

Potency of Herbal Plants Formulation as Anticholesterole agent: In Vitro Studies

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ABSTRACT

Natural materials have excellent prospects in the field of health and beauty. The use of chemicals in the field of health and beauty has negative impacts. Indonesia is an extraordinarily rich country of natural materials. Natural materials that can be used include fruit, leaves, tubers, wood, fish, and animals. These natural ingredients are also called herbs. Herbal Plants used in traditional medicine in Indonesian to decrease cholesterol. Two herbal plant formulation used in this experiment. Formula A : *Andropogus paniculata* (35%), *Piper battle* (25%), *Zingiber officinale* (25%), *Myrista fragrans* (15%) and formula B : *Dyospora kaki* (50%), *Apium grafeolens* (20%), *Guazuma uilmifolia* (20%), *Hisbiscus sabdarifa* (10%). Control used green coconut water. The aim of the study determine the potency of this herbal formulation used in vitro methods. Cholesterol blood liquid made from isotonic liquid, calcium and yellow eggs similar to cholesterol content in blood 200 mg/dl. Formula herbal plant used 20 mg/dl, 40 mg/dl, and 60 mg/dl. Control used green coconut water. Proximate analysis used SNI methods and cholesterol analysis worked on the Centre of Agro-Based

Industry Bogor used MU/INST/4 (GC) methods. The result of this experiment showed the major ingredient of proximate analysis is carbohydrate. Average cholesterol level in formula A decrease from 200 ml/dl to 23.3 mg/dl. In Formula B, cholesterol level decreased from 200 mg/dl to 86.9 mg/dl. Average cholesterol content in control 130.7 mg/dl. The study suggests that herbal plants formulation potential to decrease cholesterol.

Keywords: in vitro studies, herbal plants, cholesterol, potential, decrease

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INTRODUCTION

Indonesia is an extraordinarily rich country of natural material. This plant grows around our house. We called family medicinal plant "TOGA (tanaman obat keluarga)". The use of a medicinal plant is usually only boiled. This method was very helpful for family health. Developing of herbal technology used simplifier (powder), extraction and now Nanotechnology era. The resulting product is more specific to many kinds of diseases. Herbal nutrition need to complementary with chemical product in human health or animal nutrition and health. We hope can make nutrition formula to increase productivity of animal husbandry too, especially to be controlled of lipid or cholesterol

Lifestyle changes in era globalization. New types of diseases from fast food such as burgers, fried chicken, beefsteak, and soft drinks have great potential to cause disease because of high cholesterol, lipid, and sugar. Therefore, it is necessary to find an ingredient to reduce cholesterol levels with good efficacy. Currently, the popular drug is natural medicine because it supports the slogan "Back to Nature", in Indonesia natural medicine that has been used by generations (Batubara et al. 2017).

In encouraging wider use of herbal medicine, the Ministry of Health of the Republic of Indonesia launched the science of herbal medicine program and has approved the National Commission on scientific Herbs through Decree Number 172 / Menkes / SK / V / 2012. This national commission has the duty and authority to propose the feasibility of research results to become a

synergistic, integrated program. Therefore, traditional herbs that have been used by generations can be tested clinically to become a scientific herbal medicine. Plant raw materials that are generally used as cholesterol-lowering ingredients are *Andropogus paniculata*, *Piper battle*, *Zingiber officinale*, *Myrista fragrans*, *Dyospora kaki*, *Apium grafeolens*, *Guazuma uilmifolia*, and *Hisbiscus sabdarifa*.

This research design and innovation by using natural sources to decrease cholesterol in blood concentration and fiber content will help regulate blood pressure. cholesterol concentration in the blood. This research aimed to determine the potential of herbal plant formulation in decreasing blood cholesterol level concentration.

MATERIAL AND METHODS

Preparing Herbal Plants Formulation

Origin of herbal raw materials.

Herbal plants used to grow in Cirebon. Persimmon (*Dyospiros kaki*) plant in the village of Gunung Manik, Talaga, Majalengka. *Apium grafeolens*, *Guazuma uilmifolia*, *Hisbiscus sabdarifa*, *Zingiber officinale*, and *Myristica fragrans* bought on the market in Cirebon. *Andropogus paniculata* and *Piper battle* growth inland of house.

Preparation of Persimmon as liquid extraction

Persimmon is washed clean, then cut into pieces and put in a sterile torn and tap-mounted faucets to collect the liquid that comes out. Persimmon liquid is collected and closed tightly for the auto fermentation process until the pH becomes 3.

Herbal plant formulation

Herbal plant formula A: mixed 35% *Andropogus paniculata*, 25% *Piper betle*, 25% *Zingiber officinale*, 15% *Myrista fragrans*. The mixture is left for 3 days in a closed container and then filtered then dried in the sun and finally sterilized in open 40°C. Finally, the blender is smooth and ready to use.

Herbal plant formula B: mixed *Dyospiros kaki* (50%), *Apium grafeolens* (20%), *Guazuma ulmifolia* (20%) and *Hibiscus sabdarifa* (10%). The mixture is left for 3 days in a closed container and then filtered then dried in the sun and finally sterilized in open 40°C. Finally, the blender is smooth and ready to use.

In Vitro Method

In Vitro studies used composition of blood cholesterol (200 mg/dl) consist of isotonic liquid (100 ml), and yellow egg (5 grams). Treatment 1 added herbal plant formulation (20 mg/dl), treatment 2 (40 mg/dl), and treatment 3 (60 mg/dl).

Chemical Analysis

Proximate analysis

Methods to proximate analysis of water SNI 01-2891-1992, 5.1; ash SNI 01-2891-1992, 6.1; protein SNI 01-2891-1992,7.1; fat SNI 01-2891-1992,8.2, and carbohydrate IK 5.4.5. Methods for measuring cholesterol was MU/INS/4 (GC). Analysis was done at Analytical and Calibration Laboratories, Centre for Agro-based Industry, Bogor.

Bioactive compound analysis

Saponin

Into the beaker, the sample powder is added as much as 4 grams, then added with 25 mL of ethanol, then boiled for 25 minutes, then filtered in a hot state with cotton put in a vaporizer cup and evaporated carefully. The remaining evaporation is titrated with ether, stirring. Pour immediately into the drip plate, allow to dry. Add a few drops of Liebermann-Burchard reagent. If it appears blue to green indicates the presence of steroids. The insoluble part in ether (vaporizer cup) is added with 10 ml of water and stirred. Part of the solution that occurs is put into the test tube, shake strongly. If the foam is stable, it shows the presence of saponins.

Terpenoid

Into the beaker the sample powder is added as much as 4 grams, then added with 25 mL of ethanol then boiled for 25 minutes, then filtered in a hot state with cotton put in a vaporizer cup and evaporated carefully. The remaining evaporation is titrated with ether, stirring. Pour immediately into the drip plate, allow to dry. Add a few drops of Liebermann-Burchard reagent. If it appears blue to green indicates the presence of steroids. The insoluble part in ether (vaporizer cup) is added with 10 ml of water and stirred. Part of the solution that occurs is put into the test tube, shake strongly. Some are added to the drip plate, then add a few drops of FeCl₃ reagent. If there is a black-blue or green-brown color indicates terpenoids.

Flavonoid

Into the beaker the sample powder is added as much as 4 grams, then added with 20 mL of ethanol-water (9: 1) and then boiled for 25 minutes, then filtered in a hot state with cotton put into a vaporizer cup. Concentrate with direct fire until the volume remains a third. Pipette into the drip plate, then add a little metal Mg and concentrated HCL. Mix well with a stirring rod. If a methyl orange appears, the sample contains flavonoids.

Cholesterol Analysis

Cholesterol content test had done in the Centre of Agro-based Industry Bogor, used MU/INST/4 (GC) method.





RESULT

Herbal formulation contains nutrients shown in table1 and material used to see in Figure 1.

Table 1. Proximate analysis of herbal plant formulation

Parameters	Formula A	Formula B
Water (%)	11.6	10.8
Ash (%)	7.74	8.8
Protein (%)	8.03	8.67
Fat (%)	1.83	1.44
Carbohydrate (%)	70.8	74.7

Composition of formula A

			
<i>Andropogus paniculata</i>	<i>Piper betle</i>	<i>Zingiber officinale</i>	<i>Myristica fragrans</i>

Composition of formula B





			
<i>Dyospiros kaki</i>	<i>Avium graveolens</i>	<i>Guazuma ulmifolia</i>	<i>Hibiscus sabdarifa</i>

Figure 1. Materials Used in the Herbal plant's Formulation

Carbohydrate concentration of herbal formulation was high i.e. formula A, 70.8% and formula B, 74.7%. The component of formulation that are all plants which rich in Carbon (C). *Andropogus paniculata* as a plant, *Zingiber officinale* as

rhizome, *Myrista fragrans* as a fruit, *Dyospiros kaki* is a fruit, *Piper battle*, *Apium grafeolens*, and *Guzuma ulmifolia* are leaf, *Hibiscus sabdarifa* is a flower. Proximate analyses done in Balitvet Bogor. The result showed that cholesterol concentration in vitro study can be seen in Table 2.

Table 2. Bioactive compound analysis of herbal plant formulation

Parameters	Formula A	Formula B
Saponin	+	+
Terpenoid	+	+
flavonoid	+	+

Cholesterol concentration in control used in this study was 200 mg/dl. The used of herbal formulation A on a dosage of 20 mg/dl could decrease cholesterol concentration to 8.81 mg/dl (decrease by 95%). The used of herbal formulation on a dosage of 40 mg/dl could decrease cholesterol concentration to 8.79 mg/dl (decrease by 95%). The used of herbal formulation on dosage of 60 mg/dl could decrease cholesterol concentration to 52.0 mg/dl (decrease by 74%) The used of herbal formulation B on dosage of 20 mg/dl could decrease cholesterol concentration to 102 mg/dl (decrease by 49%). The used of herbal formulation on a dosage of 40 mg/dl could decrease cholesterol concentration to 64.5 mg/dl (decrease by 67%). The used of herbal formulation on a dosage of 60 mg/dl could decrease cholesterol concentration to 94.2 mg/dl (decrease by 53%), see Table 2. Average cholesterol content decrease in formula A, 23.2 mg/dl, formula B, 86.9 mg/dl. and control 130.7mg/dl see in Figure 2.

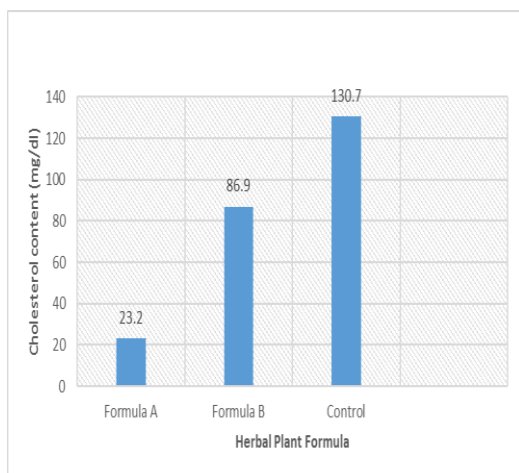


Figure 2. Cholesterol concentrations in vitro study. (A) *Andropogus paniculata* (35%), *Piper beetle* (25%), *Zingiber officinale* (25%), *Myristica fragrans* (15%). (B) *Dyospiros kaki* (50%), *Avium graveolens* (20%), *Guazuma ulmifolia* (20%). *Hibiscus sabdarifa* (10%).

DISCUSSION

There are approximately 250,000 to 500,000 species of plants with pharmacological activity on this planet. (Hong, Lee, and Kim 2018). Southeast Asian countries especially Indonesia has an

abundance of plant species. Tropical climate that supports plants' growth. One of the raw materials for plants that are generally used as cholesterol-lowering ingredients is the leaves of *Guazuma ulmifolia*. This plant leaves in Indonesia have long been used as slimming and cholesterol-lowering. The results of previous studies indicate that the leaves of *Guazuma ulmifolia* can reduce blood cholesterol levels in experimental animals. At present, this leaf has also been used as a mixture given to patients in health care facilities (Batubara et al. 2017).

It can be seen in Table 1, proximate analysis indicated that carbohydrate is a major component in herbal plants. For formula A (70.8%) and formula B (74.7%). Carbohydrates function as fuel to be used the body. The main benefits of carbohydrates are as a source of energy for the body in carrying out various functions (Ginting, Rosidi, and Noor 2013). The function of carbohydrates can also prevent various diseases. The fiber contained in carbohydrates can prevent various diseases and the system of immune in the body. The next carbohydrates function is to maintain heart health. Water-soluble fiber can reduce serum cholesterol levels (Yustika 2018). It can be seen in Table 2, bioactive component formula A and B, positive contain saponin, terpenoid, and flavonoid. Flavonoid is a group of the most phenol compounds found in nature. Pharmacological activities are ascribed to routine (flavonol glycosides) which are used to strengthen capillary structures, reduce permeability and fragility of blood vessels, etc. Flavonoids, terpenoid, and saponin can be used as drugs because they have various kinds of bio-function such as anti-inflammatory, anti-cancer, anti-fertility, antiviral, antidiabetic properties. antidepressants, diuretics, etc. (Ikhwan Habibi et al. 2018)

Table 3. Cholesterol concentrations in vitro studies

Concentration	Formula		Control
	A	B	
20	8.81	102	214
40	8.79	64.5	114
60	52.0	94.2	64.2
Average	23.2	86.9	130.7

Can be seen in table 3, cholesterol concentrations in *in vitro* studies, the average cholesterol level in formula A decreases from 200 ml/dl to 23.3 mg/dl. In Formula B, the cholesterol level decreased from 200 mg/dl to 86.9 mg/dl. Average cholesterol content in control 130.7 mg/dl. Herbal plants in this experiment contain flavonoid, terpenoid and saponin, caused decrease cholesterol levels. The other researcher, a flavonoid was separated and purified from celery leaf through ethanol extraction, collum chromatography, and crystallization. Reactive oxygen species (ROS) generated by NADPH oxidase during oxidative phosphorylation, are normal components of a healthy cell. ROS is also the mediator of the first defensive action of the cell and is involved in phagocytosis, apoptosis, and detoxification (Li et al. 2014).

Can be seen in figure 1, formula A composition are *Andropogus paniculata* (35%), *Piper battle* (25%), *Zingiber officinale* (25%), *Myrista fragrans* (15%) and formula B composition are *Dyospora kaki* (50%), *Apium grafeolens* (20%), *Guazuma uilmifollia* (20%), *Hibiscus sabdarifa* (10%).

Andropogus paniculata

A. paniculata can reduce triglycerides, LDL cholesterol, and glucosa. Research published by the Indian Journal of Pharmacology in 2012 concluded that the active andrographolide compounds contained in *A. paniculata* have hypoglycemic and hypolipidemic effects. The addition of 0.3% *Andropogus paniculata* leaves could replace tetracycline in broiler production with the advantages of improving the economics condition of broiler production. However, further researches are needed to test the effectiveness of *Andropogus paniculata* leaves on the broiler carcass quality (Maria Ulfah 2008)

Piper battle

Betel is a native plant of Indonesia that grows vines or rests on other tree trunks. Betel is used as a medicinal plant (fitofarmaka). Essential oils from betel leaves contain flavonoid (Muhammad Iqbal Mustamin, Nuraisyah Rustam 2016) sesquiterpenes, starches, diatases, sugars and tanners and kavikol which have the lethal power of germs, antioxidants and fungicides, anti-fungi. Betel efficacious eliminates body odor caused by bacteria and fungi (Rachmawati et al. 2008). Betel leaf is also to hold bleeding, heal wounds on the skin, and disorders of the digestive tract. It also is frowning, expectoration, shed saliva, hemostatic, and stop bleeding.

Zingiber officinale

Zingiber officinale used as nutrition and medicine widely. Ginger is a very popular spice used worldwide; whether it be used to spice up meals, or as a medicine, the demand for ginger all over the world has been consistent throughout history. Fresh ginger contains volatile oils consisting of 1-3%, of zingerone, shogaols, and gingerols with [6]-gingerol (1-[4'-hydroxy-3'-methoxyphenyl]-5-hydroxy-3-decanone) (Keijin An, Dandan Zhao, Zhengfu Wang, Jijun Wu, Yujian Xu 2016).

Myrista fragrans

Indonesian native nutmeg contains many substances that are beneficial to the human body. For example Atsiri, Saponin, Lipase Enzyme, to Pectin. Research using *Myristica* done for broiler chicks. The use of additive levels on enclosure density affected the consumption of feed, gain of body weight, conversion of feed, total leucocytes, meat glycogen, and meat lactic acid. There was an interaction space of floor with the additive level on the consumption of broiler feed. The use of 2% nutmeg powder on floor space 0.10 m² /bird can improve the average gain of weight and efficiency of feed (Siti Utami, Zuprizal 2012). Aromatherapy candles are the alternative application of aromatherapy by inhalation, i.e inhalation of aroma produced by several drops of essential oils. Aromatherapy candles when burnt produce scent

that has therapeutic effect (Sophia G Sipahelut, Gillian Telelepta, John Patty 2018)

Dyospora kaki

Dyospiros kaki has been favored as a tea for healthcare in Southeast Asia for its beneficial effects on homeostasis, hypertension, apoplexy, atherosclerosis, the anti-diabetic, antigen toxic, and neuroprotective activities (El-Hawary et al. 2019). *Diospyros kaki* L. progressively consumed in the market and export. The effect of bioprotective with the alcoholic extract of fruits as well as leaves of *Dyospiros kaki* using in-vivo rat models research has been conducted. Petroleum ether used to extract fruits and leaves and GC/MS used to analyze characterized for saponifiable and unsaponifiable compounds. Aqueous methanol used to extract leaves to isolate flavonoid. Chemical evaluation for fruits and leaves namely, the content of moisture, ash, proteins, fatty acids, amino acids, fat and water-soluble vitamins, minerals, carotenoids were carried out. Total antioxidant activity was determined by radical scavenging effects using DPPH assay. The effect on biochemical and biological activity was also performed. Identification of the major compounds of saponifiable and unsaponifiable matters of fruits and leaves. Scopoletin, rutin, luteolin, kaempferol, and apigenin 7-O-glucoside were isolated and identified. It showed that this plant can provide a good nutritional value and it is safe regarding the kidney and liver functions, a good source that helps in enhancing the antioxidant defense against free radicals. No abnormal effects were found in lipids profile on experimental animals and there were good results in the ratio of HDL and LDL cholesterol. Also, this plant can help in optimizing blood sugar, enhancing the level of blood hemoglobin. *Dyospiros kaki* is a good source of compounds nutrients and bioactive. That may contribute benefit of therapeutic against the risk of disease complications (El-Hawary et al. 2019). The current review of persimmon fruit with special reference to its phytochemistry and used to health claims. Accordingly, the role of its certain bioactive molecules like proanthocyanidin, carotenoids, tannins, flavonoids, anthocyanidin, catechin, etc. is highlighted. The potential antioxidant is responsible for perspectives of anti-malignant and anti-melanogenic, persimmon functional ingredients. Lifestyle-related disparities e.g cardiovascular disorders and diabetes mellitus. are proven facts that pharmacological of persimmon functional ingredients. Proanthocyanidin may help against hyperlipidemia and hyperglycemia. Persimmon and its components potential as one of the effective modules in nutrition and diet based therapy; however, integrated research and meta-analysis are still required to enhance meticulousness (Butt et al. 2015). Fibrinolytic enzymes prevents the formation of plaque in the blood vessel. Fibrinolysis in the natural process that is required by the body (human and animal) to prevent blood clotting that covers the course of blood. This fact indicated that *Bacillus sp* on *Dyospiros kaki* has a great potential to be used in the stroke case, the disease from a new lifestyle of the new generation now.

Apium grafeolens

Celery or *Apium graveolens* is a plant from the family of Apiaceae that has been used to lower blood pressure. This study aimed to review systematically the effect of *Apium graveolens* on the reduction of blood pressure. Celery extract had a significant effect to help lower the blood pressure in hypertension. The celery was extracted with ethanol, hexane, ethyl acetate, methanol, and pure water. All study were used laboratory experiments method with experimental animals. Most of them showed hypotensive effects through bradycardia and vasodilation from the administration of celery extract. Celery extract has a significant effect to help lower the blood pressure in experimental animals with hypertension (Marsita 2019).

Guazuma ulmifolia

The use of traditional *Guazuma ulmifolia* leaf extract as a slimming drug has been done but there is still very little research that addresses the problem. From several studies that have been conducted on rat animals, slimming activity from the extracts of *Guazuma ulmifolia* leaves is usually caused by the presence of tannin and gum linders in the extract. Steroids which are the main component in chloroform extract have a slimming effect. Besides, what active substances play a role is not yet known, so in this study using the active fraction of steroid extracts from the *Guazuma ulmifolia* leaves directly to see the effect of these active substances on the rabbit body weight. *Guazuma ulmifolia* leaf extract water with the main component of tannin and ethanol extract with the main component of flavonoids used as a comparison (Andriani, 2005).

The results of the separation on the teak leaves of *Guazuma ulmifolia* shows the existence of quercetin. Quercetin is contained in the extracts of *Guazuma ulmifolia* leaves with quite high levels and has properties related to a decrease in cholesterol levels, therefore quercetin can be a distinguishing compound on *Guazuma ulmifolia* leaves (Batubara et al. 2017).

This (Budiarto, Yusuf, and Yuniwati 2016) research aimed to find preventing increased fat of broiler chickens was by using natural ingredients (herbs) as a feed supplement. *Guazuma* leaf was supposed to be formed broiler with low-fat content. This research aimed to know the effect of *Guazuma* leaves wheat on decrease triglyceride levels of blood and abdominal fat percentage of broiler chickens. One hundred one-day-old broiler chickens used the research. The method applied was completely randomized designs (CRD) using 5 groups and 5 repetitions for each group, and if there is a difference will be followed by the least significant difference (LSD) test with a significant level of 95%. The assessment of influence on decreasing triglyceride levels of blood and abdominal fat of broiler chickens was collected after 28 days of treatment. The conclusion of this study was the addition of *Guazuma* (*Guazuma ulmifolia* Lamk.) leaves powder to 5 g, 10 g, 15 g, 20 g in 1 kg of standards feed could reduce the triglycerides levels of blood and abdominal fat percentage.

Hibiscus sabdarifa

Infusion of *Hibiscus sabdariffa* is a very popular drink in many parts of the world. Phytochemical composition is associated with hypotensive, antioxidant, and antiatherosclerotic effects. However, the mechanisms of molecular involved in these processes are not well known. This review aimed to report the scientific evidence supporting that regular use of *H. sabdariffa* decreases oxidative stress, atherosclerosis, lipid profile, and blood pressure (Guardiola and Mach 2014).

Can be seen in figure 2, the average cholesterol level in formula A decreases from 200 mg/dl to 23.3 mg/dl. In Formula B, cholesterol level decreased from 200 mg/dl to 86.9 mg/dl. Average cholesterol content in control 130.7 mg/dl. Based on this research, this fact also gives hope to make nutrition for human and animal nutrition that is free cholesterol to be used as it a herbal formulation in the future.

CONCLUSIONS

The result of this study showed that cholesterol level in Formula A cholesterol level decreased from 200 mg/dl to 8.81 mg/100 gram at dose 20 mg/dl, 8.79 mg/100 gram at dose 40 mg/dl, and 52.0 mg/100 gram at dose 60 mg/dl. Formula B decreased from 200 mg/dl to 102 mg/dl at dose 20 mg/dl, 64.5 mg/dl at dose 40 mg/dl, and 94.5 mg/dl at dose 60 mg/dl. The average cholesterol level in formula A decrease from 200 mg/dl to 23.3 mg/dl. In Formula B, cholesterol level decreased from 200 mg/dl to 86.9 mg/dl. Average cholesterol content in control 130.7 mg/dl. The study suggests that herbal plant formulation potential to decrease cholesterol, so this study indicated that herbal has activity as an anti-cholesterol agent.

CONFLICT OF INTEREST

They have no conflict of interest in this research.

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