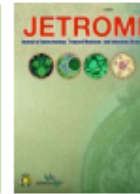




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Correlation between Low-Density Lipoprotein Cholesterol and Certain Lipid Profiles in The Treatment of Bay Leaf Extract (*Syzygium Polyanthum* (*Wight*) Walp) to Dyslipidemia Patients

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ABSTRACT.

Background: The use of herbal medicine has long been practiced throughout the world, and the production and processing of herbal medicines are constantly being improved to treat various diseases. This study aimed to assess the correlation between low-density lipoprotein cholesterol and certain lipid profiles in the treatment of bay leaf extract (*syzygium polyanthum* (*Wight*) Walp) to dyslipidemia patients.

Method: We recruit dyslipidemia patients, and the search project was given an explanation and asked to give written consent (informed consent) to participate in the research. Then anamnesis is carried out and examination: measurement of BMI, measurement of waist circumference, after fasting for 10-12 hours, the patient then took blood samples by the laboratory, to examine hs-CRP levels, lipid profiles (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), routine blood, kidney function (ureum, creatinine). Blood samples are taken before and after 30 days of study. Bay leaf extract 150 mg is taken two times per day.

Result: Subjects who participate in the study were 15 people as a treatment group and ages 47.47±11,507 years old. There is a significant decrease in cholesterol total, LDL-C, and

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Apo=B (all, $p < 0,01$). There is a correlation between LDL-C and Total Cholesterol, Triglyceride, FPG, and Apo-B (all, $p < 0.05$).

Conclusion: In this study, bay leaf administration of 2x150 mg for 30 days, improved lipid profiles of total cholesterol, LDL, and ApoB in dyslipidemic patients. Bay leaf extract administration has the potential to prevent and improve cardiovascular disease in dyslipidemic patients

Keywords: LDL-C, Bay Leaf Extract (*Syzgium Polyanthum* (Wight) Walp)

ABSTRAK.

Latar Belakang: Penggunaan obat herbal telah lama dipraktikkan di seluruh dunia, produksi serta pengolahan obat-obatan herbal terus ditingkatkan untuk mengobati berbagai penyakit. Penelitian ini bertujuan untuk mengkaji korelasi antara kolesterol low-density lipoprotein dengan profil lipid tertentu dalam pengobatan ekstrak daun salam (*Syzgium polyanthum* (Wight) Walp) terhadap pasien dislipidemia.

Metode: Kami merekrut pasien dislipidemia, diberi penjelasan dan diminta untuk memberikan persetujuan tertulis (*informed consent*) untuk berpartisipasi dalam penelitian. Kemudian dilakukan anamnesis dan pemeriksaan: pengukuran IMT, pengukuran lingkaran pinggang, setelah puasa selama 10-12 jam, pasien diambil sampel darah oleh laboratorium, untuk memeriksa kadar hs-CRP, profil lipid (kolesterol total, kolesterol LDL, kolesterol HDL, dan trigliserida), darah rutin, fungsi ginjal (ureum, kreatinin). Sampel darah diambil sebelum dan sesudah 30 hari studi. Ekstrak daun salam 150 mg diminum dua kali sehari.

Hasil: Subjek yang berpartisipasi dalam penelitian ini adalah 15 orang sebagai kelompok perlakuan dan usia $47,47 \pm 11.507$ tahun. Ada perbedaan signifikan dalam kolesterol total, LDL-C dan Apo = B (semua, $p < 0,01$). Ada korelasi antara LDL-C dan Kolesterol Total, Trigliserida, FPG, dan Apo-B (semua, $p < 0,05$).

Kesimpulan: Pada penelitian ini, pemberian daun salam 2x150 mg selama 30 hari, menurunkan secara signifikan pada kolesterol total, LDL, dan ApoB pada pasien dislipidemia. Pemberian ekstrak daun salam memiliki potensi untuk mencegah dan memperbaiki penyakit kardiovaskular pada pasien dislipidemia

Kata kunci: LDL-C, Ekstrak Daun Salam (*Syzgium Polyanthum* (Wight) Walp)

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1 Introduction

The use of herbal medicine has long been practiced throughout the world. It is estimated that as many as 75-80% of people in developing countries and 25% in developed countries use traditional medicine as a first-line treatment. Therefore, the production and processing of herbal medicines are constantly being improved to treat various diseases.[1] The market potential of herbal

medicines and phytopharmaceuticals in Indonesia is very large because Indonesia has more than 30,000 species of plants and 940 of them are efficacious plants.[2] Many phytopharmaceuticals are effective in improving metabolic function, one of which is Dhawalsan-1 (*Curanga fel-terrae*), which also significantly increases adiponectin levels in patients with new type 2 diabetes and has a potency equivalent to metformin.[3] Bay leaf contains tannins, flavonoids, saponins (triterpenoids), galokatekin, and essential oils (sesquiterpenes). In addition, bay leaves also contain several vitamins, including vitamin A, vitamin C, vitamin E, thiamine, riboflavin, niacin, vitamin B6, vitamin B12, and folate. The results of *in vitro* studies show flavonoids work as inhibitors of the enzyme 3-hydroxy-3-methylglutaryl *coenzyme* A reductase (HMG-C oA reductase) so that cholesterol synthesis decreases. Saponins can form complex insoluble bonds with cholesterol derived from food, bind to bile acids from *micelles*, and increase the binding of cholesterol by fiber so that cholesterol cannot be absorbed by the intestine. Tannins inhibit the absorption of fat in the intestine by reacting with mucosal proteins and intestinal epithelial cells. The bay leaf infusion concentrations of 5%, 10%, and 20% significantly reduced total cholesterol levels ($p\text{-value} < 0.05$). Bay leaf infusion concentrations of 5%, 10%, and 20% had the same effect in lowering total blood cholesterol levels in dyslipidemia model rats and its potency was equivalent to simvastatin. In several studies, bay leaf (*Syzygium polyanthum* Wight.) has been found to contain a variety of compounds, including tannins, flavonoids, and essential oils including citric acid and eugenol. Chemical compounds with antiinflammatory activities are flavonoids, according to numerous research findings.[4] Based on research by Liliwirianis bay leaves contain alkaloids, saponins, steroids, phenolics, and flavonoids.[5] Meanwhile, bay leaves show the presence of flavonoids, terpenoids, and phenolic compounds. The anti-inflammatory ability of bay leaf infusion is influenced by the flavonoid compounds contained in it. Flavonoids are one of the important secondary metabolites in plants. Flavonoids are a type of secondary metabolite found in plants. Flavonoids are polyphenolic substances that help the body's defensive system by acting as antiviral, antibacterial, anti-allergic, antiplatelet, anti-inflammatory, anticancer, and antioxidant.[6] Bay leaves include the flavonoids quercetin and fluorethin.[7] Flavonoids' ability to prevent the production of histamine (one of the mediators of inflammation) is the mechanism by which inflammation is inhibited. Histamine release is inhibited, due to a reduction in inflammation.[8] Flavonoids can inhibit cyclooxygenase or lipoxygenase.[9] as well as the buildup of leukocytes in the area, resulting in them being anti-inflammatory.[10] The efficiency of bay leaf ethanol extract and aqueous extract as an anti-inflammatory in rats was compared to that of diclofenac sodium as a positive control in this study. Chemical anti-inflammatory drugs are widely used by the public because they have a rapid effect in eliminating inflammation but also have the risk of dangerous side effects such as disorders of the gastrointestinal tract, blood, respiration, metabolic processes, hypersensitivity, and Reye's syndrome.[11] Diclofenac sodium is a non-steroidal anti-inflammatory drug (NSAID) with analgesic, anti-inflammatory, and antipyretic effects. Diclofenac sodium is an NSAID with high potency and good tolerance.[12] Sodium acetate or often called sodium diclofenac is one of the

drugs that has the potential to be developed as a candidate for COX inhibitors. Diclofenac sodium is a nonselective NSAID, acetic acid group, and a derivative of phenylacetic acid. This drug is a strong COX inhibitor with anti-inflammatory, analgesic, and antipyretic effects. Diclofenac sodium has COX-inhibiting activity by inhibiting the formation of prostaglandins which are pain mediators, so it can be used to treat all kinds of pain, migraines, and gout.[13]

This study aimed to assess the correlation between low-density lipoprotein cholesterol and certain lipid profiles in the treatment of bay leaf extract (*Syzygium polyanthum* (Wight) Walp) to dyslipidemia patients

2 Method

We recruit 15 dyslipidemia patients, and the search project was given an explanation and asked to give written consent (informed consent) to participate in the research. Then anamnesis is carried out and the examination is as follows:

a. Anamnesis was carried out to obtain data: age, gender, and other personal data, smoking history, comorbidities (DM, SKA, stroke, infectious diseases, food intake disorders due to gastrointestinal diseases), and family history of the disease.

b. Measurement of body height is carried out in an upright position barefoot. Measurements ranging from the soles of the feet to the top of the head using microscopes. Body height measurement results are expressed in meters (m). Body weight is measured in an upright position using a Camry brand digital scale, the measurement results are expressed in kilograms (kg), and BMI assessment is carried out in units of kg / m^2 .

c. Measurement of waist circumference is carried out in an upright position barefoot with a distance between the two legs 25-30 cm using a tape measure. Measurements were made horizontally circularly from the midpoint between the summit of *Cristae iliac* and the lower edge of the last costa on the axillaries media. The measurement results are seen from the medial and expressed in centimeters (cm).

d. After being satisfied for 10-12 hours, the patient then took blood samples by the laboratory in the cubital fossa area of the research subject to examine hs-CRP levels, lipid profiles (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides), routine blood, kidney function (ureum, creatinine), liver function (*Serum Glutamic Oxaloacetic Transaminase* (SGOT), *Serum Glutamate Pyruvate Transaminase* (SGPT)), fasting blood glucose levels. Blood samples are taken before and after the study

Making bay leaf extract is carried out by percolation. Bay leaf simplistic powder with a certain amount is put in a closed vessel, and 70% ethanol is added so that all simplistic is submerged, stir

and let stand for 3 hours. Transfer little by little into the percolator while each time pressed carefully, pour enough filter liquid until the liquid begins to drip, and on top of the simplistic, there is still a layer of filter liquid, close the percolator, and leave for 24 hours. Open the percolator faucet, let the liquid drip at a rate of 1 ml per minute, and add enough filter liquid repeatedly until there is always a layer of filter liquid on top of the simple. Percolation is stopped if the last 500 mg of percolate is evaporated, leaving no residue. Furthermore, the liquid extract is concentrated using a rotavapor, and a thick extract is obtained. The formula used in the test capsule is as follows: Bay leaf extract 150 mg, Amilum Manihot 5%, Amilum maydis 2.5% and Lactose ad 500 mg then the extract is put into the capsules.(Harrizul Rivai, 2015). Bay leaf extract capsule is taken two times per day

Statistical Analysis

Data analysis using *Statistical Package for Social Sciences* (SPSS) software. Data from each study variable were tested for normality with the Shapiro-Wilk test. When p values > 0.05 it is concluded that the data are normally distributed, and the T-test is paired (to compare numerical variables before and after therapy in one group of study subjects)

3 Result

Table 1, shows the subjects of the study were 15 people as a treatment group and ages $47.47 \pm 11,507$ years old. There is significant differences in cholesterol total, LDL-C and Apo=B (all, $p < 0,01$)

Table 1 Comparison before and after 30 days of treatment with bay leaf extract (*Syzygium polyanthum* (Wight) Walp)

Parameters		H0 (n=15)	H1 (n=15)	p
		$\bar{x}\pm SD$	$\bar{x}\pm SD$	
WC (cm)	cm	92.4± 8.5	92.3±8.8	0.527
BW (kg)	kg	65.6±10.7	65.1±10.8	0.074
BMI (kg/m ²)	kg/m ²	26.0±3.4	25.9±3.6	0.152
hs-CRP (mg/L)	mg/dl	2.8±1.9	2.2±2.3	0.570
Cholesrerol Total (mg/dL)	mg/dl	233.6±49.5	200.2±56.1	0.003*
LDL-C (mg/dL)	mg/dl	159.6±41.9	131.9±47.7	0.004*
HDL-C (mg/dL)	mg/dl	43.3±2.5	42.3±2.8	0.362
TG-C (mg/dL)	mg/dl	159.9±2.8	152.8±71.0	0.955
FPG ((mg/dL)	mg/dl	85.3±9.7	85.4±6.7	0.910
Apo-B (mg/dL)	mg/dl	117.4± 27.1	101.8± 30.0	0.002*
Ureum (mg/dL)	mg/dl	18.3±6.4	17.3±4.2	0.682
Creatinin (mg/dL)	mg/dl	0.8±0.2	0.8±0.1	0.889

WC, waist circumference; BW, Body weight; BMI, body mass index; FPG, fasting plasma glucose

In Table 2, there is a correlation between LDL-C and cholesterol total, triglyceride, FPG, and Apo-B (all, $p < 0.05$)

Table 2 Correlation between LDL-C and Cardiovascular Risk Factors

Parameters		r	p
WC	cm	-0.070	0.402
BW	Kg	-0.204	0.233
BMI	Kg/m ²	-0.175	0.266
hs-CRP	mg/dL	0.168	0.275
Cholesrerol Total	mg/dL	0.896	0.001*
HDL-C	mg/dL	0.190	0.249
Triglyceride	mg/dL	0.461	0.042*
FPG	mg/dL	0.535	0.020*
Apo-B		0.919	0.001*
Ureum	mg/dL	0.269	0.166
Creatinin	mg/dL	0.273	0.163

WC, waist circumference; BW, Body weight; BMI, body mass index; FPG, fasting plasma glucose

4 Discussion

Leaves, fruits, and barks of *S. polyanthum* are traditionally used for various medicinal and nonmedicinal purposes. The roots and the fruits are consumed to reverse the hangover effect of alcohol, whereas the leaves are traditionally consumed for treating various illnesses such as diabetes mellitus, hypertension, gastritis, ulcers, diarrhea, skin diseases, as well as infections.[15]

To further test for antihyperglycemic activity, the same treatment was administered to glucose-loaded (intraperitoneal glucose tolerance test, IPGTT) and streptozotocin (STZ)-induced diabetic rats, respectively. Hypoglycemic tests in normal rats did not show a significant reduction in blood glucose levels (BGLs) by the extract. Furthermore, IPGTT conducted on glucose-loaded normal rats also did not show a significant reduction of BGLs. However, repeated administration of metformin and three doses of ME (250, 500, and 1000 mg/kg) for six days caused a significant reduction of fasting BGLs in STZ-induced diabetic rats. The possible mechanisms of action of *S. polyanthum* antihyperglycemic activity were assessed by measurement of intestinal glucose absorption and glucose uptake by isolated rat abdominal muscle. It was found that the extract not only inhibited glucose absorption from the intestine but also significantly increased glucose uptake in muscle tissue.[16] The study demonstrated that *S. polyanthum* leaf methanol extract at 25–200 µg/mL decreased extracellular melanin formation ca. 20–80%, with high cell viability. Compounds 1–4 were found to be active in melanogenesis and tyrosinase inhibition. Compound 3 was the most active against tyrosinase activity (83.98 µM), particularly when L-tyrosine was the substrate. Compounds 1–4 significantly diminished extracellular melanin formation in B16 melanoma cells (> 80%), with high cell viability. Thus, our study suggested that compounds 1–4 isolated from the methanol extract of *S. polyanthum* leaf play important roles in decreasing extracellular melanogenesis and inhibiting tyrosinase.[17]

The nutritional aspect of *S. polyanthum* is also an important aspect to be studied as the leaves are edible and regularly incorporated into local Malay dishes. Karim *et al.* determined the content of Vitamins (B2, B3, and C) in *S. polyanthum* leaves. It was found that every 100 mg of dry powder of *S. polyanthum* leaves contains 1.24 mg of riboflavin (Vitamin B2), 0.58 mg of niacin (Vitamin B3), and 0.40 mg of ascorbic acid (Vitamin C), with the total vitamin content of 2.22 mg. The human body requires vitamins in trace amounts to maintain normal physiological functions; therefore, deficiencies of vitamins may lead to various detrimental consequences such as scurvy due to the lack of Vitamin C and pellagra for niacin deficiency.[18]

The pharmacological properties of the ripe and unripe fruits, the bark, and mostly the leaves of *S. polyanthum* were widely studied. Currently, *S. polyanthum* leaves were reported to have antioxidant, antidiabetic, antimicrobial, antihypertensive, antitumor, antidiarrheal, acetylcholinesterase inhibitory, and lipase inhibitory activities. [19]

The essential oils of the leaves of two *Syzygium* species commonly used as spices in Indonesia (*Syzygium polyanthum* and *S. aromaticum*) were analyzed by gas chromatography/mass spectrometry (GC/MS) and evaluated for their minimum inhibitory concentration (MIC) against five food-borne microorganisms. The essential oils of both plants were obtained by the hydro distillation method. The major constituents of essential oil of *S. polyanthum* were cis-4-decanal (43.489%), 1-decyl aldehyde (19.752%), and capryl aldehyde (14.092%), while the major constituents of essential oil of *S. aromaticum* were p-eugenol (75.190%) and β -caryophyllene (18.364%). Beta-caryophyllene, α -humulene, α -farnesene, and caryophyllene oxide were detected in both essential oils of *S. polyanthum* and *S. aromaticum*. Both essential oils strongly inhibited *Bacillus subtilis* growth. Essential oil of *S. aromaticum* showed a stronger inhibitory activity against *Staphylococcus aureus*, *Salmonella typhimurium*, and *Vibrio cholera* than that of *S. polyanthum*. Both essential oils did not inhibit the growth of *Escherichia coli*. [20]

Evidence has shown that there is a strong relationship between hypertension and kidney disorder. *Syzygium polyanthum* is a local plant that has been claimed traditionally as anti-hypertensive and believed to be an effective remedy for kidney problems as well. This study aimed to investigate the oral effect of 4-week administration of a methanolic extract from *S. polyanthum* (MESP) leaves towards renal structural improvement in hypertensive renal damage among spontaneous-hypertensive (SHR) and normotensive-rats (WKY). The study utilized 15 males; 10 SHR and 5 WKY rats. The methanolic extract was successively prepared via the ultrasound-assisted method. Both Group 1 (n=5) and Group 2 (n=5) received distilled water and served as negative control groups of WKY and SHR respectively. The treatment group of SHR; Group 3 (n=5) received 2000 mg/kg MESP. At the end of the study, all rats were euthanized and kidney tissues were isolated for histopathological studies using light microscopy (H&E-stain) and scanning electron microscopy. The study revealed that there was an improvement in the renal structure of the MESP-treated group; similar to the normal structure of WKY. The Bowman's capsule is well capsulated and the Bowman's space is well-defined. Meanwhile, the podocyte had better morphology. In contrast to untreated SHR, the appearance of kidney structure is slightly attenuated due to distortion and engorgement of the glomerulus. In conclusion, the result suggests that oral administration of *S. polyanthum* has a renoprotective effect in improving renal morphology in hypertensive-renal damage of SHR rats. [21]

In this study, bay leaf administration of 2x150 mg for 30 days, improved lipid profiles: total cholesterol, LDL, and ApoB in dyslipidemic patients. Furthermore, foliar feeding has the potential to prevent and improve cardiovascular disease.

5 Conclusion.

In this study, bay leaf administration of 2x150 mg for 30 days to dyslipidemia patients, can improve lipid profiles of total cholesterol, LDL, and ApoB. All these parameters are responsible for cardiovascular events such as stroke, coronary artery disease, and PAD. Bay leaf extract administration has the potential to prevent and improve cardiovascular disease in dyslipidemic patients.

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