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Curcumin: Compound in Turmeric that Has the Potential to Increase Serum Interleukin-10 (IL-10) Levels After High-Intensity Exercise

Curcumina: compuesto de la cúrcuma que tiene el potencial de aumentar los niveles séricos de interleucina-10 (IL-10) después del ejercicio de alta intensidad

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Abstract. This study aims to analyze the effect of curcumin on serum IL-10 levels after high-intensity exercise. This experimental research uses pre and post-control group design. Research subjects were selected using purposive sampling technique. Next, the subjects were divided into 2 groups, namely group (K1) given placebo and group (K2) given curcumin. A total of 20 healthy men participated in this study who were selected based on inclusion and exclusion criteria. On the first day, all subjects collected data on the characteristics of the research subjects, then warmed up, then the subjects did exercises in the form of squad exercises and leg presses with an intensity of 80-90% of their maximum ability. Exercises are done in 4 sets, 10 repetitions for each form of exercise and rest between sets for approximately 60 seconds. On the second day, after 24 hours, all subjects had pre-test blood samples taken to measure serum IL-10 levels and were given intervention according to group. On the third day, after 24 hours, all subjects had post-test blood samples taken to measure serum IL-10 levels. Blood samples were analyzed in the laboratory using the ELISA method with the Human IL-10 ELISA kit catalog number MDBEH6154. The results of this study reported that the group given curcumin at a dose of 400 mg had significantly increased serum IL-10 levels ($p<0.05$). Increasing serum IL-10 levels, which is an anti-inflammatory cytokine, has the potential to control uncontrolled inflammation after exercise. So in this case, the anti-inflammatory properties of curcumin also have the potential to reduce post-exercise muscle pain. Reducing the intensity of pain after high intensity exercise is necessary to support body function.
Keywords: Curcumin, Inflammation, Cytokines, Pain Intensity, Exercise

Abstracto. Este estudio tiene como objetivo analizar el efecto de la curcumina sobre los niveles séricos de IL-10 después del ejercicio de alta intensidad. Esta investigación experimental utiliza un diseño de grupo de control previo y posterior. Los sujetos de investigación fueron seleccionados mediante la técnica de muestreo intencional. A continuación, los sujetos se dividieron en 2 grupos, a saber, el grupo (K1) que recibió placebo y el grupo (K2) que recibió curcumina. En este estudio participaron un total de 20 hombres sanos que fueron seleccionados según criterios de inclusión y exclusión. El primer día, todos los sujetos recopilaron datos sobre las características de los sujetos de investigación, luego calentaron, luego los sujetos hicieron ejercicios en forma de ejercicios de escuadrón y prensas de piernas con una intensidad del 80-90% de su capacidad máxima. Los ejercicios se realizan en 4 series, 10 repeticiones para cada forma de ejercicio y descanso entre series durante aproximadamente 60 segundos. El segundo día, después de 24 horas, a todos los sujetos se les tomaron muestras de sangre previas a la prueba para medir los niveles séricos de IL-10 y Se les dio intervención según grupo. Al tercer día, después de 24 horas, a todos los sujetos se les tomaron muestras de sangre posteriores a la prueba para medir los niveles séricos de IL-10. Las muestras de sangre se analizaron en el laboratorio mediante el método ELISA con el kit ELISA Human IL-10 número de catálogo MDBEH6154. Los resultados de este estudio informaron que el grupo que recibió curcumina en una dosis de 400 mg había aumentado significativamente los niveles séricos de IL-10 ($p<0,05$). El aumento de los niveles séricos de IL-10, que es una citocina antiinflamatoria, tiene el potencial de controlar la inflamación incontrolada después del ejercicio. Entonces, en este caso, las propiedades antiinflamatorias de la curcumina también tienen el potencial de reducir el dolor muscular post-ejercicio. Es necesario reducir la intensidad del dolor después del ejercicio de alta intensidad para apoyar la función corporal.
Palabras clave: curcumina, inflamación, citocinas, intensidad del dolor, ejercicio

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Introduction

High-intensity training such as resistance training, especially with eccentric movements, will cause metabolic stress in the form of energy deficiency and muscle damage (Devi et al., 2023; Harty et al., 2019). Muscle damage caused by exercise or Exercise-Induced Muscle Damage (EIMD) is characterized by the emergence of muscle pain (Casanova et al., 2018). Thus, the resulting muscle pain can limit performance after a training session (Owens et al., 2019; Romero-Parra et al., 2021; Viribay et al., 2020; Xin & Eshaghi, 2021). Several studies report that muscle pain is caused by an increase in pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-a) and interleukin 6 (IL-6) in the body in response to muscle damage. (Ayubi, Kusnanik, Herawati, Komaini, Mutohir, Callixte, et al., 2023; Dupuy et al., 2018).

In most cases, inflammation peaks 1 to 2 days after an exercise session (Chang et al., 2021; Hung et al., 2021; Muljadi et al., 2021). The current phenomenon is that around 30 million people worldwide who experience pain are usually treated with non-steroidal anti-inflammatory drugs (NSAIDs). (Ayubi & Sastika Putri, 2021; Kyriakidou et al., 2021). Giving NSAIDs after exercise is a wrong alternative for managing pain, this is because NSAIDs have a disruptive effect on the muscle growth response which has an impact on hypertrophy and muscle strength (Lundberg & Howatson, 2018). As a result, giving NSAIDs will actually negate the results of the exercise carried out.

Other alternative solutions need to be sought to overcome this problem. One natural ingredient that is easy to find is curcumin. Curcumin is known for its anti-

inflammatory properties. Blockade of pro-inflammatory cytokine signals by activating protein responses in muscles thereby accelerating recovery from exercise-induced muscle damage (Srivastava et al., 2017). In this regard, anti-inflammatory cytokines such as interleukin 10 (IL-10) play an important role in controlling the inflammatory response (Srivastava et al., 2017). Curcumin has been widely used to increase endurance and VO2Max (Hamidie et al., 2017). Curcumin has also been used in the world of medicine and health to speed up wound healing (Alqahtani et al., 2020). Our previous research has reported that curcumin is able to reduce pro-inflammatory cytokines such as TNF-a, but until now curcumin has not been tested for its effectiveness against anti-inflammatory cytokines such as IL-10.

This study aims to analyze the effect of curcumin on serum IL-10 levels during high intensity exercise.

Methods

Study Design

This experimental research uses pre and post-control group design. Research subjects were selected using purposive sampling technique. Next, the subjects were divided into 2 groups, namely group (K1) given placebo and group (K2) given curcumin.

Subjects

A total of 20 healthy men participated in this study (subject characteristics are shown in table 1). The inclusion criteria in this study were men aged 20 to 30 years, with a normal BMI, and no sports training. The exclusion criteria in this study were subjects under 20 years of age and abnormal blood pressure before exercise. The drop out criteria in this study were consuming coffee, consuming foods containing turmeric, consuming non-steroidal anti-inflammatory drugs (NSAIDs), and having a massage. Research subjects receive instructions about research procedures and sign a letter of agreement willing to become research subjects.

Procedure

1. At the start, we prepare administration such as permits for ethical suitability and permits for borrowing facilities and infrastructure.
2. We screened respondents who were used as research subjects based on inclusion and exclusion criteria and filled out a form willing to become research subjects (Informed Consent) by the research subjects.
3. Subjects were divided into two groups, namely the group that received placebo and the group that received curcumin. Placebo was given in the form of empty capsules and curcumin was given at a dose of 400 mg.
4. On the first day, all subjects collected data on the characteristics of the research subjects, then warmed up, then the subjects did exercises in the form of squad exercises and leg presses with an intensity of 80-90% of their maximum ability. Exercises are done in 4 sets, 10 repetitions for each form of exercise and rest between sets for approximately 60 seconds.
5. On the second day, after 24 hours, all subjects had a pre-test blood sample taken to measure serum IL-10 levels and were given intervention according to group.
6. On the third day, after 24 hours, all subjects took post-test blood samples to measure serum IL-10 levels.
7. Blood samples were analyzed in the laboratory using the ELISA method with catalog number Human IL-10 ELISA kit MDBEH6154.

CONSORT flowchart

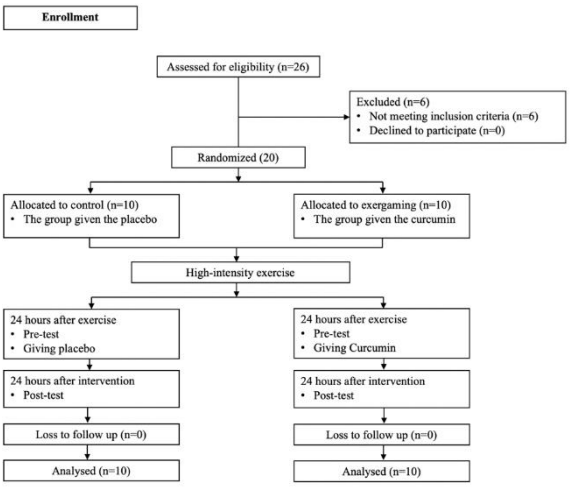

Figure 1. The CONSORT flowchart

Statistical analysis

Statistical analysis in this study used the IBM SPSS version 27 application, a descriptive test was performed to obtain the mean, standard deviation and standard error. Furthermore, the normality test was carried out using the Shapiro-Wilk method, if the data were normally distributed the different test was carried out using the paired t-test, but if the data was not normally distributed, the difference was carried out using the Wilcoxon signed rank test.

Ethics

This research protocol has been declared ethical in accordance with 7 (seven) WHO 2011 standards, namely 1) social value, 2) scientific value, 3) distribution of burdens and benefits, 4) risk, 5) seduction / exploitation, 6) confidentiality and privacy 7) Approval after explanation, which refers to the 2016 CIOMS guidelines. This is shown by the fulfillment of indicators for each standard. Declaration of ethics was approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Airlangga with registration number (No.118/EC/KEPK/FKUA/2022).

Results

Data on the characteristics of the research subjects are shown in Table 1-5. All data from the table above did not differ significantly in each group.

Table 1.
Characteristics of research subjects

Data	Group	N	x̄±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	

Table 2.
Characteristic subject: body temperature, blood pressure and pulse

Data	Group	N	x̄±SD	Shapiro-Wilk	p-value
Body temperature (°)	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 (mmHg)	K1	10	84.70±5.45	0.053	0.165
	K2	10	88.70±6.83	0.779	

Curcumin does not lower IL-10 levels

The results of the analysis of serum IL-10 levels between the pre-test and post-test in each group are presented in Figure 2.

Table 3.
Normality Test Results for serum IL-10 Levels

Data	Group	Shapiro-Wilk	
		n	p-value
IL-10 levels (Pre-test)	K1	10	0.253
	K2	10	0.001
IL-10 levels (Post-test)	K1	10	0.502
	K2	10	0.098

Information:
P>0.05 = Data is normally distributed
P<0.05 = Data is not normally distributed

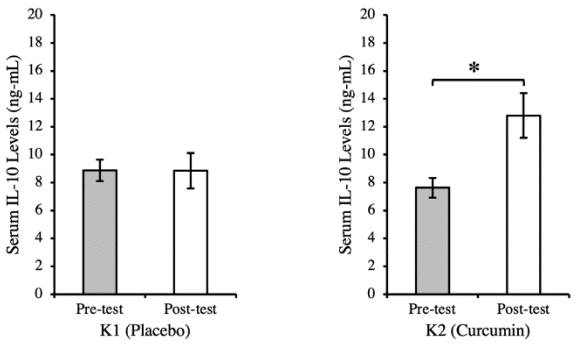

Figure 2. The group (K1) that was given a placebo after high intensity exercise did not increase serum IL-10 levels significantly (p>0.05) and there was a significant increase in serum IL-10 levels in the group (K2) that was given curcumin (p<0.05). Data are presented as Mean ± Std Error. P-value was obtained using the Paired t-test and Wilcoxon signed rank test to compare the pre-test and post-test of each group

Table 4.
IL-10 Levels Different Test Results

Difference Test Method	Group	P
Paired t-test	K1 (pre-test and post-test)	0.646
Wilcoxon signed rank test	K2 (pre-test and post-test)	0,074

Information:
There was no significant difference between the two groups

Discussion

This study aims to analyze the effect of curcumin on Interleukin 10 levels during high-intensity exercise. We observed that the placebo group did not significantly increase IL-10 levels after high-intensity exercise, whereas the curcumin group administered at a dose of 400 mg significantly increased serum IL-10 levels (p<0.05). Our study answers and confirms literature studies reporting findings that curcumin has positive effects on inflammatory responses (Dias et al., 2021; Ayubi et al., 2023).

High intensity exercise, especially with eccentric movements, will result in muscle damage and an inflammatory response (Markus et al., 2021; Nanavati et al., 2022). Eccentric movements contribute to high mechanical stress and produce bone extracellular matrix fragments that are recognized by receptors expressed by innate immune cells (Nanavati et al., 2022). In this case the role of curcumin is very necessary. A study reports that curcumin has anti-inflammatory properties (Bisht et al., 2020; Peng et al., 2021). Curcumin, which has anti-inflammatory properties, works by controlling uncontrolled inflammatory responses, especially by controlling pro-inflammatory cytokines such as TNF-a and IL-6 (Ayubi, Kusnanik, Herawati, Komaini, Mutohir, Gemaini, et al., 2023). Many studies report that increasing levels of TNF-a in the blood is a cause of delayed onset of muscle pain (Anugrah et al., 2023; Ayubi et al., 2022; Boarescu et al., 2022; Li et al., 2017). In histological studies, TNF-a levels in the blood will reach their peak 24-48 hours after exercise (Chang et al., 2021; Hung et al., 2021; Muljadi et al., 2021). Our previous research reported that omega 3 given at a dose of 1000 mg after weight training was able to reduce pain intensity through reducing TNF-a levels (Ayubi et al., 2022). In this regard, interestingly, our study provided curcumin intervention at the peak of increased inflammation at 24 post-exercise. So in this case uncontrolled inflammation due to an increase in pro-inflammatory cytokines can be controlled, as evidenced by the increase in IL-10 levels in the blood in the group given curcumin. Indeed, exercise has many benefits for health and fitness (Martin-Smith et al., 2020; Ruegsegger & Booth, 2018). However, on the other hand, when training is done at high intensity, especially for people who are not trained, this can reduce performance due to complaints of post-exercise muscle pain (Sonkodi, 2021).

In this study, the limitation is that we only investigated and analyzed the acute effects of curcumin. Apart from that, we also have not analyzed physical performance such as muscle strength. As a future perspective, we intend to analyze the chronic effects of curcumin on inflammatory biomarkers, performance parameters and adaptive responses to physical exercise. Thus we report that administration of

curcumin after high-intensity physical exercise is able to increase serum IL-10 cytokine levels which is very useful for controlling the increase in pro-inflammatory cytokines.

Conclusion

Giving a dose of 400 mg of curcumin after high-intensity exercise can increase serum IL-10 levels. Increasing levels of IL-10, which is an anti-inflammatory cytokine, has the potential to control uncontrolled inflammation after exercise. So in this case, the anti-inflammatory properties of curcumin also have the potential to reduce post-exercise muscle pain. Reducing the intensity of pain after high-intensity exercise is necessary to support body function.

Conflict of interest

The authors declare no conflict of interest

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