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The Effect of Administering Mangosteen Rind Extract *Garcia mangosta L.* to Decrease The Low Density Lipoprotein (LDL) Serum Level of A White Male Rat with Hypercholesterolemia

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Abstract
Hypercholesterolemia plays a role in the etiology of atherosclerosis that contributes in cases of coronary heart disease which is the leading cause of death worldwide. Stress, smoking, and consumption of a high cholesterol diet resulted in an increase in serum LDL. Modification of diet and management with hypolipidemic drugs including sourced from herbs one of which is Garcinia mangostana L. containing mangosteen will affect the decrease in serum LDL. The research design of posttest control group design between independent variables Garcinia mangostana L. rind extract with variable dependent serum LDL level. Types of research was the laboratory experimental studies. The population was the male white rat (Ratus norvegicus) 3-4 weeks old with weight 100-200 gram. Hypercholesterolemia was in male white rats with MDLT induction (high-fat diet foods). The data collection of measuring LDL serum level used an enzymatic method with spectrophotometer. The data analysis of this research used the Analysis of Variance (Anova). The effects of Garcinia mangostana L. rind extract on LDL levels in hypercholesterolemic white rats in experiments grouped to 7 consisted of a negative control group, a positive control group and a treatment group with 4 doses of 50, 150, 250 and 350 mg / kgBW. Serum LDL examination was performed on day 8 to see hypercholesterolemia and day 22 to see the effect of rind-enhancing Garcinia mangostana L on decreased serum LDL levels. The result of observation showed that a mangosteen rind extract Garcinia mangostana L on all given doses caused decreasing a LDL serum level significantly.

Keywords: *Garcinia mangostana L, LDL, Hypercholesterolemia*

I. INTRODUCTION

WHO data showed that a hypercholesterolemia gave 56% contribution to the coronary heart cases which caused 4.4 million people death a year. On 2020, It estimates that a coronary heart and stroke will be a main cause of death in the world and increasing more than 20 million or 24 million on 2030 (AHA, 2004). A hypercholesterolemia played a role in an atherosclerosis etiology that contributed to the coronary heart attack cases which was a main cause of death all around the world (AHA, 2004). Unhealthy lifestyle such as stress, smoking, high cholesterol diet consumption will increase the VLDL secretion by heart that causes the enhancement of LDL, then forming LDL (Murray *et al.*, 2003). High LDL concentration causes a saturation of receptor and then a change of LDL modification with oxidation into an oxidized LDL. Therefore, it is absorbed by a system with a less affinity in macrophage and other cells which is called *scavanger receptor*. It is not all oxidized LDL that taken from macrophage, as a result an oxidized LDL was excess and macrophage would change into "foam cell" encountered in an early atherosclerotic lesions (Brown *et al*, 2000).

The purpose of administering a medicine of hypolipidemic is to inhibit an enterohepatic circulation of bile acids, cholesterol absorption from gastrointestinal, and to prevent LDL oxidation (Murray *et al*, 2003). It also causes side effects that are gastrointestinal disorders, rin rash to liver dysfunction, and contra indication which it couldn't be consumed by everyone (suyatna dkk, 2005). A diet modification and management using a medicine of hypolipidemic which sourced from herbs is *Garcinia mangostana L.* It contained mangosteen that takes effect to the decreasing of Serum LDL Level. Mangosteen is effective as antioxidants to prevent the oxidation of unsaturated fats in LDL by metal ion (Cu^{2+}). Therefore, it results in a reactive aldehyde which as a kind of Malondialdehyde (MDA). As a result, the forming of adduct between aldehyde and a side chain of amino acids from Apolipoprotein B-100 in an oxidized LDL decreased. (Steinbrecher et al., 1989 ; Haberland et al,1984). So that the serum LDL level decreased.

II. METHODS

This study was a laboratory experimental that used a posttest control group design, between an independent variable that was a mangosteen rind extract *Garcinia mangostana L* and a dependent variable that was a LDL serum level. The population was a white male rat (*Ratus Norvegicus)*, 3-4 weeks old with weight 100-200 gram. There were six

rates of each group. The data collection of measuring LDL serum level used an enzymatic method with spectrophotometer. The data analysis of this study was Analysis of Variance (Anova).

III. RESULTS

Table 1. The result of a dependent variable test on on the groups of pre-induced MDTL and post-induced MTDL

Dependent Variable	Group		Sig. (p)
	Pre- (K.1), N = 6	Post- (K.2), N = 6	
Cholesterol LDL (Mean ±SD)	7.50 ± 0.83	14.67 ± 2.06	0.000

The result of study on table 1 showed that LDL cholesterol on post-induced MTDL group increased significantly compared to post-induced MTD group with p = 0.000 for LDL cholesterol.

A. The data of LDL serum level of a control group and intervention group

Table 2. The mean score and standard deviation of dependent variables on two groups

Groups		LDL serum level (mg/dl)
Control (K.3) n = 6	Mean	13.67
	Standard Deviation	4.67
Extract: 50 mg (K.4) n = 6	Mean	9.00
	Standard Deviation	2.75
Extract: 150 mg (K.5) n = 6	Mean	7.83
	Standard Deviation	0,75
Extract: 250 mg (K.6) n = 6	Mean	8.17
	Standard Deviation	0.98
Extract: 350 mg (K.7) n = 6	Mean	8.67
	Standard Deviation	0.516

B. The result of Analysis of Variance

Table 3. The result of Analysis of Variance of dependent variable on a control group and intervention group (used rind extract *Garcinia mangostana L.*)

Dependent Variable	F	Sig.
LDL serum level	5.482	0.003 *

The table above was based on the mean of LDL serum level of control group and intervention group which administered by using rind extract *Garcinia mangostana L.* on doses 50 mg/kgBB, 150 mg/kgBB, 250 mg/kgBB and 350 mg/kgBB. From the table could be derived a result that showed p value < 0.05 on LDL serum level p = 0.003.

C. The result of LSD Test

The result of LSD Test was conducted on the LDL serum level which is significantly decreasing on LDL serum level p = 0.003.

Table 4. The result of LSD Test

Dependent Variable	Group (I)	Group (J)	Deferential Mean (I-J)	Std. Error	Sig.
LDL serum level	Control (K. 3) N = 6	Exctract 50 mg (K.4)	4.667*	1.444	0.003
		Exctract 150 mg (K.5)	5.833*	1.444	0.000
		Exctract 250 mg (K.6)	5.500*	1.444	0.001
		Exctract 350 mg (K.7)	5.000*	1.444	0.002
	Exctract 50 mg (K.4) N = 6	Control (K.3)	-4.667*	1.444	0.003
		Exctract 150 mg (K.5)	1.167	1.444	0.427
		Exctract 250 mg (K.6)	0.833	1.444	0.569

Dependent Variable	Group (I)	Group (J)	Deferential Mean (I-J)	Std. Error	Sig.
		Exctract 350 mg (K.7)	0.333	1.444	0.819
	Exctract 150 mg(K.5) N = 6	Control (K.3)	-5.833*	1.444	0.000
		Exctract 50 mg (K.4)	-1.167	1.444	0.427
		Exctract 250 mg(K.6)	-0.333	1.444	0.819
		Exctract 350 mg (K.7)	-0.833	1.444	0.569
	Exctract 250 mg (K.6) N = 6	Control (K.3)	-5.500*	1.444	0.001
		Exctract 50 mg (K.4)	-0.833	1.444	0.569
		Exctract 150 mg (K.5)	0.333	1.444	0.819
		Exctract 350 mg (K.7)	-0.500	1.444	0.732
	Exctract 350 mg (K.7) N = 6	Control (K.3)	-5.000*	1.444	0.002
		Exctract 50 mg (K.4)	-0.333	1.444	0.819
		Exctract 150 mg (K.5)	0.833	1.444	0.569
		Exctract 250 mg (K.7)	0.500	1.444	0.732

Based on table 4, there was a significant decrease in the difference ($p < 0.05$) for serum LDL levels between controlled group and rin extract group of Garcinia mangostana L. dose of extract 50 mg / kg bb ($p = 0,003$), 150 mg / kgBB ($p = 0.000$), dose of extract 250 mg / kgBB ($p = 0,001$) and dose of extract 350 mg / kgBB ($p = 0,002$). While the dose of extract 50 mg / kgBB showed no significant relationship with the dose of extract 150 mg / kgBB ($p = 0,427$), dose of extract 250 mg / kgBB ($p = 0,569$) and dose of extract 350 mg / kgBB ($p = 0,552$).

Table 4 shows a significant decrease between dose 150 mg / kgBW with control ($p = 0.000$) and no significant decrease with dose of 250 mg / kgBW ($p = 0,819$) and 350 mg / kgBB extract dose ($p = 0,569$). While at a dose of 250 mg / kgBB.

At dose of extract 250 mg / kgBB showed significant relation with control group ($p = 0,001$) and not significant with dose of extract 50 mg / kgBB ($p = 0,569$), dose of extract 150 mg / kgBB ($p = 0,819$) and dose of extract 350 mg / kgBB ($p = 0.732$). While the dose of extract 350 mg / kgBB showed a significant relation with control ($p = 0,002$) and not significant with dose of extract 50 mg / kgBB ($p = 0,819$), dose extract 150 mg / kgBB ($p = 0,569$) and dose of extract 250 mg / kgBB ($p = 0.732$).

IV. DISCUSSION

The induction of high-fat diet (MDTL) foods in white rat derived from a mixture of cow's fat with palm oil in a ratio of 1: 5 as much as 2% of body weight for 7 days aimed at optimizing blood cholesterol levels of rat. The induction of high-fat diet foods (MDTL) containing saturated fats of sterols and triglycerides is thought to lead to a decrease in LDL receptors and the formation of smaller VLDL particles containing more cholesterol (Murray et al., 2003). The increase in LDL due to increased VLDL resulted in the taking up of LDL receptors in saturation so that LDL was converted to a modified LDL with oxidation not recognized by LDL receptors (Murray et al., 2003). Oxidized LDL occurs due to the increase of triacylglycerol in VLDL that is not lipolysis by lipoprotein lipase enzyme to be transferred by CETP (cholesteryl esters transfer prootein) into LDL, resulting in an increase in the formation of LDL rich in triacylglycerol called small dense LDL. This increase in LDL levels facilitates the oxidation process of LDL compounds (Godberg, 2001). The oxidized LDL interacts well and is absorbed by the lower-affinity system within the macrophages and other cells called the scavanger receptor. But not all oxidized LDLs are taken macrophages. This is due to the availability of fatty acyl co-substrates by the Asyl-CoA enzyme; cholesterol transferase (ACAT) is limited to the macrophages containing the oxidized LDL (Brown et al., 2000). Unacceptably oxidized LDLs in the cell membrane are not able to inhibit the enzyme HMG-CoA reductase, so the synthesis of cholesterol in the cell itself persists. This leads to an increase in blood cholesterol (Murray et al., 2003).

The variance analysis showed significant effect ($p < 0.05$) on serum LDL level between control group and dose group of Garcinia mangostana L. rin extract, containing Mangostin, 50 mg / kg bb ($p = 0,003$) extract dose, 150 mg / kgBW ($p = 0.000$), dose of extract 250 mg / kgBB ($p = 0,001$) and dose extract 350 mg / kgBB ($p = 0,02$). This is because Mangostin is effective in saving the use of α-tocopherol as an antioxidant chain breaker so that the role of α-tocopherol as a hydrogen phenolic donor and a less reactive tocopheroxyl substitute (α -TO) or as a direct reactant

with initiation radicals to prevent LOO formation to form non radical products (NRP) (Upston et al., 1999) one of which is Malondialdehyde also decreased (William et al., 1995). The reduction of Malondialdehyde reduces adducts by amino acid side chain from apolipoprotein B-100 (Gillote et al 2000) resulted in decreased interaction and absorption of LDL oxidized by a lower-affinity system called scavanger receptor (Gillote et al 2000) which resulted in decreased LDL oxidation or malondialdehyde damage, results in reduced adducts between malondialdehyde and amino acid side chains of apolipoprotein B-100 (Gillote et al 2000) and reduces the interaction and absorption of oxidized LDL by lower-affinity systems called scavanger receptor (Gillote et al 2000). Due to the reduced interaction and absorption of oxidized LDL, the oxidized LDL is also removed by macrophages so that the co-substrates of fatty acyl by Asyl-CoA enzyme; cholesterol transferase (ACAT) in macrophages containing sufficiently oxidized LDL and will be able to inhibit the enzyme HMG-CoA reductase in cell membrane (Brown et al., 2000) so that cholesterol synthesis is reduced (Murray et al., 2003).

V. CONCLUSION

Giving of Garcinia mangostana L. rin extract with dose 50 mg / kgBB, 150 mg / kgBW, 250 mg / kgBW and dose 350 mg / kgBW significantly decreased LDL serum level of hypercholesterolemia male white rat.

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