

## Quercetin and Vitamin C Supplementation: Effects on Lipid Profile and Muscle Damage in Male Athletes

Gholamreza Askari<sup>1,2</sup>, Maryam Hajishafiee<sup>3</sup>, Reza Ghiasvand<sup>1,2</sup>, Mitra Hariri<sup>1,2</sup>, Leila Darvishi<sup>1,2</sup>, Shekoofeh Ghassemi<sup>1,2</sup>, Bijan Iraj<sup>1,2</sup>, Volga Hovsepian<sup>1,2</sup>

<sup>1</sup>Food Security Research Center, Isfahan University of Medical Sciences, Isfahan, Iran, <sup>2</sup>Department of Community Nutrition, School of Nutrition and Food Science, Isfahan University of Medical Sciences, Isfahan, Iran, <sup>3</sup>Child Growth and Development Research Center, Isfahan University of Medical Sciences, Isfahan, Iran

### Correspondence to:

Mrs. Leila Darvishi,  
Food Security Research Center,  
School of Nutrition and Food  
Science, Isfahan University of  
Medical Sciences, Isfahan, Iran.  
E-mail: leilad\_78@yahoo.com.

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### ABSTRACT

**Background:** Quercetin, which is considered as a health-promoting antioxidant, belongs to the broad flavonoids group. Numerous experimental studies have proved that quercetin and vitamin C provide anti-inflammatory and antioxidant properties. The aim of this study is to assess the effects of both quercetin and vitamin C on lipid profile and muscle damage in human subjects.

**Methods:** A randomized, placebo-controlled, double-blind clinical trial was carried out on 60 males for eight weeks. The subjects were randomly assigned to one of the four groups: 1) quercetin + vitamin C (500mg/day quercetin+200mg/day vitamin C) 2) quercetin (500mg/day quercetin + 200 mg/day placebo) 3) vitamin C (500 mg/day vitamin C + 200 mg/day placebo) and 4) placebo (500 mg/day placebo + 200 mg/day placebo). Blood samples, body weight and percent of body fat were measured before and after intervention. In addition, dietary intake was estimated using 24-h recall.

**Results:** No significant changes occurred in high-density lipoprotein levels between groups and in the four groups before and after supplementation. Low density lipoprotein values decreased significantly ( $P = 0.048$ ) in the “Quercetin + Vit C” group but decrease was not considerable in other groups before and after intervention and among groups. Fat-soluble vitamins’ intake was significantly high among 4 groups.

**Conclusions:** Quercetin and vitamin C supplementation may not be beneficial in lipid profile improvement, although it may reduce induce muscle damage and body fat percent.

**Keywords:** Athletes, lipid profiles, quercetin

### INTRODUCTION

Quercetin, which is considered as a health-promoting antioxidant, belongs to the broad flavonoids group.<sup>[1-3]</sup> Flavonoids present in a variety of natural fruits and vegetables ranging from apple, cranberry to onion, broccoli and teas,<sup>[4-7]</sup> and along with some nutrients may have positive effects in athletes.<sup>[8,9]</sup> A large number of epidemiological studies have demonstrated

that quercetin provides anti-inflammatory and antioxidant properties.<sup>[10-12]</sup> Endothelial function is one of the exercise performance determinants and its dysfunction caused by oxidative stress and may induce atherosclerosis.<sup>[13]</sup> Within a clinic-based study, it has been proved that quercetin improves oxidant status among renal patients through raised serum paraoxonase. Paraoxonase is known as a marker of high-density lipoprotein antioxidant activity which inhibits low-density lipoprotein oxidation.<sup>[14]</sup> Yi *et al.*, reported that quercetin can reduce oxidized-low-density lipoprotein level and prevent atherosclerosis.<sup>[13]</sup> In 2011, Yeekh *et al.*, demonstrated that quercetin supplementation significantly alleviates low-density lipoprotein cholesterol concentration and increases serum high-density lipoprotein in the study group.<sup>[15]</sup> Cadmium oral administration results in an increase in low-density lipoprotein, three acylglycerol, free fatty acids and phospholipids and decrease in high-density lipoprotein. After an experimental investigation, it declared that quercetin can escalate serum high-density lipoprotein and reduce low-density lipoprotein and TG among rats. In addition it eradicates detrimental cadmium effects.<sup>[16]</sup> Lack of well-documented information about quercetin and vitamin C supplementation containing comprehensive laboratory measurements among athletes draws attention to design more clinical trials in order to define mechanisms. The present study aimed at conducting a research on the effects of both quercetin and vitamin C on lipid profile and muscle damage in human subjects.

## METHODS

A randomized, placebo-controlled, double-blind clinical trial was carried out on 60 male athletes who were active, but not involved in professional sports. They were recruited voluntarily and informed about the procedures of study. The exclusion criteria were consumption of quercetin or any other dietary supplements for at least 3 months before the study onset. Participants were requested to abstain from exhaustive exercise 24 h before the beginning of the trial and to keep a record of their recent physical activity and dietary intake. Four subjects left the study due to the gastrointestinal side-effects of supplements. A signed consent was obtained from all participants before the

study began. This trial was done in order to test the hypothesis of the beneficial effects quercetin and vitamin C supplementation on male athletes within eight weeks. Participants were randomly assigned to one of four groups including quercetin + vitamin C (500 mg/day quercetin + 200 mg/day vitamin C), quercetin (500 mg/day quercetin + 200mg/day placebo), vitamin C (500mg/day vitamin C + 200 mg/day placebo) and placebo (500 mg/day placebo + 200 mg/day placebo). Quercetin, vitamin C and their placebos had a similar appearance. All supplements were orally administrated in capsule form including 500 mg quercetin (Solaray, USA, Inc), 200 mg vitamin C (Razi, Iran, Inc) and placebo (Pharmacy faculty, Isfahan University of Medical Science, Iran) each day after meals. Blood samples were obtained from all subjects between 5:00 pm and 6:00 pm, after intensive exercising, at the outset and after intervention. All measurements were taken at the beginning of the supplementation and end of intervention. Body weight and percentage of body fat were measured using a body composition analyzer (PlusAvis 333, Korea). In addition, plasma samples were collected for the determination of serum lipid profile containing high-density lipoprotein and low-density lipoprotein concentration. high-density lipoprotein and low-density lipoprotein were measured at baseline and again at eight weeks utilizing the Cholestech LDX System (Hayward, CA), according to the manufacturer's instructions. LDH concentrations were measured by the ELISA method, according to the manufacturer's protocol. These ELISA kits were obtained from Bender Medsystems GmbH (Vienna, Austria). Dietary intake was estimated using 24-h recall. Nutrient analyses were performed using nutritionist IV software. Statistical analyses were conducted using the statistical program for social sciences (SPSS Version 13, Inc., Chicago, IL) computer software package. The results are presented as mean  $\pm$  standard error. One-way multivariate analysis of covariance (MANCOVA) controlling for the pre-test differences followed by Dunnett's *post hoc* comparison was used for multiple comparisons between groups. Within-group comparisons were done using paired *t*-test. Due to non-normality of the studied variables (positive skewed distribution) logarithmic transformation was done and homogeneity of covariance matrix was tested via BOX'M statistics. Analyses were performed with the

SPSS Version 16 (SPSS Inc, Chicago, IL) statistical package. The registration number of this clinical trial is IRCT201112055062N4.

## RESULTS

The general mean  $\pm$  SD of subjects for age (years), weight (kg) and body mass index (BMI, kg/m<sup>2</sup>) was 21.0  $\pm$  1.6, 67.5  $\pm$  10.8 and 22.3  $\pm$  3.3 respectively. Table 1 shows the mean  $\pm$  SD values of high-density lipoprotein (HDL), and lactate dehydrogenase (LDH) pre and post supplementation. We did not detect any significant changes in high-density lipoprotein levels between groups and in the four groups before and after

supplementation. While LDH values decreased significantly ( $P = 0.048$ ) in "Quercetin + Vit C" group it was not considerable in other treatments and between groups. Micronutrient intakes are demonstrated in Table 2. Intake of fat-soluble vitamins was significantly high among 4 groups.

## DISCUSSION

The results of our study represent that supplementation with quercetin and vitamin C did not improve the lipid profile as measured by high-density lipoprotein. In contrast to our study, Amengual *et al.*, in a clinical trial study, observed an improved high-density lipoprotein level among renal patients.<sup>[14]</sup> Different

**Table 1:** The comparison of lactate dehydrogenase and high-density lipoprotein levels between 4 groups

Variables	Quercetin+vit C	Quercetin+placebo	Placebo+vit C	Placebo+placebo	P value*
LDH (IU/L)					
Before	212.8 $\pm$ 25.2	275.9 $\pm$ 33.5	185.7 $\pm$ 19.4	167.8 $\pm$ 68.2	0.035
After	170.4 $\pm$ 58.8	250.1 $\pm$ 48.5	205.9 $\pm$ 35.3	195.1 $\pm$ 42.1	
P value**	0.048	0.34	0.28	0.232	
High-density lipoprotein (mg/dl)					
Before	64.7 $\pm$ 9.3	60.6 $\pm$ 7.6	62.3 $\pm$ 11.01	63.3 $\pm$ 7.8	0.23
After	62.5 $\pm$ 5.6	61.5 $\pm$ 5.1	64.3 $\pm$ 8.5	62.5 $\pm$ 8.5	
P value**	0.66	0.26	0.41	0.52	

LDH=Lactate dehydrogenase, \*MANCOVA=Multivariate analysis of covariance, \*\*Paired *t*-test

**Table 2:** The comparison of mean nutrient intakes between 4 groups

Variables	Quercetin+Vit C	Quercetin+Placebo	Placebo+Vit C	Placebo+Placebo	P value
Vit. A ( $\mu$ g)	740/78 $\pm$ 534/2	578/8 $\pm$ 377/0	980/68 $\pm$ 442/8	630/5 $\pm$ 394/4	0/03
Vit. D ( $\mu$ g)	2/2 $\pm$ 1/4	1/5 $\pm$ 0/9	0/8 $\pm$ 1/0	1/8 $\pm$ 1/2	0/015
Vit. E (Mg)	18/5 $\pm$ 8/8	11/7 $\pm$ 6/6	12/5 $\pm$ 6/8	15/5 $\pm$ 9/5	0/003
Vit. K ( $\mu$ g)	115/7 $\pm$ 96/8	78/1 $\pm$ 52/5	91/7 $\pm$ 66/8	142/7 $\pm$ 106/1	0/002
B <sub>1</sub> (Mg)	2/5 $\pm$ 1/6	2/3 $\pm$ 0/46	2/1 $\pm$ 0/64	1/9 $\pm$ 1/4	0/15
B <sub>2</sub> (Mg)	2/6 $\pm$ 0/8	2/3 $\pm$ 0/6	1/9 $\pm$ 0/6	2/5 $\pm$ 0/9	0/08
B <sub>3</sub> (Mg)	22/6 $\pm$ 12/8	25/8 $\pm$ 15/1	21/9 $\pm$ 10/5	18/6 $\pm$ 12/6	0/06
B <sub>5</sub> (Mg)	3/9 $\pm$ 1/0	3/5 $\pm$ 0/7	2/9 $\pm$ 1/1	3/3 $\pm$ 1/2	0/054
B <sub>6</sub> (Mg)	2/3 $\pm$ 0/5	2/6 $\pm$ 0/7	1/9 $\pm$ 0/6	2/5 $\pm$ 0/6	0/08
Folic acid ( $\mu$ g)	342/9 $\pm$ 121/2	289/8 $\pm$ 161/3	337/2 $\pm$ 142/2	298/1 $\pm$ 184/5	0/03
B <sub>12</sub> ( $\mu$ g)	5/2 $\pm$ 2/9	6/4 $\pm$ 4/6	5/6 $\pm$ 0/9	5/1 $\pm$ 1/7	0/04
VC (Mg)	125/2 $\pm$ 60/2	156/9 $\pm$ 84/3	142/1 $\pm$ 80/4	185/1 $\pm$ 92/6	0/03
Ca (Mg)	827/5 $\pm$ 384/7	683/4 $\pm$ 305/6	913/4 $\pm$ 424/6	775/5 $\pm$ 285/5	0/03
Mg (Mg)	238/8 $\pm$ 73/9	275/5 $\pm$ 106/7	246/2 $\pm$ 97/1	258/6 $\pm$ 101/3	0/11
K (Mg)	2635/4 $\pm$ 984/6	2458/3 $\pm$ 1285/8	2530/5 $\pm$ 897/5	2722/1 $\pm$ 1125/6	0/44
Fe (Mg)	14/7 $\pm$ 5/6	17/8 $\pm$ 6/2	12/5 $\pm$ 4/2	10/7 $\pm$ 5/4	0/05
Zn (Mg)	9/8 $\pm$ 3/1	7/5 $\pm$ 2/9	12/8 $\pm$ 4/0	10/6 $\pm$ 5/2	0/06

study populations and supplementation dosages might be the possible reasons for the differences in results between the two studies. In line with the previous study, Yeekh *et al.*, reported a significant increase in high-density lipoprotein and decrease in low-density lipoprotein after quercetin supplementation.<sup>[15]</sup> Another investigation conducted among rats showed different results.<sup>[16]</sup> The anti-inflammatory and antioxidant properties of quercetin result in reduction of exercise-induced muscle damage.<sup>[1,17,18]</sup> In accordance with this fact, we observed significant muscle damage as measured by LDH in the quercetin and vitamin C group. The attainable mechanism is that quercetin alleviates the free radical generation during physical activity in skeletal muscle.<sup>[18-21]</sup>

## CONCLUSION

However, in our study, we detected an increase in nutrient intake, notably the fat-soluble vitamins, calcium and folic acid. That may be owing to a gain in dietary intake among all groups. To provide an overview, intake of quercetin and vitamin C supplementation may not be beneficial in lipid profile improvement, although it would probably induce reduction of muscle damage. Hence, more controlled clinical trials considering longer periods of supplementation and larger dosages are needed. The limitations of our study were the limited study population and different physical activity history of athletes. The strengths of this study were human nature of samples and accurate follow-up.

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