RESEARCH ARTICLE

Beetroot (*Beta vulgaris* L.) Extract Gives Superior Effect than Beetroot Juice on Increasing HDL and Decreasing LDL and IL-6 in Dyslipidemic Rats Model

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Abstract

BACKGROUND: Dyslipidemia derives from disturbances in lipid metabolism as an interaction between genetic and environmental factors, characterized by increased levels of cholesterol, triglycerides, low-density lipoprotein (LDL) and decreased levels of high-density lipoprotein (HDL). Continuous dyslipidemia will increase the risk of atherosclerosis. In dyslipidemia, macrophages release inflammatory cytokines such as interleukin (IL)-1, IL-6, IL-12, IL-15, IL-18, and then induce T-cell infiltration formed atherosclerotic plaques. Beet (*Beta vulgaris* L.) which contains active compounds and antioxidant, such as flavonoids and betacyanin, has the ability to reduce dyslipidemia. This study evaluated effect of beetroot juice and beetroot extract on dyslipidemic rat models by evaluating the level of HDL, LDL and IL-6.

METHODS: Fourty-two male Sprague Dawley rats were divided into seven groups. Rats were fed either with standard food or high fat diet (HFD) for 28 days, then different interventions using either single combination of simvastatin, beetroot juice, or beetroot extract were given alongside the standard food or HFD diet for another 28 days. LDL and HDL were measured pre- and post-intervention, while IL-6 was measured only post-treatment.

RESULTS: Daily administration of a single beetroot juice or beetroot extract or in combination with simvastatin reduced LDL significantly compared to pre-intervention. The interventions also increased HDL significantly and lower IL-6 concentrations compared to group that received no intervention.

CONCLUSION: Administration of beetroot juice and beetroot extract can lower LDL, increase HDL, and decrease IL-6 either alone or in combination treatment with simvastatin, it is indicated beetroot have a potential benefit for prevention and therapeutic in dyslipidemia.

KEYWORDS: beetroot juice, beetroot extract, LDL, HDL, IL-6

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Introduction

Dyslipidemia, a risk factor for cardiovascular diseases (CVDs), can be resulted from an intrinsic, extrinsic, or a combination of genetic predisposition and external factors. Dyslipidemia is a disorder, characterized by increased levels of cholesterol, triglycerides, low density lipoprotein (LDL) and decreased levels of high density lipoprotein (HDL). LDL level is the main target in managing dyslipidemia.(1,2) If HDL decreases and LDL increases continuously, it can cause lipid deposition in the walls of blood vessels, leading to atherosclerosis.(3) Dyslipidemia can cause an inflammatory processed in blood vessels which develops atherosclerosis. (4) CVDs, which account for approximately 12 million deaths annually, is one of the leading causes of death and disability worldwide.(5) World Health Organization (WHO) in 2021 showed 4 out of 5 deaths worldwide were caused

by heart attacks or strokes. Increased levels of lipids in the blood, blood pressure, blood glucose levels, overweight, and obesity are some risk factors that cause CVDs.(6)

In dyslipidemia, macrophage or foam cells release inflammatory cytokines and chemokines which promote inflammation and induce the infiltration of monocyte or T-cell. Macrophages presence in the atherosclerotic plaques will produce various proinflammatory cytokines such as interleukin (IL)-1, IL-6, IL-12, IL-15, IL-18, tumor necrosis factor (TNF), and macrophage migration inhibitory factor (MIF), as well as anti-inflammatory cytokines such as IL-10 and transforming growth factor beta (TGF-β).(7) Adipose tissue as a fat storage depot also plays an active role in producing proinflammatory cytokines such as IL-6, and it is approximately 25% of IL-6 circulating in the blood circulation is released by subcutaneous adipose tissue, which stimulates the liver to produce acute phase proteins. (8) IL-6 is a proinflammatory cytokine that functions in the inflammatory process as a defense for the body and tissues.(9)

The current management of dyslipidemia is a combination of pharmacological and non-pharmacological therapy. Pharmacological therapy is therapy given in the form of anti-lipid drugs, whereas non-pharmacological therapy includes a healthy lifestyle such as an increased of physical activity and exercise, weight loss, medical nutrition therapy, smoking cessation, and administration of natural ingredients proven decreasing lipid profile levels.(10) Based on food consumption habits and several studies, there are several examples of food and processed ingredients can be used as non-pharmacological therapies, both herbal and functional food, including beetroot (*Beta vulgaris* L.).

Beetroot is a traditional plant with high levels of antioxidants.(11) Betalain is one of the main antioxidants in beetroot, and are classified into betaxanthin, orange-yellow, and betacyanin, purplish red.(12) Based on the results of quantitative and qualitative analysis, 100 grams of beetroot contains 128.9 mg alkaloids, 115.5 mg terpenoids, 16.4 mg steroids, 6.4 mg flavonoids, 6.1 mg tannins, 3.8 mg saponins, 0.7 mg glycosides.(13) The flavonoids and saponins in beetroot have the effect of lowering total cholesterol and triglyceride levels.(14,15) Beetroot extract using methanol solvent could significantly reduce cholesterol, triglyceride, LDL, and very low-density lipoprotein (VLDL) levels and significantly increase HDL.(16) Betalain and phenolic compounds found in beetroot can reduce oxidative damage to lipids therefore reducing the risk of dyslipidemia as a risk factor of CVDs. Whereas its nitrate compound can reduce the risk of hypertension and anti-inflammation, and iron content of beetroot is beneficial for anemia prevention. (16,17)

The preparation process can affect the antioxidants content. Fruit juice is the most popular processed fruit, as it is a high-fiber drink and can be made from fruit or vegetable.(18) Betalain is a compound contained in beetroot that can dissolve in water.(19) Ethanol solvent is a universal solvent and can be used for extracting polar and semipolar compounds.(20) Flavonoid which contained in the beetroot is a polar compound therefore it can be dissolved in polar solvents such as ethanol and water.(21-23) Based on the potential of beetroot as antioxidant, therefore it can be used for non pharmacological of dyslipidemia management therapy. This study was conducted to examine the effect of beetroot juice and extract on dyslipidemic rats model by evaluating HDL, LDL and IL-6 levels.

Methods

Preparation of Beetroot Juice dan Extract

The simplicia and fresh beetroot was purchased from UKM Kusuka Ubiku Banguntapan, Bantul, Yogyakarta. The beetroot used in this study has been classified and determined as *Beta vulgaris* L. in accordance with its taxonomy in the Biology Laboratory of Faculty of Science and Applied Technology, Universitas Ahmad Dahlan, Yogyakarta.

For the preparation of beetroot juice, after removing the sand, soil and its stalks, the beetroot was cleaned with water, drained, and prepared for beetroot juice by cutting beetroot into smaller sizes. Approximately 1.8 g of beetroot was blended by adding 1.8 mL of water. While beetroot extraction was carried out by two steps, first step by making simplicia (beetroot was dried up for 48 hours and powdered), next step the simplicia (beetroot powdered) was extracted by maceration method with adding 70% ethanol into the simplicia with a ratio 10:1 (ethanol:simplicia = 10:1). It was then left for 3 days in room temperature, and then filtered with vacuum filter, and dried up using rotary evaporator for 4.5 hours. After dried up, the condensed extract was collected.

Study Design and Animal Model

Forty-two male Sprague Dawley rats, obtained from Inter University Center (IUC), Universitas Gadjah Mada Animal Laboratory, weighing 150-200 g, were used as subjects in this study.(24) Before starting the study, rats were given an adaptation period (acclimatization) for seven days and fed with standard Comfeed PAR-s and water as *ad libitum*.

During the acclimatization period, the animals were adjusted to the environment therefore when the treatment was carried out the animals would no longer be stressed due to moving from their previous cages.(25)

The rats were then randomly divided into 7 groups: normal control (NC) as a group of healthy rats (n=6); C- group was dyslipidemic rats as a negative control (n=6); C+ group was dyslipidemic rats treated with 0.18 mg/200 g body weight (BW) simvastatin as a positive control (n=6); treatment (T)1 group was dyslipidemic rats administrated with 3.6 mL/200 g BW beetroot juice (n=6); T2 group was dyslipidemic rats administrated with 100 mg/200 g BW beetroot extract (n=6); T3 group was dyslipidemic rats administrated with 3.6 mL/200 g BW beetroot juice and 0.18 mg/200 g BW simvastatin (n=6); and T4 group was dyslipidemic rats administrated with 100 mg/200 g BW beetroot extract and 0.18 mg/200 g BW simvastatin (n=6) (Figure 1).

The determination of beetroot juice dose (3.6 mL/200 g BW) was based on previous study as the conversion dose of juice that is usually consumed by human.(13) Meanwhile for the determination of beetroot extract was based on previous study, which stated that by using the dose 500 mg/kg beetroot extract, rats body weight and plasma fasting glucose were decreased significantly as compared with type 2 diabetes melitus (T2DM) rat group, whereas in dosage 250 mg/kg the decreased was not really seen as in rats given 500 mg/kg beetroot extract.(26) Therefore, in this experiment, the dosage of beetroot extract for rat which was 100 mg/200 g BW daily was used.

Dyslipidemic rats were created by feeding the rats with high fat diet (HFD) for 28 days, which was made from Comfeed PAR-s, wheat, cholesterol, cholic acid, and lard. After 28 days, for groups using dyslipidemic rats, along with the intervention of simvastatin, beetroot juice or beetroot extract, HFD feeding was continued for 28 days. During the study, all rats were weighed once a week for 9 times before the treatment (before and after adaptation, before and after administration of HFD) and during treatment (day-0, -7, -14, -21, and -28). The protocol of this study was approved

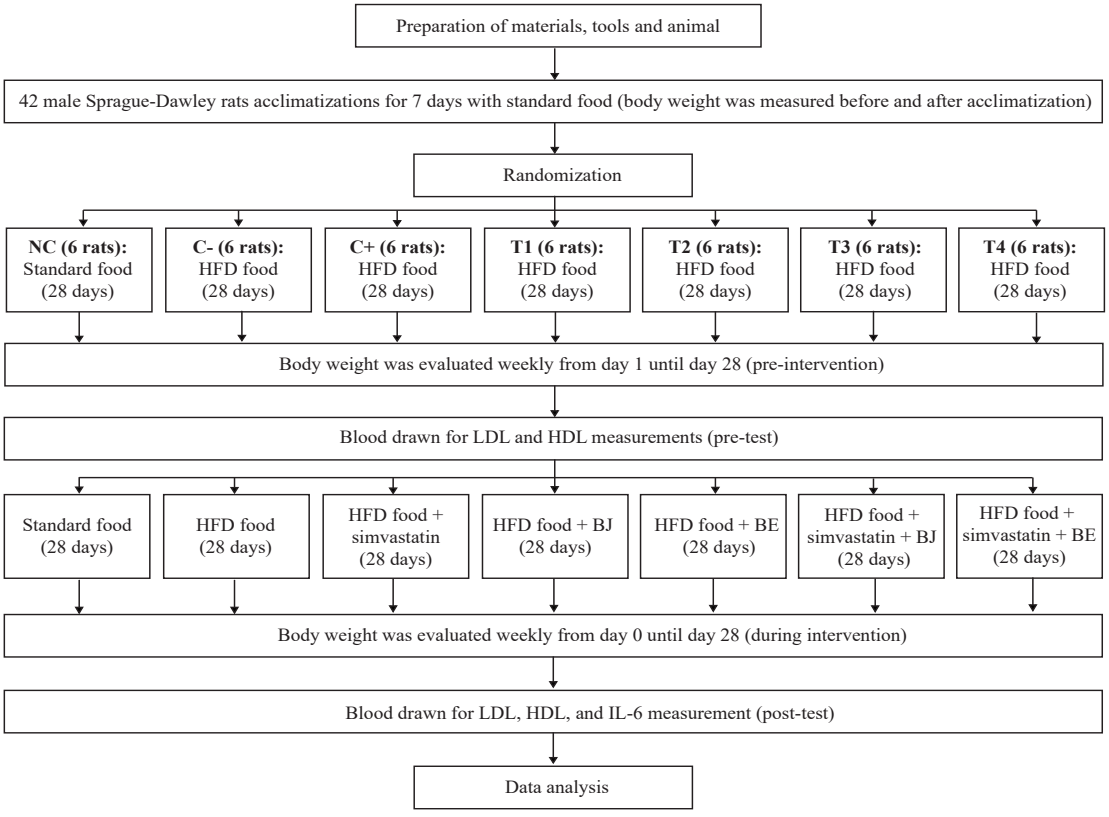

Figure 1. A schematic diagram of the study design and timeline. NC: normal control; C-: negative control (dyslipidemic rats); C+: positive control (dyslipidemic rats treated with 0.18 mg/200 g BW simvastatin); T1: dyslipidemic rats treated with 3.16 mL/200 g BW beetroot juice; T2: dyslipidemic rats treated with 100 mg/200 g BW beetroot extract; T3: dyslipidemic rats treated with 3.16 mL/200 g BW beetroot juice and 0.18 mg/200 g BW simvastatin, T4: dyslipidemic rats treated with 100 mg/200 g BW beetroot extract and 0.18 mg/200 g BW simvastatin. HFD: high fat diet; BJ: beetroot juice; BE: beetroot extract; LDL: low density lipoprotein; HDL: low density lipoprotein; IL: interleukin.

by The Research Ethic Committee of Medical Faculty of Universitas Sebelas Maret, Surakarta (No. 51/UN27.06.11/KEP/EC/2023).

LDL, HDL, and IL-6 Measurements

Blood sampling was carried out twice, as a pre-test and post-test (Figure 1). One mL blood was taken through plexus orbitalis, centrifuged at 3000 rpm for 10 minutes to collect serum samples for measuring LDL and HDL in the pre-test. While for post-test, besides LDL and HDL, IL-6 was also measured as well. LDL and HDL serum levels were measured using enzymatic cholesterol oksidase phenol amino phenazon (CHOD-PAP) photometric method with reagent from DiaSys (Waterbury, CT, USA) and measured with a spectrophotometer from Microlab 300 (Vital Scientific N.V., Diaren, Netherlands) following the manufacture protocols. The normal range for LDL was 2-27 mg/dL, whereas HDL normal range was 35-85 mg/dL.(27) IL-6 level was measured using enzyme-linked immunosorbent assay (ELISA) method with Rat IL-6 (Interleukin-6) ELISA Kit (Cat. No. ER0042; FineTest, Boulder, CO, USA), and its level was considered normal if <62.5 pg/mL.(28)

Statistical Analysis

Data were analyzed using the SPSS version 25 (IBM Corporation, Armonk, NY, USA). The normality test used Shapiro Wilk, and the homogeneity test used Levene-Statistic. Significant differences were analyzed using the one way ANOVA, Student t, and the Tukey LSD post-hoc tests. A $p<0.05$ was considered statistically significant.(29)

Results

Beetroot Juice and Extract Inhibited The Body Weight Increase of Dyslipidemic Rats

During adaptation period, all rats did not show any abnormality and all rats had significant increase of body weight with range 7.17-8.00 g. After making dyslipidemic rats model by giving HFD for 28 days, during the pre-test, each group showed significant increase of body weight with range 67.00-68.00 g in C-, C+, T1, T2, T3, and T4 group; but in the NC group, the body weight only was increased approximately 25 g. In the dyslipidemic groups, as the HFD was given for another 28 days along with the intervention for each group, there were seen increased of body weight variably (Table 1). C-, C+, T1, T2, T3, and T4 groups had increased body weight of 55.67±1.50 g, 26.00±1.09 g, 30.83±1.47 g, 25.00±1.79 g, 30.67±1.03 g, and 26.50±0.84 g, respectively; whereas in NC group also showed increasing body weight of 24.00±0.89 g. The biggest change in rat body weight was in the C- group which was 22%, while the other groups experienced a change in body weight in range of 10-12% (Table 1). There was a significant difference of body weight before and after 28 days giving intervention.

The body weights of the rats in the T1 and T3 groups were similar. This also can be seen in T2 and T4 groups. The average body weight of T4 group was close to that of the C+ group. After post hoc analysis, it was found that there was a significant difference in the body weight of rats in C-, C+, T1, T2, T3, and T4 groups as compared to NC group ($p<0.05$), and a significant body weight difference were also seen in C+, T1, T2, T3, and T4 groups when compared with C- group ($p<0.05$). The post hoc study also revealed that the body weight of T3 group was significantly different with T2 group ($p=0.016$) (Table 1).

Beetroot Juice and Extract Decreased the LDL Level of Dyslipidemic Rats

LDL level after given beetroot juice and beetroot extract in each group was measured to evaluate the effect of beetroot for 28 days of intervention. There was a decreased LDL level in the C+ and treatment groups (T1, T2, T3, T4) (Figure 2). The results proved that beetroot juice, beetroot extract, or the combination of simvastatin with beetroot juice or beetroot extract gave a good effect to LDL level. C- group had the highest level of LDL level (81.77±2.29 mg/dL) and lowest in the T4 group (30.45±1.80 mg/dL). Statistically treatment with giving beetroot juice and beetroot extract had a significant effect on LDL level among treatment groups ($p<0.05$).

The post hoc results showed significant differences among groups except for the C+ and T3 groups ($p=0.088$), C+ and T4 ($p=0.250$), and the T1 and T2 groups ($p=0.323$). These showed that the administration of beetroot juice 3.6 mL/200 g BW and simvastatin 0.18 mg/200 g BW in the T3 group and the administration of beetroot extract 100 mg/200 g BW and simvastatin 0.18 mg/200 g BW in the T4 group could suppress LDL level almost the same as the administration of simvastatin in the C+ group. There was a similar LDL levels in the T1 group and the T2 group which had a slightly changed LDL levels. There was a significant difference in LDL level of all intervention group when compared with the NC and C- groups ($p<0.05$). A comparison of LDL level in each two groups also showed a significant difference ($p<0.05$). Administration of beetroot before and after in each intervention showed the following effective treatments were T4, T3, T2, and T1, respectively.

Table 1. Changes in body weight after administration of beetroot juice and extract.

Group	Body Weight (g) (Mean±SD)		Δ Body Weight (g)	p^a	Change (%)	Post Hoc Analysis (Tukey LSD)
	Pre-Test (Day 28)	Post-Test (Day 56)				
NC	214.17±4.02	238.17±4.26	24.00±0.89	0.000*	11	
C-	255.33±4.72	311.00±4.77	55.67±1.50	0.000*	22	0.000^{*c}
C+	256.33±3.83	282.33±3.78	26.00±1.09	0.000*	10	0.000^{*c}, 0.000^{*d}
T1	253.00±4.29	283.83±3.54	30.83±1.47	0.000*	12	0.000^{*c}, 0.000^{*d}, 0.495^{e}
T2	255.17±3.87	280.17±3.31	25.00±1.79	0.000*	10	0.000^{*c}, 0.000^{*d}, 0.326^{e}, 0.100^{f}
T3	255.00±3.22	285.67±3.01	30.67±1.03	0.000*	12	0.000^{*c}, 0.000^{*d}, 0.134^{e}, 0.405^{f}, 0.016^{*g}
T4	255.33±3.26	281.83±3.37	26.50±0.84	0.000*	10	0.002^{*c}, 0.000^{*d}, 0.819^{e}, 0.364^{f}, 0.448^{g}, 0.087^{h}
p^b	0.000	0.000	0.000			

p^a: Paired Student t-test, between pre-test and post-test of each group; p^b: One way Anova test among those groups in pre-test and post-test; [c]: Post hoc analysis (Tukey LSD test) using NC group as a reference group, [d]: Post hoc analysis (Tukey LSD test) using C- group as a reference group; [e]: Post hoc analysis (Tukey LSD test) using C+ group as a reference group; [f]: Post hoc analysis (Tukey LSD test) using T1 group as a reference group; [g]: Post hoc analysis (Tukey LSD test) using T2 group as a reference group, [h]: Post hoc analysis (Tukey LSD test) using T3 group as a reference group. *p<0.05 is considered as significant.

HDL Level was Increased After Administering Beetroot Juice and Extract in Dyslipidemic Rats

The changes of HDL level in each group were analyzed to evaluate the effect of beetroot juice and beetroot extract for 28 days of treatment. Increased HDL level can be seen in the C+ and treatment groups (T1, T2, T3, T4) (Figure 3). Beetroot juice and beetroot extract, as a single or combination with simvastatin had a good effect in dyslipidemic rats. After treatment the HDL level was highest in the T4 group (68.63±4.10 mg/dL) and lowest in the C- group (24.39±1.70 mg/dL). Administration of beetroot juice and beetroot extract had a significant effect on HDL level among treatment groups. There were significant differences among groups except for the C+ and T3 groups (p=0.088). This indicated that the administration of 3.6 mL/200 g BW of beetroot juice and 0.18 mg/200 g BW of simvastatin in the T3 group increased HDL levels almost the same as the administration of simvastatin in the C+ group. NC and C- groups were compared with the dyslipidemia model rats that given interventions, it showed there was a significant difference in HDL levels (p<0.05). A comparison of the two groups also showed a significant difference (p<0.05), and the following effective treatments were seen in T4, T3, T2, and T1, respectively.

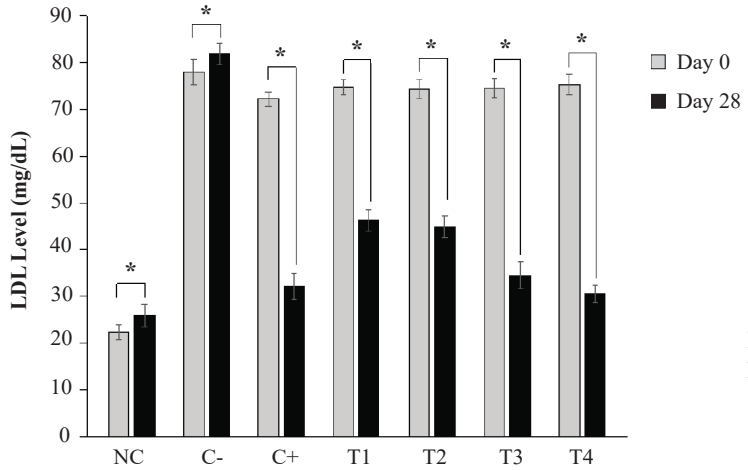

Figure 2. Pre-test and post-test LDL levels of all groups. Data were presented as mean±SD. *Tested with paired Student t-test, between pre-test and post-test of each group. *p<0.05 is considered as significant.

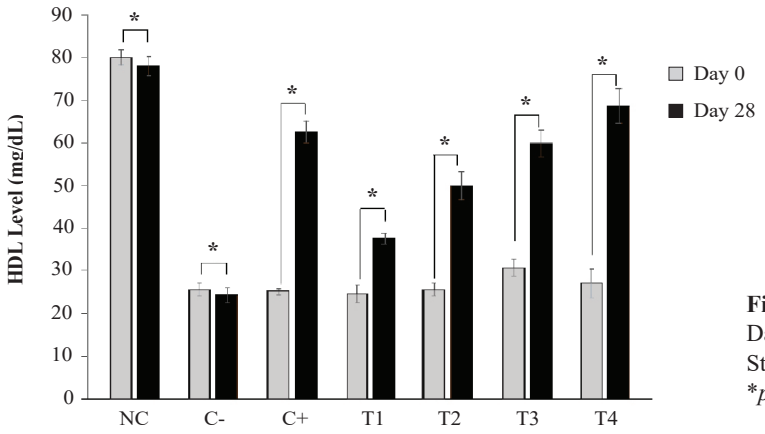

Figure 3. Pre-test and post-test HDL levels of all groups. Data were presented as mean±SD. *Tested with paired Student t-test, between pre-test and post-test of each group. *p<0.05 is considered as significant.

Beetroot Juice and Extract Reduced IL-6 Level of Dyslipidemic Rats

All intervention groups had lower IL-6 level than C- group, these results indicated that beetroot juice and beetroot extract alone, or in the combination with simvastatin had effect on lowering inflammation process dyslipidemic rats. The highest IL-6 level in intervention group was seen in the T2 group (55.39±1.18 pg/dL) whereas the lowest was shown in the T4 group (28.25±1.28 pg/dL) (Figure 4). Administration of beetroot juice and extract significantly gave an effect on IL-6 level among treatment groups. The post hoc test results showed significant differences among groups except for the C+ and T4 groups (p=0.064). This showed that the administration of beetroot extract 100 mg/200 g BW and simvastatin 0.18 mg/200 g BW in the T4 group suppressed IL-6 levels almost the same as the administration of simvastatin in the C+ group. There was a significant difference of IL-6 level in all seven groups (p<0.05). A comparison of the two groups also showed a significant difference (p<0.05) of IL-6 level, the most effective treatment was seen in T4 followed by T3, T1, and T2, respectively.

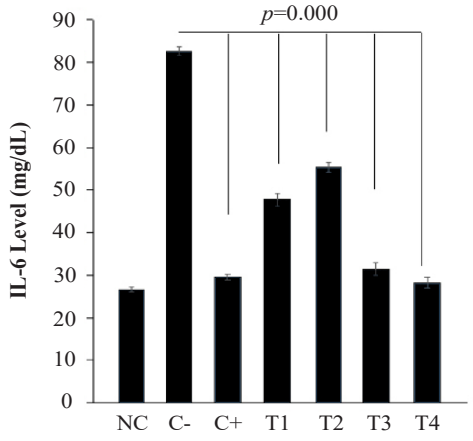

Figure 4. Changes in IL-6 Level in each grop compared to C- group. Data were presented as mean±SD. Post hoc analysis (Tukey LSD test) of each group compared to C- group. *p<0.05 is considered as significant.

Discussion

After all interventions were done in this study, there was a change in body weight during the treatment of beetroot juice and beetroot extract. The most significant change of body weight was seen in the negative control group (22%), while the other groups experienced a change in body weight of 10-12%. The body weight of dyslipidemic rats model in each group after given treatment showed a significant difference among groups. Feeding high lipid made from comfeed PAR-s, flour, cholesterol, cholic acid, and lard for 28 days was carried out to make dyslipidemia condition. It was expected that LDL-cholesterol levels will increase (normal reference: 2.00-27.00 mg/dL), and HDL-cholesterol levels will decrease (normal reference: 35.00-85.00 mg/dL). (27,28,30)

In this study, after giving beetroot juice and beetroot extract for 28 days has shown that beetroot reduced LDL level and increased HDL level in dyslipidemic rat models. There was a significant change in LDL reduction during the treatment of beetroot juice and extract. Likewise, there was a significant change in the increase in HDL level. Changes in LDL and HDL levels were greater in the administration of beetroot extract and the combination of beetroot extract and simvastatin compared to the administration of beetroot juice alone and the combination of beetroot juice and simvastatin. Beetroot contains antioxidant flavonoids and betacyanin; red dragon fruit also has this antioxidant content.(31) Administration of red dragon fruit peel infusion containing

11.38 mg/100 g of flavonoids reduced LDL and increased HDL in Sprague Dawley rats.(32) The flavonoid content in the decoction of dragon fruit peel was almost the same as the flavonoid content in this study (in beetroot juice 0.1155 mg flavonoid per 1.8 g of juice), while in beetroot extract, it was 0.516 mg per 100 mg of condensed extract. This study's results aligned with previous study which showed that beetroot extract using methanol solvent can reduce cholesterol, triglyceride, LDL, VLDL levels, and significantly increase HDL.(16) The results of this study were also in line with previous research which stated that high doses of beetroot extract could reduce LDL and have the same effectiveness as the drug simvastatin.(33) In another study conducted in human, a volume of 200 mL of beetroot juice can reduce LDL level.(34) While in another study suggested that supplementation of beetroot juice and leaves can increase HDL levels in people with dyslipidemia.(35)

Beetroot contains not only flavonoid but also high vitamin C and both compouds can escalate the activity of lecithin cholesterol acyl transferase (LCAT) by converting free cholesterol into hydrophobic cholesterol esters form from blood and peripheral tissue. The esterified cholesterol form will tie up to lipoprotein and the new HDL cholesterol is formed. Vitamin C as an antioxidant will intensify HDL cholesterol serum level by making Apo-A1 as a coezyme cofactor for LCAT, and finally LCAT activity results in more higher HDL cholesterol level. Vitamin C in the beetroot may reduce LDL oxidation by inhibiting the myeloperoxidase activity.(36)

A decreased of LDL level and an increased of HDL level impact in reducing IL-6 level. Administration of beetroot juice at a dose of 3.6 mL/200 g BW and beetroot extract at 100 mg/200 g BW reduced IL-6 levels until they reached normal value. The decrease in IL-6 level after administration of beetroot juice and extract was associated with the active flavonoid compounds in beetroot. These compounds can inhibit the secretion of proinflammatory cytokines. Reactive oxygen species (ROS) becomes stable after binding with active compund of flavonoid which results in inactivity the radicals compound and inflammation can be hampered and finally cells structure can be maintained.(28) Regarding its function, flavonoids have therapeutic potential in treating inflammation-related diseases as cytokine modulators.(37) Previous studies using *in vitro* cells experiment showed that inflammation induced by tumor necrosis factor α in macrophage treated with lipopolysaccharide, the inflammation can be reduced by culturing the cells in the presence of quercetin. During inflammation process, this flavonoid compund impedes the activity of cyclooxygenase and lipoxygenase. Macrophage released IL-6 after stimulated by IL-1 which arranged by other pathway which different from other mechanism on how IgE-induced degranulation, and quercetin can block IL-6 secretion. Quercetin affects immunity and inflammation, especially by acting on leukocytes and targeting many kinases, signaling intracellular phosphatases, enzymes, and membrane proteins, so they play an important role in specific cellular functions.(38) Plants have been used for therapeutic purposes from the ancient, and chemical based drugs medicine have some unexpected side effects, therefore many studies were conducted to find new active compound from plants, and one of them is flavonoid which have been used in many purposes such as for its antioxidant, analgesic, and anti-inflammatory effects.(39)

Both beetroot juice and extract combined with simvastatin can reduce LDL level, increase HDL level, and suppress the inflammatory response (IL-6), which can be similar to the results of the dyslipidemic rats model which given simvastatin as a single therapy. Beetroot as a single intervention (as a juice or extract) can not reduce LDL level, increase HDL level, and suppress the inflammatory response (IL-6) as much as the group given the combination with simvastatin but indeed beetroot juice and extract as a single treatment can reduce the inflammation in dyslipidemic rats model. Beetroot served as juice or extract both can decrease LDL, IL-6 and increase HDL eventhough higher LDL and HDLchanges were seen in beetroot extract than in beetroot juice as a single treatment, whereas IL-6 level was reduced with beetroot juice more than with beetroot extract.

Treatment of dyslipidemia in patients is important for changing the selection of balanced nutritional foods and increased physical activity, accompanied by food supplementation, which can reduce levels of bad fats in the blood, as well as medical therapy with lipid-lowering drug such as simvastatin especially for patient with very high level of LDL-cholesterol concentration.

Conclusion

Administration of beetroot juice and beetroot extract can lower LDL level, increase HDL level, and suppress inflammatory responses, as a single or in combination with simvastatin. The content of flavonoids and betacyanin in beetroot extract was conserved better than in beetroot juice, therefore beetroot extract is more effective than beetroot juice. Moreover, beetroot juice and beetroot extract

combined with simvastatin are more effective in reducing LDL level, increasing HDL level, and suppressing the inflammatory response (IL-6) compared to only single administration of beetroot juice or beetroot extract.

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Authors Contribution

MJR, DRH, and LOW were involved in concepting and planning the research. MJR performed all animal experimental and data collection. MJR and LOW calculated the experimental data, analysed, drafted the manuscript, designed the figures, and interpreted the results. All authors took parts in giving critical revision of the manuscript.

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