

QUERCETIN AND CURCUMIN PREVENT DECREASING OF LDL-CHOLESTEROL AND INCREASING OF HDL-CHOLESTEROL IN HIGH FAT DIET RATS

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ABSTRACT

Cardiovascular disease is number one killer disease in the world. The most common etiology is atherosclerosis. LDL and HDL-cholesterol are often associated with atherosclerosis which are affected by diet. Quercetin and curcumin considered have influenced to LDL and HDL. They are antioxidant that protect against LDL oxidation and raised HDL-cholesterol. In this study, we invest about comparison effect of prevention in LDL and HDL level change, after giving quercetin and curcumin. 20 males Rattus norvegicus rats in 200-300 grams divided into 4 groups. Group B, C, D were given high-fat diet for 4 weeks, while group A (negative control) was given standard woof. Group B was positive control and no treatment, C was given quercetin, D was given curcumin. The treatment and giving high-fat diet was done simultaneously to detect prevention effect. HDL and LDL-cholesterol evaluated two times, pre and post-treatment. Result showed the increase prevention level of LDL-cholesterol and decrease prevention level of HDL-cholesterol in group C and D significantly. The best prevention effect is quercetin, $p=0.000$. Furthermore, we showed there was no significant correlation between Δ LDL and Δ HDL-cholesterol level. In conclusion, quercetin and curcumin have a good effect in preventing hypercholesterolemia, however quercetin have better effect than curcumin.

Keywords: quercetin curcumin, HDL-cholesterol, LDL-cholesterol

INTRODUCTION

Cardiovascular disease (CVD) is the most common cause of deaths worldwide, about 80% of the burden occurs in developing countries (Kumar *et al.*, 2010). CVD includes all diseases in the heart and

blood vessels. WHO (2008) estimated 17.3 million people died by CVD, about 7.3 million were due to coronary heart disease and 6.2 million were due to stroke. Atherosclerosis is one of common causes of stroke.

Atherosclerosis is the most common pathological feature of vascular obstruction resulting in thrombotic stroke. It is characterized by intimal lesions called atheromas that protrude into vessel lumens. Atherosclerosis formation depends on lipid level in the blood. Hypercholesterolemia is a major risk factor for atherosclerosis even in the absence of other factors. The major component of serum cholesterol associated with increased risk of atherosclerosis event is low density lipoprotein cholesterol (LDL-C). LDL-C is the form of cholesterol that is delivered to peripheral tissues. In contrast, high density lipoprotein cholesterol (HDL-C) mobilizes cholesterol from tissue and transports it to the liver to be excreted in the bile. Consequently, higher levels of HDL-C correlate with reduced risk (Kumar *et al.*, 2010).

Atherosclerosis can be prevented by controlling the risk factors, particularly such as cigarette smoking, unhealthy diet, physical inactivity, high blood pressure, diabetes, and raised lipids. Lipid levels in the blood are affected by

diet including additional diet, such as antioxidant that can reduce LDL-C levels and increase HDL-C levels. It prevents targeted molecule to be oxidized by free radical. According to the oxidative modification hypothesis, Wang *et al.* (2012) said oxidation of LDL is crucial to the cellular uptake of LDL in the first stage of atherosclerotic plaque development. Because of that reason, antioxidant plays vital role in preventing atherosclerosis.

Curcumin and quercetin are antioxidants that have not been widely used. Curcumin has pharmacological effects including antitumor and anti-inflammation effects and can prevent lipid peroxidation. Sudjarwo (2011) concludes that curcumin can repair endothelium-dependent dilation at blood vessels wall and reduce lipid peroxidation in aorta wall. Quercetin is a flavonoid that can also affect lipid levels in the blood by reducing LDL-C concentrations. Flavonoids, particularly quercetin has been associated with a decreased risk of CVD. Quercetin can be found in onion, green tea, and apple. Based on

the effect of each compound, combination of both quercetin and curcumin are expected to be more effective in managing hypercholesterolemia and in preventing atherosclerosis. This study compares quercetin and curcumin, in preventing hypercholesterolemia.

METHOD

Chemicals

Quercetin and Na-CMC were of analytical grade obtained from Sigma Aldrich Chemical and the curcumin were procured from Doctor Eko Wahjuni (POM TR 023 217 101).

Animals

Animal experiments were carried out taking appropriate measures to minimize pain or discomfort with due clearance from the Medical and Health Research Ethics Committee, Faculty of Medicine Universitas Gadjah Mada (UGM)

Male wistar rats (*Rattus norvegicus*) weighing between 200-300 g each were used for this experiment. They were procured

from PAU Laboratory UGM, Yogyakarta. The rats were maintained in a controlled environment under standard condition of temperature ($28\pm 2^{\circ}\text{C}$) and humidity with an alternating light and dark cycle. The animals were housed in individual stainless steel cages were maintained on various experimental diets ad libitum. The basal diet used was AD-2 woff and the hypercholesterolemic diet consisted of AD-2 woff plus cow's fat which administered by sonde.

Experimental Procedure

After a week of acclimatization, the rats were divided into four groups with 5 rats in each group. Group I served as negative control (basal diet+1 mL Na-CMC 0.5%), Group 2 served as positive control (hypercholesterolemic diet+1 mL Na-CMC 0.5%), Group 3 treated with hypercholesterolemic diet+45mg/kgBW quercetin+1 mL Na-CMC 0.5%, Group 4 treated with hypercholesterolemic diet+45 mg/kgBW curcumin+1 mL Na-CMC 0.5%. After 4 weeks of treatment period, the animals were sacrificed

under light ether anesthesia. Blood was collected by orbital artery for two times. First, at the end of acclimatization, and second at the end of experiment. Blood was separated from serum by centrifugation and used for lipid analysis.

Lipid Profile

HDL and LDL-cholesterol were determined by homogenous enzymatic colorimetric assay method.

Statistical Analysis

Result are expressed as means \pm SD and comparison between groups were made by means of one-way ANOVA. Comparison among different groups were made applying the Tukey Post Hoc Test and were considered significant when $p < 0.05$.

RESULT AND DISCUSSION

As observed in this study, high cholesterol feeding for 4 weeks resulted in a significant increase in LDL-cholesterol concentration and a decrease in HDL-cholesterol (Table 1 and 2). The increased in LDL-cholesterol and decreased in HDL-cholesterol were variously. Dietary

quercetin or curcumin prevented the increase of LDL-cholesterol significantly. However, quercetin prevented better than curcumin.

Table I. Effect of quercetin and curcumin in HDL-cholesterol

	HDL-cholesterol (mg/dL)		Δ
	Pre-test	Post-test	
Normal	38.92 ± 1.93	38.44 ± 1.63	-0.48 ± 2.59
Control	37.17 ± 1.93	16.82 ± 1.83	-20.35 ± 1.50
Quercetin	36.09 ± 1.40	30.95 ± 1.83	-5.14 $\pm 2.37^*$
Curcumin	36.9 ± 1.11	17.38 ± 1.70	-19.51 $\pm 1.36^\#$

Tested by Tukey Post Hoc Test;

*Significantly different from control ($p < 0.05$)

$^\#p > 0.05$

HDL-cholesterol essentially decrease in all group significantly. Quercetin was prevented the decrease of HDL-cholesterol significantly in compared to control.

As shown in Table 3, there was no significant correlation between increased in LDL-cholesterol with decreased in HDL-cholesterol. Data shows that quercetin or curcumin treated group had a very weak positive correlation. It means the increased in LDL-cholesterol make HDL-cholesterol slightly increased.

Table II. Effect of quercetin and curcumin in LDL-cholesterol

	LDL-cholesterol (mg/dL)		Δ
	Pre-test	Post-test	
Normal	50.16±2.38	53.11 ±2.35	2.94 ±0.36
Control	45.02±2.31	89.76 ±2.52	44.75 ±3.42
Quercetin	48.84±6.28	63.54 ±2.99	14.7 ±8.99*
Curcumin	44.35±7.47	78.39 ±1.73	34.04 ±8.36*

Tested by Tukey Post Hoc Test;

*Significantly different from control ($p < 0.05$)

Table III. Correlation between increased in LDL and decreased in HDL-cholesterol

	r	p
Normal	-0.864	0.059
Control	-0.146	0.815
Quercetin	0.219	0.723
Curcumin	0.123	0.843

Tested by Pearson Correlation;

Significantly different if $p < 0.05$

Epidemiological studies have reported a reduced risk of coronary heart disease in subjects with high flavonoid intake (Knekt *et al.*, 1995). The protective effect of flavonoids has been attributed to many mechanisms, i.e. antioxidant properties, anti-inflammatory activity (Miller A, 1996), antiproliferative as well as antipatelet effects (Moghaddam *et al.*, 2012; Guerrero *et al.*, 2005).

In the present study, hypo-lipidemic effects was evaluated in two substance. It was demonstrated that all treatment groups showed a

positive effect in the prevention of hyper-cholesterolemia, which prevents the increase in LDL as well as prevent a significant decrease in HDL (Table I and II).

These results are consistent with the theory presented by Srinivasan *et al.* (2004) which states that curcumin has hypolipidemic activity, by increasing receptor LXR (liver X receptor) and RXR (retinoic X receptor), which causes an increase in metabolism of cholesterol, especially LDL uptake increase. Although it has an excellent effect on hypolipidemic, the major

concern of curcumin is a limited bioavailability which limits its therapeutic utility (Anand *et al.* 2007).

Earlier studies have shown that quercetin significantly inhibit in vitro LDL oxidation, and also protects macrophages from oxidized low-density lipoprotein induced apoptosis (Naderi *et al.*, 2003; Yao *et al.*, 2012). Quercetin acts to inhibit atherosclerosis through up-regulation of reverse cholesterol transport, so as to reduce cholesterol levels in the blood (Fernandes *et al.*, 2012). Quercetin inhibits sulfotransferase enzymes and also limited by poor bioavailability though it's better than curcumin (Kaur G & Meena C, 2012).

The mechanisms of each compounds lead to the prevention effects of hypercholesterolemia. However, based on this study, quercetin was more impressive effect. Quercetin was effective in prevent hypercholesterolemia by high-fat diet, after 4-weeks of the experiment. While this activity was

less prominent in the curcumin treatment.

It is well known that HDL-cholesterol levels have a protective role in cardiovascular disease (Silbernagel *et al.*, 2013). Similarly increased level of LDL-cholesterol results in increased risk of development of atherosclerosis (Warnholtz *et al.*, 2001). However, the study exhibited that there was no significant correlation between increases in LDL-cholesterol with decreases in HDL-cholesterol.

The anti-atherogenic properties were described to the antioxidant activity measured by the reduced formation of LDL-cholesterol and enhanced formation of HDL-cholesterol. Quercetin in dose 45mg/kgBW prevented hypercholesterolemia optimal, although it had not reached normal conditions.

CONCLUSION

The quercetin in 45mg/kgBW dose is the best treatment in this study, because the maximum preventive effect. Preventive effects of hypercholesterolemia slowing the formation of fatty streak which is

going from atherosclerosis, the biggest risk factor for cardiovascular diseases.

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