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Effect of Freeze-Dried Soyghurt on Malondialdehyde (MDA) Levels in Hypercholesterolemic Rats

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Abstract

Hypercholesterolemia is still one of the health problems in Indonesia, as high cholesterol levels can cause lipid peroxidase reactions that can lead to oxidative stress, which has a negative impact on health. High oxidative stress can be measured by the biomarker malondialdehyde (MDA). Soyghurt is one alternative non-pharmacological option for reducing cholesterol levels. This study aims to determine the effect of soyghurt on MDA levels, which plays a role as a marker of oxidative stress due to hypercholesterolemia. The research method used in this study is analytic experimental laboratory, using 30 male Wistar rats divided into 5 groups: negative control, positive control, treatment group 1 (high fat diet and simvastatin), treatment group 2 (high fat diet and soyghurt), and treatment group 3 (high fat diet and combination of soyghurt-simvastatin). The results of this study showed a decrease in MDA levels in treatment groups 1, 2, and 3, but the most significant results were observed in treatment group 2, which is the group of rats with a high fat diet treated with soyghurt. This is due to the biotransformation process between simvastatin and probiotic bacteria that produces metabolite M1, which can reduce the therapeutic effect of simvastatin. Therefore, further research is needed to determine the interaction between soyghurt and simvastatin.

Keyword: Hypercholesterolemia, Soyghurt, Simvastatin, Malondialdehyde

INTRODUCTION

The lifestyle of people who pay less attention to health can cause a person to fall into a state of hypercholesterolemia. Hypercholesterolemia is a condition where cholesterol levels in the blood exceed normal values. Some factors that can cause hypercholesterolemia are genetics, age, gender, physical activity, and diet ("Berapa Nilai Normal Kolesterol Total? - Direktorat P2PTM," n.d.; Zulfamidah, Abdullah Rezky Putri Indarwati, & Fajriansyah, 2022).

Hypercholesterolemic conditions can indicate the accumulation of free radicals in the body which are unpaired electron molecules and are highly reactive so that they will cause oxidative stress characterized by high levels of MDA (Tuminah, 2009).

Currently there is a lot of research on phytopharmaceutical treatments, one of which is soyghurt, soyghurt is soy milk yogurt. Soyghurt is a probiotic drink that is high in isoflavones and useful as an antioxidant. Soyghurt used is in freeze-dried form because it has higher viability than in wet form (Handayani & Wulandari, 2016; Labiba, Marjan, & Nasrullah, 2020).

Probiotics Lactobacillus acidophilus and Bifidobacterium bifidum are included in Lactic Acid Bacteria (LAB). prebiotics can reduce ROS by producing proinflammatory cytokines in the form of IFN-1 through the Toll-like Receptor-4 (TLR-4) pathway and reducing inflammatory factors through the Nuclear Factor Kappa B (NF-kB) pathway. Thus this study aims to determine the effect of freeze-dried soyghurt on MDA levels in hypercholesterolemic rats (Markowiak & Ślizewska, 2017; McNab, Mayer-Barber, Sher, Wack, & O'Garra, 2015; Yuniar Wulandari & Padaga, n.d.).

METHODS

This study uses the pretest and posttest method of probiotic administration and the method used is Laboratory Experiment because in its implementation this study uses research animals, namely 30 wistar strain rats which are divided into 5 groups, namely the negative group (KN), positive group (KP), simvastatin group (P1), soyghurt group (P2), and combination group *(soyghurt-simvastatin)* (P3) taken using a complete randomized design method which is analyzed using dependent sample T-test analysis and one way anova post hoc tukey. Before conducting the study, the researcher had obtained an ethical permit with letter number 025/UH1.09/2023, November 10, 2023.

RESULTS

This study was conducted in the animal laboratory, biochemistry laboratory, and microbiology laboratory of Jenderal Achmad Yani University with a total of 30 samples that met the research criteria. Patient data is attached in table 1.

Table 1. Comparison of cholesterol levels before and after fat induction

Group	Before	After	Difference	Percentage
KN	72	73	-1	2%
KP	76	83	-7	14%
P1	67	88	14	28%
P2	65	91	19	38%
P3	66	81	9	18%

It can be seen in table 1 that the percentage increase in all groups of rats before and after the induction of a high-fat diet, namely using a mixture of palm oil, egg yolk, and lard, shows that the provision of a high-fat diet can cause hypercholesterolemia conditions (Anggraeni, Fakhruddin, & Irawan, 2021).

Table 2. Comparison of MDA levels before and after treatment

Group	Before	After	Difference	Percentage
KN	0,0043	0,0033	0,0010	6%
KP	0,0078	0,0047	0,0031	17%
P1	0,0065	0,0017	0,0048	27 %
P2	0,0074	0,0014	0,0060	33%
P3	0,0065	0,0035	0,0030	17%

Table 2 shows the difference before and after treatment for each group, it appears that the biggest difference is in P1 and P2 with a difference of 27% and 32%, respectively, for the decrease in soyghurt, it is because soyghurt has antioxidants that can reduce oxidative stress, while in P3 there is also a decrease but not as high as P1 and P2.

Table 3. Test results of group comparison before and after treatment

Group		N	MDA Average (*mg/dl*) ± SD	Difference	SE	p
Negative	Before	6	0,0043 ± 0,00066	0,0010	0,00038	0,364
	After	6	0,0033 ± 0,00095		0,00054	
Positive	Before	6	0,0078 ± 0,0001	0,0038	0,00006	0,074
	After	6	0,0040 ± 0,0020		0,00115	
Simvastatin	Before	6	0,0065 ± 0,0013	0,0046	0,00073	0,008
	After	6	0,0019 ± 0,0007		0,00040	
Soyghurt	Before	6	0,0074 ± 0,0023	0,0060	0,00131	0,056
	After	6	0,0014 ± 0,00067		0,00038	
Combination	Before	6	0,0067 ± 0,00026	0,0031	0,00015	0,097
	After	6	0,0035 ± 0,00169		0,00097	

In Table 3. the result of p <0.05 in the simvastatin group means that there is an improvement before and after treatment in that group while in the soyghurt group has a result of p>0.05, but when viewed from the mean difference between soyghurt and simvastatin, the

difference is higher in the soyghurt group, therefore in this study there are 2 groups that have improvements, namely the soyghurt and simvastatin groups.

Table 4. Comparison test of MDA levels between groups using post hoc tests

No	Variabel		p-Value	Mean Difference	Description
1.	Negative Group (KN)	KP	0.002	-0,0045	Significantly Different
		P1	0.303	0.0017	Not Significantly Different
		P2	0.181	0.0020	Not Significantly Different
		P3	1.000	-0.0002	Not Significantly Different
2.	Positive Group (KP)	P1	0.000	0.0061	Significantly Different
		P2	0.000	0.0064	Significantly Different
		P3	0.002	0.0043	Significantly Different
3.	Treatment 1 (P1)	P2	0,995	0.0003	Not Significantly Different
		P3	0.216	-0.0019	Not Significantly Different
4.	Treatment 2 (P2)	P3	0.126	-0.0021	Not Significantly Different

From the results of the Tukey post hoc analysis test, there is a significant difference ($p < 0.05$) between the KN-KP group, this shows the difference in MDA levels between negative group rats that are not induced by fat with groups that get fat induction, where the KP group has higher MDA levels than KN, meaning that fat induction can cause oxidative stress. Significant differences ($p < 0.05$) are found in KP-P1, KP-P2 and KP-P3, this shows the administration of simvastatin, soyghurt, and a combination of both can reduce MDA levels in hypercholesterolemic rats induced by a high-fat diet, the treatment between these groups has a different decreasing effect seen from the mean difference of the soyghurt group has a higher decrease compared to simvastatin and the combination, P3 has a low mean difference compared to simvastatin and soyghurt treatment.

DISCUSSION

The results of this study are in line with the research "Simvastatin ameliorates oxidative stress levels in HepG2 cells and hyperlipidemic rats" conducted by HMG-CoA β-Hydroxy β-methylglutaryl-CoA (HMG-CoA) Verma K., et al in their research simvastatin can reduce MDA levels indirectly by inhibiting HMG-CoA β-Hydroxy β-methylglutaryl-CoA (HMG-CoA), because with high HMG-CoA can produce ROS that cause inflammation and cell damage (Verma et al., 2022). Another research that is in line is "The effect of yogurt and

cinnamon soyghurt *(Cinnamomum burmannii)* on blood glucose levels, serum insulin, and malondialdehyde of pre-metabolic syndrome rats" by Rustanti et al. (2020) where in his research soyghurt can reduce oxidative stress because it contains probiotics and antioxidants, namely isofalvone, probiotics reduce oxidative stress by producing pro-inflammatory cytokines in the form of IFN-1 which inhibits NF-kB, while isoflavone has a factor-2 that can donate hydrogen ions, namely hydroxyl and peroxyl so that free radicals will be stabilized.

The reason why the combination group of soyghurt and simvastatin was not the best group was explained in the study "Bioaccumulation and biotransformation of simvastatin in probiotic bacteria: A step towards better understanding of drug-bile acids-microbiome interactions" by Danic M. et al simvastatin is a drug with low water solubility and high permeability, in terms of its chemical structure contains an aromatic backbone attached to the dimethylbutanoic acid arm with an ester bond and an ethyl pyranyl arm that forms a C-C covalent bond to form a lactone structure, lactone acids are easily metabolized by bacterial enzymes and form metabolite M1, namely the hydroxy acid form which is the result of metabolic biotransformation of simvastatin by the esterase of probiotic bacteria L. coli. acidophillus and bifidobacterium, this causes a decrease in the therapeutic effect of simvastatin, so that the decrease in cholesterol and MDA levels is not significant (Đanić et al., 2023).

CONCLUSIONS

Based on the research that has been done, researchers can conclude that the effect of giving *soyghurt simvastatin* and a combination *(soyghurt-simvastatin)* can reduce MDA levels in hypercholesterolemic rats, after being calculated using SPSS, the best decrease is obtained in the soyghurt treatment group followed by simvastatin and a combination *(soyghurt-simvastatin)* when viewed from the mean difference. This is due to the biotransformation of simvastatin by probiotic bacteria into metabolite M1 so that there is a decrease in the content of simvastatin in the body.

CONFLICT OF INTEREST

The author's statement that there is no conflict of interest in the scientific article written.

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