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The Effectiveness of Garcinia Mangostana L. Rind extract in Reducing Total Cholesterol Levels in Hypercholesterolemic Male White Mice

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Hypercholesterolemia contributes to the incidence of coronary heart disease which is the leading cause of death in the world [1]. Diet modification and hypolipidemic drugs, including herba, one of which is Garcinia mangostana L. will effectively reduce total cholesterol [3].

A research a posttest control group design [20], type of research was a laboratory experimental research [15]. The population was male white mice aged 3 - 4 weeks weighing 100-200 grams [12]. Hypercholesterolemia in male white rats was with MDLT induction (high - fat diet food) [7]. Data collection of total cholesterol levels measurement used enzymatic spectrophotometer method, data analysis used Variant Analysis statistical test (ANOVA) with significance level $\alpha < 0.05$ [15].

The effect of Garcinia mangostana L. rind extract on total cholesterol reduction in white rats was grouped into a negative control group, positive control group and four dose treatment groups [4]. Identification of hypercholesterolaemia in white rats was examined for total cholesterol on day 8[illegible]. The effect of Garcinia Mangostana L rind extract on reducing total cholesterol was examined on day 22 [3,16] .

The results of the examination showed the administration of Garcinia mangostana L. rind extract in all dosage groups effectively reduced total cholesterol levels with a significance level of $p < 0.05$.

Keywords : *Garcinia mangostana L,* total cholesterol and hypercholesterolemia

Introduction

In 2004 World Health Organization (WHO) stated that hypercholesterolemia had a contribution of 56% of coronary heart disease which resulted in the deaths of around 4.4 million every year worldwide. The data was predicted to increase continously to 20 million per year until 2030 to 24 million per year [1]. In Indonesia deaths from heart and blood vessel disease amounted to 16.7% [12].

Hypercholesterolemia occurred because of an increase in the transport of acylglycerol from the liver to blood circulation in the form of VLDL [4,10]. In the blood circulation VLDL was hydrolyzed by lipoprotein lipase become free fatty acids and glycerol [9,10]. Then, they were transported to the tissues and became IDL which was an LDL particle precursor [6] , remained in the blood circulation. LDL in the blood circulation was then taken by LDL receptors and translocated to cell membranes, past endosomes and lysosomes [20]. The increased lipoprotein containing cholesterol by LDL receptors results in high cholesterol concentrations in cells. the lipoproteins concentration enhancement which containing cholesterol in cells resulted in an increase of total cholesterol [9,10].

At high LDL concentrations in the blood circulation there would be saturation in the process of taking lipoprotein containing cholesterol through LDL receptors [8,10] . Therefore LDL containing cholesterol was converted to oxidized LDL [4] which was not recognized by LDL receptors [9,10]. The oxidized LDL could not be taken by LDL receptors, so it was translocated to the cell membrane through scavanger receptors that had macrophage properties. Taking oxidized LDL which containing cholesterol by scavanger receptors for a

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long time resulted in the formation of foam cells in atherosclerotic lesions [2].

Decreasing LDL concentrations containing cholesterol in blood circulation is carried out through exercise and diet modification containing unsaturated fatty acids. Regular exercise can increase lipoprotein lipase expression due to increased insulin sensitivity. Diets of unsaturated fatty acids can increase the catabolic rate of LDL containing cholesterol due to the addition of the number of LDL receptors. If exercises and dietary modifications of unsaturated fatty acids fail to reduce cholesterol, it can be done by management of a plasma lipid-lowering drug (hypolipidemic) [9,10].

Hypolipidemic drugs could reduce cholesterol by mechanisms including; inhibiting enterohepatic circulation of bile acid, inhibiting cholesterol absorption from gastrointestinal [9,10], decreasing plasma triacylglycerol, inhibiting HMG-CoA reductase, and increasing lipoprotein lipase activity. However consuming hypolipidemic drugs had an impact in the form of gastrointestinal disorders, skin rashes, liver function disorders and the existence of contra-indications of use that resulting in not everyone can consume [13].

The management of herbal-derived hypolipidemic was highly recommended. Herbs were a source of compounds that had potential as a drug base, one of which was mangosteen rind (Garcinia mangostana L). In the pericarp, it contained mangostin compounds, reaching 75 mg / 100 mg [18]. Mangostin had inhibitory activity for inhibiting the release of prostaglandin E [11], that resulted in a decrease in lipolysis of adipose tissue [9,10] and was thought to increase the activity of the lipoprotein lipase enzyme [3].

The decrease in lipolysis of adipose tissue results in a decrease of free fatty acids in the blood and liver circulation. So that the esterification of free fatty acids becomes acylglycerol in the form of VLDL containing cholesterol which is transported from the liver blood circulation to decrease. Decreasing VLDL production results in decresing IDL levels. The decrease in IDL which was an LDL-forming precursor containing cholesterol in the blood circulation resulted in a decrease of total cholesterol in the blood [9,10].

Metode

This research was an experimental laboratory with a posttest control group design[20] as a study design between the independent variable of Garcinia mangostana L. Rind extract and the dependent variable of total cholesterol levels. The population was male white mice (Ratus norvegicus) aged 3-4 weeks with a weight of 100-200 grams[16]. Samples numbers were 6 for each group [5]. Data collection of measurement of total cholesterol levels used enzymatic method with a spectrophotometer, the data analysis used Variant Analysis statistical test (ANOVA)with a significance level of $\alpha < 0.05$ [15].

The Result of Study

1. The results of the total cholesterol concentration tests between the non-induced MDTL group and induced MDTL groups (High-Fat Diet Foods)

Tabel 1. The results of the total cholesterol concentration tests between the non-induced MDTL group and induced MDTL groups (High-Fat Diet Foods)

Dependent Variable	Group		Sig. (p)
	the non-induced MDTL group N = 6	induced MDTL groups N = 6	
Total Cholesterol (Mean ±SD)	56,17 ± 4,53	68,17 ± 8,61	0,010

The results of the study in table 1 showed that total cholesterol levels induced by MDTL had a significant increase compared to the group before MDTL was induced with p = 0.010

2. Data on body weight, the total cholesterol levels variable in the control group and treatment group

The analysis results of initial body weight, final weight, changes in body weight, total cholesterol levels between the control group and the treatment group which treaten by mangosteen pericarp rind extract (Garcinia mangostana L.) at a dose of 50 mg / kgBB, 150 mg / kg BW, 250 mg / kg BB and 350 mg / kg BB.

Table 2. Mean and standard deviation of initial body weight, final body weight, change in body weight and variable total cholesterol in the control and treatment groups

Group		Initial weight (gram)	Final weight (gram)	Change in body weight (gram)	Total cholesterol (mg/dl)
Control group (K 3) n = 6	Mean	165.00	188.33	23.33	95.17
	Standard deviation	30.65	29.26	8.16	10.81
Extract group of 50mg (K 4) n = 6	Mean	155.83	172.50	16.67	79.17
	Standard deviation	28,70	28,41	6,05	7,58
Extract group of 150 mg (K 5) n = 6	Mean	160.50	177.50	17.00	80.67
	Standard deviation	34,11	32,36	5,09	7,17
Extract group of 250 mg (K 6) n = 6	Mean	155.83	173.50	17.67	73.83
	Standard deviation	25.96	26.48	5.35	13.04
Extract group of 350 mg (K 7) n = 6	Mean	155.83	178.50	22.67	67.00
	Standard deviation	18.00	14.68	5.35	8.31

3. The normality test of the control group and the treatment group

The results of the Kolmogorov-Smirov normality test for one sample which administered to the changes of total cholesterol levels in the control group and the treatment group by giving mangosteen pericarp rind extract (Garcinia mangostana L.) p = 0.955. The cholesterol change data obtained p> 0.05 so that the data were normally distributed.

Table 3. The normality test of the control group and the treatment group

Variable	Sig.
The total cholesterol levels	0.955

4. The Result of Variant Analysis

Table 4. The test results were different from the ANOVA total cholesterol variable in the control group and the handling of Garcinia mangostana L skin extract

The results of the t-test with the total cholesterol variables anova in the control and treatment group of *Garcinia mangostana L* skin extract

Dependent Variable	F-count	Sig.
total cholesterol	7,009	0,001*

Sign * to show signficant meaningfullness

From the table above based on the average total cholesterol level between the control group and the treatment group given Garcinia mangostana L. rind extract showed a significant difference (p <0.05) p = 0.001

5. The result of LSD test

Table 5. The result of t-test using LSD total cholesterol variables in the control and treatment group of mangosteen pericarp rind extract *(Garcinia mangostana L.*

Dependent Variable	Group (I)	Group (J)	Difference everage	Std. Error	Sig.
total cholesterol	(Control Group 3) N = 6	Extract of 50 mg	16.000*	5.569	.008
		Extract of 150 mg	14.500*	5.569	.015
		Extract of 250 mg	21.333*	5.569	.001
		Extract of 350 mg	28.167*	5.569	.000
	Extract of 50 mg (Group 4) N = 6	Control	-16.000*	5.569	.008
		Extract of 150 mg	-1.500	5.569	.790
		Extract of 250 mg	5.333	5.569	.347
		Extract of 350 mg	12.167*	5.569	.038
	Extract of 150 mg (Group 5) N = 6	Control	-14.500*	5.569	.015
		Extract of 50 mg	1.500	5.569	.790
		Extract of 250 mg	6.833	5.569	.231
		Extract of 350 mg	13.667*	5.569	.021
	Extract of 250 mg (Group 6) N = 6	Control	-21.333*	5.569	.001
		Extract of 50 mg	-5.333	5.569	.347
		Extract of 150 mg	-6.833	5.569	.231
		Extract of 350 mg	6.833	5.569	.231
	Extract of 350 mg (Group 7) N = 6	Control	-28.167*	5.569	.000
		Extract of 50 mg	-12.167*	5.569	.038
		Extract of 150 mg	-13.667*	5.569	.021
		Extract of 250 mg	-6.833	5.569	.231

In table 5 showed that there was a decrease in total cholesterol with a significant difference (p <0.05) between the control group and the mangosteen pericarp rind extract group (*Garcinia mangostana L.*). extract dose of 50 mg / kg BB (p = 0,008), extract dose of 150 mg / kg BW (p = 0,015) and extract dose of 250 mg / kg BW (p = 0,001), while group of extract dose 350 mg / kgBB (p = 0,000)

In Table 5 showed that there was a significant decrease (p <0.05) compared to total cholesterol between the dose groups of mangosteen pericarp rind extract (Garcinia mangostana L.) 50 mg / kgBB and the control group (p = 0.008) and group extract 350 mg / kgBB (p = 0.038). However there was no significant difference of the extract dose of 150 mg / kgBB (p = 0.790) and extract dose of 250 mg / kgBB (p = 0.347).

For the total cholesterol in the dose group of mangosteen pericarp rind extract (*Garcinia mangostana L.*) of 150 mg / kgBB, there was a significant decrease (p <0.05) between the mangosteen pericarp rind extract group (*Garcinia mangostana L.*). dose of 150 mg / kgBB with control (p = 0.15) and extract dose of 350 mg / kg BB (p = 0.021), meanwhile aministering the extract dose of 50 mg / kgBB (p = 0.015) and extract dose of 250 mg / kgBB (p = 0.001) there was a significant decrease (p> 0.05).

For the total cholesterol in the dose group of mangosteen pericarp rind extract (*Garcinia mangostana L.*) 250 mg / kgBB, the ratio of significant decrease was only on the control group (p = 0.01), whereas on the group dose of 50 mg / kgBB, 150 mg / kgBB and 350 mg / kgBB there was no significant differences with p> 0.05. In comparison with the dose group of mangosteen pericarp rind extract (*Garcinia mangostana L.*) 350 mg / kgBB for the total cholesterol there was a significant decrease with the control group (p = 0,000), dose of 50 mg / kgBB (p = 0.038), and dose of 150 mg / kgBB (0.021). For the extract dose of 250 mg / kgBB there was no significant difference (p = 0.231).

Discussion

Food induction of a high-fat diet (MDTL) in white rats consisting of a mixture of beef fat and palm oil in a ratio of 1: 5 as much as 2% of body weight for 7 days

aimed to optimize rat blood cholesterol levels [7]. The induction of MDTL containing sterols and triglycerides was estimated to reduce LDL receptors and the formation of VLDL particles of smaller size and contained more cholesterol [9,10]. The enhancement of LDL containing cholesterol resulted in the taking through LDL receptors experienced saturation. Therefore it changed into modified LDL with oxidation which was not recognized by LDL receptors [9,10].Oxidized LDL interacts well and is absorbed by lower affinity systems in macrophages and other cells called *scavanger receptors*. However not all oxidized LDL were taken by macrophages. This was due to the availability of fatty acyl substrates by the enzyme Acyl-CoA; colesterol transferase (ACAT) which was limited to macrophages which were loaded by oxidized LDL [2]. Oxidized LDL was not taken by macrophages that were in the membrane as far as it was unable to inhibit the HMG-CoA reductase enzyme, so cholesterol synthesis in the cell itself continues. This situation caused an increase of cholesterol in the blood [9,10].

The variance analysis test showed that there was a significant effect ($p < 0.05$) on total cholesterol levels between the control group and the treatment group dosing *Garcinia mangostana L.* rind extract. This decrease was consistent with the results of previous studies conducted by Dachriyanus by giving as suspension of pure mangostin in mice showed a decrease in serum total cholesterol reaching 24% [3].

This decrease was due to mangosteen pericarp rind extract (Garcinia mangostana L.) which containing mangostin had an inhibitory activity against the inhibition of prostaglandin E release [11]. Prostaglandin E could cause resistance to the activity of the enzyme adenyl cyclase, an enzyme that converted ATP to cAMP. cAMP synthesis Obstacles resulted in inactive conversion of hormone-sensitive lipase enzymes into the active form of the lipase enzyme through protein kinase [17] to be disrupted. As a result the lipolysis process decreased [9.10]. The lipolysis reduction in adipose tissue resulted in a decrease in free fatty acids in the blood circulation. In this condition free fatty acids will enter the liver with low concentration. Decreasing the esterification concentration of free fatty acids to acylglycerol which transported from the liver in the form of VLDL decreased. Decreasing VLDL production resulted in a decrease of IDL levels which was the LDL former containing cholesterol. Therefore cholesterol in the blood circulation decreased [9.10].

The total cholesterol reduction also occured because of *Garcinia mangostana L.* rind extract containing mangostin is very effective in saving the use of α-tocopherols which are antioxidants and play a role in breaking the chain. α-tocopherols plays a role as donors of hydrogen phenolic and a less reactive radical tocopheroxyl substitutes (α -TO •) or as direct reactants with radical initiation to prevent the formation of LOO • to form non radical products (NRP) [14], one of which is *Malondialdehyde* [19]. Decreasing Malondialdehyde reduces *adducts* with amino acid side chains from apolipoprotein B-100 [9,10], resulting in reduced oxidation interaction and absorption of LDL by a lower affinity system called scavanger receptor which results in LDL oxidation containing cholesterol decreases [9,10]. Decreasing or damaging malondialdehyde resulted in reducing *adducts* between malondialdehyde and amino acid side chains of apolipoprotein B-100 and reducing the interaction and absorption of oxidized LDL by a lower affinity system called scavanger receptor [9,10]. As a result of reduced interaction and absorption of oxidized LDL, oxidized LDL was also reduced by macrophages resulting in fatty acyl substrates by the enzyme Acyl-CoA; colesterol transferase (ACAT) in macrophages that were filled with oxidized LDL was sufficient and would be able to inhibit the HMG-CoA reductase enzyme in cell membranes [2], so that cholesterol synthesis was reduced [9,10].

Conclusion

Giving rind extract of Garciniamangostana L. with a dose of 50 mg / kgBB, 150 mg / kgBB, 250 mg / kgBB and a dose of 350 mg / kgBB can significantly reduce total cholesterol levels of male hypercholesterolemic white mice with a significance level of $p < 0.05$.

References

1. AHA, American Heart Association : Hesrt and Stroke guide, Cholesterol statistical Update, Dallas, Texas ; 2004
2. Browns MS and Goldstein JL. : Drugs in The Treatment of Hypreproteinemias in Good mean. New York Mc.Grraw - Hill Medical Publishing Division : 2001
3. Dachriyanus, Delpa Oria Katrin, Rika Oktarina, Olivia Ernas, Suhatri and M.Husni Mukhtar : Artikel penelitian Uji efek α-mangostin terhadap kadar colesterol total, Trigliserida, kolesterol HDL, dan kolesterol LDL darah mencit putih jantan serta

penentuan letal dosis. J.Sains : Tek.Far.; 2007 : 12-2

4. Golberg. Prinsip-Prinsip Biokimia, Jakarta. Erlangga ; 2001 : 45 – 57
5. Hanafiah KA. : Rancangan Percobaan, Teori dan Aplikasi. Jakarta : Raja Grafindo Persada, 2003
6. Keigsburg KJ, Freb GB : Understanding the Essential of Blood Lipid Metabolism, Pathways of Lipid transport, 2003
7. Kusumawati D,. Bersahabat dengan hewan coba, Gajah Mada University Press, 2004 : 82-90
8. Lehniger : Dasar-Dasar Biokimia, jilid 3. Jakarta : Erlangga ; 2008
9. Robert K. Murray : Biokimia Harper. Edisi 29. Jakarta : EGC ; 2017
10. Murray RK, Granner DK, Mayes PA, Rodwell VW : Harper's Illuystrated Biochemistry, a LANGE Medical Book, 26/E. 2009 : 203-261
11. Nakatomi K, Yamakuni T, Kondo N, Arakawa T, Oosawa K, Shimura S, Inoue H, and Ohizumi Y, 2004, α Mangostin Inhibits Inhibitor-κB Kinase Activity and Decreases Lipopolysaccharide-Induced Cyclooxygenase-2 Gene Expression in C6 Rat Glioma Cells, Molecular Pharmacology 66 2004 : 667 – 674
12. Ruhyana : Hipertensi Penyebab Utama Penyakit Jantung. available from URL: http:// wordpres. com, acessed form Juni 10, 2007
13. Suyatna, Tony Handoko : Farmakologi dan terapi. Edisi 4. Universitas Indonesia Bagian Farmakologi Fakultas Kedokteran. 2008 : 370 – 373
14. Upston JM, Terentis AC, and Stocker R : Tocopherol - mediated peroxidation of lipoprotein ; implications for vitamin E as a potential anti atherogenic suplemen ; 13. The FASEB Journal. 1999 : 977- 999
15. Santoso, Buku Latihan SPSS Statistik Multivariat. Jakarta : Gramedia ; PT Elex Media Komputindo. 2002: 34-38
16. Smith JB, Soesanto Mangkoewidjojo. Pemeliharaan, pembiakan dan penggunaan hewan coba di daerah tropis. Jakarta : Universitas Indonesia. 1988 : 37-57
17. Stephen J. Mc Phee, William F. Ganong. Patofisiologi Penyakit: Pengantar Menuju Kedokteran Klinis, Edisi 5. Jakarta : EGC. 2012
18. Tati Sukarti, Roni Kastaman and Dwi Purnomo. Teknologi dan pengembangan bahan pewarna dari kulit buah manggis, available from URL: http // BPPT and Ristek : IPTEKnet , acessed form November 14, 2009
19. Williams P, Ongsakul M, Proudfoot J, Croft K, Bellin L : Mangostin inhibitits the oxidative modification of human low density lipoprotein. Harwood Academic Publishers Gmb H.23- 2, 1995 : 175 – 184
20. Zainuddin M. Metodologi Penelitian. Surabaya , Universitas Airlangga, 1995; 38 - 57

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