Comparative Assessment of Three Common Pepper Species on Plasma and Fecal Lipid Profile of High-fat Diet Fed Wistar Rats

ABSTRACT

The consumption of high-fat diets has been linked to various health conditions, including dyslipidaemia. The aim of the present study was to compare the impact of three pepper types on the plasma lipid profile [total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL) and low-density lipoprotein (LDL)] of high-fat diet fed wistar rats. The study involved forty-five wistar rats separated into nine groups of five rats each. Group 1 served as control while groups 2 to 9 were fed with high-fat diet throughout the period of the experiment. Group 2 received only high-fat diet. Groups 3 and 4 received in addition, 50mg/kg and 75mg/kg of red pepper respectively, Groups 5 and 6 received in addition, 50mg/kg and 75mg/kg of green pepper respectively, Groups 7 and 8 received in addition 50mg/kg and 75mg/kg of black pepper respectively. Group 9 received in addition 10mg/kg of simvastatin. The results showed that at a dose of 50mg/kg, both red and black pepper caused significant reduction in all the plasma lipid profile parameters while green pepper only caused reduction in TG and HDL. Comparatively, at 50mg/kg there was no significant difference in the lipid lowering effect of red and black pepper but rats fed with green pepper had significantly higher levels of LDL. At 75mg/kg, both green and black pepper caused significant reduction in all the lipid profile parameters. Comparatively at 75mg/kg, TC, TG and HDL were significantly higher in green and black pepper compared to red pepper. There was no significant difference in the LDL levels of red and black pepper but LDL was higher in the red pepper group than the green pepper. The present study suggests that all three pepper types generally have plasma lipid lowering effects, with black pepper being more potent at both the lower and higher doses. At high doses, red pepper has a higher lowering effect on TC, TG and HDL while green pepper has higher lowering effect on LDL. No significant changes in faecal lipid profile parameters were observed upon administration of 50mg/kg of the pepper varieties but green and black pepper increased faecal loss of total cholesterol compared to red pepper. Conclusively, consumption of pepper together with high-fat diet would reduce the plasma concentrations of cholesterol. Green and black peppers are more potent cholesterol lowering agents at high doses. However, the target cholesterol depends on the type of pepper.These findings show that pepper has therapeutic potential as a natural alternative or addition to current lipid-lowering drugs. Further research is necessary to completely understand the involved mechanisms and improve dosing regimens.

Key words: Pepper species, plasma and faecal lipid profile, High-fat diet.

Comment [الحاسب1]: The title could be slightly refined for clarity and conciseness. For instance, specifying the pepper species under investigation could enhance precision. Additionally, "High-fat Diet Fed Wistar Rats" could be reworded for better readability, such as "Wistar Rats Fed a High-fat Diet."

Comment [الحاسب2]: The abstract presents a well-structured and insightful study on the lipid-lowering effects of three common pepper species in high-fat diet-fed Wistar rats. The findings suggest that different pepper types exert varying degrees of influence on plasma lipid profiles, with black pepper demonstrating the most consistent effect across doses. The conclusion effectively highlights the potential therapeutic role of peppers as natural lipid-lowering agents. However, the abstract could be improved by clarifying the underlying mechanisms and emphasizing the statistical significance of the results to strengthen the validity of the findings.

Comment [الحاسب3]: The abstract lacks clarity in some comparisons. For instance, phrases like "comparatively at 75 mg/kg, TC, TG, and HDL were significantly higher in green and black pepper compared to red pepper" could be rewritten for precision.
The discussion on fecal lipid profile results is underdeveloped in the abstract, making the findings appear incomplete.
The conclusion should explicitly connect findings to potential human applications.

Introduction

Comment [الحاسب4]: The introduction provides a strong foundation by highlighting the importance of healthy dietary choices and the risks associated with excessive fat consumption. It effectively establishes the relevance of pepper as a functional food with diverse health benefits, including its lipid-lowering potential. However, it could be improved by focusing more on the specific gap in knowledge that the study aims to address and providing a clearer link between the bioactive compounds in different pepper species and their potential effects on lipid metabolism. Additionally, refining sentence structure and ensuring consistent citation formatting would enhance readability and scientific clarity.

Healthy living encompasses healthy dietary choices and lifestyle, adequate sleep and physical activity. Indiscriminate food intake and poor lifestyle which includes consumption of excessive dietary fat is associated with increased risk of dyslipidemia(1,2,3,4) and other related metabolic disorders. Pepper is a common food spice with excellent nutritional value and many proven beneficial effects including antioxidant potential, anti-inflammatory, antimicrobial, improved intestinal transit and other beneficial effects in gastrointestinal health (5,6,7,8). The commonly consumed species of pepperinclude green and red pepper (*Capiscum annuum*) and black pepper (*Piper nigrum*). Bioactive compounds from pepper species are known for their analgesic, anti-obesity, cardio-protective, pharmacological, neurological and nutritive properties. These substances display a significant antibiotic activity and the capacity to reduce serum cholesterol levels when consumed in small quantities as part of a normal diet (9,10).

Red pepper have been used as traditional food pigments, spices and medicines since ancient time (11,12); Green pepper *(Capiscum annum)* is produced with unripe pepper and have been shown to contain several bioactive compounds including phenolic compound (13) and the major extract of black pepper (piperine) have been reported to stimulate the pancreatic digestive enzymes, enhanced the digestive capacity and significantly reduced the transit time of food (8,14).

The several platforms used to educate citizens on the need to reduce the consumption of high-fat diets have not yielded the needed results. This knowledge gap prevents a comprehensive understanding of the potential benefits of the different pepper species in mitigating high-fat diet-induced dyslipidemia and limits the development of evidence-based interventions for individuals at risk.This study aimed to compare the effects of three pepper species (green, red and black) on plasma and fecal lipid profile of high-fat diet fed wistar rats.

Comment [الحاسب5]: Some sentences are overly complex or awkwardly phrased, reducing readability. Example:
"The several platforms used to educate citizens on the need to reduce the consumption of high-fat diets have not yielded the needed results."

Materials and Methods

The present study was carried out at animal house of the department of Human Physiology, faculty of Basic Medical Sciences, Rivers State University in the year 2024. Ethical approval was obtained from the Ethics Committee of faculty of Basic Medical Sciences, Rivers State University with approval number; RSU/FBMS/REC/24/063.

The present study involved a total of forty-five male wistar rats weighing 200-250g. The rats were kept in suitable conditions, including proper ventilation and temperature levels. They were housed in clean disinfected wooden cages with saw dust as beddings. The rats were acclimatized for one week and were fed *ad libitum*with normal animal chow and clean water. The animals were weighed at the commencement of the experiment and the initial weight of each rat was recorded.Simvastatin was purchased from Alpha Pharmacy and Stores, a registered pharmaceutical company in Port Harcourt, Rivers State. The three pepper species; red, green and black were purchased from Mile 3 market and properly identified. The butter was used to prepare high-fat diet was also purchased from Mile 3 market, Port Harcourt, Rivers State.

The Wistar rats were separated into nine groups of five rats each. Group 1 served as control and received distilled water. Groups 2 to 9 were fed with high-fat diet consisting of butter throughout the period of the experiment. Group 2 received only high-fat diet. Groups 3 and 4 received in addition, 50mg/kg and 75mg/kg of red pepper respectively, Groups 5 and 6 received in addition, 50mg/kg and 75mg/kg of green pepper respectively, Groups 7 and 8 received in addition 50mg/kg and 75mg/kg of black pepper respectively. Group 9 received in addition 10mg/kg of simvastatin (15).

Comment [الحاسب6]: The **Materials and Methods** section is well-detailed and systematically describes the experimental design, ethical considerations, animal housing conditions, dietary interventions, and analytical methods. The use of control and experimental groups is appropriate, and the statistical analysis is clearly outlined. However, there are some areas that could be improved for clarity and scientific rigor. The method of pepper preparation (e.g., extraction, drying, or grinding) should be explicitly stated to ensure reproducibility. Additionally, the description of sample collection and analysis could be more structured to avoid redundancy, particularly in the blood sample collection and lipid profile assessment. Overall, the methodology is robust but could benefit from minor refinements in organization and specificity.

The pepper species were administered in their respective daily oral dosages and the experiment lasted for 28days. Thereafter, the animals were sacrificed under anesthesia and blood samples collected from each animal to determine plasma lipid profile [total cholesterol (TC), triglyceride (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL)] and fecal lipid profile [Fecal total cholesterol (FTC), fecal triglyceride (FTG), fecal high density lipoprotein (FHDL) and fecal low density lipoprotein (FLDL) using standard laboratory techniques.The colon was also dissected to collect fecal pellets for fecal lipid profile.Thereafter the animals were sacrificed under anesthesia and blood samples collected for determination of lipid profile.

Comment [الحاسب7]: The phrase "Thereafter the animals were sacrificed under anesthesia" is redundant. The term "under anesthesia" is sufficient.

Statistical package for social sciences (SPSS) version 22.0 was used for data analysis. Results were presented in tables and graphs. Continuous variables were expressed as mean ± standard error of mean (SEM). Statistical difference was determined using analysis of variance (ANOVA) and significant differences noted at $p < 0.05$.

Results and Discussion

Comment [الحاسب8]: The study demonstrates that different pepper varieties modulate the plasma and fecal lipid profiles in high-fat diet-fed Wistar rats, with black and green peppers showing a more pronounced reduction in plasma LDL and TG levels compared to red pepper. The findings suggest that these peppers may exhibit lipid-lowering effects comparable to simvastatin, particularly at higher doses. However, the variations in responses among pepper types warrant further mechanistic studies to elucidate their specific bioactive compounds and lipid metabolism pathways.

Table1: Effect of different varieties of pepper on the Plasma lipid profile of high-fat diet fed wistar rats.

Group	PTC (mmol/l)	PTG (mmol/l)	PHDL (mmol/l)	PLDL (mmol/l)

Control	4.52 ± 0.38	2.42 ± 0.28	2.14 ± 0.14	3.48 ± 0.42
High fat diet (HFD)	5.20 ± 0.12	2.81 ± 0.12	2.70 ± 0.13[a]	3.77 ± 0.16
HFD + 50mg/kg of **Red** pepper	3.66 ± 0.20[b]	1.95 ± 0.07[b]	2.09 ± 0.09[b]	2.46 ± 0.11[ab]
HFD + 75mg/kg of **Red** pepper	4.90 ± 0.09[c]	2.54 ± 0.18[c]	2.59 ± 0.11[ac]	3.47 ± 0.07
HFD + 50mg/kg of **Green** pepper	4.50 ± 0.43	2.02 ± 0.17[b]	2.11 ± 0.12[b]	3.31 ± 0.39
HFD + 75mg/kg of **Green** pepper	3.58 ± 0.14[ab]	1.70 ± 0.05[ab]	1.90 ± 0.06[b]	2.45 ± 0.18[ab]
HFD + 50mg/kg of **Black** pepper	3.82 ± 0.39[b]	1.68 ± 0.15[ab]	1.81 ± 0.12[b]	2.80 ± 0.38[b]
HFD + 75mg/kg of **Black** pepper	3.98 ± 0.33[b]	1.68 ± 0.16[ab]	1.95 ± 0.19[b]	2.80 ± 0.23[b]
HFD + 10mg/kg of Simvastatin	3.88 ± 0.41[b]	1.75 ± 0.18[ab]	1.99 ± 0.20[b]	2.68 ± 0.32[b]

[a]Significantly different compared to control group
[b] Significantly different compared to High fat diet (HFD) only group
[c]Significantly different compared to HFD + 10mg/kg of Simvastatin group
P = Plasma

Table 2: Effect of different varieties of pepper on the fecal lipid profile of high-fat diet fed wistar rats.

Group	FTC (mmol/l)	FTG (mmol/l)	FHDL (mmol/l)	FLDL (mmol/l)
Control	2.26 ± 0.09	2.42 ± 0.28	1.47 ± 0.08	1.54 ± 0.15
High fat diet (HFD)	2.55 ± 0.13	2.81 ± 0.12	1.57 ± 0.07	1.63 ± 0.19
HFD + 50mg/kg of **Red** pepper	**2.55 ± 0.27**	**1.95 ± 0.07**	**1.39 ± 0.13**	**1.75 ± 0.16**

HFD + 75mg/kg of **Red** pepper	**2.13 ± 0.01[c]**	**2.54 ± 0.18**	**1.17 ± 0.02[ab]**	**1.54 ± 0.02[c]**
HFD + 50mg/kg of **Green** pepper	**2.44 ± 0.16**	**2.02 ± 0.17**	**1.23 ± 0.11[b]**	**1.77 ± 0.13**
HFD + 75mg/kg of **Green** pepper	**2.93 ± 0.14[a]**	**1.70 ± 0.05[c]**	**1.52 ± 0.15**	**2.10 ± 0.23[a]**
HFD + 50mg/kg of **Black** pepper	**2.74 ± 0.07[a]**	**1.68 ± 0.15**	**1.51 ± 0.08**	**1.86 ± 0.09**
HFD + 75mg/kg of **Black** pepper	**2.84 ± 0.10[a]**	**1.68 ± 0.16**	**1.48 ± 0.12**	**1.80 ± 0.11**
HFD + 10mg/kg of Simvastatin	**2.82 ± 0.30[a]**	**1.14 ± 0.03[ab]**	**1.31 ± 0.05**	**2.14 ± 0.29[a]**

[a]Significantly different compared to control group
[b] Significantly different compared to High fat diet (HFD) only group
[c]Significantly different compared to HFD + 10mg/kg of Simvastatin group
F = Fecal

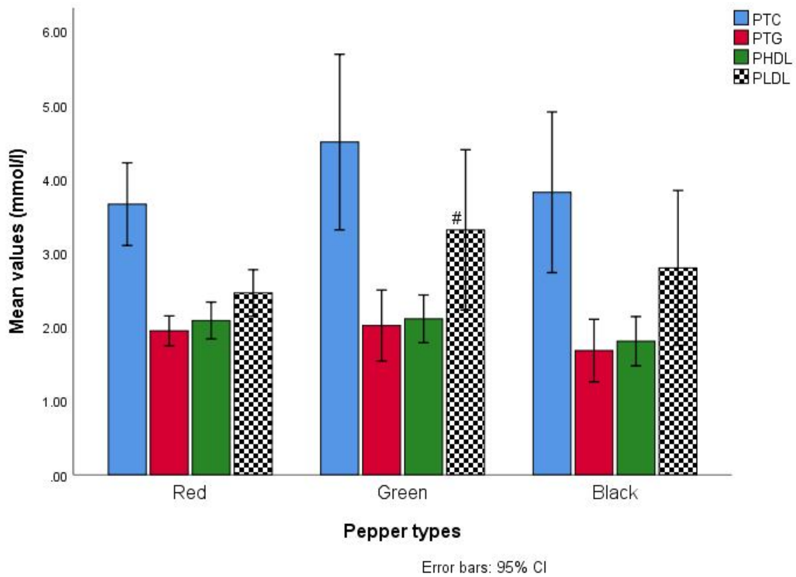

Figure 1: Comparison of the Plasma lipid profile parameters following exposure to 50mg/kg of red, green and black pepper respectively.

Plasma LDL of Green pepper was significantly higher than that of Red pepper ($p < 0.05$; Post Hoc test).There were no significant differences in the Plasma TC, TG and HDL of the animals exposed to 50mg/kg of Red, Green and Black pepper respectively.

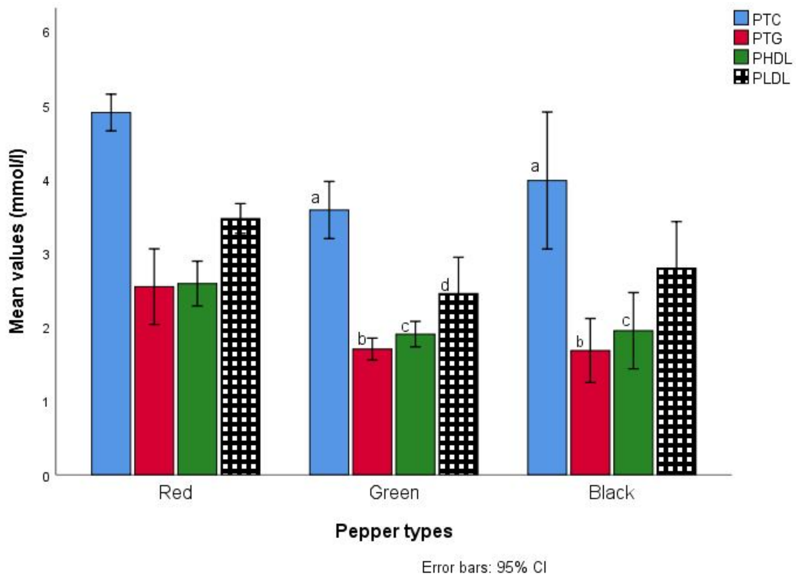

Figure 2: Comparison of the Plasma lipid profile parameters following exposure to 75mg/kg of red, green and black pepper respectively.

a = Plasma TC of Red pepper was significantly higher than that of Green and Black pepper ($p < 0.05$; Post Hoc test).

b = Plasma TG of Red pepper was significantly higher compared to Green and Black pepper respectively.

c = Plasma HDL of Red pepper was significantly higher compared to Green and Black pepper respectively.

d = Plasma LDL of Red pepper was significantly higher compared to Green pepper.

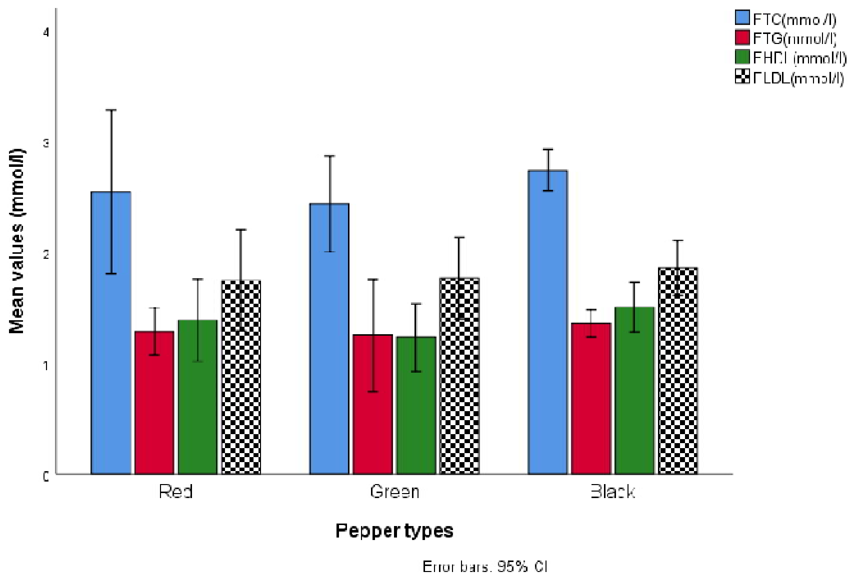

Figure 3: Comparison of the faecal lipid profile parameters following exposure to 50mg/kg of red, green and black pepper respectively.

No significant difference in the faecal lipid parameters of the different pepper types.

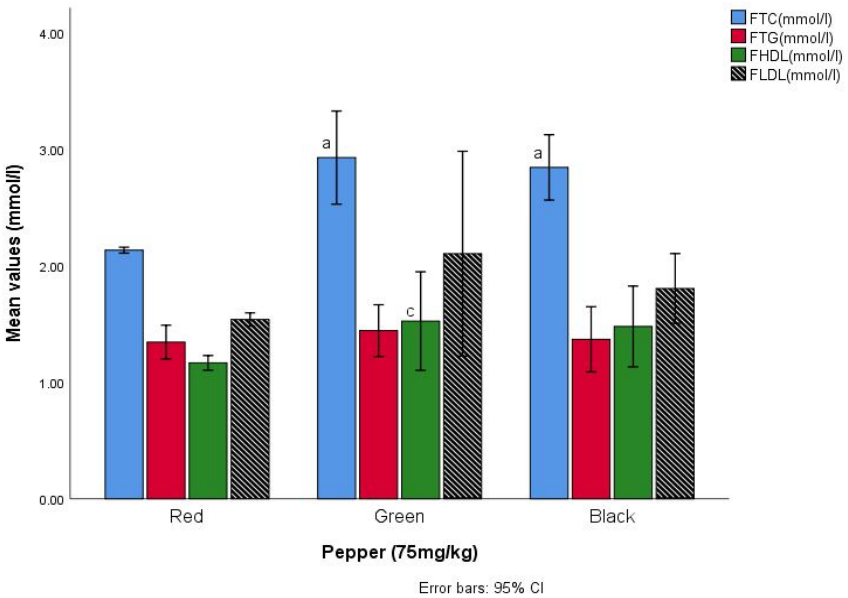

Figure 4: Comparison of the fecal lipid profile parameters following exposure to 75mg/kg of red, green and black pepper respectively.

a = Faecal TC of Red pepper was significantly higher than that of Green and Black pepper (*$p < 0.05$*; Post Hoc test).

c = Faecal HDL of Red pepper was significantly higher compared to Green and Black pepper respectively.

This study investigated and compared the effects ofthree common pepper varieties on the plasma and faecal lipid profile of rats fed with high-fat diet (HFD). The results showed that consumption of HFD caused non-significant increase in the plasma concentrations of total cholesterol (PTC), triglycerides (PTG) and low density lipoprotein (PLDL) but only significantly increased plasma high density lipoprotein (PHDL) compared to control. Although, some studies have associated the consumption of high-fat diet with hypercholesterolemia (16,17), a previous studyinvolving the administration of full-fat dairy food showed no significant changes in fasting lipid profile (18). This implies that thecommercially sold margarine used in the present study significantly

Comment [الحاسب9]: This study provides valuable insights into the lipid-lowering effects of different pepper varieties in high-fat diet-fed rats. The findings suggest that red pepper at lower doses effectively reduces PLDL while increasing PHDL at higher doses, whereas green and black pepper enhance cholesterol excretion through feces. However, the study lacks mechanistic depth regarding the bioactive compounds' precise roles in lipid metabolism and gut microbiota interactions.

raised the concentration of PHDL which is often considered to be the ‘‘good cholesterol’’. PHDL is known to play a key role in the efflux of cholesterol and other lipids from peripheral tissues and transport them either to the liver for disposal or to steroidogenic tissues for hormone synthesis (19), thus reducing the risk of cardiovascular disease.

Administration of 50mg/kg of red pepper caused significant reduction in all lipid profile parameters (PTC, PTG, PLDL and PHDL) compared to HFD-only group and no significant effect on the faecal lipid profile. The reduction is attributed to bioactive compounds like capsaicin, which influences lipid metabolism (20,21).This lipid-lowering potential of red pepper is possible because it stimulates bile formation and secretion of bile acids which is an essential route in eliminating cholesterol from the body (22). 75mg/kg of red pepper did not have any significant effect on the PTC, PTG and PLDL but significantly reduced faecal loss of HDL. 50mg/kg of green pepper did not have any significant effect on PTC and PLDL but significantly caused a reduction in PTG and PHDL. However, 75mg/kg of green pepper caused significant reduction in the plasma levels of lipid profile in a similar pattern as simvastatin, a known lipid lowering agent. 50mg/kg and 75mg/kg of black pepper respectively caused significant reduction in all the lipid profile parameters estimated. The possible mechanism of action is that piperine (the active compound in black pepper) reduces cholesterol uptake by internalizing the cholesterol transporter proteins (23).

Comparatively, there were no significant differences in the levels of PTC, PTG and PHDL following oral administration of 50mg/kg of red, green and black pepper respectively. Our study suggests that consumption of 50mg/kg of red pepper is more potent in lowering the PLDL than green pepper (Fig. 1). At a higher concentration (75mg/kg), both green and black pepper significantly lowered the concentrations of PTC, PTG and PHDL compared to red pepper. Red pepper therefore caused a significant rise in the PHDL compared to the other pepper varieties. Again, higher concentrations of red pepper caused significant elevation of PLDLlevels compared to green pepper but not significantly different from black pepper. Of the three pepper species, green pepper probably would be more beneficial in reducing the PLDL levels and also possibly reduces the risk of dyslipidaemia and other cardiovascular risks (24,25). For faecal parameters, the concentrations of FTC, FTG, FHDL and FLDL in response to administration of 50mg/kg of red, green and black pepper respectively werenot significantly different. The FTC level following oral intake of 75mg/kg of red pepper was significantly lower than that of green and black pepper.Our study therefore confirms that both green and black pepper increases faecal excretion of total cholesterol than red pepper (8). The findings suggest that at high doses green and black pepper has more potent cholesterol clearing effect than the red variety. This effect is comparable with lipid lowering potential of other natural products (25,26,27).There were no significant changes in the FTG and FLDL in response to consumption of any of the three pepper species, although FHDL was significantly higher in the green pepper group compared to the red and black pepper groups.

Consumption of pepper hasbeen associated with alterations in gut microbiota composition, which can affect lipid metabolism and absorption. Piperine, found in black pepper, has been shown to alter gut microbiota composition, potentially influencing triglyceride metabolism (28).Polyphenols and flavonoids, abundant in green pepper (Anaya-Esparza et al., 2021), have been reported to impact gut microbiota composition which in turn modulate lipid metabolism pathways and improve lipid regulatory bioavailability (29,30,31). Furthermore, antioxidant properties of green pepper might play a rolein its lipid lowering potential (32,33,34). This finding highlights the potential of green pepper as an alternative or adjunct therapy for managing triglyceride levels in dyslipidaemia. These findings underscore the potential therapeutic utility of pepper as a natural alternative or adjunct to conventional lipid-lowering medications, although further research is needed to elucidate underlying mechanisms and optimize dosing regimens.

Conclusively, at a lower dosage, red pepper reduced PLDL with increasing levels of PHDL at high doses. High doses of green and black pepper increases faecal loss of total cholesterol. These findings show that pepper has therapeutic potential as a natural alternative or addition to current lipid-lowering drugs. Further research is necessary to completely understand the involved mechanisms and improve dosing regimens.

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