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**Potency of Ethanol Extract Celery (*Apium graveolens L.*)
 Stalk as Anti-Cholesterol**

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Abstract

Increasing levels of blood cholesterol is one of the risk factors for atherosclerosis. Currently, experts have been trying used herbal medicine as an alternative treatment of atherosclerosis. One of the highlights is the use of celery stalks. Celery is generally used as a flavouring dish. In addition, celery stalks are believed able to reduce cholesterol levels because they contain flavonoids, tannins, and saponins. This study was aim to determine the effect of celery stalk ethanol extract to reduce LDL an increase of HDL level in rats after fed high-fat diet. Randomized Post Test Only Control Group Design was used to measure the HDL and LDL blood serum levels of male Wistar (*Rattus norvegicus*) rats fed a high-fat diet. This study was used 27 male Wistar rats (*Rattus norvegicus*) divided into 3 groups; K1 was only given regular feed and water, K2 was given a high-fat diet and water, K3 was given a high-fat diet and celery stalk extract at a dose of 75mg/kg BW/day for 14 days. The data were analysed by ANOVA test and Tukey HSD test. The results of the ANOVA test showed a significance value of p-value of LDL = 0.000 and HDL p-value = 0.536. Celery stalk extract (*Apium graviolens L*) had an effect on decreasing LDL levels but not on increasing HDL blood serum levels of white Wistar rats (*Rattus norvegicus*) given high-fat diet.

Keywords: Celery stalk, LDL, HDL.

Original Research Article

**Kemampuan Ekstrak Etanol Batang
 Seledri (*Apium graveolens L.*)
 sebagai Anti Kolesterol**

Abstrak

Peningkatan kadar kolesterol darah merupakan salah satu faktor resiko terjadinya aterosklerosis. Saat ini banyak ahli yang mencoba memanfaatkan obat herbal sebagai aletrnatif pengobatan arterosklerosis. Salah satu yang menarik adalah penggunaan batang seledri. Seledri pada umumnya digunakan sebagai pepadap masakan. Selain itu batang seledri dapat digunakan sebagai obat tradisional yang dipercaya oleh masyarakat dapat menurunkan kadar kolesterol karena memiliki kandungan flavonoid, tanin, dan saponin.

Penelitian ini bertujuan untuk mengetahui pengaruh pemberian ekstrak etanol batang seledri (*Apium gravolens L.*) terhadap penurunan kadar LDL dan peningkatan kadar HDL serum darah tikus putih (*Rattus norvegicus*) jantan galur wistar yang diberi diet tinggi lemak. Penelitian ini menggunakan metode Randomized Post Test Only Control Group Design dengan besar sampel 27 ekor tikus putih jantan galur wistar (*Rattus norvegicus*) yang dibagi dalam 3 kelompok; K1 hanya diberi pakan biasa dan air, K2 diberi pakan tinggi lemak dan air, K3 diberi pakan tinggi lemak dan ekstrak batang seledri dengan dosis 75mg/kgBB/hari selama 14 hari. Data dianalisis dengan uji ANOVA dan dilanjutkan dengan uji Tukey HSD. Hasil uji Anova menunjukkan nilai signifikansi p-value LDL = 0,000 dan signifikansi p-value HDL = 0,536. Pemberian ekstrak batang

seledri (Apium graveolens L) berpengaruh terhadap penurunan kadar LDL namun tidak berpengaruh terhadap peningkatan kadar HDL

serum darah tikus putih galur wistar (Rattus norvegicus) yang diberikan diet tinggi lemak.

Kata Kunci: Batang seledri, LDL, HDL

INTRODUCTION

WHO estimates that there will be more than 23 million people die from cardiovascular disease by 2030 (WHO, 2020). Coronary heart disease is the top leading cause of death in Indonesia (SKRT, 2017). Hypercholesterolemia is one of factors that triggers this disease. Some factors affect cholesterol levels in the blood, including age, weight, diet, physical activity, smoking habit, stress, and heredity, where diet takes the most proportion (Wulandari et al., 2016). For genetically susceptible individuals, high cholesterol diet increases the concentration of cholesterol, especially LDL in the blood, leading to dyslipidemia. Increased blood cholesterol level plays a major role in atherosclerosis. Recently, experts have started to use herbal medicines in atherosclerosis treatment, including the use of celery stalks. Besides as a taste enhancing food, celery has been known able to lower cholesterol levels (Dwisatyadini, 2010).

Some chemical compounds are found in celery stalks (*Apium graveolens L.*), including flavonoids, saponins, 1% tannins, 0.033% essential oils, flavoglucoisides (apiin), apigenin, choline, lipase, asparagine, bitter substances, vitamins (A, B, and C). (Dalimartha, 2016). The mechanisms of flavonoids, tannins and saponins have effects on hypolipidemia. Flavonoids are effective antioxidants for the inactivation of hydroxyl and peroxy radicals. Flavonoids are inhibitors against HMG-CoA reductase enzyme, which will decrease the cholesterol synthesis (Shi et al., 2021). Flavonoids can also form complex bonds with metal ions, and inhibit the initiation of metals to carry out lipid oxidation. Tannins are one of the natural antioxidants that prevent lipid peroxidation from free radical attack (Muchatadi, 2013). Tannins reduce the activity of HMG-CoA reductase cholesterol and LDL cholesterol and significantly increase the HDL cholesterol level. Saponins are triterpene glycosides that have a hypolipidemic mechanism which decrease the cholesterol synthesis by inhibiting HMG-CoA reductase activity and increase the conversion of cholesterol to bile acids (Meirindasari et al., 2013).

Based on research by (Meirindasari et al., 2013). and (Muchatadi, 2013) stated that celery leaves have an effect in lowering LDL levels and increasing blood serum HDL levels. Celery stalks, which contain almost the same content as celery leaves, are almost not used in the community. The number of celery stalks in volume is much more than the leaves. Celery stalks can be used as a traditional medicine which is believed by the community to reduce cholesterol levels and as an alternative treatment for atherosclerosis because it contains flavonoids, tannins and saponins. Based on this phenomenon, it is necessary to conduct research to determine the effect of ethanol extract of celery stalks (*Apium graveolens L*) on decreasing LDL levels and increasing HDL blood serum levels of male Wistar rats (*Rattus norvegicus*) given a high-fat diet.

MATERIALS AND METHOD

High-fat diet containing a mixture of 2 grams of pork oil, 0.02 grams of cholic acid and 1 gram of boiled quail egg yolk dissolved in 2 ml of water was administered. The extract was produced from celery stalks of 1 cm above the root limit and 1 cm below the first leaf branch which were dissolved in 80% ethanol obtained from Batu - Malang, East Java. A Randomized Post Test Only Control Group Design was performed; involving 27 male Wistar rats (*Rattus norvegicus*) aged 3-4 months, with body weights ranging from 150-250 grams as samples. Samples were divided into 3 groups; K1 was only given regular feed and water, K2 was given a high-fat diet and water, K3 was given a high-fat diet and celery stalk extract at a dose of 75mg/kg BW/day for 14 days. Extraction of celery stalks (*Apium graveolens L.*) was carried out by maceration method. The result of maceration in the form of celery stalk powder, 50 grams of powder was taken and dissolved in 100 ml of 80% ethanol. The suspension was filtered using a glass funnel and filter paper. The result of this process in the form of filtrate is then put into a rotary evaporator until a thick extract is obtained. The data were analysed using ANOVA test and followed up with the Tukey HSD test.

RESULTS

Twenty-seven male Wistar rats were administered by high-fat diet to obtained the hypercholesterolemia condition. In treatment

group (K3) were given high-fat diet together with the celery's stalk. In the end of treatment, data were collected from all groups including HDL and LDL level from blood serum. The mean and standard deviation of HDL and LDL level showed in Table 1.

Table 1. HDL and LDL Levels of Samples

	K1 (Negative Group)		K2 (Positive Group)		K3 (Treatment Group)	
	HDL (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	HDL (mg/dl)	LDL (mg/dl)
Mean	17.6389	31.8833	18.9033	31.7322	19.1644	24.9978
Standard deviation	2.64251	3.09823	2.49574	2.41905	3.85373	0.61747

Source: Data processed 2021

As presented in the Table 1, the highest HDL level was found in K3 (the treatment group). The highest average HDL level was found in the treatment group (19.16). Whereas, the lowest

HDL level was obtained in the negative control group (17.64). The negative control group has the highest LDL level (31.88), and the lowest one was in treatment group (24.99).

Table 2. Statistical Data Analysis

P value	Normality test	Test Homogeneity of Variance	Comparative test
HDL	0.200	0.328	0.536 (ANOVA)
LDL	0.083	0.001	0.000 (Kruskal-Wallis)*

*superscript: significant difference

In Table 2, It can be inferred from the table that the data were normally distributed with Kolmogorov-Smirnov test, and the variance of HDL were homogeneous with Levene's test, otherwise LDL's variance were heterogenous. LDL data continue with nonparametric test (Kruskal-Wallis). As presented in the table, celery stalk extract (*Apium graveolens L*) does not increase blood serum HDL levels of rats given high-fat diet as

evidenced by the significance value of p-value = 0.536, i.e. > (0.05) using ANOVA test.

On the other side, the celery stalk extract (*Apium graveolens L*) decreased the LDL levels in blood serum of white Wistar rats given high-fat diet used Kruskal-Wallis test with p-value = 0.000 < (0.05). Level of HDL and LDL continue to analyse with Tukey test to determine the significant different level between groups.

Table 3. Post-Hoc Turkey Test on HDL dan LDL

Dependent Variable	Group	Group	p-value
HDL	K1	K2	0.660
	K2	K3	0.549
		K3	0.982
LDL	K1	K2	0.989
	K2	K3	0.000*
		K3	0.000*

*superscript: significant difference

Table 3. indicates no significant difference among all groups in HDL variables, related to the increase in blood serum HDL levels of white Wistar rats given high-fat diet as evidenced by the

significance value (p-value) of > α (0.05). Variable of LDL level shows a significant difference among the treatment group, the negative group and positive control group in lower LDL levels in the

blood serum of white Wistar rats given a high-fat diet as evidenced by the significance value (p-value) of $0.000 < \alpha (0.05)$.

DISCUSSIONS

The results obtained in this study showed that celery stalk extract (*Apium graveolens L*) reduced the LDL levels in male Wistar rats given a high-fat diet as shown by the p value = $0.000 < (0.05)$. Therefore, celery stalk extract (*Apium graveolens L*) has been proven able to decrease LDL levels. The results also indicated a significant difference between the treatment group given celery stalk extract (K3) and the negative control group (K1) in terms of LDL blood serum levels of rats with p-value of $0.000 < (0.05)$. Meanwhile, no significant difference was found between negative group and the positive control group.

Celery contains flavonoids, saponins and tannins which are efficacious for lowering total and LDL cholesterol levels (Umarudin et al., 2012). Flavonoids are phenolic compounds that have antioxidant properties which can protect the body against damages from reactive oxygen species, while they also inhibit the occurrence of degenerative diseases and lipid peroxidase (Murray et al, 2017). Saponins are a large group of alicyclic compounds or higher complex ring compounds with alicyclic properties (Naim et al., 2017). Saponins can lower cholesterol levels, while also acting as antioxidant, antiviral and anti-carcinogenic agents as well as manipulators of rumen germination (Suparjo., 2018). Saponins can lower blood cholesterol by binding to bile acids in the small intestine. The bile acids are produced out of cholesterol and 98% of which are usually reabsorbed by the intestines (entero-hepatic circulation) (Guyton., 2017). By inhibiting the excretion and re-absorption of bile acids, the bile acids will be keep being produced from cholesterol, which eventually decreases the blood cholesterol (Sherwood., 2017).

As antioxidants and radicals-scavenger, saponins will form hydroperoxides which are intermediate compounds. Tannins are the polar active substances of celery. A molecule is polar if it is made up of different atoms. The polarity of a molecule is determined by the value of its dipole moment. Tannins are also polyphenolic compounds that act as antioxidants. As antioxidants, polyphenols have been known to reduce total cholesterol levels and inhibit the formation of atherosclerosis. Tannin compounds

can prevent the occurrence of oxidative stress which can disrupt the balance between the production of oxidants and antioxidants associated with free radical exposure. Tannin extracts reduce the total cholesterol levels by inhibiting the LDL oxidation. Oxidation of LDL cholesterol is a biological process that correlates with the initiation and acceleration of arterial lesions (Umarudin et al., 2012). According to Salman et al (2013), *Apium graveolens* have antioxidant properties and lipid-lowering activities that have direct effect to eliminating free radicals therefore help the cholesterol level in the healthy state

The results also showed no significant difference between the treatment group given celery stalk extract (*Apium graveolens L*) compared to the negative and positive control group in HDL blood serum levels of white Wistar rats given a high-fat diet as evidenced by a significant value (p-value) between pairs of samples of $> \alpha (0.05)$.

Based on the results of the study, it was found that the distribution of celery stalk extract (*Apium graveolens L*) was effective in reducing LDL levels and not effective in increasing HDL levels. It was believes that the effectiveness of celery stalk extract (*Apium graveolens L*) in lowering LDL levels is due to the length of time given celery stalk extract (*Apium graveolens L*) is sufficient, the dose given is also optimal, this is in accordance with research by Umarudin et al. (2012) which states that the active substances contained in celery extract (*Apium graveolens L*), namely flavonoids, saponins and tannins are efficacious for lowering total and LDL cholesterol levels. On the one hand, the result showed that during of giving administration and the dose of celery stalk extract (*Apium graveolens L*) was not optimal yet, causes HDL levels didn't increase as well. This result is different from the research of Umarudin et al. (2012) which stated that the stalk of celery extract containing flavonoids, saponins and tannins also increased HDL levels.

CONCLUSIONS

Celery stalk extract (*Apium graveolens L*) was proven able to reduce LDL levels. Celery stalk extract (*Apium graveolens L*) had no effect on increasing the blood serum HDL levels of white Wistar rats given a high-fat diet at a dose of 75mg/kg BW/day for 14 days.

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