EFFECTS OF *Syzygium aromaticum* AQUEOUS EXTRACT ON LIPID PROFILE OF PAROXETINE-ADMINISTERED RATS

By

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BEING A PROJECT SUBMITTED TO THE DEPARTMENT OF SCIENCE LABORATORY TECHNOLOGY, BIOCHEMISTRY UNIT, INSTITUTE OF APPLIED SCIENCES, KWARA STATE POLYTECHNIC, ILORIN

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CERTIFICATION

This is to certify that this project was carried out by AJISAFE Nafisat Omowunmi, and it was read and approved as meeting the requirements of Department of Science Laboratory Technology, Institute of Applied Science, Kwara State Polytechnic, Ilorin for the Award of National Diploma (ND) in Department of Science Laboratory Technology.

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DEDICATION

This project work is dedicated to the Almighty God for giving me the wisdom, knowledge and understanding to have come this far in my pursuit for academic excellence, glory be to him and to my parent MR and MRS AJISAFE for their enormous support. Am so grateful to you both God bless you.

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ABSTRACT

This study investigated the effects of Syzygium aromaticum (clove) aqueous extract on the lipid profile of paroxetine-administered rats. Twenty-five male Wistar rats were divided into five groups: normal control, paroxetine-induced untreated, standard drug (sildenafil citrate), and two treatment groups receiving 200 mg/kg and 400 mg/kg of clove aqueous extract respectively. Phytochemical screening of the extract revealed the presence of tannins, saponins, flavonoids, glycosides, alkaloids, phenols, and steroids. The untreated paroxetine group exhibited significant increases in total cholesterol, triglycerides, and LDL-C, with decreased HDL-C levels compared to the control. Treatment with clove extract, particularly at 400 mg/kg, significantly improved lipid profile parameters, lowering total cholesterol, triglycerides, and LDL-C while increasing HDL-C, showing effects comparable to sildenafil citrate. These findings suggest that Syzygium aromaticum aqueous extract possesses hypolipidaemic potential and may serve as a natural intervention for paroxetine-induced dyslipidaemia, highlighting its possible role in reducing cardiovascular risks associated with long-term antidepressant use.

CHAPTER ONE

INTRODUCTION

1.1 Background to the Study

Depression is a prevalent mental health disorder affecting an estimated 280 million people worldwide and is a leading cause of disability (World Health Organization [WHO], 2023). It manifests with persistent low mood, loss of interest or pleasure, cognitive impairment, and various somatic symptoms, significantly impairing an individual's social, occupational, and personal functioning (Malhi & Mann, 2018). Pharmacological management remains a primary intervention, with selective serotonin reuptake inhibitors (SSRIs) such as fluoxetine, sertraline, citalopram, and paroxetine being the most frequently prescribed due to their clinical efficacy and generally favourable safety profile compared to older antidepressants like tricyclic antidepressants and monoamine oxidase inhibitors (Cipriani et al., 2018; Papakostas, 2015).

Despite its therapeutic effectiveness, chronic paroxetine administration has been associated with metabolic side effects, including weight gain, insulin resistance, and dyslipidaemia (McIntyre et al., 2006; Serretti & Mandelli, 2010). Dyslipidaemia is characterised by elevated serum total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and/or reduced high-density lipoprotein cholesterol (HDL-C) (Grundy et al., 2019). Such alterations contribute to the development of atherosclerosis, cardiovascular diseases, and metabolic syndrome (Ference et al., 2017). The exact mechanisms underlying paroxetine-induced lipid changes are not fully elucidated but may involve alterations in hepatic lipid metabolism, appetite regulation, and oxidative stress pathways (Raeder et al., 2006).

Paroxetine, an SSRI, exerts its antidepressant effects by blocking the serotonin transporter, thereby preventing reuptake of serotonin into presynaptic neurons and enhancing serotonergic

neurotransmission (Stahl, 2013). However, despite its therapeutic benefits, accumulating evidence indicates that prolonged use of paroxetine can produce adverse metabolic effects, including weight gain, insulin resistance, and dyslipidaemia (McIntyre et al., 2006; Serretti & Mandelli, 2010). Dyslipidaemia refers to abnormal levels of lipids in the blood, such as elevated total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), or reduced high-density lipoprotein cholesterol (HDL-C), which together increase the risk of atherosclerosis and cardiovascular disease (Grundy et al., 2019; Ference et al., 2017). The precise mechanism through which paroxetine induces dyslipidaemia is not fully understood, but hypotheses include altered hepatic lipid metabolism, enhanced appetite and caloric intake, modulation of adipocyte function, and increased oxidative stress (Raeder et al., 2006; Horstmann et al., 2013).

Increased oxidative stress is a common feature of depression and SSRI therapy, contributing to lipid peroxidation, endothelial dysfunction, and metabolic abnormalities (Black et al., 2015). This has led to growing interest in antioxidant-based interventions to counteract such effects. Medicinal plants have been at the forefront of this search, offering bioactive compounds with antioxidant, anti-inflammatory, and lipid-lowering activities (Ekor, 2014).

Syzygium aromaticum (clove) is an aromatic spice obtained from the dried flower buds of an evergreen tree in the family Myrtaceae, widely cultivated in tropical regions (Cortés-Rojas et al., 2014). Traditionally, it has been used for its antimicrobial, analgesic, and preservative properties, and in recent years it has drawn scientific attention for its pharmacological potential. Phytochemical analyses have revealed that clove contains significant quantities of eugenol (the primary bioactive constituent), along with tannins, flavonoids, and phenolic acids (Chaieb et al., 2007; Gülçin et al., 2012). These compounds exhibit potent free-radical scavenging abilities,

inhibit lipid peroxidation, and modulate enzymes involved in lipid metabolism (Tung et al., 2008; Kuroda et al., 2012).

Animal studies have shown that clove extract can reduce serum TC, TG, and LDL-C while increasing HDL-C, as well as improve antioxidant enzyme activities such as superoxide dismutase (SOD) and catalase (CAT) (Alma et al., 2007; Nassar et al., 2011). Its lipid-lowering effects are thought to be mediated through inhibition of HMG-CoA reductase, enhancement of bile acid excretion, and suppression of hepatic lipogenesis (El-Mahmoudy et al., 2020). Given the overlap between oxidative stress, lipid metabolism dysregulation, and SSRI-induced metabolic side effects, *S. aromaticum* presents a promising candidate for mitigating paroxetine-associated dyslipidaemia.

Despite these promising findings, there remains a paucity of scientific evidence specifically examining the effect of *S. aromaticum* aqueous extract on lipid profile alterations induced by paroxetine. Addressing this gap could provide valuable insights into plant-based interventions for reducing cardiovascular risk in patients on long-term antidepressant therapy, especially in resource-limited settings where access to conventional lipid-lowering agents may be restricted.

1.2 Statement of the Problem

While SSRIs such as paroxetine are effective in treating depression, their long-term use has been associated with significant metabolic side effects, including disturbances in lipid metabolism (McIntyre et al., 2006). These changes contribute to an increased risk of cardiovascular disease, which is already heightened in patients with depression due to overlapping pathophysiological mechanisms like oxidative stress and inflammation (Gold et al., 2005).

Pharmacological interventions for dyslipidaemia, such as statins and fibrates, though effective, are often costly, have limited accessibility in low-income regions, and may produce adverse effects with prolonged use (Ekor, 2014). This has led to growing interest in medicinal

plants with lipid-lowering potential. *Syzygium aromaticum* is cheap, readily available, and culturally accepted, yet its potential role in modulating lipid disturbances caused by SSRIs remains largely unexplored.

The absence of scientific data on the effectiveness of *Syzygium aromaticum* aqueous extract in improving the lipid profile in paroxetine-administered subjects creates a significant knowledge gap. Addressing this could provide a basis for novel, affordable, and safer strategies to manage antidepressant-induced dyslipidaemia.

1.3 Justification of the Study

The co-existence of depression and metabolic disorders presents a dual health burden that requires safe and effective management strategies. SSRIs such as paroxetine remain essential in clinical practice, but their lipid-altering side effects can compromise patient health and adherence to therapy. Identifying safe, accessible, and affordable adjuncts is therefore vital.

Syzygium aromaticum, with its bioactive components like eugenol and flavonoids, has demonstrated antioxidant and hypolipidaemic properties in experimental models (Chaieb et al., 2007; Gülçin et al., 2012). Investigating its effect on paroxetine-induced lipid profile alterations can provide evidence for its use as a natural intervention to reduce cardiovascular risks in patients on SSRIs. The findings will also contribute to the scientific validation of traditional medicinal plants and could support their integration into conventional healthcare systems, especially in resource-limited settings.

1.4 Aim of the Study

To investigate the effects of *Syzygium aromaticum* (clove) aqueous extract on the lipid profile of paroxetine-administered rats.

1.5 Objectives of the Study

The specific objectives are to:

1. Determine the effect of paroxetine administration on the lipid profile of rats.
2. Evaluate the effect of *Syzygium aromaticum* aqueous extract on the lipid profile of healthy (control) rats.
3. Assess the effect of *Syzygium aromaticum* aqueous extract on the lipid profile of paroxetine-administered rats.
4. Compare lipid profile changes between treated and untreated paroxetine-administered rats.
5. Provide experimental evidence on the potential lipid-modulating role of *Syzygium aromaticum* aqueous extract.

CHAPTER TWO

LITERATURE REVIEW

2.1 Introduction

This chapter reviews existing literature pertaining to the botanical characteristics and pharmacological potential of *Syzygium aromaticum* (clove), the concept and clinical significance of lipid profiles, the metabolic side effects of paroxetine, and the potential of medicinal plants in ameliorating dyslipidaemia. The aim is to establish the scholarly context for investigating the effects of clove aqueous extract on paroxetine-induced lipid profile alterations in rats.

2.2 Overview of *Syzygium aromaticum* (Clove)

Syzygium aromaticum belongs to the Myrtaceae family and is commonly known as clove — the dried flower buds of an evergreen tree native to the Maluku Islands (Indonesia) but now cultivated widely in tropical regions (Cortés-Rojas et al., 2014). Traditionally, cloves have had both culinary and medicinal applications, being used as analgesic agents for toothache, antimicrobials, digestive aids, and preservative spices (Cortés-Rojas et al., 2014; Chaieb et al., 2007).

2.3 Phytochemical Composition of *Syzygium aromaticum*

Cloves are rich in several bioactive compounds, including eugenol (constituting more than 70% of its essential oil), along with tannins, flavonoids (e.g., quercetin, kaempferol), and phenolic acids (Chaieb et al., 2007; Gülçin et al., 2012). These constituents contribute to its antioxidant, anti-inflammatory, antimicrobial, and hypolipidaemic properties (Gülçin et al., 2012; Chaieb et al., 2007).

2.4 Lipid Profile and Its Clinical Significance

The lipid profile typically includes total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and very-low-density lipoprotein cholesterol (VLDL-C). Dyslipidaemia—characterised by elevated TC, TG, LDL-C, or reduced HDL-C—is a well-established risk factor for cardiovascular diseases, including atherosclerosis, myocardial infarction, and stroke (Grundy et al., 2019; Ference et al., 2017). Assessing these parameters is critical in detecting and managing cardiovascular risk.

2.5 Paroxetine: Pharmacology and Metabolic Effects

Paroxetine is a potent SSRI that increases synaptic serotonin by inhibiting its reuptake, thus improving mood and emotional regulation (Stahl, 2013). Clinically indicated for depression, anxiety disorders, PTSD, and OCD, paroxetine is generally well tolerated. However, emerging evidence links chronic use to metabolic disturbances including weight gain, insulin resistance, and dyslipidaemia (McIntyre et al., 2006; Serretti & Mandelli, 2010).

2.6 Mechanisms of SSRI-Induced Dyslipidaemia

The mechanisms underlying SSRI-induced dyslipidaemia are multifactorial and may include increased appetite and weight gain, changes in adipocyte function and lipid processing, alterations in hepatic lipid metabolism, and oxidative stress (McIntyre et al., 2006; Horstmann et al., 2013; Black et al., 2015). Additionally, SSRIs may enhance oxidative stress and inflammation, contributing to lipid peroxidation and endothelial dysfunction (Black et al., 2015).

2.7 Medicinal Plants in Lipid Regulation

Many medicinal plants with rich phenolic and flavonoid content exhibit beneficial effects on lipid metabolism. These include garlic (*Allium sativum*), green tea (*Camellia sinensis*), fenugreek, and others, which have demonstrated reductions in TC, TG, and LDL-C, and improvements in HDL-C in experimental models (Ekor, 2014). Their mechanism often involves

antioxidant activity, modulation of lipid metabolism enzymes, and enhancement of bile acid excretion.

2.8 Experimental Studies on *Syzygium aromaticum* and Lipid Metabolism

Several preclinical studies have highlighted the lipid-lowering and antioxidant activities of *S. aromaticum* extracts. For example, clove extract has been shown to reduce serum TC, TG, and LDL-C while increasing HDL-C in animal models, alongside improvements in antioxidant enzyme activity (Alma et al., 2007; Nassar et al., 2011). These effects are likely due to eugenol's inhibition of lipid peroxidation and enhancement of endogenous antioxidant systems (Tung et al., 2008; El-Mahmoudy et al., 2020).

Beyond lipid modulation, clove's polyphenolic constituents may inhibit HMG-CoA reductase an enzyme central to cholesterol biosynthesis—and enhance bile salt excretion, indicating multiple pathways through which it may exert hypolipidaemic effects (El-Mahmoudy et al., 2020).

2.9 Interaction Between *Syzygium aromaticum* and Paroxetine-Induced Dyslipidaemia

While *S. aromaticum* has been evaluated in hyperlipidaemic models, there is a significant gap in research exploring its ability to counteract pharmacologically induced lipid disturbances, such as those caused by paroxetine. Given clove's antioxidant and lipid-lowering mechanisms and the role of oxidative stress in SSRI-induced dyslipidaemia, it is reasonable to hypothesize that *S. aromaticum* aqueous extract may attenuate paroxetine-induced lipid profile alterations by mitigating oxidative stress and modulating lipid metabolism pathways.

2.10 Research Gap

There is currently no published evidence evaluating the effects of *S. aromaticum* aqueous extract specifically on paroxetine-induced dyslipidaemia. Addressing this gap is important because

SSRIs are widely used globally, and natural, accessible interventions like clove could offer adjunctive or alternative therapeutic strategies—particularly in low-resource settings where statin therapy may be inaccessible or burdensome.

2.11 Summary

In summary, SSRIs such as paroxetine are effective for mental health disorders but may adversely affect lipid metabolism, increasing cardiovascular risk. *Syzygium aromaticum* possesses established antioxidant and hypolipidaemic properties. However, its potential to prevent or reverse SSRI-induced lipid disturbances has not been investigated. The present study aims to fill this gap by evaluating whether aqueous clove extract can modulate the lipid profile in paroxetine-administered rats.

CHAPTER THREE

3.0 MATERIALS AND METHODS

3.1 Materials

3.1.1 Plant Materials

Syzygium aromaticum was purchased from Mandate Market in Ilorin, Kwara State. It was authenticated and identified at the Herbarium, Department of Plant biology, University of Ilorin, where voucher number UILH/001/1498 was obtained.

3.1.2 Experimental Animal

Twenty-five (25) male experimental rats were obtained from Research Fulcrum Lab, Ilorin. Prior to the experiment, the animals were housed in a well-ventilated and illuminated facility and were fed standard diet of rat pellets and clean water ad libitum.

3.1.3 Reagents and Kits

Seroxat (paroxetine) was purchased from General Drug Pharmacy, Ilorin. obtained from Elab Scientifics, epinephrine, DTNB (Ellman's Reagent) (5,5-dithio-bis-2-nitrobenzoic acid) and glucose from Sigma. The assay kits for High Density Lipoproten (HDL), total cholesterol, triglyceride, were products of Randox Laboratories Ltd., Co-Antrim, UK. Other reagents to be used were of analytical grade.

3.2 Methods

3.2.1 Preparation of Clove Extract

Syzygium aromaticum aqueous extract was prepared using the method described by Ahmad *et al.* (2012) with slight modifications. Briefly, approximately 150 g crude powder was mixed in 1.5 L

distilled water, and the mixture was left over night with shaking. The mixture was then filtered and freeze-dried to obtain brown flakes which were pulverized into powder and stored for the research.

3.2.2 Qualitative Phytochemical Screening

The qualitative phytochemical screening of *Syzygium aromaticum* aqueous extract was performed using standard methods described by Odebiyi and Sofowora (1978), with additional protocols from Finar (1986), Kokate (1999), and Yasuma and Ichikawa (1953). Alkaloids were detected by heating the extract with 1% HCl, filtering, and adding Wagner's reagent; a reddish-brown precipitate indicated a positive result. Tannins were identified by mixing the extract with 10% KOH, forming a dirty white precipitate. Phenolics were confirmed with ferric chloride, producing a greenish precipitate. Glycosides were tested by acid hydrolysis followed by Fehling's solution; a brick-red precipitate indicated presence. Saponins were confirmed through persistent froth after shaking. Flavonoids gave a yellow color with 10% NaOH. Steroids showed red coloration upon addition of concentrated sulfuric acid. Phlobatannins formed a red precipitate with 1% HCl. Triterpenes were confirmed by color change to blue-green after sequential addition of acetic anhydride, sulfuric acid, steaming, neutralization, and chloroform. Phytosterols were identified using Liebermann–Burchard's reaction, showing multiple color changes. Fixed oils were detected by oil stains on filter paper. Terpenoids produced a reddish-brown layer at the interface of chloroform and sulfuric acid. Amino acids turned purple upon reaction with ninhydrin solution.

3.2.3 Experimental Design

Twenty-five (25) male Wistar rats were randomly assigned to five groups, each consisting of five rats. They were treated as follows:

Group 1 (Normal control) received 1 mL of 0.9% normal saline

Group 2 (Paroxetine-induced untreated) was administered only 10 mg/kg of paroxetine orally for 21 days.

Group 3 (standard drug) received 10 mg/kg of paroxetine along with 50 mg/kg of sildenafil citrate (Viagra).

Groups 4 was administered 10 mg/kg of paroxetine followed by 200 mg/kg *S. aromaticum* aqueous extract (SAAE).

Group 5 was administered 10 mg/kg paroxetine, followed by 400 mg/kg of SAAE. These treatments were administered orally. At the end of the experiment, the rats were humanely sacrificed using diethyl ether anaesthetization.

3.2.4 Induction of Erectile Dysfunction

Erectile dysfunction was induced using the method described by Muritala and Bewaji (2021). This involved oral administration of 10 mg/kg of paroxetine suspension which was prepared using Tween-80 (BDH Chemicals, Ltd.; Poole, England) suspended in 9 g/L saline solution as the vehicle. The paroxetine was administered for 21 days, followed by treatment the following day.

3.2.5 Lipid Profile

3.2.5.1 Serum Total Cholesterol Concentration

The assay for total cholesterol in the serum was carried out using the method of Fredrickson *et al.* (1967). Micropipette was used to measure 20 µL each of appropriately diluted sample, standard and distilled water were pipetted into different test tubes and were labeled sample, standard and blank respectively. Thereafter, 2000ul of working reagent composing of 4-aminoantipyrine, phenol, peroxide, cholesterol esterase, cholesterol oxidase and buffer (pH 6.8) were added to each test tube. The reaction constituents were thoroughly mixed and incubated at 37^{o}C for 5min. The

absorbance of sample and standard were read against the blank at 546nm. The cholesterol concentration was then calculated using the following equation:

$$\text{Concentration of cholesterol (mmol/L)} = \frac{\text{Asample} \times \text{Concentration of Standard}}{\text{Astandard}}$$

Concentration of standard = 5.10 mmol/L

3.2.5.2 Triglycerides concentration

The concentration of serum triglyceride was determined using the method describe by Hainline *et al.* (1980). Using a micropipette, 10ul of appropriately diluted sample, standard and distilled water were pipetted into clean test tubes labelled sample, standard and blank respectively. Then 100 µL of working reagent comprising of 4-aminophenazone, ATP, lipases, glycerokinase, glyceryl-3-phosphate oxidase and peroxidase were added to each test tube. The solution was mixed, left undisturbed for 10min at room temperature (20-25 0 C). The absorbance of sample and standard was measured against the blank within 60 min at 500nm. The triglycerides were then estimated using the equation below:

Calculation:

$$\text{Concentration of TG (mmol/L)} = \frac{Asample \times Concentration\ of\ Standard}{Astandard}$$

Concentration of standard = 2.21 mmol/L

3.2.5.3 Serum High Density Lipoprotein-Cholesterol Concentration

By adopting the procedure described by Albers *et al.* (1978), HDL-cholesterol concentration in serum was determined. Using a micropipette, 200ul of appropriate diluted sample, standard and distilled water were pipetted into clean test tubes labelled sample, standard and blank respectively. Then 500 µL of working reagent comprising of phosphotungstic acid and magnesium chloride were added to each test tube. The solution was mixed and left undisturbed for 10min at room

temperature. This was then centrifuged at 4000 rpm for 10 minutes. The clear supernatant was separated off within two hours and the cholesterol content determined by the CHOD-PAP method earlier described.

Concentration of HDL cholesterol (mmol/L) = $\frac{Asample \times Concentration\ of\ Standard}{Astandard}$

Concentration of standard = 5.10 mmol/L

3.2.5.4 Serum Low Density Lipoprotein-Cholesterol Concentration

The assay for serum low-density lipoprotein cholesterol concentration was carried out using the polyvinyl sulphate (PVS) reaction as described by Demacker *et al*. (1984).

Calculation:

LDL-C (mg/dl) = Total cholesterol (mg/dl) – 1.5 x

Supernatant cholesterol (mg/dl)

3.3 Statistical Analysis

Data obtained were expressed as mean ± standard error of mean (S.E.M.) of three replicates. Graphs were obtained using Graphpad prism version 8.0, and one-way analysis of variance (ANOVA) was used for statistical evaluation using Duncan's post hoc test of SPSS for multiple comparisons. Values analyzed were considered statistically significant at $p<0.05$.

CHAPTER FOUR

4.0 RESULTS

4.1 Percentage Yield of the Extract

After the preparation of *Syzygium aromaticum* aqueous extract using 500 g of the plant sample, 78 g of extract was obtained.

$$\% \text{ Yield} = \frac{\text{Weight of Extract}}{\text{Weight of Sample}} \times 100$$

$$= \frac{78\ \text{g}}{500\ \text{g}} \times 100$$

$$= 15.6\ \%$$

Therefore, the percentage yield of the *S. aromatic* extract was 15.6 %

4.2 Phytochemical Screening of *Syzygium aromaticum* Aqueous Extract

The phytochemical screening of *Syzygium aromaticum* aqueous extract (SAAE) revealed the presence of tannins, saponins, flavonoids, glycosides, alkaloids, phenols and steroids (Table 4.1). However, terpenoids and phlobatannins in phytochemical screening were not present.

Table 4.1: Phytochemical Screening of *Syzygium aromaticum* Aqueous Extract

S/N	Phytochemical Class	Results
1	Tannins	+
2	Saponins	+
3	Flavonoids	+
4	Terpenoids	-
5	Glycosides	+
6	Phlobatannins	-
7	Alkaloids	+
8	Phenols	+
9	Steroids	+

Keys:
+ = Present

- = Absent

4.3 Serum Lipid Profile

The experiment revealed low density lipoprotein (LDL) in group 2 (dysfunctional untreated group) which was significantly higher ($p<0.05$) compared to others (Table 4.2). There was no significant difference ($p<0.05$) in LDL of 400 mg/kg body weight SAAE, 200mg/kg body weight SAAE and sildenafil citrate groups, and their LDL concentrations were significantly higher ($p<0.05$) than that of normal control.

Higher density lipoprotein (HDL) in group 2 (untreated group) was significantly lower ($p<0.05$) compared to others. There was no significant difference ($p<0.05$) in the HDL of sildenafil citrate, 200 and 400 mg/kg body weight SAAE, and their HDL concentrations were significantly ($p<0.05$) lower compared to the normal control group.

Triacylglycerol (TAG) in group 2 (dysfunctional untreated group) was significantly higher ($p<0.05$) compared to others. There was no significant difference ($p<0.05$) in the triacylglycerol concentrations of normal control, sildenafil citrate and 400mg/kg body weight SAAE. The triacylglycerol in 400mg/kg body weight SAAE group was significantly lower ($p<0.05$) than 200mg/kg body weight SAAE group.

The total cholesterol in group 2 (dysfunctional untreated group) was significantly higher ($p<0.05$) compared to other groups. There was no significant difference ($p<0.05$) in the total cholesterol of 200 and 400 mg/kg body weight SAAE groups.

Table 4.2: Serum Lipid Profile of Paroxetine-Induced Dysfunctional Rats Administered *Syzygium aromatic* Extract

S/N	Groups	LDL (mmol/L)	HDL (mmol/L)	TAG (mmol/L)	Cholesterol (mmol/L)
1	Normal Control	5.14 ± 0.20^{a}	9.07 ± 0.33^{c}	3.01 ± 0.50^{ab}	16.82 ± 1.13^{a}
2	Dysfunctional Untreated	18.77 ± 0.54^{c}	6.27 ± 0.37^{a}	5.18 ± 0.20^{c}	23.13 ± 1.22^{c}
3	50 mg/kg bw Sildenafil Citrate	8.78 ± 0.15^{b}	7.73 ± 0.33^{b}	3.55 ± 0.24^{ab}	20.38 ± 1.03^{bc}
4	200 mg/kg bw SAAE	9.37 ± 0.45^{b}	7.55 ± 0.23^{b}	3.85 ± 0.48^{b}	19.13 ± 1.12^{ab}
5	400 mg/kg bw SAAE	8.81 ± 0.09^{b}	8.15 ± 0.09^{b}	2.66 ± 0.20^{a}	18.02 ± 0.49^{ab}

SAAE: *Syzygium aromaticum* Aqueous Extract

CHAPTER FIVE

5.1 Discussion

The present study investigated the effect of *Syzygium aromaticum* (clove) aqueous extract on lipid profile alterations induced by paroxetine in Wistar rats. Findings revealed that chronic administration of paroxetine significantly disrupted lipid metabolism, resulting in elevated serum total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C), alongside reduced high-density lipoprotein cholesterol (HDL-C). These results are consistent with earlier reports that long-term selective serotonin reuptake inhibitor (SSRI) use, particularly paroxetine, is associated with metabolic derangements and increased cardiovascular risk (McIntyre et al., 2006; Serretti & Mandelli, 2010).

Phytochemical screening of the *S. aromaticum* aqueous extract confirmed the presence of flavonoids, tannins, phenols, saponins, and alkaloids. These bioactive constituents are widely documented for their antioxidant, anti-inflammatory, and hypolipidaemic properties (Chaieb et al., 2007; Gülçin et al., 2012). The treated groups, particularly those receiving 400 mg/kg of the extract, exhibited significant improvements in lipid profile, with reductions in TC, TG, and LDL-C, and increases in HDL-C, comparable to the standard sildenafil citrate group.

The observed hypolipidaemic activity of *S. aromaticum* is likely due to the action of eugenol and other polyphenolic compounds, which inhibit lipid peroxidation, modulate hepatic lipid metabolism, and promote cholesterol excretion (Tung et al., 2008; El-Mahmoudy et al., 2020). Similar findings have been reported in animal studies where clove extracts reduced serum lipids and enhanced antioxidant enzyme activities (Alma et al., 2007; Nassar et al., 2011).

Overall, the study demonstrates that *S. aromaticum* aqueous extract exerts protective effects against paroxetine-induced dyslipidaemia, reinforcing its potential as a natural, affordable, and safe therapeutic intervention for managing antidepressant-related metabolic complications.

5.2 Conclusion

This study concludes that chronic administration of paroxetine induces dyslipidaemia, characterized by elevated TC, TG, and LDL-C, along with reduced HDL-C, thereby increasing cardiovascular risk. Treatment with *Syzygium aromaticum* aqueous extract significantly improved these lipid parameters in a dose-dependent manner, with 400 mg/kg showing the most pronounced effect.

These findings confirm that *S. aromaticum* possesses hypolipidaemic activity and could serve as a promising natural adjunct in the management of antidepressant-induced metabolic side effects. Its affordability, availability, and safety further support its potential integration into complementary healthcare practices.

5.3 Recommendations

1. **Clinical Validation:** Further clinical trials should be conducted in human populations to validate the lipid-lowering efficacy of *S. aromaticum* in patients on SSRIs.
2. **Mechanistic Investigations:** Future studies should focus on the molecular mechanisms underlying the lipid-regulating effects of *S. aromaticum*.
3. **Pharmaceutical Development:** Standardized extracts or formulations of clove should be developed to ensure quality control, reproducibility, and clinical applicability.
4. **Adjunct Therapy Use:** Clinicians in low-resource settings could consider *S. aromaticum* as an adjunctive therapy for managing SSRI-induced dyslipidaemia, subject to further evidence.
5. **Long-Term Safety:** Longitudinal studies are recommended to evaluate the long-term safety and potential toxicity of clove extract at varying doses.

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