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The Activity Test of Soursop Fruit Juice (Annona muricata L) on Decreasing Cholesterol Levels in Male Mice (Mus musculus)

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The increased cases of hypercholesterolemia in Indonesia encourage the public to make prevention and treatment efforts. Soursop fruit is an option because it has properties to lower blood cholesterol levels be a potential source of antioxidants, which can inhibit oxidation reactions by binding to free radicals and highly reactive molecules. The aim of this study was to determine the effect of soursop fruit juice (Annona muricata L) on the total blood cholesterol levels of male mice (Mus musculus). This type of research is an experimental study of benefit testing, with a comparison group (pre-test and post-test with control group design). This research was conducted at the Pharmacology and Natural Materials Laboratory of STIK Siti Khadijah Palembang for 21 days. The sample in this study was male mice aged 6-8 weeks with an average body weight of 20-30 grams of normal mice, which met the inclusion and exclusion criteria. The number of samples is 25 male mice. There was a significant relationship between the cholesterol levels of mice before and after being given soursop fruit juice. It was concluded that the administration of soursop fruit juice effected reducing blood cholesterol levels. It is recommended that further research be conducted on human samples.

Kata kunci:

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A B S T R A K

Meningkatnya kasus hiperkolesterolemia di Indonesia mendorong masyarakat untuk melakukan usaha pencegahan dan pengobatan. Buah sirsak menjadi pilihan karena memiliki khasiat untuk menurunkan kadar kolesterol darah, menjadi sumber antioksidan yang potensial. yang mampu menghambat reaksi oksidasi dengan mengikat radikal bebas dan molekul yang sangat reaktif. Tujuan penelitian ini adalah untuk mengetahui pengaruh jus buah sirsak (AnnonamuricataL) terhadap kadar kolesterol total darah mencit jantan (Mus musculus). Jenis penelitian ini adalah penelitian eksperimental uji manfaat, dengan kelompok pembanding (pre-test and pos-test with control group design). Penelitian ini dilakukan di laboratorium Farmakologi dan Bahan Alam STIK Siti Khadijah Palembang selama 21 hari. Sampel dalam penelitian ini adalah mencit jantan berusia 6–8 minggu dengan rerata berat badan mencit normal adalah 20–30 gram, yang memenuhi kriteria inklusi dan eksklusi. Jumlah sampel adalah 25 mencit jantan. Ada hubungan yang bermakna kadar kolesterol mencit sebelum dan setelah diberikan jus buah sirsak. Disimpulkan bahwa pemberian jus buah sirsak berpengaruh terhadap penurunan kadar kolesterol darah. Disaran untuk dilakukan penelitian lebih lanjut pada sampel manusia.

INTRODUCTION

The shift in people's lifestyles with the rise of online food ordering applications prefers to consume fast food and snacks high in fat and cholesterol. Suspected to be a trigger factor for the high incidence of hypercholesterolemia. (Tia, HD., 2014). Hypercholesterolemia is a lipid metabolism disorder characterized by an increase or decrease in the lipid fraction in plasma. The main increase in the lipid fraction is total cholesterol, Low-Density Lipoprotein (LDL) accompanied by a decrease in High Density Lipoprotein (HDL) (Guyton and Hall, 2014; Tia, HD., 2014; Iswandi, 2019).

Lipidsare physiologically synthesized by the liver and intestines (Tia, HD., 2014; Moghadamtousi, S. Z. 2015). Lipids are needed by the body as cell formation, steroid hormone synthesis, prostaglandin precursors, and as a source of energy for the body (Guyton and Hall, 2014; Iswandi, 2019). Hypercholesterolemia can change the structure of blood vessels resulting in impaired endothelial function which results in the buildup of cholesterol plaques. Cholesterol plaques can make blood vessels narrow so that blood flow becomes less smooth (Humphries, S. E., 2013 Sofi Ariani, 2016).

Cholesterol plaques on the walls of blood vessels are fragile, break easily, and leave scars on the walls of blood vessels that can activate the formation of blood clots. Because the blood vessels have been narrowed and hardened by cholesterol plaques, these clots can easily clog the blood vessels completely. This condition is known as atherosclerosis. Atherosclerosis can occur in the arteries in the brain, heart, kidneys, arms, legs, and other vital organs. If atherosclerosis occurs in the arteries leading to the brain or the carotid arteries, a stroke can occur. If it occurs in the arteries leading to the heart to the coronary arteries, a heart attack can occur (Humphries, S. E., 2013; Sofi Ariani, 2016).

Data from the World Health Organization (WHO) shows that 20% of strokes and more than 50% of heart attacks are caused by high cholesterol levels. The case in Indonesia increases by 28 percent per year and attacks the productive age, namely those under 40 years old (Iswandi 2019).

The Increasing public understanding, along with the increasing number of cases in Indonesia, encourages to make efforts for prevention and treatment (Tia, HD., 2014; Moghadamtousi, SZ 2015; Iswandi, 2019), diet, exercise are the chosen alternatives in addition to treatment using drugs. Usually, synthetic drugs are often used to decrease cholesterol levels. Consuming the drug in the long term effects the body's organs, especially the liver and kidneys. Now many people switch to using herbal remedies derived from traditional plants. Based on the results of several studies, it is relatively safer. (Rizky, IS., 2014; Ramadhono, DA., 2014; Fatimah 2019), traditional treatment is recommended because it has almost no side effects (Rizky, IS., 2014; Ramadhono, DA., 2014; Moghadamtousi, SZ 2015; Fatimah 2019; Tiencheu, B., 2021).

Annona muricata is a lowland tropical fruit-producing tree of the Annonaceae family found in the rainforests of Africa, South America, and Southeast Asia (Rady, I., 2018; Kim, J. Y., 2018). Soursop fruit known by the Latin name A. muricata L., commonly known as graviola, guanabana, (Adefegha, 2015; Moghadamtousi, 2015), Brazilian claw (Rady, I., 2018) and paw-pawis a member of the family Annonaceae which consists of about 130 genera and 2300 species, (Moghadamtousi, SZ 2015; Abbas, SI., 2015; Fatimah, S., 2019). has large, glossy, dark green leaves (Rady, I., 2018). with edible green heart-shaped fruit. Soursop fruit has a fairly large size of 20-30 cm, weighing up to 2.5 kg per fruit. Soft, curved spines cover the leathery skin of the fruit, each containing 55-170 black seeds distributed in creamy white flesh with a distinctive aroma and taste. All parts of A. muricata, pericarp leaves, fruit, seeds, and roots have been used for traditional medicine, the most parts used for making traditional medicinal herbs are the bark, roots, seeds, and leaves (Rady, I., 2018; Neputty, J.P., 2013).

This fruit contains a lot of carbohydrates, especially fructose and vitamins such as vitamin C, vitamin B1, and B21 (Prasetyorini, 2014; Garnadi, Y. 2012; Sudaryati, 2013; Sayuti, 2015). Soursop fruit has many benefits in curing several diseases, including overcoming gout, increasing immunity and warding off colds, helping treat gallstones, hypercholesterolemia (Rizky, IS., 2014; Ramadhono, DA., 2014; Fatimah, 2019). Soursop leaves can be used as a medicine for hemorrhoids, bladder pain, diarrhea in infants, dysentery, and as a source of vitamin C. Soursop is a sweat laxative, anti-spasmodic, and accelerates the cooking of boils (Prasetyorini, 2014; Garnadi, Y. 2012).

Soursop contains flavonoid compounds, tannins, phytosterols, calcium oxalate, and alkaloids (Moghadamtousi, S.Z., 2015; Fatimah). Flavonoid compounds function as antioxidants, antimicrobials, anti-viruses, photosynthetic regulators, and growth regulators (Prasetyorini, 2014). Flavonoids can reduce blood cholesterol levels by increasing bile acid excretion and reducing blood viscosity, thereby reducing the occurrence of fat deposition in blood vessels (Irwandi, 2019). Flavonoids are efficacious in reducing blood cholesterol levels by increasing bile acid excretion and reducing viscosity (Irwandi, 2019). viscosity) of the blood, thereby reducing the occurrence of fat deposition in the blood vessels (Prasetyorini, 2014; Irwandi, 2019).

According to research by Moghadamtousi, (2015), Prasetyorini (2014), and research by Fatimah (2019), soursop fruit is a potential source of antioxidants. Antioxidants are important substances in the body that can inhibit oxidation reactions by binding free radicals and highly reactive molecules. An Antioxidant is a compound that has a small molecular weight, this antioxidant can prevent the formation of free radicals. The Oxidation reaction is by inhibiting the occurrence of cell damage in degenerative diseases. Antioxidants are enzymes (superoxide dismutase, catalase, and glutathione peroxidase), vitamins (vitamins E, C, A, -carotene), and other compounds (flavonoids, albumin, bilirubin, and ceruloplasmin) (Fatimah, S., 2019)

Flavonoids are a large group of plant polyphenol compounds that are widely distributed in various foodstuffs (vegetables and fruits) in various concentrations (Fatimah, S., 2019). Flavonoids act as LDL-reducing antioxidants in the body, increase the density of LDL receptors in the liver and increase Apolipoprotein B. Flavonoids also act as compounds that reduce triglycerides and increase HDL and can activate multi-enzyme systems such as cytochrome-450 and b5 that affect lipid and acid metabolism. bile (Fatimah, S., 2019).

Free radicals have a good effect on the body, such as helping the destruction of microorganisms and cancer cells. Excessive production of free radicals and inadequate production of antioxidants can cause damage to tissue cells and enzymes. Soursop fruit has a high content of polyphenol compounds. Phenol and flavonoid compounds that are widely contained in plants can act as antioxidants because they have a molecular structure that can donate electrons to free radical molecules. The content of phenols and flavonoids is directly proportional to the antioxidant activity. The

content of vitamin C also affects antioxidant activity (Prasetyorini, 2014).

According to research by Presetyorini (2014), 100 grams of soursop juice contains 98.18 mg of polyphenols, 0.77 percent of vitamin C, and 282.61 ppm for antioxidants. Soursop fruit is not only used as fresh food, but has been used as industrial ingredients such as syrup, sweets, jams, juices, and other cake mixes that have added value.

This study aimed to determine the effect of soursop fruit juice (Annona muricata L) on the total blood cholesterol levels of male mice (Mus musculus). Research related to the cholesterol-lowering activity of soursop fruit juice in male mice (Mus musculus) has not been done much, therefore further research on the use of soursop fruit juice to reduce cholesterol levels still needs to be continued. To find out the benefits of soursop fruit to lower blood cholesterol levels.

METHODS

This type of research is an experimental study of benefit testing, with a comparison group (pretest and posttest with control group design). This research was conducted at the Pharmacology and Natural Materials Laboratory of STIK Siti Khadijah Palembang, for 21 days. The sample in this study was male mice aged 6-8 weeks with an average body weight of 20-30 grams of normal mice, which met the inclusion and exclusion criteria. The number of samples was 25 male mice, which were ordered from the Palembang center rat farm. The reason for choosing male mice is because male mice are relatively more stable than female mice, where female mice experience hormonal changes that can affect their psychological condition.

The dependent variable in this study was cholesterol levels and the independent variable was the concentration of soursop fruit juice. The treatment of the research sample, for 7 days the mice were adapted in the pharmacology laboratory, during the adaptation period the mice were given pig pellets and sufficient water, the purpose of adaptation was so that the mice could adjust to the new environment and so as not to stress the mice. The treatment of mice is guided by research ethics in experimental animals (Marwati, F and Putri, S. 2018), which include: separating the experimental animal treatment site from other mice, preventing oral injection in the wrong channel, calculating the concentration correctly. Hold the mice properly to avoid bites, hold the tail end of the mice with the right hand, and place it on a flat, non-slippery place such as a wire ram on the cage cover. The tools used in this study included: digital animal scales, analytical balance, drip plate, measuring cup, glucometer, cholesterol check strip, blender, while the research materials were: CMC 0.5%, aquadest, simvastatin, soursop fruit, eggs quail, pellets.

The work procedure consists of, 1. The procedure for making soursop fruit juice is: weighing 500 grams of ripe soursop fruit and then separating the skin, seeds, and flesh of the soursop fruit. After that, put the soursop flesh into a blender for as much as 150 grams, add 150 ml of distilled water, then puree using a blender. The procedure for making induction feed is high-fat feed to increase cholesterol levels is given every day for 7 days, 250grams of quail eggs are separated from the whites and then the yolk is taken, and probed to mice with a dose of 1ml, given 2x a day.3. The dose of simvastatin given is a dose that includes a human therapeutic dose of 10mg (ISO 2014) with a conversion factor from humans (70kg) to mice (20gr) of 0.0026. Human therapy dose = 10 mg Human to mouse conversion factor 20g = 10 x 0.0026 = 0.026 mg/20 g mice body weight. Simvastatin was dissolved in 0.5% CMC–Na as a suspending agent. 4. Preparation of 0.5% CMC-Na solution is, as much as 0.5 g of CMC Na is sprinkled into a mortar containing 100 ml of hot/warm aqua dest and let stand for 15 minutes to obtain a transparent mass and then ground until homogeneous. Then it was diluted using aqua dest and put into a 100 ml volumetric flask. 5. The dosage of Soursop Fruit Juice is, the concentration of fruit juice used is 20%, 50%, and 80%. 6. Blood samples were taken after male mice were adapted for 7 days in laboratory conditions for pre-test blood total cholesterol levels (initial level, 1 week after high-fat diet) and 1 week later given soursop fruit juice orally. Each study subject fasted for 16 hours before blood was taken.

Phytochemical screening includes: a. examination of Alkaloids by taking 3 drops of juice added 2 drops of Mayer's reagent to produce a white/yellow precipitate, 2 drops of Bouchardat's reagent which produces a brown precipitate, and finally 2 drops of Dragendrof's reagent which produces a brick-red precipitate. 8. Flavonoid examination is, the juice obtained is taken as much as 5 ml, and then added 0.1 g of Mg powder, and 1 ml of concentrated HCL, and 2 ml of amyl alcohol, shaken and allowed to separate. Positive flavonoids if there is a red, yellow, orange color on the amyl alcohol layer. 9. Examination of Tannins, namely, the juice obtained is taken as much as 2 ml, and then 1-2 drops of iron (III) chloride reagent is added. A blue or blackish green color occurs indicating the presence of tannins. The procedure for examining mice's cholesterol levels was carried out intravenously by cutting the mice's tails. Before being cut, the tails of the mice were cleaned first.

The research procedure was, 25 male mice were adapted for 7 days in the laboratory, fasted for 16 hours, then pre-cholesterol levels were checked, then all samples were fed a high-fat diet for 7 days. Furthermore, the samples were grouped into 5 groups, with each group consisting of 5 mice, namely, group 1, given CMC 0.5% given at a dose of 1x a day, group 2, given soursop juice concentration of 20%, group 3, given soursop juice concentration 50%, group 4, were given soursop juice concentration 80%, and group 5, given Simvastatin with a dose of 0.026 mg. On the 8th day, all samples were fasted for 16 hours, for further examination of post cholesterol levels.

RESULTS AND DISCUSSION

The data obtained in this study were data before, and after 14 days of treatment. The data obtained in this study were then analyzed statistically using statistical applications, which included a sample homogeneity test using homogeneity of variances test, descriptive analysis to determine the mean, and standard deviation, and the One-way ANOVA test. The resulting data is homogeneously distributed.

From Table 1. It is known that after the phytochemical screening, it was found that soursop fruit juice (Annona muricata L) contains secondary metabolites of alkaloids, flavonoids, saponins, and tannins. The results of phytochemical screening in a study conducted by Gavamukulya (2014), found that soursop plants are rich in secondary metabolic compounds such as saponins, terpenoids, flavonoids, coumarins and lactones, anthraquinones, tannins, glycosides, and phytosterols. The results of this study are in line with the research of

Gavamukulya et al. (2014) on the results of phytochemical screening found that this plant is rich in second-class metabolites such as saponins, terpenoids, flavonoids, coumarins and lactones, anthraquinones, tannins, cardiac glycosides, and phytosterols. The same results were found in the research of Gbaguidi et al (2017). The results of the phytochemical screening found compounds includingtanin gallic, tanin catechins, flavonoids, *leucoanthocyanins*, and mucilage found in the leaves of *A. muricata*. However, quinone and cyanogenic derivatives and saponins were not detected.

Table 1.
The Results of Soursop Fruit Juice (*Annona muricata L*) Phytochemical Screening

Metabolite Compounds	Correction	Color	Result
Alkaloid	Fruit juice + Mayen	- White/yellow	+
	Fruit juice + Bouchardat	- Dark chocolate	
	Fruit juice + Dragendrof	- Brick Red	
Flavonoid	Mg powder + concentrated HCL + Amyl alcohol	- Red Yellow, Orange	+
Tanin	Fruit juice + Iron (III) Chloride	- Blue / green black	+
Saponin	Fruit juice + Aqua dest	- Formed foam	+

Flavonoids are one of the polyphenolic compounds that have antioxidant properties. Flavonoids are secondary metabolites of polyphenols, found widely in plants, and food and have a variety of bioactive effects including anti-viral, anti-inflammatory (Adefegha, SA, 2015; Qinghu Wang et al, 2016), cardioprotective, anti-diabetic, anti-cancer (Marzouk, MM., 2016) anti-aging, antioxidant (Vanessa et al, 2014). Flavonoids act as LDL-reducing antioxidants in the body, increasing Apolipoprotein B. Flavonoids also act as compounds that reduce triglycerides, increase HDL, and activate multi-enzyme systems such as cytochrome-45 and b5 that affect lipid and bile acid metabolism (Rizky, 2014).

A literature study of several studies found that more than 200 chemical compounds have been identified and isolated from this plant. The most important compounds are alkaloids, phenols, and acetogenins (Gavamukulya et al., 2017; Franyoto, 2019). The total phenol found in the aqueous extract was 683.69±0.09 g/mL gallic acid equivalents (GAE), while in the ethanol extract it was 372.92±0.15 g/mL GAE. Phytochemical screening also found that this plant is rich in second-class metabolites such as saponins, terpenoids, flavonoids, coumarins and lactones, anthraquinones, tannins, cardiac glycosides, and phytosterols (Gavamukulya et al., 2017). Gallic tannins, catechin tannins, flavonoids, leucoanthocyanins, and mucilage are present in the leaves of A. muricata. However, quinone and cyanogenic derivatives and saponosides were not detected (Gbaguidi et al., 2017).

Alkaloids are naturally occurring chemical compounds that contain a basic nitrogen atom. Alkaloids are produced by a wide variety of organisms, including bacteria, fungi, plants, and animals. The content of alkaloids contained in soursop fruit is used as medicine. Research conducted by Franyoto (2019) showed that alkaloids have various kinds of biological activities, such as anti-microbial, antioxidant, anti-cancer, anti-inflammatory, and anti-viral activities

The other chemical compounds contained in soursop fruit juice are tannins, which can bind and precipitate protein compounds caused by the presence of several functional bonding groups that will interact strongly with protein molecules which in turn will produce large and complex cross-links, namely tannins. protein (Fauziah, N., 2020; Hasan, 2003).

According to Subandi (2019), alkaloid, flavonoid, and saponin compounds have activity as pancreatic lipase inhibitors. Pancreatic lipase is an enzyme that is responsible for breaking down fat in the human digestive tract, by converting the triglyceride substrate present in dietary fat into monoglycerides and free fatty acids so that fat can enter and be absorbed by the small intestine. Saponins are complex glycosides formed from triterpenoids or steroidal alkaloids, which are nonvolatile and amphiphilic (Waziiroh, E., 2018). Saponins as a support to increase endurance (Waziiroh, E., 2018).

Soursop fruit contains tannin, which is useful in reducing triglyceride levels, also contains flavonoids that can inhibit the HMG CoA reductase enzyme in the cholesterol synthesis process. Inhibition of this enzyme activity resulted in the absence of mevalonate from HMG-CoA; mevalonate will be converted into squalene, lanosterol, dihydrolanosterol, D8-dimethylsterol, 7-dihydrocholesterol, and finally cholesterol. In addition, flavonoids also have a positive effect in reducing total cholesterol levels (Alatas, H., 2018).

Table 2.
Differences in Mean Cholesterol Levels Before and After Cholesterol Induction and Giving Soursop Juicen (treatment group and control group)

Variable	n	Mean			%
		Pre (mg/dL)	Induction post Cholesterol (mg/dL)	Gift post Soursop juice (mg/dL)	
Negative Control Na-CMC 0.5%	5	131.8	226.4	243.6	-
Positive Control Simvastatin	5	116.6	241.0	133.2	44.73
Treatment Group Soursop Juice 20%	5	125.0	204.0	123.4	39.50
Treatment Group Soursop Juice 50%	5	109.0	215.4	127.4	40.85
Treatment Group Soursop Juice 80%	5	138.4	226.0	128.6	43.09

From Table 2. above, it is known that the average decrease in cholesterol levels after administration of soursop juice was in the positive control group given simvastatin was 133.2 g/dL with a decrease of 107.8 g/dL (44.73%). The highest reduction in cholesterol levels was in the treatment group with 80% soursop juice, which was 128 gr/dL with a decrease in cholesterol levels of 97.4 gr/dL (43.09%). This indicates that the greater the concentration of soursop juiceeffects reducing blood cholesterol levels, relatively close to the effect of Simvastatin.

The results of this study are in line with the research of Fatimah, S (2019). There was a significant decrease in mice given soursop fruit extract. According to research by Fatimah, S (2019) and Abbas (2015), cholesterol levels decreased significantly, soursop fruit extract given to experimental animals contained many antioxidants such as alkaloids, tannins, saponins, flavonoids, and polyphenols. Flavonoids are known to function to inhibit macrophage-modified LDL oxidation by reducing -tocopherol contained in LDL particles, alkaloids by inhibiting pancreatic lipase enzymes, and tannins will react with mucosal proteins. Research conducted by Cahyawati (2020); Gavamukulya et al., (2017), revealed that soursop fruit has anxiolytic, anti-stress, anti-inflammatory, contraceptive, antitumor, anti-ulcer, wound healing, hepatoprotection, anti-icteric, and hypoglycemic effects.

There was an increase in post cholesterol levels in the treatment group and the control group which was induced by food containing high cholesterol. The highest increase in post-cholesterol levels was in the Simvastatin positive control group, which was 241.0 g/dL, with an increase of 124.4 g/dL. These results are in line with the research of Tia, HD (2014), there was an increase in cholesterol levels in white rats induced by a diet high in lard. The Cholesterol contained in lard is absorbed, then transported to the liver. In this process, HMG-CoA reductase will be inhibited, so that cholesterol synthesis by the liver itself will be reduced. When cholesterol intake is excessive, there is a buildup of cholesterol molecules in the liver which are packaged for distribution throughout the body by VLDL. During this process, VLDL is turned into a VLDL remnant which is then converted into intermediate-density lipoprotein (IDL), then IDL is converted into LDL.

When the need for cholesterol in the cells is fulfilled, LDL will return to the liver, captured by vascular endothelial macrophages, and foam cells are formed. HDL is then tasked with clearing cholesterol from endothelial macrophage cells to be degraded and repackaged into VLDL. However, this process is not perfect because there is still a lot of cholesterol in the liver that comes from food intake. The amount of cholesterol in the liver reduces LDL and HDL receptorsso that LDL cannot enter the liver and causes LDL to increase in the blood8 (Tia. HD., 2014)

In the digestive system, the metabolic process starts from the process of digestion of food, absorption, and transportation of lipids. The process of digestion of lipids has begun. When food is chewed in the mouth, the chewing process plays a role in separating fats. Lingual lipase enzymes support the hydrolysis of fat. Hydrochloric acid separates fats from other food substances and lipase enzymes hydrolyze fats in the stomach. Bile acids play a role in emulsifying and breaking down fats so that the lipase enzyme from the pancreas hydrolyzes triglycerides into diglycerides, monoglycerides, and fatty acids. Diglycerides and monoglycerides are hydrolyzed into fatty acid components and glycerol in the small intestine (Guyton and hall, 2014; Humphries, 2013).

Absorption Lipid absorption occurs mainly in the duodenum. Most of the products of digestion are absorbed into the mucous membrane of the small intestine by passive diffusion. The results of fat digestion in the form of monoglycerides and long-chain fatty acids in the intestine are converted back into triglycerides (TG). Long-chain fatty acids bind to coenzyme A through the enzyme acyl co A synthetase and then undergo reesterification into triglycerides (TG), phosphatidylcholine (FK), and cholesterol esters (KE). Short-chain fatty acids directly bind to albumin for transport to tissues. Cholesterol is then taken up by fat vesicles which then fuse with the Golgi apparatus to form chylomicrons (CM) (Guyton and hall, 2014; Humphries, 2013).

Table3.
Differences in Average Cholesterol Levels in Soursop Juice Treatment Groups

Variable	Sum of Squares	SD	Mean	F	P-value
Cholesterol Pre-Induction					
Between Groups	2744.160	4	686.040	,600	,667
Within Groups	22853.200	20	1142,660		
Total	25597.360	24			
Cholesterol Post Induction					
Between Groups	3811,760	4	952.940	1,458	,252
Within Groups	13068.400	20	653.420		
Total	16880.160	24			
3rd day Check					
Between Groups	22351.760	4	5587.940	5,272	,005
Within Groups	21200.000	20	1060.000		
Total	43551.760	24			
7th day Check					
Between Groups	51882.100	4	12970.525	49,127	,0001
Within Groups	5016.400	19	264.021		
Total	56898.500	23			

Note: (+) contains the test compound group

Lipids and blood do not mix, as long as they are in the bloodstream, lipids combine with proteins. There are 2 lipid transport pathways namely, the exogenous pathway and endogenous pathway. The exogenous pathway is the

transport of lipids from the tissues to the liver and the endogenous pathway is the transport of lipids from the liver to the peripheral tissues and vice versa. This transport of most of the hydrophobic lipids in the circulation is accomplished by the conjugation of lipids and proteins called lipoproteins. Lipoprotein components consist of TG, free cholesterol (K), KE, and phospholipids (FL) 1,2. Total cholesterol in the blood is about 140 grams, and about 8 grams of cholesterol is in the plasma. About 1 gram of cholesterol enters the body every day, 400 mg of cholesterol comes from absorption in the intestine, and 600 mg from biosynthesis in the body.

The process of regulating cholesterol homeostasis in the body consists of 3 phases, namely: regulating cholesterol synthesis, 3-hydroxy-3-methylglutaryl co-enzyme A (HMG-Coa) reductase, regulating the synthesis and recycling of LDL receptors, and finally activating the process of esterification of intracellular cholesterol by enzymes. Acyl-CoA: cholesterol-acyltransferase (ACAT) These three mechanisms together regulate and prevent an increase in intracellular cholesterol concentrations (Guyton and hall, 2014; Humphries, 2013).

From Table 3. It is known that the average cholesterol level in the treatment group with soursop juice had a significant increase on the 3rd day of checking with a p-value of 0.005 and on the 7th day of checking with a p-value of 0.0001.

The results of this study are in line with Cahyawati's research (2020) which found that A. muricata leaf extract significantly reduced LDL levels, increased HDL levels, and glucose tolerance at a dose of 150 mg/kg. This extract was also able to reduce the levels of very low-density lipoprotein (VLDL) and adipocyte area in epididymal adipocytes at doses of 100 mg/kg and 150 mg/kg.

The results of Jimoh's study, OA (2018), showed that there was a significant decrease in cholesterol levels in samples given soursop fruit juice for 5 days, compared to the treatment in the 1-4 day group. This shows that soursop fruit juice reduces total cholesterol levels. Giving soursop fruit juice reduced serum lipid peroxide in the treatment group. Hypercholesterolemia is associated with increased lipid peroxidation (Jimoh, 2018). Soursop fruit juice is very effective given to patients who experience long-term oxidative stress and chronic diseases such as hypercholesterolemia (Jimoh, 2018).

According to the research of Tran, N,YT, (2020) revealed that soursop fruit stored at a low temperature (1°C) was able to maintain TAA (36.13%), TPC (45.13%), antioxidant activity (58.97%)

CONCLUSION AND SUGGESTIONS

Based on the analysis of the discussion, it was found that the results of phytochemical screening obtained secondary compounds in soursop fruit juice, namely, Alkaloids, Flavonoids, Tannins, and Saponins. Therewas a significant decrease in cholesterollevels in the treatment group given soursop fruit juice. It can be concluded that soursop fruit juice lowers blood cholesterol levels. It is recommended to conduct future research that involve human samples.

Conflict of Interest Statement

The authors declared that no potential conflict of interests with respect to the authorship and publication of this article.

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