ISSN XXXX-XXXX (Online) | XXXX-XXXX (Print) | Vol. 1, No. 2, April (2023), pp. 55-60

Published by: IARN Institute

International Journal on Health and Medical Sciences

Journal homepage: https://journals.iarn.or.id/index.php/HealMed/index

Effect of gambir catechins on cholesterol levels of mice hypercholerolemia

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Article Info

Article history:

Received Mar 6, 2023
Revised Mar 17, 2023
Accepted Apr 14, 2023

Keywords:

Gambir;
Catechin;
Cholesterol.

ABSTRACT

Hypercholesterolemia is a condition characterized by increased level of cholesterol in the blood exceeding the normal threshold. Gambir (*Uncari gambir Roxb.*) contains chemical compounds, namely flavonoid, specifically catechin. Catechin in gambir has the potential to increase fat metabolism therefore it has the potential to reduce cholesterol level in the body of mice. The purpose of this study is to determine the effect of gambir catechin on cholesterol levels in hypercholesterolemic mice. The study is an experiment with a Completely Randomized Design (CRD) with two control groups and three treatment groups those are K negative was not given treatment, K positive was induced by simvastatin after induction of a high-fat diet, P1, P2 and P3 were induced by catechin with different concentrations of 50%, 80% and 90% after being induced by a high-fat diet. Cholesterol level was checked with Easy touch GCU. Data was analyzed by One Way of Variance (ANOVA) followed by 5%-degree DMRT test. The result shows that gambir catechin has the effect ($p<0.05$) on reducing cholesterol level in hypercholesterolemic patients. The most effective using of catechin with the level of concentration of catechin is at 90%.

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1. INTRODUCTION

Uncaria gambir is a typical plant from West Sumatra, North Sumatra, Riau, and South Sumatra. Gambir is a plant commodity that has high economic value for Indonesia. Indonesia is the largest supplier of gambier in the world, which is 80%, and 90% of Indonesia's gambier supply is produced from West Sumatra. Gambir is widely used by the community for betel, tanning. Gambir is a product produced from plants with Latin (U. *gambir*) (Dhalimi, 2006). This plant contains the main components of catechins and tannins (Rauf & Siregar, 2015). According to Ermiati, (2004), gambier can be used as a mixture of drugs, for burns, headaches, diarrhea, dysentery, canker sores, skin pain medication and complementary to betel consumption. Amalia (2009) stated that gambier extract can act as an immunomodulator (Anggraini et al., 2011; Hadad, 2007).

The potential of gambier cannot be separated from the bioactive compounds contained in it. According to Heitzman et al., (2005), gambier contains polyphenols such as alkaloids, terpenoids, flavonoids and other polyphenolic compounds. Flavonoids are the largest phenolic compounds in nature. The flavonoid components contained in gambier include catechin (7-33%), pyrocatechol (20-30%) and quercetin (2-4%). The catechins in gambier are polyphenolic compounds that act as antimicrobial and antioxidant compounds, in gambier it was also found to contain Fe. The Fe content in gambier can trigger an increase in red blood cell levels in the blood, so that it can increase Hb levels and prevent anemia. Consumption of gambier is safe to use, even in high doses (up to 200 µg mL-1). (Nazir, 2000; Santoso, 2012) (G. P. Sari, 2010) (Alfaridz, 2018) (Latifat, 2015).

In the research, (Yeni et al., 2017; Yeni, Syamsu, et al., 2014) stated that the compounds contained in the gambier plant have considerable potential in its development as modern medicine, especially in dealing with various health problems whose prevalence is getting higher, one of which is hypercholesterolemia (a condition characterized by increased levels of cholesterol in the blood exceeding the threshold). normal). Hypercholesterolemia can occur due to unhealthy eating patterns, especially the tendency of people to consume fast food, one of which is high-fat foods. The thing that causes the danger of high-fat foods is if cooking oil is used repeatedly. Hypercholesterolemia causes atherosclerosis. Hypercholesterolemia is thought to also affect the stability of blood values, such as protein albumin, hemoglobin and hematocrit (Soeharjo, 1989; Waspadji, 2007).

Hypercholesterolemia is a disorder of fat levels in the blood (dyslipidemia) where cholesterol levels in the blood are more than 240 mg/dl, Low Density Lipoprotein (LDL) levels are more than 160 mg/dL and High-Density Lipoprotein (HDL) levels are less than 40 mg/dl. dL.1 Hypercholesterolemia is a condition in which the level of cholesterol in the blood exceeds the required limit. This occurs due to changes in blood vessel walls, increased hypoxide in the colon tissue, changes in homeostasis of hereditary age cells, dietary errors, lifestyle, environmental pollution, alcohol consumption and smoking in the long term. In addition, hypercholesterolemia can occur due to several factors, such as body weight, age, the aging process, decreased estrogen levels in postmenopausal women and daily food consumption patterns that are high in cholesterol (H. Sari, 2010) (Suyatna & Handoko, 2007; Wibowo, 2009).

WHO reports that 30% of the number of deaths in the world is caused by cardiovascular disease and is predicted to be the leading cause of death in the world in the next two decades and will affect almost 23.3 million people in the world by 2030. Southeast Asia has contributed to the death toll. 28% of all deaths from cardiovascular disease. Deaths due to coronary heart disease (CHD) were ranked the most at 7.2 million deaths, with details for people aged 15-59 years at 1.332 million and aged 60 years and over 5.825 million. Indonesia has contributed about 37% of deaths per year for cardiovascular disease and the reported death rate from CHD was around 100,000 – 499,999 people in 2002. Based on the Riskesdas, cases of cardiovascular disease in West Sumatra reached 700,000 thousand people per year. Coronary heart disease (CHD) is the most frequent cause of death and in Indonesia is ranked 3rd (three) causes of death due to CHD and more than half of these deaths occur due to hypercholesterolemia.

One of the efforts made in diet modification is to consume functional foods that can provide physiological benefits to the body. One of the uses of functional food in controlling and reducing blood cholesterol levels including blood LDL levels is the use of gambir catechin isolates (Rauf & Siregar, 2015). Gambir catechin is a compound consisting of epicatechin-3-gallte, epigallocatechin-3-3 gallate, and epigallocatechin. The catechin isolate has potential as an antioxidant, anticardiogenic, anti-inflammatory, thermogenic, probiotic and anti-microbiological. The presence of catechins in gambier extract has high antioxidant activity, works as a free radical scavenger and can be used to repair or restore vascular endothelial function which is characterized by an increase in the amount of endothelium derived relaxing factor (EDRF) or nitric oxide (NO) (Sitompul, 2003; Winarsi, 2007). In addition, catechins have anti-obesity, hypoglycemic and hypolipidemic effects and have the potential to increase fat metabolism and reduce fat levels in the body.

2. RESEARCH METHOD

This research is experimental research. This research was carried out in August December 2021 at the Animal Physiology Laboratory and Animal House, Department of Biology, Faculty of Mathematics and Natural Sciences, Universitas Negeri Padang.

The tools used in this study were rat cages, cables, fans, rat feeding containers, drinking bottles, analytical scales, measuring cups, beakers, stirring rods, solution bottles, 1 ml sonde, cholesterol strips (easy touch), strips and scissors. medical. The materials used in this study were gambir catechins, male mice aged 8-10 weeks weighing 30-35 grams, pellets, drinking water, rice husks, quail egg yolk, aquades, alcohol swabs, and red medicine, PTU (Propiltiourasil).

This study is an experimental study with a completely randomized design (CRD), with 2 control groups and 3 treatment groups consisting of positive control given simvastatin, negative control, P1, P2, P3, using 25 samples of mice with a duration of 30 days (Rauf & Siregar, 2015).

Sampling of mice by acclimatization for 7 days, then fasted for 12 hours. Then the mice were induced to eat a high-fat diet in the form of fresh quail egg yolk 30 mg. homogeneous volume of quail egg yolk given to mice is 0.5 ml/20 mg g BW for 14 days orally. Cholesterol levels were measured 3 times, namely on the 8th day, 23rd day and 30th day. Measurement of cholesterol levels in mice was carried out by taking blood from the tails of mice and measured using cholesterol strips (easy touch). Data were analyzed by oneway variance (ANOVA) followed by a 5% DMRT follow-up test.

3. RESULTS AND DISCUSSIONS

Cholesterol in mice before the experiment under normal conditions, then induced by quail egg yolk and propyltyouracil for 14 days to make mice hypercholesterolemia. Where the change from normal to hypercholesterolemia can be seen clearly in table 1.

Tabel 1. Cholesterol levels in mice under normal conditions to hypercholesterolemia.

Rancangan	No. Sampel	Kadar Kolesterol (mg/dL)				
		Day First	Acclimatization for 7 days until the 8th day	PDTL 0.5 ml for 14 days	Administration of simvastatin 0.5 ml for 7 days	Induction Catechin 0.5 ml for 14 days until day 30
K-	1	Lo	102	THERE ISN'T ANY TREATMENT	THERE ISN'T ANY TREATMENT	THERE ISN'T ANY TREATMENT
	2	Lo	105			
	3	Lo	107			
	4	Lo	101			
K+	1	Lo	102	210	125	THERE ISN'T ANY TREATMENT
	2	Lo	109	185	108	
	3	Lo	112	174	119	
	4	Lo	105	172	102	
P1 Katekin 50% Dosis 100 mg/kg	1	Lo	103	157	THERE ISN'T ANY TREATMENT	168
	2	Lo	98	152		162
	3	Lo	106	167		158
	4	Lo	108	148		148
P2 Katekin 80% Dosis 100 mg/kg	1	Lo	120	196	THERE ISN'T ANY TREATMENT	142
	2	Lo	108	206		138
	3	Lo	112	176		135
	4	Lo	107	193		132
P3 Katekin 90% Dosis 100 mg/kg	1	Lo	103	172	THERE ISN'T ANY TREATMENT	105
	2	Lo	106	192		102
	3	Lo	100	165		104
	4	Lo	97	158		111

The results of the study on the effect of giving gambir catechins on cholesterol levels in hypercholesterolemic mice show the following results in table 2.

Tabel 2. average cholesterol levels of mice in hypercholesterolemic conditions and after giving gambier catechin.

Average cholesterol levels in mice				
Treatment	PREE	POST	STD PREE	STD POST
K-	103,75	103,75	2,745	2,745
K+	164,25	118,5	17,462	10,41
P1 50% 100	154	159	8,206	8,406
P2 80% 100	156,25	136,75	12,473	4,272
P3 90% 100	185,25	105,5	14,66	3,873

Based on Table 2. Shows the average cholesterol levels of mice during hypercholesterolemia (after a high-fat diet) and after treatment with gambir catechin intake at various concentrations with the same dose according to the experimental design which showed an increase and decrease in cholesterol levels in mice.

Tabel 3. Percentage reduction in cholesterol levels in mice.

Group	Average Cholesterol Levels mg/dL
K-	103,7 [a]
K+	113,5 [a]
P1	157,25 [c]
P2	138,9 [b]
P3	108,5 [a]

Table 3. Shows cholesterol levels of mice after intake of gambir catechins, where the table shows that the most optimum decrease at 90% concentration P3 is 108.5 mg/dL, at K+ shows the optimum decrease is 113.5 mg/dL, while at P2 there is a slight optimum decrease in concentration of 80% and at P3 there was no significant decrease in the concentration of 50% catechins. This research has been successfully carried out by obtaining data on cholesterol levels of mice after treatment with gambir catechins with various concentrations used with the same dose, the results showed that gambir catechins had an effect on cholesterol levels in hypercholesterolemic mice (Lewis & Rader, 2005; Mu'nisa et al., 2018).

Giving quail egg yolk is thought to increase fat accumulation in the liver. Guyton. A. C and J. E. Hall, (2006) stated that a saturated fatty acid diet causes an increase in fat accumulation in the liver, resulting in an increase in acetyl CoA in liver cells to produce cholesterol, as a result, cholesterol levels in the blood increase. Free radicals contained in frying oil are thought to be able to oxidize LDL, causing various damage.

Usoh et al., (2005) stated that free radicals contained in quail egg yolks can damage nucleic acids, proteins and lipid membranes so that they can cause liver damage(Fajrin, 2010). Added that liver damage can interfere with the metabolism and excretion of cholesterol from the body so that total cholesterol levels can increase. Giving gambier with various dose levels can inhibit the increase in cholesterol in mice given quail egg yolk compared to control. This is because gambier contains compounds that are antioxidants, one of which is catechins. This is in accordance with what was stated by Ekawati, (2007) catechins are strong antioxidants with the ability to scavenge free radicals originating from oxygen, including reactive OH (Yeni, Syamsu, et al., 2014).

The dose in each experimental group showed a significant decrease in cholesterol levels in the P2, P3 and K+ groups. While in P1 there was an increase in cholesterol levels. At P2 the concentration of 80% and a dose of 100 mg/kgBW showed a decrease from 192.75 mg/dL to 136.75 mg/dL with an average decrease of 56 mg/dL. Whereas in P3 which was given a concentration of 90% with a dose of 100 mg/kgBW, there was a decrease from 171.75 mg/dL to 105.5 mg/dL with an average decrease of 66.25 mg/dL. And for K+ given a dose of simvastatin which is a commercial cholesterol-lowering drug, it can reduce cholesterol levels in mice from 185.25 mg/dL to 118.5 mg/dL with an average decrease of 66.75 mg/dL.

According to Diaz et al., (1997), antioxidants play a role in protecting LDL against oxidation. In addition, according to Langseth, (1995) antioxidants protect cells from reactive oxygen species

(RO) or other radical species through oxygen-radical scavenger mechanisms such as catalase enzymes, super-oxidation mutases and glutathione peroxidase. Catechins can reduce cholesterol, LDL and triglyceride levels. The mechanism of this reduction is by increasing Lipoprotein lipase, so that the catabolism of triglyceride-rich lipoproteins such as VLDL (Very Low-Density Lipoprotein) and IDL (Internediet Density Lipoprotein) increases. HDL (High Density Lipoprotein) cholesterol levels increase indirectly due to decreased VLDL triglyceride levels. The effect of lowering LDL cholesterol is thought to be related to increased clearance of VLDL and IDL in the liver so that LDL production decreases. Sitompul, (2003) added that antioxidants through their mechanism can inhibit and prevent LDL damage due to oxidation, which in turn can reduce cholesterol levels in the blood (Yeni, Sa'id, et al., 2014).

Induction of a diet high in cholesterol and fat for 28 days was able to significantly increase triglyceride levels when compared to mice without food induction. Increased intake of fat, cholesterol, cholic acid and PTU from food in the high cholesterol and fat diet group caused an increase in the lipogenesis activity of experimental animals, so that the free fatty acids formed increased. Furthermore, there is mobilization of free fatty acids from fatty tissue to the liver and binds to glycerol to form triglycerides. Thus, the higher the consumption of fat, the higher the synthesis of triglycerides in the liver so that the level of triglycerides in the blood will increase.

This decrease in cholesterol levels occurred at concentrations of 80%, 90%, and in positive controls who were given a dose of simvastatin. Simvastatin used as a comparison also has an anticholesterol mechanism by competitively inhibiting the HMG-CoA reductase enzyme which functions as a catalyst in the formation of cholesterol. However, the K+ group gave a higher decrease than the P1 and P2 groups because the P1 and P2 groups did not give a significant result.

Meanwhile, the right concentration and dose of gambir catechins to reduce cholesterol levels in the body of mice is a concentration of 90%. As well as a concentration of 80% can reduce cholesterol levels well, this proves that the decrease in cholesterol levels in the body of mice is influenced by high concentrations in. Based on the results of the 5% DMRT test, it was concluded that the treatment that could reduce cholesterol levels was the treatment at P3 which was 108.5 mg/dl, because it had a significant effect on cholesterol levels. This shows that the consumption of gambier catechins with a concentration of 90% at a dose of 100 mg/kg BW has proven to be effective in reducing cholesterol levels in the body of mice. Due to the high levels of catechins contained in gambier, gambier has strong antioxidant activity so that it can help lower triglyceride levels in the blood and make cholesterol levels normal (Wibowo, 2009).

4. CONCLUSION

Gambier catechins (*Uncaria gambir* Roxb.) affect cholesterol levels in mice (Mus musculus L.) Hypercholesterolemia. Gambier catechin (*Uncaria gambir* Roxb.) with a concentration of 90% has the most effective effect on reducing cholesterol levels in mice (Mus musculus L.) Hypercholesterolemia. Data was analyzed by One Way of Variance (ANOVA) followed by 5%-degree DMRT test. The result shows that gambir catechin has the effect ($p<0.05$) on reducing cholesterol level in hypercholesterolemic patients.

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