje, C. C., and Chuku, L. C. (2019). Phytochemical composition of ethanol extract of a cocktail herbal mixture (Aju Mbaise). *Journal of Advances in Biology and Biotechnology*, 22(1), 1-11. 10.9734/JABB/2019/v22i130103

Nnadiukwu, C. U., Nnadiukwu, T. A., Ajuru, G., and Ogono, T. G. (2024). Synergistic effect of combined multiple plants extracts on some blood cell indices of diabetic rats. *Scientia Africana*, 23(2), 165-179. 10.4314/sa.v23i2.15

Nnadiukwu, T. A., Ighorodje, C. C., and Chuku, L. C. (2020). Nutritional composition of 'AjuMbaise' herbal cocktail. *Asian Journal of Research in Biochemistry*, 7(2), 30-37. 10.9734/AJRB/2020/v7i230136

Nnadiukwu, T. A., Monago-Ighorodje, C. C., and Chuku, L. C. (2023). Anti-diabetic impact of 'Aju Mbaise' herbal cocktail in streptozotocin-induced diabetic female rats. Scientia Africana, 22(3), 85-106. 10.4314/sa.v22i3.8

Nnadiukwu, T. A., Monago, C. C., and Chuku, L. C. (2016). Effects of the combined treatment of ethanol extract of moringa oleifera and Pleurotus ostreatus on blood glucose, amylase and lipid profile of alloxan-induced diabetic Wistar albino rats. *British Biotechnology Journal*, 14(4), 1 9. https://doi.org/10.9734/BBJ/2016/27365

Otieno, J. N., Hosea, K. M. M., Lyaruu, H. V., and Mahunnah, R. L. A. (2008). Multi-plant or single-plant extracts, which is the most effective for local healing in Tanzania? *African Journal of Traditional, Complementary and Alternative Medicines*, 5(2), 165-172. 10.4314/ajtcam.v5i2.31269

Ouimet, M., Barrett, T. J., and Fisher, E. A. (2019). HDL and reverse cholesterol transport: Basic mechanisms and their roles in vascular health and disease. *Circulation Research*, 124(10), 1505 1518. https://doi.org/10.1161/CIRCRESAHA.119.312617

Pulipati, V. P., Brinton, E. A., and Hatipoglu, B. (2022). Management of mild-to-moderate hypertriglyceridemia. Endocrine Practice, 28(11), 1187-1195. https://doi.org/10.1016/j.eprac.2022.07.003

Saponaro, C., Gaggini, M., Carli, F., and Gastaldelli, A. (2015). The subtle balance between lipolysis and lipogenesis: a critical point in metabolic homeostasis. *Nutrients*, 7(11), 9453 - 9474. https://doi.org/10.3390/nu7115475

Shattat, G. F. (2015). A review article on hyperlipidemia: types, treatments and new drug targets. *Biomedical and Pharmacology Journal*, 7(1), 399-409. https://dx.doi.org/10.13005/bpj/504

Sunil, B., and Ashraf, A. P. (2020). Dyslipidemia in pediatric type 2 diabetes mellitus. *Current Diabetes Reports*, 20(53), 1-9. https://doi.org/10.1007/s11892-020-01336-6

Tomkin, G. H., and Owens, D. (2017). Diabetes and dyslipidemia: characterizing lipoprotein metabolism. Diabetes, metabolic syndrome and obesity: *Targets and Therapy*, 333-343. http://dx.doi.org/10.2147/DMSO.S115855

Vaou, N., Stavropoulou, E., Voidarou, C., Tsakris, Z., Rozos, G., Tsigalou, C., and Bezirtzoglou, E. (2022). Interactions between medical plant-derived bioactive compounds: Focus on antimicrobial combination effects. *Antibiotics*, 11(8), 1014. https://doi.org/10.3390/antibiotics11081014

Zhou, X., Zhang, W., Liu, X., Zhang, W., and Li, Y. (2015). Interrelationship between diabetes and periodontitis: role of hyperlipidemia. *Archives of Oral Biology*, 60(4), 667-674. https://doi.org/10.1016/j.archoralbio.2014.11.008