Original Article

The Effects of Curcumin Supplementation on Muscle Damage, Oxidative Stress, and Inflammatory Markers in Healthy Females with Moderate Physical Activity: A Randomized, Double-Blind, Placebo-Controlled Clinical Trial

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Abstract

Background: Exercise-induced oxidative stress, muscle damage, and inflammation represent major contributors to why athletes use ergogenic aids. Turmeric is used as a spice because of its polyphenol ingredient named curcumin. We assessed the effects of curcumin supplementation on inflammatory, oxidative stress markers, muscle damage, and anthropometric indices in women with moderate physical activity. **Methods:** This double-blind, placebo-controlled clinical trial was conducted on 80 women with moderate physical activity levels (defined as walking or swimming for at least 1 h per day) for 8 weeks. Mean ± SD of age (years) all participants was 21 ± 2. Participants were randomly assigned into two groups: curcumin (500 mg/day) and placebo (500 mg/day cornstarch). Serum C-reactive protein (CRP), total antioxidant capacity (TAC), malondialdehyde (MDA), lactate dehydrogenase (LDH) levels, body composition, and maximum oxygen uptake (VO2 max) were evaluated before and after an intervention. **Results:** Sixty-five subjects completed the 8-week intervention. Within analysis indicated a significant decrease in CRP, LDH, MDA levels, and a significant increase in VO2 max in the curcumin group after an intervention ($P < 0.05$). There were significant decreases in CRP ($P = 0.002$), LDH ($P = 0.041$), and MDA ($P = 0.005$), no significant increase in TAC, and significant increase in VO2 max ($P = 0.0001$) levels in the curcumin group compared with placebo group. There were no significant changes in weight, body mass index, body fat, and lean body mass between two groups. **Conclusions:** Our findings indicated that 8-week curcumin administration could significantly improve CRP, LDH, MDA, and VO2 max. Curcumin supplementation did not elicit significant changes in anthropometric indices in this study.

Keywords: *Body composition, curcumin, inflammation, muscle damage, oxidative stress*

Introduction

Regular physical exercise has been considered as an important part of healthy life in adulthood and old age.[1] Moreover, there is growing evidence supporting the fact that physical activity has a positive effect on the risk of sarcopenia, chronic disease,[1] and cardiovascular disease.[2] Although previous evidence indicated that regular exercise has a role in the prevention of metabolic disorders such as cardiovascular disease, diabetes, cancer, hypertension, and obesity,[3] recent studies demonstrate that prolonged exercise increases reactive oxygen species level (ROS),[4] muscle fatigue, and inflammation in athletes.[1] Interestingly, it has been suggested that long-term oxidative stress and inflammation are responsible for the beginning or progression of several diseases such as diabetes, cancer, and cardiovascular disease.[5] Therefore, there has been significant interest in taking nonsteroidal antiinflammatory drugs (NSAIDs) to prevent inflammation among athletes.[6] However, several deleterious side effects have been observed following the over-consumption of these medications.[7] Therefore, identifying natural dietary compounds that contain antioxidant and antiinflammatory properties is of paramount importance.[1]

Contemporary interest in the use of herbal extracts has increased significantly in recent years, and is largely attributable to their potential positive impact on mental and physical performance, maintaining health and preventing diseases,[8,9] easy-access, low

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cost, and fewer side effects than synthetic medications.[8] Curcumin is one of the primary components in turmeric and curry powders derived from the rhizome of the plant *Curcuma longa*, which widely used in Asian countries in order to add color and flavor of food.[10] These spices also contain abundant polyphenol ingredients and have been recognized as antiinflammatory, antioxidant,[11] and anticancer agents.[12]

Given the reports of positive effects attributed to curcumin, many studies have investigated the antioxidant and antiinflammatory properties of curcumin;[13-15] however, the results of these studies remain controversial. A previous report by Sahin *et al*. declared that curcumin administration can decrease muscle damage by regulating the nuclear factor-kappa B (NF-κB) in male Wister rats.[16] In addition, the results of another study that performed on 90 rats with poly cystic ovarian syndrome (PCOS) showed a significant reduction in C-reactive protein (CRP) levels in the curcumin-treated rats.[17] In contrast, 500 mg curcumin with a midday meal for three days and 500 mg consumption just before exercise had no significant effects on CRP levels in human athletes.[18] Thus, to our knowledge, the effect of dietary curcumin supplementation on inflammatory markers and muscle damage has not been comprehensively explored. In addition, the positive effects of curcumin on healthy women with moderate physical activity levels are unclear. Because previous studies have shown that CRP levels are different in men and women,[19] and the aim of our study was to investigate the effects of curcumin in adults, we recruited women aged over 20 years. Therefore, in the present study, we sought to assess the effects of curcumin supplementation on inflammatory markers, oxidative stress, muscle damage, and anthropometric indices in female with moderate physical activity level.

Methods

Study design and participants

This double-blind, placebo-controlled clinical trial involved 80 healthy females without history of illness from January 2018 to April 2018. The sample size was estimated based on $n=\left(\frac{\varphi+1}{\varphi}\right)\frac{\left(z_{1-\frac{\gamma}{2}}+z_{1-\beta}\right)^2}{a^2}+\frac{z^2_{1-\frac{\gamma}{2}}}{4}$ considering statistical power 1-β = 80, type one error rate alpha = 5% for detecting the standardized effect size 0.5 for the CRP as main study's outcome. The estimated sample size was 32 per group. Finally, 40 people were recruited for subject dropout probability.[18]

Study protocols were approved by the bioethics Committee of Isfahan University of Medical Sciences, Isfahan, Iran, in October 2017 (Ethics committee reference number: IR.MUI.REC.1396.2.045) and registered in the Iranian Registry of Clinical Trials (www.irct.ir) with IRCT registration number: IRCT20121216011763N33. Following a health-screening questionnaire, all volunteers provided a written, informed consent. Before the intervention, study protocol, benefits, and possible side effects were described. The inclusion criteria were: female participants aged 20–30 years, not using antioxidant supplements or antiinflammatory drugs, and history of at least 3 years of continuous exercise (walking or swimming for at least 1 h per day). Exclusion criteria were less than 70% compliance of the study protocol, unwillingness to continue the study, diseases afflicting individuals during the study, and smoking.

Study procedures and assessment of variables

In this double-blind study (investigators and participants), 80 eligible subjects were randomly assigned into two groups (using random selection option in SPSS Version 23 (SPSS Inc., Chicago, IL) randomization). Subjects consumed 500 mg/day encapsulated curcumin or 500 mg/day encapsulated cornstarch as placebo for 8 weeks according to the previous study.[20] Supplement used in this trial was an extract of Turmeric (*Curcuma longa L*; ginger), manufacturing by Karen Pharma (Tehran, Iran). Counting the remaining capsules of each participant was used as a measure of compliance with the study.

Anthropometrics indices including fat mass and lean body mass (LBM) were measured by bioimpedance device at the beginning and the end of study (Body compositions AVIS 333 PLUS, Jawon Medical, Korea). In addition, the height of subjects was measured in standing position without shoes using a stadiometer with a precision of 0.1 cm. Weight was evaluated to the nearest 0.1 kg by means of a digital scale with light clothing worn and without shoes. FFQ was used to measure dietary intake and analyzed using nutritionist IV software at the baseline.[21,22] Queen College step test (QCT) was used to measure VO2max.[23] Furthermore, 10cc blood was obtained from participants twice at the beginning and the end of study to assess inflammatory, oxidative stress, and muscle damage markers. Inflammation was measured by CRP levels. CRP levels were evaluated quantitatively using the Bionik kit. Oxidative stress was assessed by total antioxidant capacity (TAC) and malondialdehyde (MDA) levels. These were measured according to the ferric reducing/antioxidant power assay (FRAP)[24] and thiobarbituric acid-reactive substances (TBARs)[25] method, respectively, and LDH was measured to assess muscle damage using spectrophotometry and DGKC method.

Statistical analysis

Results of the study were analyzed by SPSS Version 23 (SPSS Inc., Chicago, IL). Normality of continuous data was evaluated using Kolmogorov–Smirnov and Q-Q plot. Nonnormally distributed data were subjected to logarithmic transformation. Continuous and categorical data were reported as mean ± standard deviation and

frequency (percentage). Continuous basic characteristics and antioxidant content based micro and macro nutrients were compared between two groups using independent samples t-test. Within-group comparisons were performed by using paired samples *t*-test and between group comparisons were performed by using analysis of covariance (ANCOVA) and adjustment was made for initial values of dependent variables and some possible confounding nutrients.

Results

The present study was conducted using 80 healthy females for 8 weeks, of which 65 completed the intervention. Four participants were excluded because of gastrointestinal complications during the study and eleven subjects were unwilling to continue the study [Figure 1]. Mean ± SD of age (years) all participants was 21 ± 2.

Anthropometric indices at baseline and after intervention in the two groups are shown in Table 1. Between group analysis indicated that mean values of weight (P = 0.550), body mass index (BMI, P = 0.699), body fat (BF, P = 0.441), and LBM (P = 0.902) were not significantly different after the 8-week intervention across the two groups.

Table 2 details the dietary intake of key nutrients for each group. The analysis of FFQ indicated that there were no statistically significant differences in mean intakes of overall energy, carbohydrate, protein, fat, beta-carotene, vitamin C, vitamin E, zinc, and selenium between the two groups.

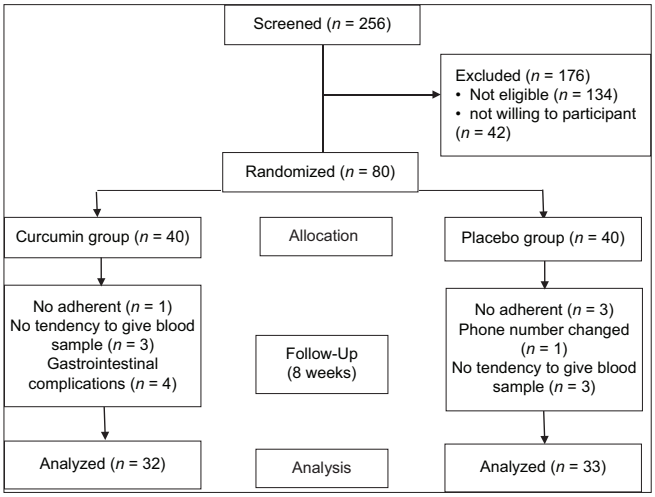

Figure 1: Flow diagram of participant's recruitment and follow-up

Baseline and after intervention serum biomarkers of inflammation, oxidative stress, muscle damage, and data of VO2 max are shown in Table 3. Within group analysis indicated a significant decrease in CRP (P = 0.004), LDH (P = 0.010), and MDA (P = 0.027) and a significant increase in VO2 max (P = 0.016) in curcumin group after 8-week intervention; and while compared with baseline, an increase in TAC was seen after 8-week intervention but it is not significant (P = 0.263). Moreover, this analysis illustrated an increase in CRP (P = 0.044), LDH (P = 0.360), and MDA (P = 0.195) and decrease in TAC (P = 0.694) and in VO2 max (P = 0.063) in placebo group. However, these changes were only significant for CRP. Between group analyses demonstrated a statistically significant decrease in CRP (P = 0.002), LDH (P = 0.041), and MDA (P = 0.005), and increase in VO2 max (P = 0.0001), and no significant increase in TAC (P = 0.439) in the curcumin group compared with placebo group.

Discussion

The present findings demonstrate that 500 mg/day oral curcumin administration for 8 weeks is well tolerated and elicits a significant decrease in CRP and LDH levels. Further, curcumin supplementation had a positive effect on oxidative stress through a significant reduction in MDA and no significant increase in TAC in healthy female young adults. No significant changes on body composition indices were observed after 8 weeks of curcumin supplementation.

To our knowledge, few studies have assessed the effects of curcumin supplementation on inflammatory markers and oxidative stress in young-adult athletes. In the current study, we show that 8 weeks of oral curcumin supplementation improves exercise-induced muscle damage and inflammation. Consistent with our study, the results of a recent meta-analysis indicated that curcumin supplementation could decrease high sensitivity C-reactive protein (hs-CRP) concentration among patients with metabolic syndrome.[26] Moreover, Panahi *et al.* previously indicated that 1 g/day curcumin supplementation can significantly reduce plasma levels of high sensitivity C-reactive protein in patients suffering from chronic

Table 1: The comparison of anthropometric indices between two groups

Variables	Curcumin group (n=32)				Placebo group (n=33)				P^{b}*
	Before	After	Mean±SE	P^{a}	Before	After	Mean±SE	P^{a}	
Weight (kg)	57.13±8.25	56.88±8.24	−0.25±0.24	0.301	59.81±10.22	59.71±10.23	−0.1±0.19	0.619	0.550
BMI (kg/m^2)	21.75±3.22	21.65±3.28	−0.09±0.09	0.292	22.20±3.24	22.15±3.26	−0.05±0.07	0.466	0.699
BF (kg)	15.45±5.06	15.38±5.13	−0.78±0.17	0.660	16.49±5.53	16.54±5.37	0.05±0.13	0.742	0.441
LBM (kg)	41.67±3.64	41.5±3.55	−0.17±0.09	0.090	43.32±5.35	43.16±5.64	−0.15±0.77	0.262	0.902

[a]Within group comparisons (paired samples *t*-test), [b]between group comparisons (ANCOVA), *Adjusted for baseline values, BMI=Body mass index, BF=Body fat, LBM=Lean body mass

SM-induced cutaneous complications.[27] In addition, the positive effect of curcumin administration in reducing circulating tumor necrosis factor α (TNF-α) concentrations has been demonstrated in clinical practice.[28] Previous findings indicated that curcumin can inhibit phospholipase A_2 (PLA_2) by preventing its phosphorylation, cyclooxygenase (COX-2) by inhibiting its transcription in cultured cells.[29] On the other hand, curcumin is an inhibitor of nuclear factor-kappa B,[30] which regulates gene expression and inflammatory proteins.[31] Thus, agents such as curcumin inhibit nuclear factor-kappa B and have a preventive role against inflammatory diseases.[12] However, a clinical trial on athletes indicated that 500 mg curcumin with a midday meal and 500 mg consumption just before exercise had no significant effects on CRP levels.[18] It is plausible that the short duration of the intervention (3 days) did not provide enough time for curcumin to act as antiinflammatory agent and thus decrease CRP levels.

In the present study, we found that 8 weeks of curcumin administration attenuates MDA in females with moderate activity. In agreement with these findings, a previous study revealed that curcumin (1000 mg/day co-administered with piperine 10 mg/day) supplementation for 8 weeks led to a significant decrease in serum MDA and increase TAC and superoxide dismutase (SOD) activities in subjects with type 2 diabetes mellitus (T2DM).[32] Concordantly, 6-week supplementation of 1500 mg/day curcumin elicited significant improvements in antioxidant status and a significant decrease in MDA concentrations in patients with knee osteoarthritis.[33,34] It is well known that aerobic and anaerobic exercise can induce ROS overproduction, leading to increased oxidative stress.[35] Curcumin, as an antioxidant agent, can increase superoxide dismutase level via inhibiting ROS-generating enzymes.[12] In addition, it can increase serum activities of antioxidants.[11,34,36] Another positive action of curcumin is related to scavenging properties[11] to decrease oxidative damage.

Curcumin administration did not yield any changes in BMI, weight, BF, and LBM. Our finding for anthropometric measures, including body composition, is inconsistent with previous work, which has indicated that curcumin can significantly decrease body weight and fat content and improve lean tissue mass in metabolic syndrome or overweight subjects.[37] The effects of curcumin on weight are related to the reduction of adipose tissue inflammation and insulin resistance.[38] Further, the effects of curcumin in terms of appetite reduction, due to cortisol lowering properties, have been described previously.[39] It is conceivable that we saw no changes in the previously mentioned variables due to our participants being normal weight and not possessing any complications such as metabolic syndrome. Hence, the controversial results between studies might be using different groups (metabolic syndrome, athletes, healthy individuals, etc.).

Several strength points should be addressed about the present study. This study is the first investigation to have assessed the effects of curcumin in healthy females and in subjects with moderate physical activity levels. Using the lowest dose of curcumin supplementation is another strength point of this study. This study results cannot be generalized as this study did not include men or professional athletes, and find whether any ethnic differences exist on the effects of curcumin. Moreover, we did not investigate the gene expression and molecular mechanisms of curcumin on inflammation and oxidative stress. In addition, FFQ usually evaluates the usual diet for a long time and might not be suitable in trials. However, it might provide an overview of diet. Thus, we had recall bias because of using FFQ to assess dietary intake. Therefore, it is suggested that future studies assess such gene markers and evaluate the effects of different doses of curcumin on anthropometric indices.

Table 2: Estimated average intake of some nutrients

Variables	Mean±SD		*P**
	Curcumin group (*n*=32)	Placebo group (*n*=33)	
Energy (kcal)	2140.5±434.67	2139.73±466.81	0.994
Carbohydrate (g)	319.17±78.33	302.53±74.23	0.332
Protein (g)	75.96±17.83	75.96±21.26	0.960
Fat (g)	69.62±15.72	76.51±24.57	0.139
Beta-carotene (µg)	3135.44±1738.08	3646.38±2306.45	0.267
Vitamin C (mg)	176.81±80.73	157.93±91.45	0.331
Vitamin E (mg)	9.90±3.15	12±7.59	0.110
Zinc (mg)	10.83±2.59	11.07±3.32	0.719
Selenium (µg)	84.1±20.1	89.75±23	0.246

*Resulted from independent *t*-test

Table 3: The comparison of inflammatory indice, oxidative stress, and muscle damage indices between two groups

Variables	Curcumin group (*n*=32)				Placebo group (*n*=33)				*P*b*
	Before	After	Mean±SE	*P*a	Before	After	Mean±SE	*P*a	
CRP (mg/L)	5.6±2.54	4.21±2.12	−1.38±0.44	0.004	4.53±2.48	5.71±2.16	1.18±0.56	0.044	0.002
LDH (U/L)	248.79±74.63	210.69±69.27	−38.1±13.78	0.010	214.05±80.70	228.46±79.11	14.4±15.5	0.360	0.041
TAC (mMOL/L)	0.99±0.23	1.06±0.25	0.06±0.05	0.263	1.13±0.25	1.10±0.25	−0.02±0.06	0.694	0.439
MDA (nMOL/mL)	1.27±0.29	1.15±0.17	−1.18±0.05	0.027	1.22±0.26	1.29±0.24	0.06±0.04	0.195	0.005
$VO2_{max}$ (mL/kg.min)	45.91±1.24	46.75±1.79	0.84±0.32	0.016	45.74±1.6	45.16±1.4	−0.58±0.3	0.063	0.0001

[a]Within group comparison (paired samples *t*-test), bbetween group comparisons (ANCOVA), *Adjusted for baseline values, CRP=C-reactive protein, TAC=Total antioxidant capacity, MDA=Malondialdehyde, LDH=Lactatedehydrogenase, $VO2_{max}$=Maximum oxygen uptake

Conclusions

In healthy young adult women, 8 weeks of curcumin supplementation yielded significant improvements in CRP, LDH, MDA, and VO_2 max. In contrast, curcumin supplementation did not affect weight, body fat, and lean body mass in this study.

Declaration of participant consent

The authors certify that they have obtained all appropriate participant consent forms. In the form, the participants have given their consent for their images and other clinical information to be reported in the journal. The participants understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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This study was extracted from MSc dissertation, which was approved by School of Nutrition & Food Science, Isfahan University of Medical Sciences (code: IR.MUI.REC.1396.2.045).

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Conflicts of interest

There are no conflicts of interest.

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