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# Acute effect of curcumin on interleukin-6 (IL-6) levels and C-reactive protein (CRP) levels after high-intensity physical exercises

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**Abstract**
**Introduction. Around 30 million people worldwide experience pain are usually treated with NSAIDs. Providing complementary and therapeutic therapies as means of pain management would benefit those individual suffering with chronic pain. One such non-pharmacological natural compound reported to offer therapeutic application is curcumin. Aim of Study. This study aims to analyze the acute effect of curcumin on IL-6 levels and CRP levels after high-intensity physical exercises. Material and Methods. This experimental research uses pre- and post-control group design. Research subjects were selected using random sampling technique. Next, the subjects were divided into two groups: K1, which was given a placebo, and K2, which received curcumin. A total of 20 healthy men, who were selected according to inclusion and exclusion criteria, participated in this study. Blood samples were analyzed in a laboratory using the ELISA method. Results. The results of the study reported that there was no significant change in the serum IL-6 levels in the placebo group or in the group given curcumin at a dose of 400 mg ($p > 0.05$). Furthermore, the significant decrease in the serum CRP levels has been observed in the group given curcumin at the dose of 400 mg ($p < 0.05$). Conclusions. Curcumin given at the dose of 400 mg 24 hours after the high-intensity physical exercises had no effect on the IL-6 levels because it had already exceeded the maximum levels in blood. However, curcumin given at the dose of 400 mg after the high-intensity physical exercises was observed to reduce the CRP levels.**

**KEYWORDS:** **exercise, inflammation, therapeutic, curcumin, pain.**

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## Introduction

High-intensity physical exercise, such as resistance training and/or plyometrics, that target eccentric muscle actions, can result in significant metabolic stress and exercise-induced muscle damage (EIMD) [12]. EIMD is often characterized by increased muscle pain and reduce range of motion [5]. Collectively, this may limit physical performance after a training session [19, 20, 26, 27]. Studies have reported a cascade of events leading to pain, such as uncontrolled inflammatory process due to increased levels of tumor necrosis factor alpha (TNF-α) and interleukin 6 (IL-6) levels during EIMD [9]. Meanwhile, C-reactive protein (CRP) is believed to be a biomarker for inflammation [10, 18]. In most cases, inflammation tends to peak one to two days post-exercise [6, 14, 17].

Currently, the Exercise is Medicine approach is recommended to assist individuals suffering chronic conditions, such as persistent pain. This is an important consideration, given that approximately 30 million people worldwide experience persistent pain, and are usually treated with nonsteroidal anti-inflammatory drugs (NSAIDs) [4, 16]. Administering NSAIDs after exercise in those experiencing persistent pain may interfere with the both the acute and chronic neuromuscular response to exercise. Furthermore, the use of NSAIDs may specifically negate the positive, anabolic effects of strength exercises [22].

Therefore, alternative complementary therapies as means of pain management would benefit individuals suffering with persistent pain. One such non-pharmacological natural compound, known for its anti-inflammatory properties is curcumin. Curcumin is reported to inhibit inflammation through modulating NF-κB signals and blocking proinflammatory cytokine signals by activating protein responses in muscles, thereby accelerating recovery from EIMD [24, 25]. Moreover, curcumin also offers antioxidant properties, and plays a role in suppressing prooxidant activity by increasing the heme oxygenase 1 (HO-1) and glutathione peroxidase (GPx) genes [15]. Furthermore, curcumin has been linked to improved cardiovascular endurance [11]. It has also been applied in the world of medicine and health to accelerate wound healing [1]. Our previous research has reported that curcumin can reduce creatine kinase (CK) levels after physical exercises. Until now, it has not been known whether curcumin can reduce IL-6 and CRP levels as inflammatory biomarkers after high-intensity physical exercises.

## Aim of Study

This study aims to analyze the acute effect of curcumin on IL-6 levels and CRP levels after high-intensity physical exercise in recreationally active men.

## Material and Methods

*Study design*

This experimental research uses pre- and post-control group design. Research subjects were selected using a random sampling technique, then the subjects were divided into two groups, namely a group which was given a placebo (K1) and a group which received curcumin (K2).

*Subjects*

A total of 20 healthy, recreationally active men participated in this study (subject characteristics are shown in Table 1). Inclusion criteria for this study were recreationally active males, 20-30 years old, normal BMI and pre-exercise blood pressure, not participating in sports. Participants were asked to refrain from consumption of coffee, foods containing turmeric, use of NSAIDs, and massage therapy. Participants received instructions on research procedures, and signed a consent form, agreeing to become research subjects.

**Table 1.** The characteristics of the research subjects

| Data | Group | n | $\bar{x} \pm SD$ | Shapiro–Wilk | p-value |
|---|---|---|---|---|---|
| Age (y) | K1 | 10 | 22.60 ± 1.83 | 0.149 | 0.389 |
| | K2 | 10 | 23.30 ± 1.70 | 0.850 | |
| Height (cm) | K1 | 10 | 166.95 ± 4.46 | 0.891 | 0.179 |
| | K2 | 10 | 169.80 ± 4.64 | 0.243 | |
| Weight (kg) | K1 | 10 | 63.55 ± 9.11 | 0.823 | 0.938 |
| | K2 | 10 | 63.20 ± 10.68 | 0.386 | |
| BMI (kg/m$^2$) | K1 | 10 | 23.13 ± 4.20 | 0.046 | 0.173 |
| | K2 | 10 | 21.70 ± 3.17 | 0.477 | |

There were no significant differences in the data for each group presented in the table above.

*Procedure*

Administration preparations included obtaining ethical suitability approvals and permits for borrowing facilities and infrastructure was followed by screening of the respondents to be selected as research subjects according to the inclusion and exclusion criteria, and completion of a form by the research subjects, indicating their willingness to participate in the study (the Informed Consent). The subjects were divided into two groups, namely the group that received a placebo, and the group that received curcumin. The placebo was provided in a form of empty capsules and curcumin was given in a form of natural supplement capsules at a dose of 400 mg. The 400 mg dose of curcumin was chosen based on our previous literature studies [2].

On the first day, the research subjects' characteristics were collected. Then the subjects warmed up and performed exercises in a form of squats and leg presses with 80-90% intensity of their maximum capacity. The intensity for each subject was determined using the one-repetition maximum (1RM) test. The 1RM is the maximum weight that can be lifted in one repetition of a movement. The exercise is performed in four sets of 10 repetitions with a recovery time of approximately 60 seconds between sets. On the second day, after

24 hours, all subjects had their pain intensity measured, pre-test blood samples were taken to determine the IL-6 levels and the CRP levels, and intervention was given according to the group. On the third day, after 24 hours, all subjects had their pain intensity measured and post-test blood samples were taken to determine the IL-6 levels and the CRP levels. Blood samples were analyzed in a laboratory using the ELISA method with the human IL-6 ELISA kit (cat. no. E0090Hu) and the human CRP ELISA kit (cat. no. MDBE1798Hu). Figure 1 displays the CONSORT flowchart.

*Statistical analysis*

Statistical analysis included descriptive tests to obtain a mean, a standard deviation and a standard error. A normality test was performed using the Shapiro–Wilk method if data was normally distributed. A difference test was conducted using a paired t-test, however if

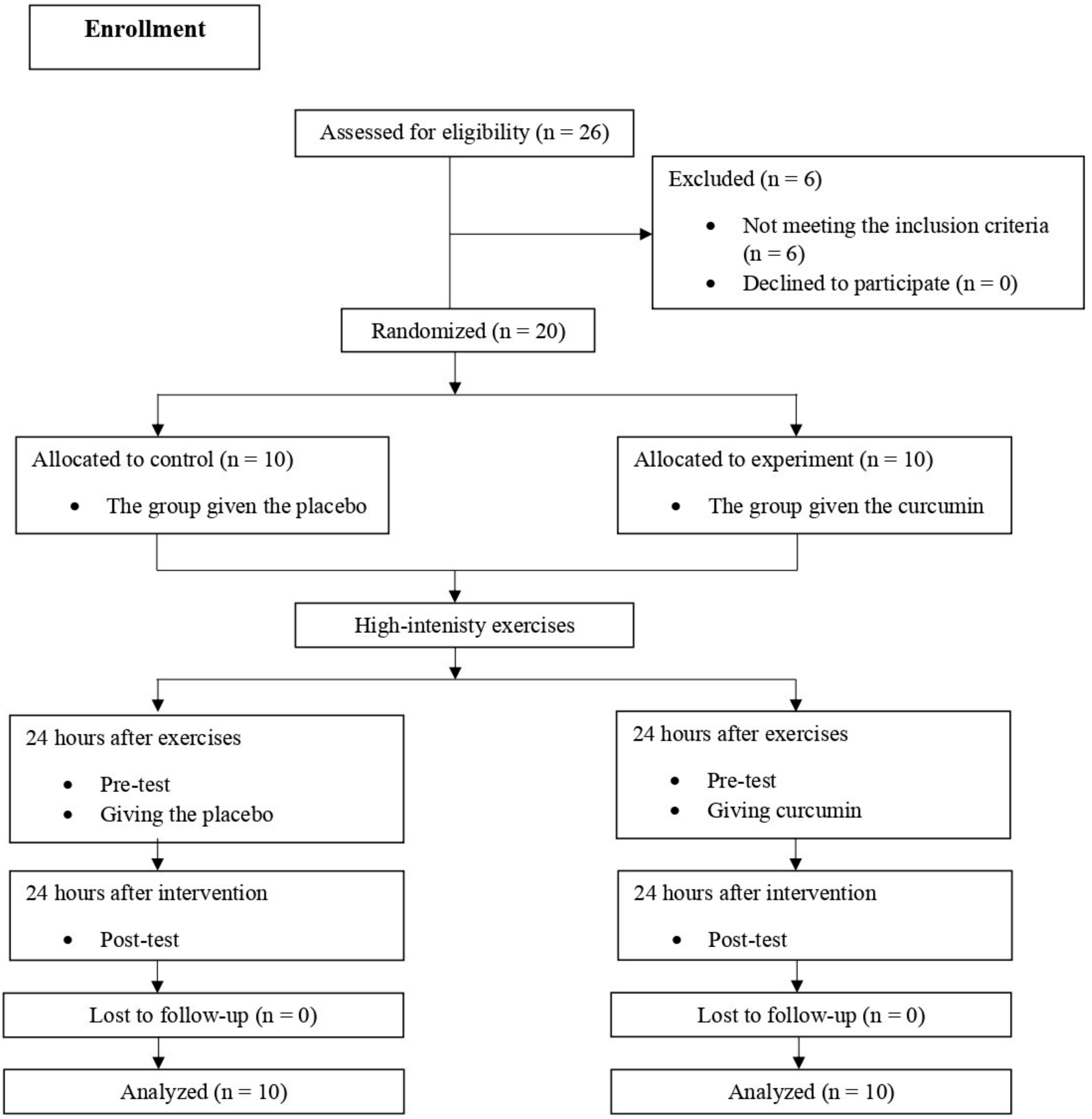


**Figure 1.** The CONSORT flowchart [4]

data was not normally distributed, a difference test was performed using the Wilcoxon signed rank test.

*Ethics*

Declaration of ethics was approved by the Health Research Ethics Committee of the Faculty of Medicine, Airlangga University (registration No. 118/EC/KEPK/FKUA/2022).

**Results**

Data on the characteristics of the research subjects are shown in Tables 1-5.

**Table 2.** The characteristic of the research subjects: body temperature, blood pressure and pulse

| Data | Group | n | x̄ ± SD | Shapiro–Wilk | p-value |
|---|---|---|---|---|---|
| Body temperature (°C) | K1 | 10 | 36.56 ± 0.26 | 0.184 | 0.619 |
| | K2 | 10 | 36.47 ± 0.49 | 0.523 | |
| Systolic blood pressure (mmHg) | K1 | 10 | 123.00 ± 6.27 | 0.475 | 0.355 |
| | K2 | 10 | 119.80 ± 8.62 | 0.987 | |
| Diastolic blood pressure (mmHg) | K1 | 10 | 75.30 ± 6.66 | 0.100 | 0.385 |
| | K2 | 10 | 71.60 ± 11.31 | 0.385 | |
| Pulse (bpm) | K1 | 10 | 84.70 ± 5.45 | 0.053 | 0.165 |
| | K2 | 10 | 88.70 ± 6.83 | 0.779 | |

**Table 3.** The normality test results for the IL-6 levels

| Data | Group | Shapiro–Wilk | |
|---|---|---|---|
| | | n | p-value |
| IL-6 levels (pre-test) | K1 | 10 | 0.249 |
| | K2 | 10 | 0.005 |
| IL-6 levels (post-test) | K1 | 10 | 0.004 |
| | K2 | 10 | 0.290 |

$p > 0.05$ = data is normally distributed; $p < 0.05$ = data is not normally distributed

The results of the analysis of the IL-6 levels between the pre- and post-test blood samples in each group are presented in Figure 2.

There was no significant reduction in the IL-6 levels ($p > 0.05$) observed in either the group K1, that was administered the placebo, or the group K2, that received curcumin after the high-intensity exercises.

**Table 4.** The difference test results for the IL-6 levels

| Difference test method | Group | p |
|---|---|---|
| Wilcoxon signed ranks test | K1 (pre-test and post-test) | 0.646 |
| | K2 (pre-test and post-test) | 0.074 |

There was no significant difference between the two groups.

The results of the analysis of CRP levels between the pre- and post-test blood samples in each group are presented in Figure 3.

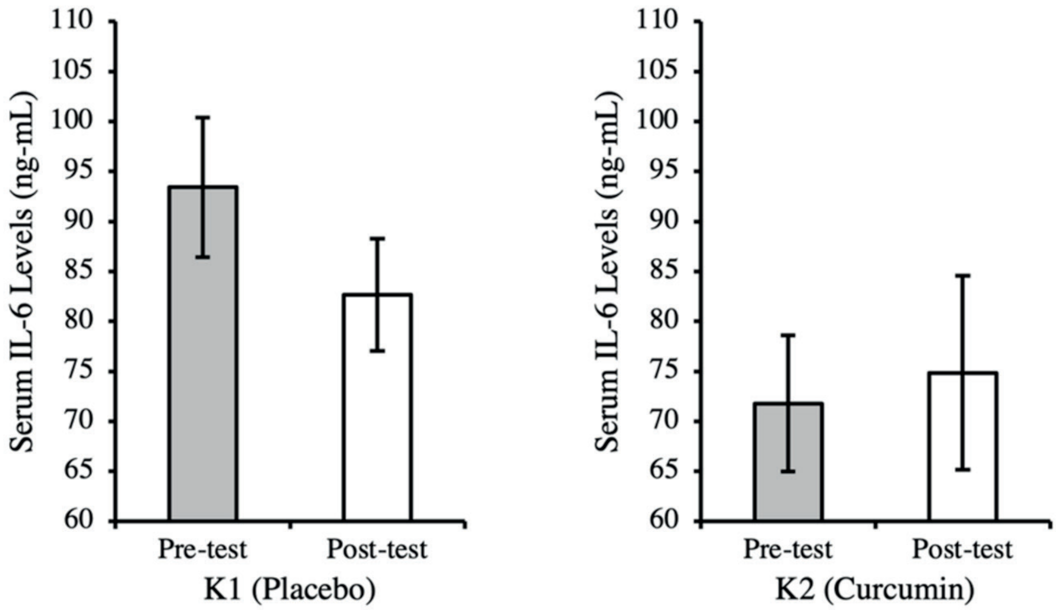


**Figure 2.** Serum IL-6 levels before and after the high-intensity exercises (data is presented as mean ± standard error)

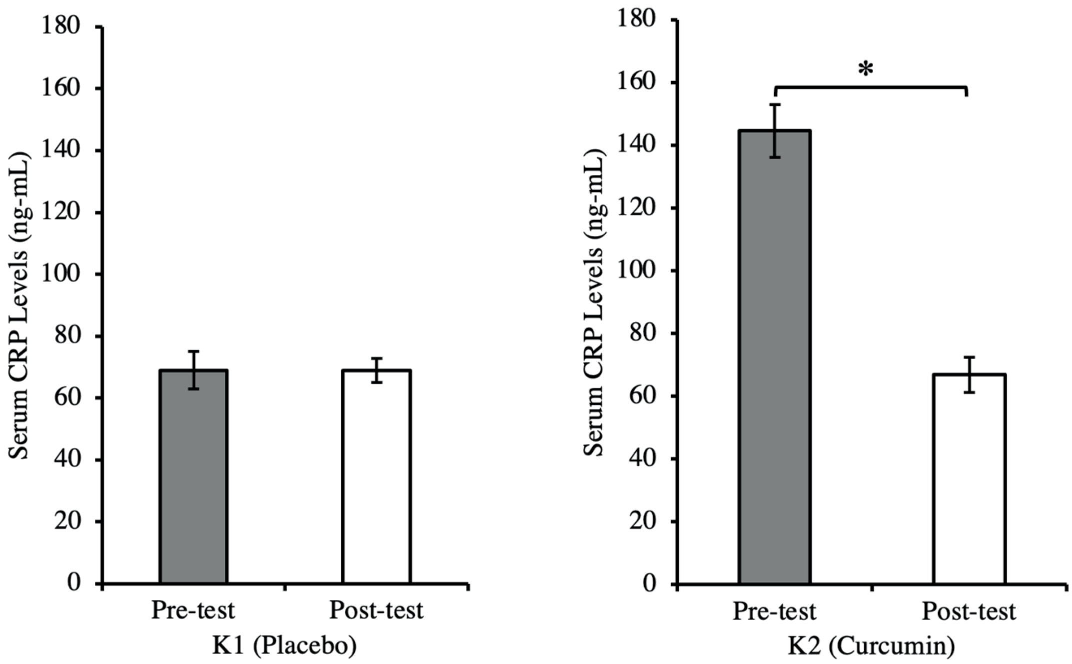


**Figure 3.** CRP levels before after the high-intensity exercises (data is presented as mean, standard error)

**Table 5.** The normality test results for the CRP levels

| Data | Group | Shapiro–Wilk | |
|---|---|---|---|
| | | n | p-value |
| CRP levels (pre-test) | K1 | 10 | 0.101 |
| | K2 | 10 | 0.362 |
| CRP levels (post-test) | K1 | 10 | 0.274 |
| | K2 | 10 | 0.081 |

$p > 0.05$ = data is normally distributed

The significant reduction in CRP levels (* $p < 0.05$) was observed in the group K2 that was given curcumin after the high-intensity exercises, compared to the group K1 that was administered the placebo.

**Table 6.** The difference test results for the CRP levels

| Difference test method | Group | p |
|---|---|---|
| Paired t-test | K1 (pre-test and post-test) | 0.925 |
| | K2 (pre-test and post-test) | 0.000* |

* There is a significant difference in the paired t-test ($p < 0.05$).

## Discussion

No significant change in the serum IL-6 levels was observed in the placebo group or the group treated with curcumin. Some studies reported that a value of IL-6 secretion in muscle cells, which can be measured in a blood sample, increases 6 hours after exercising and a value of IL-6 secretion in immune cells increases again after 12 hours [13, 21]. Supporting these results, in the present study curcumin was administered 24 hours after exercises. Therefore, it does not necessarily have a significant effect because IL-6 concentration exceeds the maximum levels in blood.

Furthermore, the significant decrease in the serum CRP levels was observed in the group which was given 400 mg of curcumin ($p < 0.05$). CRP is an acute-phase protein that increases after exercising, especially when muscle damage occurs. One theory suggests that CRP reaches its peak one day after doing exercises [8]. The present study responds, confirming that curcumin has the potential to have positive effects on inflammatory responses [2, 7]. This research is supported by a study in rats reporting that curcumin is able to inhibit aldosterone-induced CRP in vascular smooth muscle cells through blocking reactive oxygen species (ROS)-ERK1/2 signaling [28]. Furthermore, other studies report that curcumin at doses of 200 and 400 mg/kg body weight has the potential to slow aging processes by modulating CRP levels [23]. Post-exercise inflammation triggers increased muscle pain. In this regard, the recent study reports that curcumin administered at a dose of 400 mg is able to reduce pain intensity and increase range of motion (ROM) during EIMD [3]. Thus, this study demonstrates that the anti-inflammatory properties of curcumin have the potential to reduce CRP levels as a marker of inflammation after high-intensity exercises.

Based on the conducted laboratory tests, it can be concluded that the decrease in CRP occurred due to the anti-inflammatory effects of curcumin. Meanwhile, all aspects of research and measurement have been carefully considered. Acknowledging the limitations of the study regarding the lack of measurements of curcumin effects 12 hours after exercises, the authors believe that the strengths of these findings outweigh the shortcomings. For future research, the authors hope to test the effect of curcumin on the IL-6 biomarker 12 hours after exercising.

## Conclusions

Curcumin administered at the dose of 400 mg 24 hours after high-intensity physical exercises had no effect on the IL-6 levels because it had already exceeded the maximum values in blood. However, curcumin given at the dose of 400 mg after the high-intensity physical exercise was able to reduce the CRP levels. It is highly recommended to use curcumin, which proves to have many benefits for sportsmen.

## Conflict of Interest

The authors declare no conflict of interest.

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