International Journal of Engineering Inventions
e-ISSN: 2278-7461, p-ISSN: 2319-6491
Volume 12, Issue 9 [September. 2023] PP: 21-25

Analysis Of Anti-Dyslipedemia Effect Of Mangosteen Fruit Peel Extract (Garcinia Mangostana L.) In Male Rats

CHEN JUN
Email: chenjunch1@gmail.com
Master of Clinical Medicine Program, Faculty of Medicine, Dentistry, Health Sciences Prima Indonesia University

ABSTRACT
Mangosteen peels are Natural ingredients that can potentially be an alternative treatment for dyslipidemia. The utilization of mangosteen fruit peel for treatment in Indonesia is still not much. Therefore, this study aims to analyze mangosteen fruit peel extract as an anti-dislipidemia drug in male Wistar rats. This type of research is experimental with a Pre-test and Post-test group-only control design approach. The samples used were mangosteen peel ethanol extract and male Wistar rats, with the sample size calculated by the Federer formula so that at least four rats were needed. The results of SGOT and SGPT levels in all rat treatment groups showed significant differences; this can be seen from the P value <0.05. It is concluded that mangosteen peel ethanol extract significantly reduces total cholesterol, triglyceride levels, LDL levels, and SGOT levels compared to the control group. Mangosteen peel ethanol extract can significantly increase HDL levels compared to the control group.

Keywords.: *Anti-Dyslipedemia, Mangosteen Fruit, Extract*

Date of Submission: 02-09-2023 Date of acceptance: 13-09-2023

I. Introduction

Based on data from the World Health Organization (WHO) in 2008 estimates that the prevalence of dyslipidemia in various regions varies, namely 30.3% in Southeast Asia and 47.7% in America (3); (4). High cholesterol is a frequent etiology that causes atherosclerosis, stroke, and cardiovascular disease (5). Dyslipidemia is a significant risk factor for coronary heart disease. It is often defined as an abnormality or disruption of lipid metabolism due to the interaction of genetic and environmental factors (1,2). Management of dyslipidemia: there are several anti-dyslipidemia drugs on the market, including statins, fibrates, niacin, ezetimibe, and bile acid binding resins (7). Still, the use of these drugs shows several side effects that are detrimental to health (8).

One of the natural ingredients that has the potential to be an alternative treatment is mangosteen peel. So far, the utilization of mangosteen peels is only for tanning leather, traditional medicine, and the making of anti-rust substances and textile dyes. The utilization of mangosteen rind for treatment in Indonesia is still not much, especially as Anti-Dyslipidemia. Therefore, this study aims to determine the effectiveness of mangosteen fruit peel ethanol extract as anti-dyslipidemia in male Wistar rats given a high-fat diet.

II. Research Methods

This type of research is experimental with the Pre-test and Post-test group-only control design approach. The samples used were mangosteen peel ethanol extract and male Wistar rats, with the sample size calculated by the Federer formula, so at least four male Wistar rats (Rattus norvegicus) were needed in each treatment group. Surgical tools, laboratory glassware, aluminum foil, blender (Miyako), porcelain cup, desiccator, incubator, object glass, cover glass, porcelain crust, drying cabinet, microtube, light microscope, analytical balance (Vibra AJ), oral sonde, electric oven (Stork), water bath (Yenaco), tube clamp, test tube rack, rotary evaporator, centrifugator, set of water content determination tools, UV spectrophotometer (Microlet 3000), injection syringe, furnace (Nabertherm), test tube, animal scales (Presica).

The materials used in this study were mangosteen fruit, methanol, distilled water, Na-CMC (Sodium-Carboxyl methylcellulose), simvastatin, husk, rat food pellets, phytochemical screening reagents, and ketamine. The doses of mangosteen peel ethanol extract and simvastatin as the standard group were determined based on previous studies (11-14). The treatments experienced by each rat in the group were as follows:

Table 1. Treatment Overview of Each Group

No	Test Group	Treatment
1.	Normal	Test animals were not given specific treatment, only food and drink ad libitium.
2.	Control	Test animals were given 1 ml of 0.5% Na CMC suspense daily for 14 days. Food and drink were provided ad libitum.
3.	Standard	Test animals were given oral simvastatin 5 ml/ kgBB daily for 14 days. Food and drink were provided ad libitum.
4.	(25 mg/kgBB)	Test animals were given mangosteen peel ethanol extract at 4 ml/ kgBB daily for 14 days. Food and drink were provided ad libitum.
5.	Ethanol Extract of Mangosteen Fruit Peel - I (400 mg/ kgBB)	Test animals were given mangosteen peel ethanol extract at 8 ml / kgBB daily for 14 days. Food and drink were provided ad libitum.
6.	Ethanol Extract of Mangosteen Fruit Peel - II	Test animals were given mangosteen peel ethanol extract at 12 ml / kgBB daily for 14 days. Food and drink were provided ad libitum.

Data analysis One-Way Anova test if the data is usually distributed with a further test in the form of Post Hoc Tukey HSD test to see fundamental differences between treatments. However, as an alternative test, if the data is not normally distributed, the Kruskall-Wallis test is used.

III. Results and Discussion

Table 2. Comparison of Initial Body Weight of Mice in All Treatment Groups

Treatment Group	Body Weight (grams)		P-value
	Mean	SD	
Normal	241.00	31.62	0.867
Standard	231.61	13.62	
Control	246.47	23.63	
Mangosteen Peel Ethanol Extract I	247.48	22.58	
Mangosteen Fruit Peel Ethanol Extract -II	237.23	22.61	
Ethanol Extract of Mangosteen Fruit Peel -III	244.74	16.82	

From the data table above, it can be seen that the P value> 0.05 (P value = 0.867) means that there is no significant difference in the initial body weight of the rats used in this study. The body weight of rats used in this study ranged from 232-250 grams, evenly distributed in each treatment group.

Total cholesterol

To evaluate the anti-dyslipidemia effect of mangosteen peel, a high-fat diet was administered to the control, standard, mangosteen peel extract I, II, and III groups. Before and after the administration of the high-fat diet, the total cholesterol in all rats was measured, and non-parametric statistics analyzed all total cholesterol data. The results of the analysis can be seen in the following table.

Table 3. Comparison of Total Cholesterol Before and After Administration of High Fat Diet in All Treatment Groups

Treatment Group	Total cholesterol (mg/dL)	
	Before Induction	After Induction
Normal	115.30 (110-116)	115.50 (112-127)^{b}
Standard	113.00 (100-114)	216.00 (209-219)^{a}
Control	112.30 (110-118)	217.50 (210-216)^{b}
Mangosteen Peel Ethanol Extract I	116.50 (110-116)	213.50 (208-216)^{b}
Mangosteen Fruit Peel Ethanol Extract -II	111.50 (100-115)	213.00 (207-216)^{b}
Ethanol Extract of Mangosteen Fruit Peel -III	111.40 (117-12)	208.50 (207-213)^{b}
P-value	**0.836**	**0.011**

Data are shown as Median (Range). P values obtained from Kruskal-Wallis analysis; different superscripts in the same column indicate significant differences.

From the data table above, it can be seen that before being given a high-fat diet, the total cholesterol of rats before giving a high-fat diet in all treatment groups did not show significant differences (P value =0.836). This indicates that the entire cholesterol data of rats before being given a high-fat diet is uniform. However, the total cholesterol in all groups of rats after the high-fat diet showed a different distribution, where only the control, standard, mangosteen peel ethanol extract-I, II, and III groups showed uniform total cholesterol.

Table 4. Comparison of Lipid Profile in All Rat Treatment Groups

Treatment Group	Profil Lipid			
	Total cholesterol *	Triglycerides **	LDL*	HDL**
Normal	134.00 ± 2.40a	98.30 (97-100)a	53.70 ± 1.72a	63.20 (61-63)a
Standard	142.00 ± 0.27b	193.50 (101-104)b	63.40 ±1.19b	62.50 (60-64)a
Control	172.15 ± 6.02c	164.00 (160-169)c	108.24 ±3.30c	28.40 (37-40)b
Mangosteen Peel Ethanol Extract -I	162.15 ± 1.52d	133.50 (131-136)d	83.75 ±2.62d	57.50 (56-58)b
Mangosteen Fruit Peel Ethanol Extract -II	163.15 ± 2.22e	120.50 (119-123)e	77.50 ± 1.29e	61.50 (61-62)a
Ethanol Extract of Mangosteen Fruit Peel -III	151.25 ± 0.96e	110.00 (109-113)f	67.50 ±1.23f	60.00 (60-62)a
P-value	**< 0.05**	**0.016**	**< 0.05**	**0.016**

*Data are shown as Mean ± SD. P values obtained from One Way ANOVA analysis; **Data are shown as Median (Range). P values obtained from Kruskal-Wallis analysis; Different superscript in the same column indicates significant difference.

From the data table above, it can be seen that all lipid profile data in all treatment groups show significant differences.

a. Total cholesterol in all rat treatment groups showed significant differences; this can be seen from the P value <0.05. The lowest average total cholesterol was found in the standard group, which was 134.00 ± 2.40 mg/dL, followed by the legal group at 142.00 ± 0.27 mg/dL, mangosteen rind ethanol extract group I, II, III, and the group with the highest total cholesterol was the control group at 172.15 ± 6.02 mg/dL;

b. Triglyceride levels in all treatment groups also showed significant differences; this can be seen from the P value <0.05 (P value = 0.016). The trend of the lowest triglyceride levels was found in the standard group at 97.50 mg/dL, followed by the legal group at 98.30 mg/dL, mangosteen rind ethanol extract groups I, II, III, and the group with the highest triglyceride levels were the control group at 193.50 mg/dL.

c. LDL levels also showed significant differences in all treatment groups; this can be seen from the P value <0.05. The lowest average LDL level was found in the standard group at 53.70 ± 1.72 mg/dL, followed by the legal group at 63.40 ± 1.19 mg/dL, mangosteen rind ethanol extract group I, II, III, and the group with the highest LDL level was the control group at 108.24 ± 3.30 mg/dL.

d. HDL levels also showed significant differences in all treatment groups; this can be seen from the P value <0.05 (P value = 0.016). The highest HDL level trend was found in the standard group at 63.20 mg/dL, followed by the legal group at 62.50 mg/dL, mangosteen rind ethanol extract group I, II, and III, and the group with the lowest HDL level was the control group at 28.40 mg/dL.

Table 5. Comparison of SGOT and SGPT Levels in All Treatment Groups

Treatment Group	SGOT levels (U/L)	SGPT levels (U/L)
Normal	110.50 (108-112)^{b}	156.00 ± 1.59^{b}
Standard	178.20 (161-170)^{c}	97.25 ± 1.50^{c}
Control	117.50 (117-120)^{d}	100.70 ± 3.29^{d}
Mangosteen Peel Ethanol Extract -I	120.00 (120-125)^{e}	115.50 ± 4.50^{e}
Mangosteen Fruit Peel Ethanol Extract -II	130.00 (129-122)^{f}	142.00 ± 2.08^{b}
Ethanol Extract of Mangosteen Fruit Peel -III	0.028	< 0.05
P-value	**29.40 (26-31)^{a}**	**44.20 ± 1.40^{a}**

*Data are shown as Mean ± SD. P values obtained from One Way ANOVA analysis; **Data are shown as Median (Range). P values obtained from Kruskal-Wallis analysis; Different superscript in the same column indicates significant difference.

From the data table above, it can be seen that the SGOT and SGPT levels in all rat treatment groups show significant differences; this can be seen from the P value <0.05. The highest trend of SGOT levels was found in the control group, 178.20 U/L, and the lowest in the standard group, 29.40 U/L. Meanwhile, a similar picture was found in the SGPT level; the group with the highest SGPT level was found in the control group, which was 156.00 U/L, and the lowest was found in the standard group, 44.20 U/L.

IV. Discussion

The highest mangosteen peel ethanol extract dose showed the most optimal lipid profile improvement. This can be seen from the decrease in total cholesterol, triglyceride, and LDL levels and the increase in HDL levels of mangosteen peel ethanol groups II and III. However, this improvement in lipid profile in the mangosteen rind ethanol extract-III group did not exceed the modification shown in the standard group. The anti-dyslipidemia

effect of mangosteen rind ethanol extract may be related to the content of various phytochemicals in mangosteen fruit.

Several studies have shown the potential of phytochemicals as anti-dyslipidemia. Polyphenols may cause down-regulation of pro-inflammatory cell signaling such as nuclear factor-κB, activated protein-1, and mitogen-activated protein kinase by inhibiting the arachidonic acid cascade and eicosanoid derivatives. Another possible mechanism for the anti-dyslipidemia effect of polyphenolic compounds is the regulation of intestinal mycobiota. Polyphenolic compounds in the gut will interact with the gut microbiota to increase various beneficial metabolite products such as short-chain free fatty acids, and gut microbiota such as Akkermansia municiphilia sp. restore inflammatory conditions in the gut, improve gut permeability and insulin sensitivity. Furthermore, these improvements to the gut microbiota protect the gut-liver axis, thereby reducing the lipid profile in the body. (15,16). The diagnosis of dyslipidemia can be made based on elevated plasma LDL levels. Xanthone found in mangosteen rind is antioxidant, antidiabetic, anticancer, anti-inflammatory, hepatoprotective, immunomodulatory, aromatase inhibitor, antibacterial, and other functional properties. Mangosteen rind (Garcinia mangostana. L) is beneficial for health because it contains anthocyanins, tannins, phenol/polyphenol compounds, epicatechin, and xanthone (17).

Thong and Quynh (2021) reported that SGOT and SGPT correlate with NAFLD, but using SGOT and SGPT separately may show errors in confirming mild NAFLD. In severe NAFLD cases, SGOT will increase slightly; SGOT levels can be found in average amounts in milder cases. Therefore, using SGOT and SGPT unilaterally may allow errors in confirming mild NAFLD (18). In this study, the SGOT and SGPT levels in the group of rats receiving mangosteen peel ethanol extract were lower than the SGOT and SGPT levels of the control group. This suggests that mangosteen peel ethanol extract may protect liver tissue from NAFLD compared to the group that did not receive mangosteen peel ethanol extract. However, the possibility of mild NAFLD in the rats that received mangosteen peel ethanol extract cannot be ruled out.

Garcinia mangostana L. (mangosteen, Clusiaceae) has long been used as a medicinal plant. Traditionally, mangosteen is well known for its anti-inflammatory properties and is used in treating skin infections and wounds (19). The main phytochemicals present in this species are the terisoprenylated xanthones, a class of secondary metabolites with many reported biological effects, such as antioxidant, pro-apoptotic, anti-proliferative, antinociceptive, anti-inflammatory (20), neuroprotective, hypoglycemic, and anti-obesity. Mangosteen rind is widely developed as a new drug to treat chronic and degenerative diseases (21). According to (22), mangosteen rind contains organic compounds, namely xanthones. Pasaribu et al. (2012) stated that 96% ethanol extract from mangosteen fruit peel contains chemical compounds of alkaloids, flavonoids, glycosides, saponins, tannins, and steroids/triterpenoids (23). The flavonoid and alkaloid content of mangosteen skin can have an effect as an analgesic. In addition, flavonoids can inhibit prostaglandins so that they have an antipyretic effect (24). Dyslipidemia is a lipid metabolism disorder characterized by an increase or decrease in the lipid fraction in plasma.

V. Conclusion.

This study concluded that mangosteen peel ethanol extract significantly reduced total cholesterol, triglyceride levels, LDL levels, and SGOT levels compared to the control group. Mangosteen peel ethanol extract can significantly increase HDL levels compared to the control group.

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