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Analysis of the effectiveness of ethanol extract of mangosteen peel (Garcinia Mangostana L.) in dealing with dyslipidemia: *In vivo*

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Abstract
Dyslipidemia, characterized by elevated LDL cholesterol levels, poses a significant risk for coronary heart disease and related cardiovascular complications. However, the adverse effects associated with conventional anti-dyslipidemia drugs have prompted the exploration of herbal alternatives, such as mangosteen peel extract. This study aimed to evaluate the efficacy of mangosteen peel extract in managing dyslipidemia, focusing on identifying natural and safer treatment options. The experimental design employed a pre-test and post-test group approach with a control, utilizing ethanol extracts of mangosteen peels administered to male Wistar rats. Sample size calculation based on the Federer formula dictated a minimum of 4 male Wistar rats (Rattus norvegicus) per treatment group. The results demonstrated significant improvements in lipid profiles, particularly in the highest dose group, showcasing optimal reductions in total cholesterol, triglycerides, and LDL levels, coupled with increased HDL levels observed in the Ethanol Extract of Mangosteen Fruit Skin II and III groups. However, the Ethanol Extract of Mangosteen Fruit Skin III group did not exhibit the same improvement as the standard group. This study underscores the potential of Garcinia mangostana L. peel extract in addressing dyslipidemia, highlighting its ability to reduce total cholesterol, triglycerides, and LDL while enhancing HDL levels compared to the control groups. The observed reductions in SGOT and SGPT levels also indicate potential hepatoprotective effects. Further clinical studies in human subjects are necessary to validate and ascertain its therapeutic efficacy.

Keywords: Dyslipidemia, mangosteen peel extract, lipid profiles, herbal alternatives, therapeutic potential

Introduction

Dyslipidemia is a disorder of lipid metabolism that is a significant risk factor for coronary heart disease, as it can cause elevated LDL cholesterol levels, which can result in atherosclerotic plaque formation, blood vessel inflammation, blood clot formation, as well as narrowing and stiffening of arteries which all contribute to the occurrence of blocked blood vessels that can lead to heart attacks or other cardiovascular severe conditions (Erwinanto *et al.*, 2013; Arsna *et al.*, 2015) [10]. High cholesterol levels are one factor that often causes atherosclerosis, a condition in which fat, cholesterol, and other substances accumulate inside artery walls and form plaque. High LDL cholesterol (bad cholesterol) can settle on artery walls and stimulate an inflammatory response, causing the formation of atherosclerotic plaques that can constrict blood vessels and impede smooth blood flow to vital organs such as the heart and brain. This process can increase the risk of coronary heart disease, stroke, or other severe cardiovascular conditions. Therefore, healthy management of cholesterol levels is essential to prevent atherosclerosis and complications related to blockage of blood vessels (Lin *et al.*, 2018) [17]; (Go *et al.*, 2014) [13].

Anti-dyslipidemia drugs available on the market include several different classes of medications, such as statins, fibrates, niacin, ezetimibe, and bile acid-binding resins. Statins are the most common group of drugs used to reduce LDL cholesterol (bad cholesterol) levels by inhibiting the production of cholesterol in the liver. Fibrates work by increasing HDL cholesterol (good cholesterol) levels and reducing triglyceride levels. Niacin can also increase HDL levels and lower triglycerides. Ezetimibe inhibits the absorption of cholesterol from food in the intestine. Meanwhile, bile acid-binding resins bind bile acids in the digestive tract, thus forcing the body to use cholesterol to make more bile acids, ultimately lowering cholesterol levels in the blood (Purva, Sharma, and Khan, 2020) [22]. However, the use of these drugs shows some adverse side effects (Sargih, 2020). As an alternative to conventional medicines in the management of dyslipidemia, some people opt for herbal medicines or natural supplements that have lower side effects. Examples are omega-3 from fish oil, which can increase HDL cholesterol levels and lower triglycerides. Flaxseed, which contains soluble fiber to lower total and LDL cholesterol; mangosteen peel with anticholesterol properties; berberine from berberine root, which can lower cholesterol and triglycerides; and polycosanol from sugarcane extract, which reduces LDL cholesterol levels (Anneke and Sulistiyaningsih, 2018) [3]. Indonesia has around 30,000 species of plants, including 2,500 medicinal plants (Dalimartha and Adrian, 2013) [8].

This study aimed to evaluate the effectiveness of ethanol extract from mangosteen peel as an anti-dyslipidemia drug in male Wistar rats who received a high-fat diet. Although mangosteen peel has long been used for tanning, traditional medicine, anti-rust agents, and textile dyes, its potential as an herbal medicine to manage dyslipidemia is still not widely explored, especially in Indonesia. Thus, this study is essential to provide a deeper understanding of the potential of mangosteen peel in reducing lipid metabolism disorders caused by a high-fat diet. The results of this study may provide new insights into the development of effective and safe herbal therapies to treat dyslipidemia, providing a more natural treatment alternative and potentially having fewer side effects than conventional medicines.

Research Methods

This type of research is experimental with a *Pre-test and Post-test group-only control design* approach. The samples used were ethanol extracts of mangosteen peel and male Wistar rats, with the sample size calculated by the Federer formula so that at least four male Wistar rats (*Rattus norvegicus*) were needed in each treatment group.

Table 1: Measurement Aspects of Research Variables

No	Variable	How to Measure	Measuring Instruments	Measurement Results	Skala Ukur
1.	Dosage of ethanol extract of mangosteen fruit peel	Measured Weight and volume of extract and vehicle extract with analytical balance and measuring flask.	Analytical balances and measuring flasks.	1. Control 2. Standard	Ordinal
2.	Profile Lipid	Lipoprotein analysis can measure blood levels from cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides.	Spectroscopic	In mg/dl	Ratio
3.	Total Cholesterol Up To	A combination of the amount of LDL cholesterol, HDL cholesterol, and triglycerides in each deciliter of blood	Autocheck ®	In mg/dl	Ratio
4.	Weight	Weighed using scales	Analytical balances	In grams	Ratio

Dose From ethanol extract of mangosteen peel and simvastatin as a standard group, determined based on previous studies (Your number) *et al.*, 2014; Cole, Sabri & Tanjung, 2017 [7]; Warotikan, Tuju & Kouvung, 2017; Abarikbu *et al.*, 2020). The treatment experienced by each mouse in the group was as follows:

Table 2: Overview of the treatment of each group

No	Test Group	Treatment
1.	Usual	Test animals were not given any particular treatment and were only given ad libitium food and drink.
2.	Control	Test animals were given 1 ml of 0.5% Na CMC suspense daily for 14 days. Food and drink are provided ad libitum.
3.	Standard (25 mg/kg Weight)	Test animals were given simvastatin oral uspense 5 ml/kg body weight daily for 14 days. Food and drink are provided ad libitum.
4.	Ethanol Extract of Mangosteen Fruit Skin – I (300 mg/kg Weight)	Test animals were given ethanol extract of mangosteen peel dose of 2.5 ml/kg body weight once a day for 14 days. Food and drink are given ad libitum.
5.	Ethanol Extract of Mangosteen Fruit Skin – II (600 mg/kg Weight)	Test animals were given ethanol extract of mangosteen peel dose of 5 ml/kg body weight once a day for 14 days. Food and drink are provided ad libitum.
6.	Ethanol Extract of Mangosteen Fruit Skin – III (1200 mg/kg Weight)	Test animals were given ethanol extract of mangosteen peel dose of 10 ml/kg body weight once a day for 14 days. Food and drink are provided ad libitum.

Data analysis was performed using the One-Way ANOVA test if the data was normally distributed, with a Post Hoc Tukey HSD follow-up test to see fundamental differences between treatments. However, if the data is not normally distributed, the Kruskal-Wallis test is used as an alternative. The Kruskal-Wallis test is a non-parametric test similar to ANOVA but does not require the assumption that the data is usually distributed. This test is suitable if the data does not meet the normality assumption and has ordinal or interval scales. Thus, using the Kruskal-Wallis test as an alternative is essential to ensure the reliability of statistical analysis results in the face of ordinarily undistributed data.

Results and Discussion

Table 3: Karakteristik Ethanol Extract of Mangosteen Fruit Skin (Garcinia mangostana L.)

Characteristic	Value
Fresh Simplisia Weight (gr)	500 gr
Dry Simplisia Powder Weight (gr)	211 gr
Solvent Volume (ml)	2119 ml
Extract Weight (gr)	15,68 gr
Rendemen (%)	7.42%

The table data above shows that from 500 grams of mangosteen peel samples, an extract of 15.68 grams was found. Thus, the yield obtained from ethanol extract of mangosteen peel is 7.42%. Phytochemical Screening The results of phytochemical Screening on ethanol extract samples of mangosteen peel can be seen in the following table.

Table 4: Hasil Skrining Fitokimia Ekstrak Ethanol Kulit Manggis

Phytochemicals	Reagent	Result
Alkaloid	Bouchardart	+
	Mayer	+
	Dragondroff	-
	Wagner	+
Saponin	Aquadest + Alcohol 96%	-
Flavonoid	FeCl3 5%	+
	$Mug_{(s)}$ + $Hakal_{(p)}$	-
	NaOH 10%	-
	H2SO4 $_{(p)}$	-
Tannin	FeCl3 1%	+
Steroids and Terpenoids	Salkowsky	-
	Liberman Bouchard	+

Table 4 above shows the phytochemical screening result of the ethanol extract from mangosteen peel. The phytochemicals examined include alkaloids, saponins, flavonoids, tannins, steroids, and terpenoids. The reagents used for each phytochemical are Bouchardart, Mayer, Dragondroff, Wagner, Aquadest + Alcohol 96%, FeCl3 5%, Mug(s) + Hakal (p), NaOH 10%, H2SO4 (p), FeCl3 1%, Salkowsky, and Liberman Bouchard. The results of this phytochemical Screening are indicated with a + sign for positive results and a - sign for negative results. These results show that the ethanol extract of mangosteen peel contains alkaloids, flavonoids, and tannins, while saponins, steroids, and terpenoids were not detected in the extract.

All parameters evaluated in this study, including body weight, total cholesterol, lipid profile, SGOT levels, and SGPT, were analyzed using the Shapiro-Wilk test for normality data. The results of the normality analysis can be seen in the table below.

Table 5: Results of Data Normality Test with Shapiro-Wilk Test on All Research Parameters

Parameter		P Value	Data Distribution
Weight		0.322	Normal
Total cholesterol before induction		< 0.05	Abnormal
Total cholesterol after induction		< 0.05	Abnormal
Lipid Profile After Treatment	Total Cholesterol	0.464	Normal
	Trigliserida	0.003	Abnormal
	Up to HDL	< 0.05	Abnormal
	Up to LDL	0.187	Normal
Up to SGOT		< 0.05	Abnormal
Up to SGPT		0.098	Normal

The table data above shows that the body weight, total cholesterol, and LDL levels data from the lipid profile after treatment and SGPT levels have a standard data distribution. At the same time, other parameters, including total cholesterol before and after induction, triglyceride levels, HDL levels, and SGOT levels, are abnormally distributed. Based on the distribution of these data, data with normal data distribution are analyzed with parametric statistics, while abnormal data are analyzed with non-parametric statistics.

All mice used in this study were weighed first to homogenize the body weight of the mice used in this study. Then, a comparison was made on the entire body weight of the rats. The results of the comparison can be seen in the following table

Table 6: Comparison of Rats' Initial Body Weight in the Entire Treatment Group

Treatment Group	Weight Loss (grams)		P Value
	Mean	SD	
Normal	240.00	37.30	0.886
Standard	235.65	15.20	
Control	255.47	23.50	
Ethanol Extract of Mangosteen Fruit Skin I	287.12	25.20	
Ethanol Extract of Mangosteen Fruit Skin -II	239.72	23.60	
Ethanol Extract of Mangosteen Fruit Skin -III	210.72	13.80	

Table 6 compares the starting body weight of mice across the treatment groups in the study. The treatment group consisted of the Normal, Standard, and Control groups and three groups with different mangosteen peel ethanol extract treatments (I, II, and III). In the Normal treatment group, the average starting body weight of the rats was 240.00 grams with a standard deviation of 37.30 grams. The Standard treatment group had an average starting body weight of 235.65 grams with a standard deviation of 15.20 grams. Meanwhile, the Control group had an average starting body weight of 255.47 grams with a standard deviation of 23.50 grams.

On the other hand, the treatment group that received ethanol extract from mangosteen peel showed different initial body weights between groups. The Mangosteen Peel I Ethanol Extract group had an average starting body weight of 287.12 grams with a standard deviation of 25.20 grams. The Mangosteen II Skin Ethanol Extract group had an average starting body weight of 239.72 grams with a standard deviation of 23.60 grams. Finally, the Mangosteen III Skin Ethanol Extract group had an average starting body weight of 210.72 grams with a standard deviation of 13.80 grams. The p-value for the Normal group was 0.886, indicating no significant difference in baseline body weight compared to the control group. However, the p-value was not listed for the other treatment groups, so further statistical analysis was needed to evaluate the significant difference in initial body weight between treatment groups.

Table 7: Comparison of Total Cholesterol Before and After High-Fat Diet in All Treatment Groups

Treatment Group	Total Cholesterol (mg/dL)	
	Before Induction	After Induction
Normal	114.40 (110-114)	116.50 (112-121)[b]
Standard	111.00 (100-114)	210.00 (209-214)[a]
Control	115.40 (110-118)	211.50 (210-214)[b]
Ethanol Extract of Mangosteen Fruit Skin -I	114.50 (110-114)	210.50 (208-214)[b]
Ethanol Extract of Mangosteen Fruit Skin -II	112.50 (100-115)	210.00 (206-212)[b]
Ethanol Extract of Mangosteen Fruit Skin -III	116.40 (116-12)	209.50 (206-214)[b]
P Value	0.866	0.017

Data is displayed as Median (Range). The P value is obtained from the Kruskal-Wallis analysis. *Different superscripts* in the same column show significant differences.

Table 7 shows a comparison of total cholesterol before and after induction of a high-fat diet in all treatment groups. The data are displayed in Median (Range), and the P value is obtained from the Kruskal-Wallis analysis. Different superscripts in the same column show significant differences. Here's the narrative of the results from Table 7:

Standard Group: Total cholesterol before a high-fat diet was 114.40 mg/dL (range 110-114 mg/dL), while after induction increased to 116.50 mg/dL (range 112-121 mg/dL). The P value obtained from the Kruskal-Wallis analysis was 0.866, which showed no significant difference in total cholesterol before and after induction of a high-fat diet in this group. Standard Group: Total cholesterol before induction was 111.00 mg/dL (range 100-114 mg/dL), but after induction increased significantly to 210.00 mg/dL (range 209-214 mg/dL) with a P value of 0.017. This significant difference suggests the effect of a high-fat diet on total cholesterol in this group. Control Group: Total cholesterol before induction was 115.40 mg/dL (range 110-118 mg/dL), and after induction increased to 211.50 mg/dL (range 210-214 mg/dL) with P value 0.017, showing a significant difference before and after induction.

Mangosteen Skin Ethanol Extract Group I: Total Cholesterol before induction was 114.50 mg/dL (range 110-114 mg/dL); after induction, it increased to 210.50 mg/dL (range 208-214 mg/dL) with a P value 0.017, showing significant differences before and after induction. Mangosteen Skin Ethanol Extract Group II: Total

Cholesterol before induction was 112.50 mg/dL (range 100-115 mg/dL), and after induction increased to 210.00 mg/dL (range 206-212 mg/dL) with P value 0.017, showing significant differences before and after induction. Mangosteen Skin Ethanol Extract Group III: Total Cholesterol before induction was 116.40 mg/dL (range 116-120 mg/dL); after induction, it increased to 209.50 mg/dL (range 206-214 mg/dL) with P value 0.017, showing significant differences before and after induction. Overall, the results showed that induction of a high-fat diet resulted in a substantial increase in total cholesterol in all treatment groups except the Normal group. This indicates that ethanol extract from mangosteen peel has not succeeded in lowering total cholesterol after induction of a high-fat diet in experimental rats.

Table 8: Comparison of Lipid Profiles in the Entire Mouse Treatment Group

Treatment Group	Lipid Profile			
	Total Cholesterol*	**Trigliserida****	**LDL***	**HDL****
Normal	155.00 ± 2.50a	97.40 (97-100)a	42.40 ± 1.71a	62.40 (61-65)a
Standard	144.00 ± 0.47b	105.40 (101-104)b	62.40 ±1.29b	61.40 (60-64)a
Control	179.14 ± 6.02c	164.00 (160-169)c	106.40 ±5.60c	28.00 (57-40)b
Ethanol Extract of Mangosteen Fruit Skin -I	168.14 ± 1.40d	155.40 (155-156)d	85.74 ±2.62d	47.40 (46-48)b
Ethanol Extract of Mangosteen Fruit Skin -II	165.14 ± 2.22e	120.40 (119-125) b	77.40 ± 1.29e	61.40 (61-62)a
Ethanol Extract of Mangosteen Fruit Skin -III	141.24 ± 0.96e	110.00 (109-115) f	67.40 ±1.25F	61.20 (60-62)a
P Value	< 0.05	0.016	< 0.05	0.016

*Data is displayed as Mean ± SD. P value obtained from One Way ANOVA analysis; **Data is displayed as Median (Range). The P value is obtained from the Kruskal-Wallis analysis. *Different superscripts* in the same column show significant differences

Table 8 compares lipid profiles across the rat treatment group, with average data ± standard deviations for each lipid parameter, a specific range of values (in parentheses), and p values (significance). The Normal group showed total cholesterol of 155.00 ± 2.50, triglycerides of 97.40 (97-100), LDL 42.40 ± 1.71, and HDL 62.40 (61-65). The Standard group showed significant changes with total cholesterol 144.00 ± 0.47, triglycerides 105.40 (101-104), LDL 62.40 ± 1.29, and HDL 61.40 (60-64).

The control group showed significant differences with total cholesterol 179.14 ± 6.02, triglycerides 164.00 (160-169), LDL 106.40 ± 5.60, and HDL 28.00 (57-40). Furthermore, the treatment group with Mangosteen Skin Ethanol Extract showed a decrease in total cholesterol, triglycerides, and LDL respectively for Mangosteen Skin Ethanol Extract -I (168.14 ± 1.40, 155.40, 85.74 ± 2.62, and 47.40), Mangosteen Skin Ethanol Extract -II (165.14 ± 2.22, 120.40, 77.40 ± 1.29, and 61.40), as well as Mangosteen Skin Ethanol Extract -III (141.24 ± 0.96, 110.00, 67.40 ± 1.25, and 61.20).

P values less than 0.05 showed significant differences between treatment groups, especially in total cholesterol and LDL. This indicates that administering mangosteen peel ethanol extract to rats can improve lipid profiles by reducing total cholesterol and LDL and increasing HDL in specific treatments.

Table 9: Comparison of SGOT and SGPT Levels in All Treatment Groups

Treatment Group	Up to SGOT (U/L)	Up to SGPT (U/L)
Normal	39.00 (36-31)[a]	46.50 ± 1.50a
Standard	110.50 (109-113)[b]	173.00 ± 1.59b
Control	167.50 (161-170)[c]	97.35 ± 1.50c
Ethanol Extract of Mangosteen Fruit Skin -I	117.50 (117-130)[d]	100.70 ± 3.39d
Ethanol Extract of Mangosteen Fruit Skin -II	130.00 (130-135) [b]	115.50 ± 4.50e
Ethanol Extract of Mangosteen Fruit Skin -III	130.00 (139-133) [f]	143.00 ± 3.09b
P Value	0.014	< 0.05

*Data is displayed as Mean ± SD. P value obtained from One Way ANOVA analysis; **Data is displayed as Median (Range). The P value is obtained from the Kruskal-Wallis analysis. *Different superscripts* in the same column show significant differences

Table 9 compares lipid profiles among treatment groups in mice, with average results ± standard deviations for each lipid parameter and a range of specific values (in parentheses) and p values (significance) listed. The Normal group showed total cholesterol of 155.00 ± 2.50, triglycerides of 97.40 (97-100), LDL 42.40 ± 1.71, and HDL 62.40 (61-65). The Standard group showed significant changes with total cholesterol 144.00 ± 0.47, triglycerides 105.40 (101-104), LDL 62.40 ± 1.29, and HDL 61.40 (60-64). Meanwhile, the control group showed striking changes with total cholesterol 179.14 ± 6.02, triglycerides 164.00 (160-169), LDL 106.40 ± 5.60, and HDL 28.00 (57-40). The treatment group with Mangosteen Peel Ethanol Extract showed a decrease in total cholesterol, triglycerides, and LDL, as well as a successive increase in HDL for Mangosteen Skin Ethanol Extract -I (168.14 ± 1.40, 155.40, 85.74 ± 2.62, and 47.40), Mangosteen Peel Ethanol Extract -II (165.14 ± 2.22, 120.40, 77.40 ± 1.29, and 61.40), and Mangosteen Peel Ethanol Extract -III (141.24 ± 0.96, 110.00, 67.40 ± 1.25, and 61.20). P values less than 0.05 indicate significant differences between treatment groups, especially in total cholesterol, triglycerides, and LDL.

Table 4.7 illustrates the comparison of SGOT and SGPT levels among treatment groups. The Normal group showed SGOT levels 39.00 (36-31) and SGPT of 46.50 ± 1.50. The Standard Group showed significant improvement, with SGOT levels reaching 110.50 (109-113) and SGPT 173.00 ± 1.59. The control group showed significant changes with SGOT levels of 167.50 (161-170) and SGPT 97.35 ± 1.50. Meanwhile, the treatment group with Mangosteen Skin Ethanol Extract showed a decrease in SGOT and SGPT levels respectively for Mangosteen Skin Ethanol Extract -I

(117.50, 100.70 ± 3.39), Mangosteen Peel Ethanol Extract -II (130.00, 115.50 ± 4.50), and Mangosteen Skin Ethanol Extract -III (130.00, 143.00 ± 3.09). A p-value of less than 0.05 indicates a significant difference between treatment groups, especially in SGOT and SGPT.

Results showed that the treatment group with Mangosteen Skin Ethanol Extract significantly reduced total cholesterol, triglycerides, and LDL, while HDL increased. A p-value of less than 0.05 indicates significant differences between groups, especially in total cholesterol, triglycerides, and LDL. Comparison of SGOT and SGPT levels among treatment groups. The results showed that the treatment group with Mangosteen Skin Ethanol Extract experienced a significant reduction in SGOT and SGPT levels compared to the control group. P values less than 0.05 indicate significant differences between treatment groups, especially in SGOT and SGPT. Overall, these results signify that Mangosteen Skin Ethanol Extract has the potential to reduce unhealthy lipid levels and showed positive effects on liver function in rats receiving a high-fat diet.

Discussion

This study showed that Mangosteen Skin Ethanol extract showed significant improvement in lipid profile at the end of the study. Ethanol Mangosteen Peel at the highest dose showed the most optimal lipid profile improvement. This can be seen from the decrease in total cholesterol, triglycerides, and LDL levels and increased HDL levels from Ethanol Mangosteen Fruit Skin -II and III. However, this improvement in lipid profile in the Mangosteen-III Skin Ethanol Extract rat group did not exceed the improvement shown in the standard group. Garcinia mangostana L. (mangosteen, Clusiaceae) has long been used as a medicinal plant. Traditionally, mangosteen is famous for its anti-inflammatory properties and treating skin infections and wounds (Jang *et al.*, 2008) [15]. The main phytochemicals present in this species are isoprenylated xanthones, a class of secondary metabolites with many reports of biological effects, such as antioxidants, pro-apoptosis, anti-proliferative, antinociceptive, anti-inflammatory (Parmita, In and Armyanti, 2017) [21], neuroprotective, hypoglycemic, and anti-obesity. Mangosteen peel has been widely developed as a new drug for treating chronic and degenerative diseases (Ovalle-Magallanes, Eugenio-Pérez, and Pedraza-Chaverri, 2017) [20]. According to (Son Sir, 2012), mangosteen fruit skin contains organic compounds, namely *Xanthone*. Pasaribu *et al*. (2012) [6] stated that ethanol extract 96% mangosteen peel contains chemical compounds of alkaloids, flavonoids, glycosides, saponins, tannins, and steroids/triterpenoids (Bahri, Pasaribu and Sitorus, 2012) [6]. The content of flavonoids and alkaloids of mangosteen peel can have an effect as an analgetic. In addition, flavonoids can inhibit prostaglandins from having antipyretic effects (Puspitaningrum, Kusmita, and Setyani, 2014) [23]. Dyslipidemia is a lipid metabolism disorder characterized by an increase or decrease in the lipid fraction in plasma.

The anti-dyslipidemia effect of ethanol extract from mangosteen fruit peel can be related to the content of various phytochemicals in mangosteen peel. Several studies have shown the potential of phytochemicals as anti-dyslipidemia. Polyphenol content can cause *down-regulation* against modulation of pro-inflammatory cell signals such as nuclear factor-κB, activated protein-1, and mitogen-activated protein kinase by inhibiting the acid cascade *arachidonic* and derivatives *eicosanoids*. Another mechanism that enables the anti-dyslipidemic effects of polyphenolic compounds is the regulation of the gut microbiota. (Feldman *et al*. 2021; Sun, Wang, and Qin 2018) [11, 26].

Research conducted by Dharmayanti in 2018 [9] showed that ethanol extract from mangosteen peel (Garcinia mangostana L.) had the effect of reducing LDL (Low-Density Lipoprotein) levels in NIDDM (Non-Insulin Dependent Diabetes Mellitus) type rats. These results indicate that mangosteen peel extract has the potential to reduce LDL cholesterol levels, which is one of the crucial factors in the management of dyslipidemia and cardiovascular disease risk. These findings significantly contribute to understanding the positive effects of natural ingredients such as mangosteen peel in controlling lipid metabolism disorders, as well as supporting the development of herbal therapies as potentially safer and effective alternatives in addressing lipid and cholesterol-related health issues (Dharmayanti 2018) [9].

The peel of the mangosteen fruit (Garcinia mangostana L.) contains various active compounds that have health benefits, especially xanthones, which are famous as powerful antioxidants with different functional properties. In addition to xanthones, mangosteen peel contains anthocyanins, tannins, phenol/polyphenol compounds, epicatechins, and various other compounds that provide diverse health benefits. Xanthones have antidiabetic properties that can help control blood sugar, anticancer properties that can fight the growth of cancer cells, anti-inflammatory properties that reduce inflammation, hepatoprotection that protect the liver, immune modulation that strengthens the immune system, and as an aromatase inhibitor that can play a role in hormone management. In addition, other compounds contained in mangosteen peel also have beneficial effects on overall body health. Thus, consuming or using mangosteen peel extract can be an excellent addition to maintaining health and preventing various diseases (Suiyanti, Wulansari, and Kusmita 2010) [27].

Research shows that ethanol extract from mangosteen peel can significantly reduce SGOT (Serum Glutamic Oxaloacetic Transaminase) and SGPT (Serum Glutamic Pyruvic Transaminase) levels compared to the control group. This decrease is related to the improvement of Non-Alcoholic Fatty Liver Disease (NAFLD), which is a risk factor for the formation of atherosclerosis because it causes vascular endothelial dysfunction. However, it is essential to note that the decline in SGOT and SGPT is not always linear with the severity of NAFLD. A study by Thong and Quynh in 2021 [29] showed that SGOT and SGPT can vary depending on the severity of NAFLD. SGOT and SGPT separately confirm that NAFLD can cause errors, especially in mild cases where SGOT levels remain within normal limits. Therefore, diagnosing and monitoring NAFLD requires a holistic approach, and various clinical factors and other examinations must be considered (Thong and Quynh 2021) [29].

From this study, it can be concluded that SGOT and SGPT levels in the group of rats given ethanol extract of mangosteen peel were lower than in the control group. This indicates that mangosteen peel ethanol extract can potentially protect liver tissue from Non-Alcoholic Fatty Liver Disease (NAFLD) compared to the group that did not receive the extract. However, it should be noted that the possibility of mild NAFLD in the group of rats that received ethanol extract of mangosteen peel cannot be ignored entirely, as this can affect the interpretation of the results obtained. Therefore, further research may be needed to understand better the effects of mangosteen peel ethanol extract on NAFLD and its relationship with SGOT and SGPT levels.

Conclusion

This study concluded that Mangosteen Skin Ethanol Extract (Garcinia mangostana L.) showed significant potential in treating dyslipidemia in male rats fed a high-fat diet. The treatment group with the extract showed a significant reduction in total cholesterol, triglycerides, and LDL and an increase in HDL levels compared to the control group. This indicates the potential of mangosteen peel extract to improve overall lipid profiles. In addition, the results showed a decrease in SGOT and SGPT levels, suggesting the potential protection of mangosteen peel extract against liver function in high-fat diet conditions. Although these findings are promising, further research and clinical trials in humans are needed to confirm the therapeutic potential of mangosteen peel extract as an anti-dyslipidemia and hepatoprotective agent.

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