

# Antihyperlipidemic Activity of *Plectranthus neochilus* Leaf Ethanolic Extract on Fat-Fed Male Wistar Rats

Hamza Lawal, Ahmad Mallam Ado, Moshood Usman and Usman Sani Garba

Department of Biochemistry, Faculty of Science, Sa'adu Zungur University, Gadau, Itas-Gadau LGA, Nigeria

Corresponding Author's Email: hamzamaccidolawal@gmail.com

Received on: April, 2024

Revised and Accepted on: May, 2024

Published on: July, 2024

## ABSTRACT

*Plectranthus neochilus* (*P. neochilus*), a perennial shrub-like flowering plant have been used in Brazilian and Southern African folk medicine to treat liver related diseases amongst other ailments. Lifestyle choices, specifically continuous consumption of foods with high fat content have been identified as one of the major causes of non-alcoholic fatty liver disease. In this study, the antihyperlipidemic effect of *P. neochilus* leaves ethanolic extracts (PNEE) in fat-fed male Wistar rats was evaluated. *In-vitro* antioxidant activity of the extract was evaluated using DPPH assay. Hyperlipidaemia was induced by feeding with fat-supplemented feed (FSF) (35% beef fat) for 21 days *ad libitum*. DPPH scavenging assay indicated antioxidant activity with an IC<sub>50</sub> of 27.48±3.85 µg/mL. While the FSF resulted to significant ( $p < 0.05$ ) elevations in total cholesterol (TC) level, and triglycerides (TG) level, coupled with reduction in HDL-C level in the hyperlipidaemic control compared to the non-FSF fed rats (normal control). Interestingly, treatment with PNEE at 150 mg/kg/day, 300 mg/kg/day and Atorvastatin at 10mg/kg/day (as standard control) for 14 days with continuation of the fat-supplemented regimen, revealed significant ( $p < 0.05$ ) reduction in serum levels of TC and TG as well as elevations in serum level of HDL-C in PNEE-treated groups compared to the hyperlipidemic control. These findings suggested that the PNEE possess hyperlipidemic potentials which could be used for the development of therapies against diet associated dyslipidaemia as well as non-alcoholic fatty liver disease.

**Keywords:** Lobstar plant, *Plectranthus neochilus*, Hyperlipidemia, Hypercholestremia

## 1.0 INTRODUCTION

Obesity, cardiovascular disease, and type 2 diabetes mellitus are the main indicators of hyperlipidaemia and are the major causes of death and morbidity worldwide as well as a large contributor to the burden of disease globally (La Sala and Pontiroli, 2020). Hyperlipidaemia is a heterogeneous disorder characterized by a persistent excess of lipids in the blood, such as triglycerides, cholesterol, cholesterol esters, and phospholipids. It is caused by abnormal lipid metabolism and can lead to various complications, like hypertension, atherosclerosis, myocardial infarction, cerebral stroke, renal failure, and insulin resistance. These complications are major global health concerns (Pirillo et al., 2021).

The primary strategy for treatment of hyperlipidaemia remains the use of allopathic medicine, which comes with individual based intolerance and side effects, thereby making plant sources of medicine a noteworthy alternative (Najmi et al., 2022; Sharma et al., 2024). Natural products researchers are focusing on developing safe and effective drugs with hypolipidaemic activity, exclusively from plant sources (Najmi et al., 2022). Recent preclinical studies have reported potent anti-hyperlipidemic effects of different phytochemicals that were administered in specific, effective and safe doses (Gong et al., 2020; Hussain et al., 2024). Moreover, the adherence to plant

based medicine promotes green health care concept, encourages chemoprevention and provides a cost-effective approach to the prevention and treatment chronic metabolic diseases like hyperlipidaemia (Cena and Calder, 2020).

*Plectranthus neochilus* Schltr. (*P. neochilus*) is a small perennial aromatic herb that grows robustly and fast to the height of about 0.5 m and spreads to about 1.5 m wide with purple lobster shaped flowers. This plant which is endemic to Africa, India and South America is widely used in traditional and folk medicine by locals where infusions or aqueous extract of its leaves are prepared and used for treatment of skin infections, indigestion, dyspepsia, respiratory illness among others (Lambrechts and Lall, 2020; Ramborger et al., 2020).

Studies on phytochemical constituents of *P. neochilus* have reported that rosmarinic acid and chlorogenic acid have been isolated from its leaves (Lambrechts and Lall, 2020). Most phytochemical analysis however, have been on essential oil isolated from the plant which revealed compounds as monoterpenoids like citronellyl formate, citronellol, linalool, and isomethone as well as the sesquiterpene, citronellyl propionate (Lawal et al., 2010). Others are  $\alpha$ -terpenyl acetate,  $\beta$ -pinene,  $\alpha$ -thujone,  $\beta$ -caryophyllene, and  $\alpha$ -pinene (da Silva et al., 2023; Mota et al., 2014).

While extracts and essential oil of *P. neochilus* are yet to be extensively explored, few studies have researched its pharmacological potentials. Mota et al investigated the antioxidant activity of *P. neochilus* essential oil using the diphenylpicrylhydrazyl (DPPH) radical scavenging assay and the thiobarbituric acid reactive substances (TBARS) assay. They reported 60% inhibition of lipid peroxidation and moderate free radical scavenging property at 1000 mg/L (Mota et al., 2014). Also, moderate antimicrobial activity of *P. neochilus* has been previously reported (de Souza et al., 2012). Cytotoxicity studies conducted on n-hexane extracts of *P. neochilus* leaves reported anti-tumour activity on tongue squamous cell carcinoma (SCC-25) and hypopharyngeal carcinoma (FaDu) cell lines (Borges et al., 2016). De Souza et al reported inhibition of alpha-glucosidase activity at 48.11 mg/mL and 30.63 mg/mL for n-hexane and aqueous extracts respectively (de Souza et al., 2012). While these studies provide evidence of potent wide range bioactivities, the antihyperlipidaemic properties of this plant remains to be explored.

Therefore, this study investigates the anti-hyperlipidemic potentials of *P. neochilus* leaves extract in reversing high fat diet-induced hyperlipidaemia in male wistar rats, which can be beneficial to the management of obesity, cardiovascular disease as well as diabetic dyslipidaemia.

## 2.0 MATERIALS AND METHODS

### 2.1 Plant Material

Fresh six months old whole *P. neochilus* plants were harvested from the Botanical Garden of Bauchi State University Gadau, Bauchi, Nigeria. The plants were identified and authenticated by the Herbarium, Federal College of Forestry, Jos, Plateau State Nigeria. The leaves were plucked, washed and shade dried over a period of 15 days after which they were ground into fine powder.

### 2.2 Extract Preparation

The powdered leaves were subjected to ethanol extraction using 70% ethanol as solvent. Five hundred grams of the powder was soaked in the solvent and was kept overnight. The mixture was then separated using separating funnel. The residue was soaked again in the solvent and kept for 48 hours and which was filtered. The solvent in both filtrates was then evaporated under reduced pressure in a rotavapor (R-100, BUCHI, Russia) at 50 °C and the residue obtained was termed *Plectranthus neochilus* ethanolic extract (PNEE) and stored at 4 °C until analysis.

### 2.3 Diphenylpicrylhydrazyl (DPPH) Radical Scavenging Assay

Antioxidant activity of PNEE was evaluated using DPPH photometric assay as described by Sahin et al. The extract was diluted in ethanol to concentration of

100 µg/mL, after which serial dilutions to 80, 60, 40 and 20 µg/mL concentrations were made. To 1 mL of the different concentration, 2 mL of 0.3 mM DPPH ethanol solution was added and the mixture was vortexed, and then kept in a dark room for 30 minutes (Şahin et al., 2004). The absorbance was measured using a spectrophotometer CM-5 (Konica Minolta, Japan) at 517 nm wavelength against blank. The percentage inhibition was calculated using the formula below.

$$\% \text{ Inhibition} = \frac{(A_0 - A_1)}{A_0} \times 100$$

Where  $A_0$  is absorbance of ethanol + DPPH and  $A_1$  is absorbance of sample + DPPH. Butylated toluene (BHT) was used as positive control. The  $IC_{50}$  value was calculated using GraphPad Prism software version 9.

### 2.4 Preparation of Fat-Supplemented Feed

An optimised fat supplementation method, modified from (Al-Hayder et al., 2020), was used in this study. Beef fat was purchased from the local market, homogenized by melting in low heat (< 50 °C) and mixed with the animal feed powder along with groundnut and salt. The relative component fraction (by weight) of the fat-fortified animal feed was; Animal feed powder 60 %, Beef fat 35 %, Groundnut 5 %. The components were properly mixed. The dried powder obtained was then sprinkled with distilled water to make small balls of feed, stored in self-sealing plastic covers and refrigerated at 2°C to 8°C until use. This preparation of feed was done once in every three days for all the animals. The unsaturated fatty acids vs. saturated fatty acids (UFA: SFA) ratio of the fat-supplemented and non-supplemented animal feed was evaluated by analysing relative concentrations of Palmitic (16:0) and Stearic (18:0) for saturated fatty acids, against Oleic (18:1) and Linoleic (18:2) for unsaturated fatty acids. The ratios were then computed.

### 2.5 Experimental Animals

A total of 20 male Wistar rats were acclimatized to the environment in five different groups of 4 rats each. Hyperlipidaemia was induced by feeding the rats with the fat-supplemented animal feed and water *ad libitum* while the group serving as normal control received non-supplemented feed.

The animals were fed for a total of 35 days; however, after day 21 of feeding, oral treatment with PNEE and Atorvastatin commenced on the test and positive control groups, once daily in the morning orally for 14 consecutive days. The feeding pattern of the test and control groups as described above was maintained all through the experiment.

Group 1: Fed with non-supplemented feed and served as normal control.

Group 2: Fed with fat-supplemented feed and served as positive control.

Group 3: Administered PNEE (150mg/kg), p.o., and fed with fat-supplemented feed.

Group 4: Administered PNEE (300mg/kg), p.o., and fed with fat-supplemented feed.

Group 5: Administered Atorvastatin (10mg/kg), p.o., and fed with fat-supplemented feed as standard control.

## 2.5 Analyses of Biochemical Parameters

After treatment, the animals were anaesthetized with chloroform, blood samples were collected and centrifuged for 15 minutes at 2500 rpm to obtain serum. The collected serum was analysed for serum total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C) using Hitachi 902 Chemistry Analyzer (Hitachi, Japan). Low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were calculated

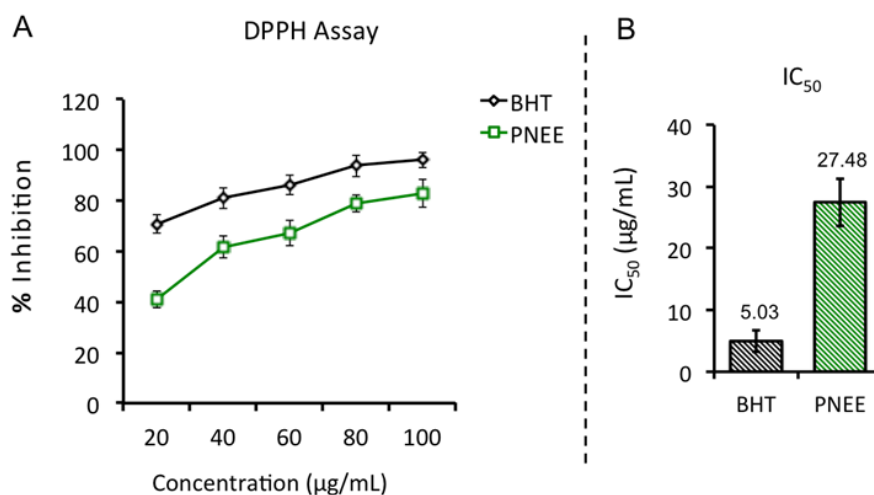
using formula described previously (Friedewald et al., 1972) while atherogenic index (AI) was computed using formula described previously (Abbott et al., 1988)

## 2.7 Statistical Analysis

All values were presented in form of mean  $\pm$  standard deviation and student's t test was used to determine statistical significance between the test and control groups with p value set at  $< 0.05$ .

## 3.0 RESULTS

The evaluation of antioxidant activity of the extract using DPPH assay revealed a concentration-dependent increase in free-radical scavenging ability. Figure 1A shows the concentration response curve of PNEE as it compares with butylated hydroxytoluene (BHT). The  $IC_{50}$  obtained was  $27.48 \pm 3.85 \mu\text{g/mL}$  for PNEE and  $5.03 \pm 1.79 \mu\text{g/mL}$  for BHT (Figure 1B).



**Figure 1: DPPH Scavenging Activity of PNEE**

Figure 1A shows the concentration response curve of PNEE as it compares with BHT. The  $IC_{50}$  obtained was  $27.48 \pm 3.85 \mu\text{g/mL}$  for PNEE and  $5.03 \pm 1.79 \mu\text{g/mL}$  for butylated hydroxytoluene (BHT) (Figure 1B).

The fatty acid composition of the fat-supplemented feed (FSF) and non-fat supplemented feed (NSF), which were used for induction of hyperlipidaemia and as normal feed respectively, is presented in Table 1.

**Table 1: Fatty acid composition of the FSF and NSF**

Fatty Acids	FSF (%/100 g)	NSF (%/100 g)
Palmitic (16:0)	20.71 $\pm$ 0.3	11.39 $\pm$ 0.8
Stearic (18:0)	8.87 $\pm$ 0.7	3.92 $\pm$ 0.3
Oleic (18:1)	47.59 $\pm$ 1.2	51.11 $\pm$ 1.7
Linoleic (18:2)	16.11 $\pm$ 1.4	26.23 $\pm$ 2.0
Others	6.72 $\pm$ 0.4	7.35 $\pm$ 0.8
UFA	67.06 $\pm$ 0.9	81.01 $\pm$ 0.3
SFA	32.94 $\pm$ 0.4	18.99 $\pm$ 0.3
UFA:SFA ratio	2.04:1	4.26:1

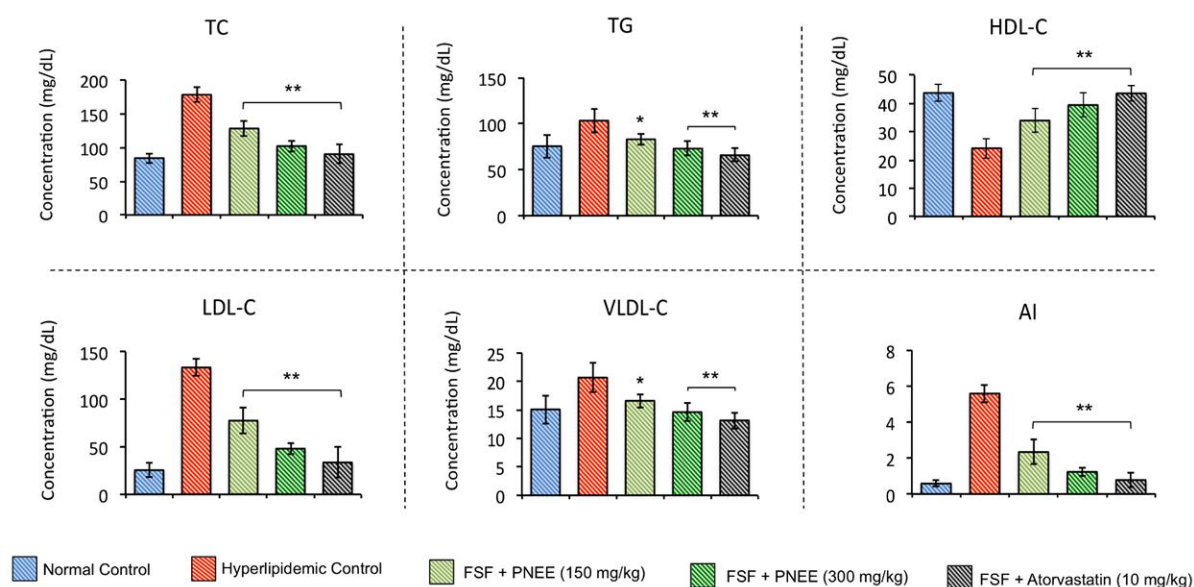
Following the addition of animal fat, the UFA:SFA ratio of the non-supplemented animal feed decreased from 4.26:1 to 2.04:1.

The FSF had a higher amount of saturated fatty acids, specifically palmitic and stearic acids. On the other hand, the NSF had a higher concentration of unsaturated fatty acids, specifically oleic and linoleic acids. The relative UFA percentage was higher in non-supplemented feed compared to the fat-supplemented feed (i.e. 67.06 $\pm$ 0.9 % FSF vs. 81.01 $\pm$ 0.3 % NSF), while SFA percentage was higher in fat-supplemented feed compared to the non-supplemented feed (i.e. 32.94 $\pm$ 0.4 % FSF vs. 18.99 $\pm$ 0.3 % NSF). Therefore as expected, the UFA:SFA ratio of the non-supplemented animal feed reduced by 52 % after supplementation with animal fat.

Significant elevations in serum levels of TC, LDL-C, VLDL-C and the AI, as well as significant decrease in serum HDL-C level was observed in the experimental animals fed with the FSF compared with the normal

control group ( $p < 0.05$ ). The data presented in Figure 2, demonstrated that treatment with PNEE at concentrations of 150 mg/kg and 300 mg/kg as well as with atorvastatin significantly reduced serum levels of TC, LDL-C and the AI in the fat diet fed animals compared with the hyperlipidaemic control group at  $p < 0.01$ . While treatment with 300 mg/kg PNEE and atorvastatin was able to significantly reduce serum levels of TG and VLDL-C in the fat diet fed animals

compared to the hyperlipidaemic control group at  $p < 0.01$ , 150 mg/kg PNEE was only able exert significant reduction of serum TG and VLDL-C level in the fat diet fed animals compared to the hyperlipidaemic control group at  $p < 0.05$ . Also, treatment with PNEE at concentrations of 150 mg/kg and 300 mg/kg as well as with atorvastatin significantly elevated serum level of HDL-C in the fat diet fed animals compared with the hyperlipidaemic control group at  $p < 0.01$ .



**Figure 2: Lipid Profile of the Experimental Animals**

Significant reductions in serum HDL-C levels and increases in serum levels TG, TC, LDL-C, VLDL-C, and the atherogenic index (AI) were observed in the hyperlipidaemic control. PNEE at doses of 150 mg/kg/day and 300 mg/kg/day, as well as Atorvastatin at 10 mg/kg/day (used as a positive control), resulted to statistically significant reductions in serum TG, TC, LDL-C, VLDL-C, and the AI. Additionally, there were increases in serum HDL-C levels in the PNEE-treated groups compared to the hyperlipidaemic control group.

\* indicates statistically significant difference at  $p < 0.05$

\*\* indicates statistically significant difference at  $p < 0.01$

#### 4.0 DISCUSSION

According to a review of the global estimates from the Global Burden of Disease, Injuries, and Risk Factors Study 2019 (Vos et al., 2020), it was projected that in 2019, there were 43.8 million cases of type 2 diabetes mellitus, 18.5 million cases of hypertension, and 1.2 billion cases of non-alcoholic fatty liver disease. Type 2 diabetes mellitus, hypertension, non-alcoholic fatty liver disease, and obesity accounted for the highest number of fatalities between 2000 and 2019, with mortality rates steadily increasing over this period (Chew et al., 2023). These findings underscores the significance of antihyperlipidaemic studies. In this study, we evaluated the antihyperlipidaemic activity of a locally available plant material which is easily accessible, explored and utilized. The PNEE revealed a competitive potency (i.e.  $IC_{50}$  of 27.48  $\mu\text{g/mL}$ ) regarding *in-vitro* antioxidant capacity which

comparable with extracts of other medicinal plant materials reported in previous studies; pomegranate peels (28.84  $\mu\text{g/mL}$ ), guava leaves (28.00  $\mu\text{g/mL}$ ) (Farag et al., 2020) as well as *Bergenia pacumbis* 25.97  $\mu\text{g/mL}$  (Pandey et al., 2020).

To ascertain whether the observed antioxidant capacity translates to hypolipidaemic effects *in-vivo*, the experimental animals were fed with a fat supplemented feed with a UFA: SFA ratio 2.04:1. This resulted to significant elevations in serum TC and TG as well as induced dyslipidaemia evident by lowered levels of HDL-C in the fat fed animals compared to the control. However, a statistically significant dose dependant reversal of the hyperlipidaemic trend coupled with elevations in serum levels of “good cholesterol” i.e. HDL-C in the PNEE treated animals is indicative of a potent antihyperlipidaemic prowess.

It is widely known that hypertriglyceridemia has a clinically significant role in predicting the onset of cardiovascular disease. Patients undergoing coronary angiography who have hypertriglyceridemia typically have significant coronary heart disease, and low HDL-C levels are closely associated with the development of cardiovascular disease and its consequent death (Chait, 2022; Choe et al., 2022). It has been investigated whether the ratio of high triglycerides to HDL-C (TG/HDL-C) could serve as a biomarker to identify people with unfavourable cardiometabolic risk profiles. It is well recognized that the pathophysiology of atherosclerosis and chronic inflammation are influenced by the interaction between triglyceride and HDL-C levels (Chait, 2022). Reverse cholesterol transport, which includes taking cholesterol out of peripheral cells and transferring it to the liver via several routes for recycling, is where HDL-C comes into play (Wieczorek et al., 2022).

In our study, we observed significantly higher levels of LDL-C and VLDL-C in the hyperlipidaemic control group compared to the normal control group and the animals treated with PNEE in a dose-dependent manner. The TG/HDL ratio, an important parameter, has been investigated as a novel biomarker for adverse cardiometabolic risk profiles and insulin resistance (Kosmas et al., 2023). Insulin resistance is considered a key feature of metabolic syndrome, which precedes the development of conditions such as diabetes mellitus, coronary heart disease, and cardiovascular disease (Zhao et al., 2023). As the TG/HDL-C ratio increases, LDL particles tend to become smaller and denser, which are known to be pro-atherogenic and linked to the initiation and progression of atherosclerotic lesions in coronary arteries (Sultani et al., 2020).

Here, we also evaluated the atherogenic index (AI), calculated as the logarithm of the TG/HDL-C ratio, to assess the levels of triglycerides and HDL-C cholesterol. AI serves as a robust biomarker for dyslipidaemia, metabolic syndrome, and cardiometabolic risk profiles. Studies have suggested that AI may be more closely associated with cardiovascular and cerebrovascular disease risk than individual lipoprotein cholesterol concentrations alone, making it a valuable prognostic marker (Edwards et al., 2017; Sadeghi et al., 2021). Higher AI values indicate worsening dyslipidaemia, while lower values suggest improvement (Chen et al., 2023). Our results showed significantly higher AI in the hyperlipidemic group compared to the non-induced rats, with a significant reduction in AI observed in the PNEE-treated animals ( $p < 0.01$ ).

## 5.0 CONCLUSION

In conclusion, our findings demonstrate the strong antihyperlipidaemic activity of PNEE in experimental rats, as shown by the reversal of dyslipidaemia induced by a fat-rich diet. This highlights the potential of *P. neochilus* leaves as a promising source for the development of anti-dyslipidaemic interventions. However, further research is needed to explore the molecular mechanisms underlying these observed antihyperlipidaemic effects in future studies.

## REFERENCES

- Abbott, R. D., Wilson, P., Kannel, W. B., & Castelli, W. P. (1988). High density lipoprotein cholesterol, total cholesterol screening, and myocardial infarction. The Framingham Study. *Arteriosclerosis: An Official Journal of the American Heart Association, Inc.*, 8(3), 207-211. <https://doi.org/10.1161/01.ATV.8.3.207>
- Al-Hayder, M. N., Al-Mayyahi, R. S., & Abdul-Razak, A. S. (2020). Effects of sunflower oils and beef tallow on serum parameters and liver histopathology in experimental rats. *Obesity Medicine*, 18, 100232.
- Borges, G. A., Ferreira, J. F., Elias, S. T., Guerra, E. N. S., & Simeoni, L. A. (2016). Cytotoxic effect of *Plectranthus neochilus* extracts in head and neck carcinoma cell lines. *African Journal of Pharmacy and Pharmacology*, 10(10), 157-163. DOI: 10.5897/AJPP2015.4355
- Cena, H., & Calder, P. C. (2020). Defining a healthy diet: evidence for the role of contemporary dietary patterns in health and disease. *Nutrients*, 12(2), 334.
- Chait, A. (2022). Hypertriglyceridemia. *Endocrinology and Metabolism Clinics*, 51(3), 539-555.
- Chen, M., Fang, C.-y., Guo, J.-c., Pang, L.-m., Zhou, Y., Hong, Y., Yang, L.-f., Zhang, J., Zhang, T., & Zhou, B.-f. (2023). Predictive value of atherogenic index of plasma and atherogenic index of plasma combined with low-density lipoprotein cholesterol for the risk of acute myocardial infarction. *Frontiers in Cardiovascular Medicine*, 10, 1117362.
- Chew, N. W., Ng, C. H., Tan, D. J. H., Kong, G., Lin, C., Chin, Y. H., Lim, W. H., Huang, D. Q., Quek, J., & Fu, C. E. (2023). The global burden of metabolic disease: Data from 2000 to 2019. *Cell Metabolism*, 35(3), 414-428. e413.
- Choe, H. J., Park, S., Han, K.-D., Moon, M. K., & Koo, B. K. (2022). Contribution of hypertriglyceridemia to ischemic cardiovascular disease in Korean women: A nationwide population-based study. *Journal of Clinical Lipidology*, 16(1), 83-93.
- da Silva, L. R. R., Correia, Z. A., Gurgel, E. S. C., Ribeiro, O., Silva, S. G., Ferreira, O. O., Andrade, E. H. d. A., & de Oliveira, M. S. (2023). Morphoanatomical, histochemical, and essential oil composition of the *Plectranthus ornatus* Codd. (Lamiaceae). *Molecules*, 28(18), 6482.

- de Souza, P. M., de Sales, P. M., Simeoni, L. A., Silva, E. C., Silveira, D., & de Oliveira Magalhães, P. (2012). Inhibitory activity of  $\alpha$ -amylase and  $\alpha$ -glucosidase by plant extracts from the Brazilian cerrado. *Planta Medica*, 78(04), 393-399.
- Edwards, M. K., Blaha, M. J., & Loprinzi, P. D. (2017). Atherogenic index of plasma and triglyceride/high-density lipoprotein cholesterol ratio predict mortality risk better than individual cholesterol risk factors, among an older adult population. *Mayo Clinic Proceedings*.
- Farag, R. S., Abdel-Latif, M. S., Abd El Baky, H. H., & Tawfeek, L. S. (2020). Phytochemical screening and antioxidant activity of some medicinal plants' crude juices. *Biotechnology Reports*, 28, e00536.
- Friedewald, W. T., Levy, R. I., & 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.
- Gong, X., Li, X., Xia, Y., Xu, J., Li, Q., Zhang, C., & Li, M. (2020). Effects of phytochemicals from plant-based functional foods on hyperlipidemia and their underpinning mechanisms. *Trends in Food Science & Technology*, 103, 304-320.
- Hussain, M. A., Muhammad, G., Raza, M. A., Ashraf, A., Haseeb, M. T., Mushtaq, M., & Shafiq, Z. (2024). A comprehensive review on phytochemistry, pharmacology, preclinical, and clinical trials of *Cydonia oblonga*. *Phytochemistry Reviews*, 1-34.
- Kosmas, C. E., Rodriguez Polanco, S., Bousvarou, M. D., Papakonstantinou, E. J., Peña Genao, E., Guzman, E., & Kostara, C. E. (2023). The triglyceride/high-density lipoprotein cholesterol (TG/HDL-C) ratio as a risk marker for metabolic syndrome and cardiovascular disease. *Diagnostics*, 13(5), 929.
- La Sala, L., & Pontiroli, A. E. (2020). Prevention of diabetes and cardiovascular disease in obesity. *International journal of molecular sciences*, 21(21), 8178.
- Lambrechts, I. A., & Lall, N. (2020). *Plectranthus neochilus*. In *Underexplored Medicinal Plants from Sub-Saharan Africa* (pp. 235-240). Elsevier.
- Lawal, O., Hutchings, A., & Oyediji, O. (2010). Chemical composition of the leaf oil of *Plectranthus neochilus* Schltr. *Journal of Essential Oil Research*, 22(6), 546-547.
- Mota, L., Figueiredo, A. C., Pedro, L. G., Barroso, J. G., Miguel, M. G., Faleiro, M. L., & Ascensao, L. (2014). Volatile-Oils Composition, and Bioactivity of the Essential Oils of *Plectranthus barbatus*, *P. neochilus*, and *P. ornatus* Grown in Portugal. *Chemistry & biodiversity*, 11(5), 719-732.
- Najmi, A., Javed, S. A., Al Bratty, M., & Alhazmi, H. A. (2022). Modern approaches in the discovery and development of plant-based natural products and their analogues as potential therapeutic agents. *Molecules*, 27(2), 349.
- Pandey, B. P., Adhikari, K., Pradhan, S. P., Shin, H. J., Lee, E. K., & Jung, H. J. (2020). In-vitro antioxidant, anti-cancer, and anti-inflammatory activities of selected medicinal plants from western Nepal. *Future Journal of Pharmaceutical Sciences*, 6, 1-12.
- Pirillo, A., Casula, M., Olmastroni, E., Norata, G. D., & Catapano, A. L. (2021). Global epidemiology of dyslipidaemias. *Nature Reviews Cardiology*, 18(10), 689-700.
- Ramborger, B. P., Paz, M. E. G., Denardin, E. L. G., de Jesus Soares, J., & Roehrs, R. (2020). A review of anatomical, physiological, biological characteristics and uses of *Plectranthus neochilus*. *Ciência e Natura*, 42, e12-e12.
- Sadeghi, M., Heshmat-Gahdarijani, K., Talaei, M., Safaei, A., Sarrafzadegan, N., & Roohafza, H. (2021). The predictive value of atherogenic index of plasma in the prediction of cardiovascular events; a fifteen-year cohort study. *Advances in Medical Sciences*, 66(2), 418-423.
- Şahin, F., Güllüce, M., Daferera, D., Sökmen, A., Sökmen, M., Polissiou, M., Agar, G., & Özer, H. (2004). Biological activities of the essential oils and methanol extract of *Origanum vulgare* ssp. *vulgare* in the Eastern Anatolia region of Turkey. *Food control*, 15(7), 549-557.
- Sharma, P., Singh, V., & Baldi, A. (2024). Allo-polyherbal Approaches for Managing Metabolic Syndrome: A Narrative Review. *The Natural Products Journal*, 14(5), 1-27.
- Sultani, R., Tong, D. C., Peverelle, M., Lee, Y. S., Baradi, A., & Wilson, A. M. (2020). Elevated triglycerides to high-density lipoprotein cholesterol (TG/HDL-C) ratio predicts long-term mortality in high-risk patients. *Heart, Lung and Circulation*, 29(3), 414-421.
- Vos, T., Lim, S. S., Abbafati, C., Abbas, K. M., Abbasi, M., Abbasifard, M., ... & Bhutta, Z. A. (2020). Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The lancet*, 396(10258), 1204-1222. [https://doi.org/10.1016/S0140-6736\(20\)30925-9](https://doi.org/10.1016/S0140-6736(20)30925-9).
- Wieczorek, E., Ćwiklińska, A., & Jankowski, M. (2022). Hypertriglyceridemia, a causal risk factor for atherosclerosis, and its laboratory assessment. *Clinical Chemistry and Laboratory Medicine (CCLM)*, 60(8), 1145-1159.
- Zhao, X., An, X., Yang, C., Sun, W., Ji, H., & Lian, F. (2023). The crucial role and mechanism of insulin resistance in metabolic disease. *Frontiers in endocrinology*, 14, 1149239.