International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2019): 7.583

Comparison between Oral Administration of *Kaempferia galanga* Rhizome Extract and Simvastatin in Improving Lipid Profile of Dyslipidemic Male Wistar Rats

Sonia Hermawan[1], IGM Aman[2], Ni Nyoman Ayu Dewi[3]

[1]Program Studi S2 Biomedik, Fakultas Kedokteran Universitas Udayana, Bali, Indonesia

[2]Departemen Farmakologi dan Terapi, Fakultas Kedokteran Universitas Udayana, Bali, Indonesia

[3]Departemen Biokimia, Fakultas Kedokteran Universitas Udayana, Bali, Indonesia
soniahermawan1792[at]gmail.com

Abstract: ***Introduction: Dyslipidemia has the potential to cause atherosclerosis which leads to cardiovascular disease. Kaempferia galanga rhizome is known to contain various components as antioxidants those affect on lipid profile improvement. This study aimed to determine the effect of Kaempferia galanga rhizome extract on improving the lipid profile of male Wistar rats with dyslipidemia. Methods: An experimental study with a randomized pretest-posttest control group design was conducted on 14 male Wistar rats, aged 2-2.5 months which suffered from dyslipidemia. Subjects were divided into two balanced groups, namely the control group (administrated with simvastatin 0.36mg) and the study group (administrated with Kaempferia galanga rhizome extract 100 mg) for 14 days. Lipid profiles were measured before and after treatment. The data were analyzed using a compare mean test. Results: The results showed no significant difference in total cholesterol levels between the two groups pretest (p = 0.336) and posttest (p = 0.038) , triglycerides between the two groups pretest (p = 0.447) and posttest (p =0.923), LDL between the two groups pretest (p = 0.515) and posttest (p = 0.052), and HDL between the two groups pretest (p = 0.354) and after posttest (p = 0.574). Although there was significant difference in p-total cholesterol values in the two groups pretest and posttest, the pre-post mean difference between the two groups showed no significant difference from the difference between pre-post total cholesterol (p = 0.117). Conclusion: The results of this study indicated that there was a significant improvement in the lipid profile with both Kaempferia galanga rhizome extract and simvastatin. The improvement in lipid profile was not significantly different from the administration of Kaempferia galanga rhizome extract or simvastatin.***

Keywords: Cholesterol, Dyslipidemia, Kaempferia galanga Rhizome Extract

1. Introductions

There has been a transition in Indonesia epidemiology, namely a reduction in infectious diseases and an increased number of non-communicable diseases incidents.[1] According to data from the World Health Organization (WHO), cardiovascular disease ranks first as the cause of global death , specifically about 17.9 million people died in 2016, and it is predicted that the number will be increased continually to 23.6 million in 2030.[2,3] The root of cardiovascular disease is atherosclerosis and dyslipidemia is one of the main risk factors.[4]

Dyslipidemia itself is described as a disorder of lipid metabolism, characterized by plasma fraction abnormalities, including increased levels of total cholesterol (≥200 mg/dl), Low Density Lipoprotein (LDL) cholesterol (≥130 mg/dl), triglycerides (TG) (≥ 150 mg / dl), or a decrease in High Density Lipoprotein (HDL) cholesterol levels. [5,6] In addition to hypertension and diabetes mellitus, dyslipidemia is also included in the metabolic syndrome triad, which is a major factor in the emergence of atherosclerosis that causes cardiovascular diseases such as stroke and coronary heart disease. [7]

The keys to managing dyslipidemia include a low calorie and minimally cholesterol diet, avoiding alcohol and cigarettes, doing regular physical activity, and a good lifestyle, including adequate sleep and good stress control. If pharmacological approaches are difficult to achieve, then pharmacological therapy is the next option.[8]

The main pharmacological therapy in the management of dyslipidemia is the statin group. Statin works by lowering blood cholesterol levels and LDL in patients.[9] In addition, it is also able to increase HDL and Apolipoprotein AI (apo AI) levels. By inhibiting the coenzyme HMG-CoA reductase, an enzyme that plays a role in cholesterol formation, it can reduce the risk of cardiovascular disease eventually in the long term. However, regardless of the benefits obtained, it is necessary to consider the side effects associated with synthetic drugs that can possibly occur, such as myopathy, changes in hepatic function, renal function, and effects on the digestive organs.[10]

One of the alternative plants that can be used is *Kaempferia galanga*. In a study by Subbaian and Ragavan (2020), giving *Kaempferia galanga* extract of 250 grams / kg BW and 500 grams / kg BW in streptozotocin-induced diabetic albino rats showed a significant decreased in cholesterol, triglyceride, LDL, VLDL levels, and improved HDL. The lipid profile

difference was significant when compared to the control group using saline solution. [11]

The ethanol extract of *Kaempferia galanga* rhizome is also known to have antioxidant, anti-inflammatory, anti-cancer, analgesic, nematicide, vasorelaxant and antimicrobial activity.[12] The flavonoid content of *Kaempferia galanga* has a strong correlation (R2 = 0.985, p <0.05) with nitric oxide scavenging activity. The content of all phenols and flavonoids from the methanol extract of *Kaempferia galanga* is 15.40 ± 0.50 mg equivalent of catechin / g extract.[13]

Kaempferia galanga has a potential effect on the lipid profile improvement, therefore this study was carried out on dyslipidemic male Wistar rats to compare improvements in lipid profiles between *Kaempferia galanga* extract and simvastatin. Simvastatin is an HMG-CoA inhibitor which included in the statin group as a reference because it is a dyslipidemia first-line drug.[14]

2. Methods

Extract Preparation

Kaempferia galanga were bought at a traditional market and then dried for several days before cut and soaked with 95% ethanol with ratio of 1:6 for 72 hours in room temperature. Afterwards, submerged *Kaempferia galanga* were filtered by filter paper and being evaporated using vacuum rotator to obtain crude extract. Phytochemical analysis was performed using spectrophotometer.

Animal Subjects

The sample of this study were male Wistar Rats (*Rattus norvegicus*), aged between 2-2.5 months, and weighing 160-220 grams. The sample size was calculated using Pocock (2008) formula, with a minimum sample size per group at 7 rats/group. The variables measured were levels of lipid profiles after 14 days treatment. The rats were adapted for 7 days, before given a high cholesterol diet such as chicken egg yolk (5%), lard (15%) for 30 days to achieve dyslipidemia condition (cholesterol levels ≥200 mg/dl).[8]

Sample Collection

After 30 days of high cholesterol diet, all rats were being weighed and examined their lipid profiles for pretest data. Then, they divided randomly into 2 groups. The control group was treated with 0.36 mg of simvastatin and the treatment group was treated with 100mg *Kaempferia galanga* rhizome extract every 5 pm for 14 days. After being treated, the rats from each group were fasted for 8 hours then anesthetized using Ketamine 40mg/kg BW and Xylazine 5mg/kg BW by intramuscular injection. 1.2ml were drawn through the medial canthus of orbital sinus to measure blood lipid profile.

Lipid Profile Measurement

Lipid profile (total cholesterol, triglyceride, LDL, and HDL) was determined by quantitative-enzymatic-colorimetric methods, according to manufacturer's instructions ('Stanbio Laboratory' Kit). One ml blood serum was put inside a tube along with reagent and standard. Then incubated in 37ºc for 5 minutes before reading the results in microplate reader.

Statistical Analysis

After collecting all data, the lipid profile and body weight were analyzed to obtain data description, data normality, data homogenicity, and comparison of mean. Lipid profile and body weight data were tested using T-Independent Test. All statistical analysis was performed by SPSS 21 for Windows. P value was considered signigicant if less than 0.05.

3. Results & Discussion

Kaempferia galanga is known for its potential as an antioxidant, which contains several active compounds.[15] This, in line with the results of the phytochemical test of *Kaempferia galanga* rhizome extract conducted at the UPT Analytical Laboratory of Udayana Bali University, which showed that the levels of flavonoids were 1322 mg / 100g, phenol 298mg / 100g, and tannins of 222 / 100g. While the IC50 results obtained 928.13 ppm.

Table 1: Phytochemical Results Test of *Kaempferia galanga*

Parameter	Unit	Results
IC 50	Ppm	928.13
Antioxidant Capacity	mg/L GAEAC	83.54
Fenol	mg/100g	298.02
Flavonoid	mg/100g	1322.19
Tannin	mg/100g	222.85

When compared to the South African leaf extract research which conducted by Nurdiastuti (2016), it was found that the IC50 level was 1.31 ppm, then the IC50 of South African leaf extract was better.[16] When compared with another study by Valentina (2016) which used chayote extract as a comparison of simvastatin in improving lipid profiles, it showed that chayote extract had tannin levels of 451.2929 mg / 100g, flavonoids 3.9089 mg / 100 g, and phenol 87. 43/100 g, then the antioxidant activity of *Kaempferia galanga* rhizome extract is higher.[17]

Comparative mean tests for total cholesterol, triglycerides, LDL, HDL, and body weight are also shown in table 2. The results showed there were significant differences in the total cholesterol mean of pretest (214.59±4.20 mg/dl) and posttest (198.14±6.12 mg/dl) in control group (p<0.001) and mean of pretest (217.51±6.78 mg/dl) and posttest (205.94±6.42 mg/dl) in the study group (p<0.001), triglyceride mean of pretest (161.43±7.36 mg/dl) and posttest (143.61±11.69 mg/dl) in control group (p=0.001) and mean of pretest (157.62±10.49 mg/dl) and posttest (144.22±11.28 mg/dl) in the study group (p=0.001), LDL mean of pretest (141.81±6.19 mg/dl) and posttest (123.24±3.58 mg/dl) in control group (p<0.001) and mean of pretest (144.23±7.27 mg/dl) and posttest (129.96±7.43 mg/dl) in study group (p=0.001), and HDL mean of pretest (40.49±2.29 mg/dl) and posttest (46.18±2.53 mg/dl) in control group (p=0.003) and study group (p=0.002). However, body weight showed that there was no significant difference in the mean of pretest (184.43±9.11 g) and posttest (200.43±17.23 g) in control group (p=0.060) and mean of pretest (175.29±28.12) and posttest (183.43±43.35) in study group (p=0.501).

The results of the comparability test between the two groups showed that there were no significant difference in the mean total cholesterol between the two groups pretest (p=0.336) and posttest (p=0.038), the mean triglycerides between the two groups pretest (p=0.447) and posttest (p=0.923), the mean LDL between pretest (p=0.515) and posttest (p=0.052) groups, the mean HDL between pretest (p=0.354) and posttest (p=0.574) groups, and the average body weight between the two pretest groups (p=0.429) and posttest (p=0.354). Although there was a significant difference in the p value of total cholesterol posttest, the pre-post difference (Δ) between the two groups showed no significant difference (p=0.117).

Table 2: Comparison of Lipid Profile and Body Weight Before and after Treatment

Variable	Group	Pre test Mean±SD	Post test Mean±SD	ΔPre-Post Mean±SD	P**
Cholesterol (mg/dl)	Control	214.59±4.20	198.14±6.12	16.45±5.99	<0.001
	Treatment	217.61±6.78	205.94±6.42	11.67±4.48	<0.001
	P*	0.336	0.038	0.117	
Triglycerides (mg/dl)	Control	161.43±7.36	143.61±11.69	17.82±8.04	0.001
	Treatment	157.62±10.49	144.22±11.28	13.40±5.25	0.001
	P*	0.447	0.923	0.247	
LDL (mg/dl)	Control	141.81±6.19	123.24±3.58	18.56±6.76	<0.001
	Treatment	144.23±7.27	129.96±7.43	14.27±5.87	0.001
	P*	0.515	0.052	0.228	
HDL (mg/dl)	Control	40.49±2.29	46.18±2.53	5.68±3.02	0.003
	Treatment	41.85±2.93	47.13±3.57	5.28±2.55	0.002
	P*	0.354	0.574	0.492	
Body Weight (gram)	Control	184.43±9.11	200.43±17.23	16.00±18.27	0.060
	Treatment	175.29±28.12	183.43±43.35	8.14±30.11	0.501
	P*	0.429	0.354	0.566	

*p** was analyzed using Independent T Test; *p*** was analyzed using T-Paired Test

The improvement of the lipid profile by administration of *Kaempferia galanga* rhizome extract was influenced by various active compounds, such as flavonoids, polyphenols and tannins. Flavonoids work as inhibitors of the HMG-CoA reductase enzyme preventing the formation of mevalonate, resulting in lowering cholesterol in the liver. In addition, it could also increased the HDL level by stimulating Lecithin Cholesterol Acyl Transferase (LCAT) enzyme .[14] Polyphenols are classified as antioxidants which take a positive role in endothelial function, by reducing LDL oxidation and increasing the amount of Nitric Oxide (NO) .[18] Tannins are also able to inhibit HMG-CoA reductase, reducing the secretion of lipoproteins in the liver and intestines, and lowering cholesterol esters which could inhibit the cholesterol esterification process.[19]

The comparability test showed no difference in the mean total cholesterol levels in the pretest group (p> 0.05), but there was a significant difference in the post-test group (p <0.05). The test in the control group and the treatment group obtained p value = 0.001, it could be seen that there was a significant decreased in the mean of total cholesterol. The mean reduction value of the treatment group was 11.67 which was lower than the mean value in the control group which was 16.45. The results of this study are in accordance with the expectations of the study because although in the control group the number of decreases was greater than the treatment group, there was a decrease in total cholesterol in the paired T-test in the two groups showing a significant difference (p <0.05).

There was no difference in the mean HDL levels in the comparability test between the pretest and posttest groups (p> 0.05). The treatment effect test in the control group and the treatment group obtained p value <0.05, which indicated a significant increase in the mean HDL. The increased value in the control group was 5.69 which was greater when compared with the increased value in the treatment group, namely 5.28.

The LDL comparability test showed that there was no difference in the mean LDL between the two groups pretest and posttest (p> 0.05) The treatment effect test in the control group and the treatment group obtained p value <0.05 which indicates that there was a significant decrease in the mean LDL in both groups . The mean value of reduction was greater in the control group of 18.57 when compared to the average value of decline in the treatment group which was 14.27.

As explained above, the results of the phytochemical examination of *K. galang*a rhizome extract showed the content of flavonoids, phenols, and tannins, which are antioxidant components. In the concept of Anti Aging Medicine, antioxidants have a crucial role to reduce the effects of free radicals that play a role in the aging process.[20]

As far as we know, our study is the first report on comparison between *K. galanga* and simvastatin on lipid profile in Indonesia. Our findings indicated that *K.galanga* rhizome extract improved lipid profile as effective as simvastatin. However, our study did not identify the mechanism of the decrease in triglyceride due to statin administration. It may cause by a diet change from a high fat diet to the standard diet. This needs to be further studied because even though simvastatin can indeed lower triglyceride levels, simvastatin is not the drug of choice like fibrate in lowering triglyceride levels. Therefore, the initial lipid profile measurement prior to the study is highly suggested. It is hoped that this research can provide alternative therapy in dealing with dyslipidemia and various

degenerative diseases that could arise from the incidence of dyslipidemia, including obesity and cardiovascular disease.

4. Conclusion

Based in the data, it can be conluded that there was no significant difference in lipid profile by administration of *Kaempferia galanga* rhizome compared to simvastatin given to rats (*Rattus norvegicus*) with dyslipidemia. Further studies are needed to make sure the effectivity of *Kaempferia galanga* whether it's reversible or not in the management of dyslipidemia. Toxicity study is also needed to study about the safety of consuming it in a period time. And last but not least, to measure the lipid profile levels in the initial condition before conducted the research to determine the exact starting point of the lipid profile levels.

5. Conflict of Interest

All authors declared that there is no conflict of interest regarding this publication

6. Author Contribution

All author contributed equally in the writing of this article

7. Funding

This study was self-funded without any contribution from third party.

8. Ethic Approval

This study had been ethically approved by ethical commission of Faculty of Medicine Udayana University with approval letter number 87/UN14.2.9/PT.01.04/2020.

References

[1] PERKENI. (2015). Panduan Pengelolaan Dislipidemia Panduan Pengelolaan Dislipidemia di Indonesia 2015. *PB. Perkeni.*

[2] WHO. (2017). Fact Sheet: cardiovascular disease. *Cardiovascular Diseases*.

[3] World Health Organization. (2013). WHO | Cardiovascular diseases (CVDs) factsheet. Retrieved from http://www.who.int/cardiovascular_diseases/about_cvd/en

[4] Rahmawansa S. Sany. Dislipidemia sebagai Risiko Utama Penyakit Jantung Koroner (PJK). Cermin Dunia Kedokt 169. 2009;36(3):181–4.

[5] Kavey R-EW, Daniels SR, Lauer RM, Atkins DL, Hayman LL, Taubert K. American Heart Association Guidelines for Primary Prevention of Atherosclerotic Cardiovascular Disease Beginning in Childhood. AHA J. 2003;107(11):1562–6.

[6] Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002 Dec 17;106(25):3143–421.

[7] Raal FJ. Pathogenesis and Management of the Dyslipidemia of the Metabolic Syndrome. Metab Syndr Relat Disord [Internet]. 2009 Apr [cited 2020 Jan 8];7(2):83–8. Available from: http://www.liebertpub.com/doi/10.1089/met.2008.0079

[8] American Heart Association (AHA). 2013. 2013 *ACCF/AHA guideline for the management of heart failure: A report of the American College of Cardiology Foundation/American Heart Association task force on practice guidelines*. J Am Coll Cardio, 62(16), e240-e327.

[9] McFarland, A. J., Anoopkumar-Dukie, S., Arora, D. S., Grant, G. D., McDermott, C. M., Perkins, A. V., dan Davey, A. K. 2014. *Molecular Mechanism Underlying the Effect of Statins in the Central Nervous System*. International Journal of Molecular Sciences, 20607 – 20637

[10] PERKENI. 2019. Pedoman Pengelolan Dislipidemia di Indonesia. Jakarta. PB PERKENI.

[11] Subbaian, K., & Ragavan, B. 2020. *Antihyperlipidemic effect of Kaempferia galanga in streptozotocin-induced diabetic rats Collection of Plant Material.* Drug Intervention Today, 14(3), 7–10.

[12] Muhafidzah, Z., Dali, S., Syarif, R. A. 2018. Aktivitas Antioksidan Fraksi Rimpang Kencur (*Kaempferia galanga*) dengan Menggunakan Metode Peredaman 1,1 Diphenyl-2-picrylhydrazil (DPPH). 10(01), 44–50

[13] Ali, H., Yesmin, R., Satter, M. A., Habib, R., dan Yeasmin, T. 2018. *Antioxidant and antineoplastic activities of methanolic extract of Kaempferia galanga Linn. Rhizome against Ehrlich ascites carcinoma cells.* Journal of King Saud University - Science, 30(3), 386–392. https://doi.org/10.1016/j.jksus.2017.05.009

[14] Ekananda, N. A. (2015). Bay Leaf in Dyslipidemia Therapy. *Dyslipidemia Therapy J Majority*, *4*(4), 64–69.

[15] Hasanah, A. N., Fikri, N., Ellin, F., & Ade, Z. 2011. Analisis kandungan minyak atsiri dan uji aktivitas antiinflamasi ekstrak rimpang kencur (*Kaempferia galanga L.*). Jurnal Matematika & Sains, 3, 16, 147-152.

[16] Artha, C., Mustika, A., dan Sulistyawati, S. W. 2017. Pengaruh Ekstrak Daun Singawalang terhadap Kadar LDL Tikus Putih Jantan Hiperkolesterolemia. Artikel Penelitian. Surabaya : Universitas Airlangga.

[17] Nurdiastuti, T. 2016. Efek Daun Afrika Selatan (*Vernonia amygdalina*) Memperbaiki Profil Lipid Tikus Wistar Jantan Dislipidemia. https://anzdoc.com/ekstrak-daun-afrika-selatan-vernoniaamygdalina-memperbaiki-.html

[18] Umarudin dan Susanti, R. 2012. Efektivitas Ekstrak Tanin Seledri Terhadap Profil Lipid Tikus Putih Hiperkolesterolemi. Unnes Journal of Life Science Volume 1, no 2. Halaman 78-85.

[19] Puspita, R., Ardiaria, M., dan Syauqty, A. 2016. Perbedaan Efek Seduhan Kulit dan Jus Buah Naga Merah (*Hylocereus polyrhizus*) Terhadap Kadar Kolesterol LDL Serum Tikus Sprague Dawley Dislipidemia. Jurnal Kedokteran Diponegoro, vol 5, no. 4, hlm. 1559-1567.

[20] Valentina, C. 2016. Pemberian Ekstrak Labu Siam (*Sechium Edule*) Memperbaiki Profil Lipid Tikus Putih Jantan (*Rattus norvegicus*) Dislipidemia Lebih Baik Daripada Simvastatin. Denpasar. Universitas Udayana Denpasar.
[21] Pangkahila, W. 2011. *Anti-Aging.* Tetap Muda dan Sehat. Jakarta:PT. Kompas Media Nusantara.