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Curcumin: The Active Compound in Turmeric has the Potential to Reduce Pain Intensity and Increase Range of Motion During Exercise-Induced Muscle Damage

Curcumina: el compuesto activo de la cúrcuma tiene el potencial de reducir la intensidad del dolor y aumentar el rango de movimiento durante el daño muscular inducido por el ejercicio

*Novadri Ayubi, *Nining Widyah Kusnanik, **Lilik Herawati, *Heryanto Nur Muhammad, ***Anton Komaini, ****Mohammed Nashrudin Bin Naharudin, *Donny Ardy Kusuma, *Dwi Cahyo Kartiko, *Gigih Siantoro, *Awang Firmansyah

*Universitas Negeri Surabaya (Indonesia), **Universitas Airlangga (Indonesia), *** Universitas Negeri Padang (Indonesia), ****Universiti Malaya (Malaysia)

Abstract. This study aims to analyze and prove the effect of curcumin on pain intensity and ROM during EIMD. This experimental study used a pre and post-control group design. Research subjects were selected using a purposive sampling technique and then the subjects were divided into 2 groups, namely the group given a placebo and the group was given curcumin at a dose of 400 mg. A total of 24 healthy men aged between 20-30 years participated in this study. On the first day, all subjects took data on the characteristics of research subjects, then warmed up. Then the subjects did the high-intensity physical exercise in the form of squad and leg press exercises with an intensity of 80-90% of maximum ability. The exercise was carried out in 4 sets for each form of exercise and rest between sets for about 1 minute. On the second day, after 24 hours the subject took pre-test data to measure pain intensity and ROM, then the intervention was given based on each group. On the third day, after 24 hours the subject took post-test data to measure pain intensity and ROM. Measurement of pain intensity using the Visual Analytical Scale (VAS) and measurement of ROM performed in the knee joint using a goniometer. After the data was obtained, the data were analyzed using the IBM SPSS version 26 application. The results of this study reported that the group given curcumin during EIMD was able to significantly reduce pain intensity (*p<0.05) compared to the group given a placebo. Furthermore, the group given curcumin during EIMD was able to increase ROM significantly (*p<0.05) compared to the placebo group. We believe that the main cause of muscle soreness is the uncontrolled increase in pro-inflammatory cytokines such as TNF-a and IL-6 during EIMD and then decreased ROM for several days after exercise. Since pain intensity and ROM are needed to support body functions, we highly recommend the use of curcumin, which has many positive benefits for sports enthusiasts to support physical performance.
Keywords: Curcumin, Pain Intensity, Range of Motion, Exercise-Induced Muscle Damage, Inflammation

Resumen. Este estudio tiene como objetivo analizar y probar el efecto de la curcumina sobre la intensidad del dolor y el ROM durante la EIMD. Este estudio experimental utilizó un diseño de grupo de control previo y posterior. Los sujetos de investigación se seleccionaron utilizando una técnica de muestreo intencional y luego los sujetos se dividieron en 2 grupos, a saber, el grupo que recibió un placebo y el grupo que recibió curcumina en una dosis de 400 mg. Un total de 24 hombres sanos de entre 20 y 30 años participaron en este estudio. El primer día, todos los sujetos tomaron datos sobre las características de los sujetos de investigación y luego calentaron. Luego, los sujetos realizaron el ejercicio físico de alta intensidad en forma de ejercicios de escuadra y prensa de piernas con una intensidad del 80-90% de la capacidad máxima. El ejercicio se realizó en 4 series para cada forma de ejercicio y descanso entre series durante aproximadamente 1 minuto. El segundo día, después de 24 horas, el sujeto tomó datos de la prueba previa para medir la intensidad del dolor y el ROM, luego se administró la intervención en función de cada grupo. El tercer día, después de 24 horas, el sujeto tomó datos posteriores a la prueba para medir la intensidad del dolor y el ROM. Medición de la intensidad del dolor mediante la Escala Analítica Visual (EVA) y medición del ROM realizada en la articulación de la rodilla mediante un goniómetro. Después de obtener los datos, los datos se analizaron utilizando la aplicación IBM SPSS versión 26. Los resultados de este estudio informaron que el grupo que recibió curcumina durante la EIMD pudo reducir significativamente la intensidad del dolor (*p<0.05) en comparación con el grupo que recibió un placebo. Además, el grupo que recibió curcumina durante la EIMD pudo aumentar significativamente el ROM (*p<0,05) en comparación con el grupo de placebo. Creemos que la causa principal del dolor muscular es el aumento descontrolado de citocinas proinflamatorias como TNF-a e IL-6 durante la EIMD y luego la disminución del ROM durante varios días después del ejercicio. Dado que la intensidad del dolor y el ROM son necesarios para respaldar las funciones corporales, recomendamos encarecidamente el uso de curcu-min, que tiene muchos beneficios positivos para los entusiastas del deporte para respaldar el rendimiento físico.
Palabras clave: curcumina, intensidad del dolor, rango de movimiento, daño muscular inducido por el ejercicio, inflamación

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Anton Komaini
antonkomaini@fik.unp.ac.id

Introduction

Physical exercise, especially with high-intensity eccentric contractions, will cause muscle damage (Nanavati *et al.*, 2022; Anugrah *et al.*, 2023). This is called exercise-induced muscle damage (EIMD) (Jamurtas, 2018). EIMD triggers an inflammatory process that is closely related to an increase in muscle pain intensity and a decrease in Range of Motion (ROM) (Fernández-Lázaro *et al.*, 2020). Pro-inflammatory cytokines such as Tumor Necrosis Factor-alpha (TNF-a) and Interleukin 6 (IL-6) are believed to be the main causes of muscle pain during the inflammatory process due to EIMD (Li, Xu and Yang, 2017; Novadri Ayubi *et al.*, 2022; Devi *et al.*, 2023).

Several studies have reported that muscle pain peaks 24 hours after exercise (Chang *et al.*, 2021; Hung *et al.*, 2021; Muljadi *et al.*, 2021; Novadri Ayubi *et al.*, 2022). The resulting muscle pain is associated with decreased ROM (Fernández-Lázaro *et al.*, 2020). Decreased ROM has been reported to reduce performance in performing daily activities (Howatson *et al.*, 2012). In this regard, the current phenomenon of around 30 million people worldwide consuming non-steroidal anti-inflammatory drugs (NSAIDs) as a solution in pain management (N Ayubi *et al.*, 2022; Kafrawi *et al.*, 2023). In this case, consuming NSAIDs for pain management is the wrong alternative to be applied after exercise, this is because NSAIDs can interfere with the muscle growth response which is closely

related to muscle hypertrophy and muscle strength so it will negate the results of the exercise that has been done (Ozaki *et al.*, 2020). In addition, NSAIDs can cause drug dependence and are certainly not good for the health of the body's organs.(Godersky *et al.*, 2017).

Alternative solutions need to be found to overcome these problems. One of the natural ingredients contained in turmeric is curcumin. Curcumin is well known for its active compounds that have anti-inflammatory activity (Boarescu *et al.*, 2022). A literature study reported that curcumin was able to attenuate EIMD by decreasing the inflammatory response (Fernández-Lázaro *et al.*, 2020). The anti-inflammatory properties of curcumin can reduce TNF-a and IL-6 (Rahardjo *et al.*, 2014; Barchitta *et al.*, 2019). In addition, in the medical world curcumin has been widely used to accelerate wound healing (Sharma *et al.*, 2018). Despite the advantages of curcumin with its anti-inflammatory properties, a study reported that curcumin given at a dose of 500-12,000 mg in one day can cause diarrhea, rash, and yellow stools (Lao *et al.*, 2006). Thus, the use of doses must also be considered.

Until now, curcumin has not been reported to reduce pain intensity and increase ROM during EIMD. This study aims to analyze and prove the effect of curcumin on pain intensity and ROM during EIMD.

Research Methods

Study Design

This experimental study used a pre and post-control group design. The research subjects were selected using a random sampling technique and then the subjects were divided into 2 groups, namely the group receiving a placebo and the group receiving curcumin.

Subjects

A total of 24 healthy men participated in this study (subject characteristics are shown in table 1). The inclusion criteria in this study were ranging in age from 20 to 30 years, with normal BMI, and not trained in sports. The exclusion criteria in this study were subjects under 20 years of age and abnormal blood pressure prior to high-intensity physical exercise. The drop-out criteria in this study were consuming coffee, consuming foods containing turmeric, consuming non-steroidal anti-inflammatory drugs (NSAIDs), and doing a massage. research subjects received instructions on research procedures and signed written consent to become research subjects.

Research Instruments

Some of the instruments used in this study were fitness centers, data collection sheets, stationery, tensimeters, visual analog scales (VAS), goniometers, curcumin, and placebo capsules.

Procedure

1. Initially, we prepared administration such as ethical feasibility permits and permits for borrowing facilities and infrastructure.
2. We screened respondents who were used as subjects in the study based on inclusion and exclusion criteria and filled out a form willing to become research subjects (Informed Consent) by research subjects.
3. Subjects were divided into two groups, namely the group receiving a placebo and the group receiving 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 took data on the characteristics of the research subjects, then warmed up. Then the subjects did a high-intensity physical exercise in the form of squad and leg press exercises with an intensity of 80-90% of maximum ability. The exercise was carried out in 4 sets of each form of exercise and rest between sets for about 1 minute.
5. On the second day, after 24 hours all subjects took pre-test data to measure pain intensity and ROM, then the intervention was given based on their respective groups.
6. On the third day, after 24 hours all subjects took post-test data to measure pain intensity and ROM.
7. Measurement of pain intensity using the Visual Analog Scale (VAS) and measurement of ROM performed in the knee joint using a goniometer.
8. The final stage of this research, data analysis and preparation of reports as the responsibility of the researcher.

CONSORT flowchart

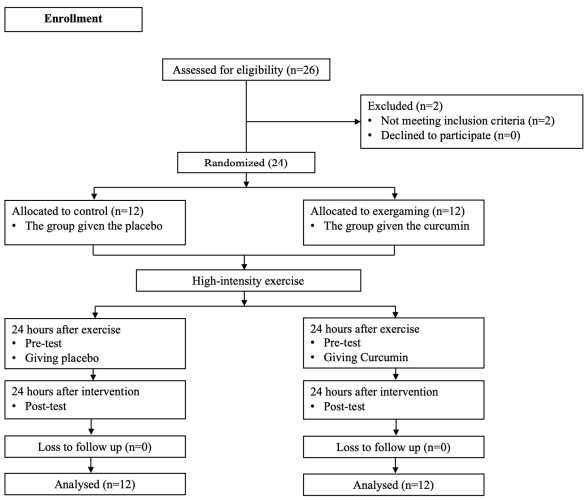

Figure 1. The CONSORT flowchart

Statistical analysis

Statistical analysis in this study used the IBM SPSS version 26 application, descriptive tests were carried out 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 difference test was performed using a paired t-test and independent t-test, but if the data were not normally

distributed, the difference was performed 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. The 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

The data on the characteristics of the research subjects are shown in table 1.

Table 1.
characteristics of research subjects

Data	Group Placebo	Group Curcumin	P value
Age (y)	22.75±1.81	23.00±1.80	0.739
Height (cm)	166.08±4.51	169.95±4.67	0.316
Weight (kg)	65.12±9.11	63.16±10.24	0.626
BMI (kg/m^2)	23.92±4.26	21.67±2.94	0.147
Body temperature (^{o})	36.55±0.29	36.49±0.13	0.712
Systolic (mmHg)	123.75±6.32	119.00±7.83	0.158
Diastolic (mmHg)	75.50±8.28	72.33±10.41	0.419

Data given as mean ± standard deviation. In the t-test, there was no significant difference in the characteristics of each group (p≥0.05).

Table 2.
Results of the normality test for Pain Intensity

Data	Group	Shapiro-Wilk	
		n	P-value
Pain Intensity (Pre-test)	Placebo	12	0.296
	Curcumin	12	0.412
Pain Intensity (Post-test)	Placebo	12	0.043
	Curcumin	12	0.632
Delta Pain Intensity	Placebo	12	0.412
	Curcumin	12	0.632

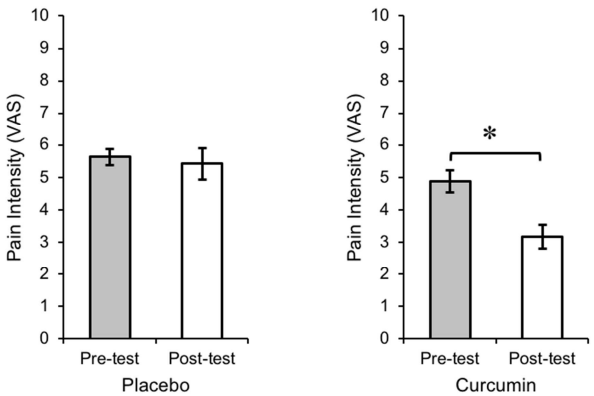

Figure 2. The group given curcumin during EIMD was able to significantly reduce pain intensity (*p<0.05) compared to the placebo group. Data are presented as Mean Std Error. P-values were obtained using the Wilcoxon signed rank test to compare the pre-test and post-test of each group.

Based on the normality test in Table 2, the post-test data on pain intensity in the placebo group were not normally distributed (p<0.05).

The results of the analysis of pain intensity between the pre-test and post-test presenting curcumin in each group are presented in Figure 2.

Table 3.
Results of Pain Intensity t-test

Different Test Method	Group	P-value
Wilcoxon signed rank tes	Placebo (pre-test and post-test)	0.683
	Curcumin (pre-test and post-test)	0,007*
Mann Whitney u-test	Delta placebo and curcumin	0,003**

Information:
* There was a significant difference in the Wilcoxon signed test (p <0.05)
** There is a significant difference in the *Mann* Whitney u-test (p <0.05)

Table 4.
Results of the normality test for ROM

Data	Group	Shapiro-Wilk	
		n	P-value
ROM (Pre-test)	Placebo	12	0.683
	Curcumin	12	0.979
ROM (Post-test)	Placebo	12	0.142
	Curcumin	12	0.246
Delta ROM	Placebo	12	0.979
	Curcumin	12	0.246

Based on the normality test in Table 4, the pre-test and post-test ROM data in the placebo group and the curcumin group were normally distributed (p>0.05).

The results of the ROM analysis between the pre-test and post-test of curcumin administration in each group are presented in Figure 3.

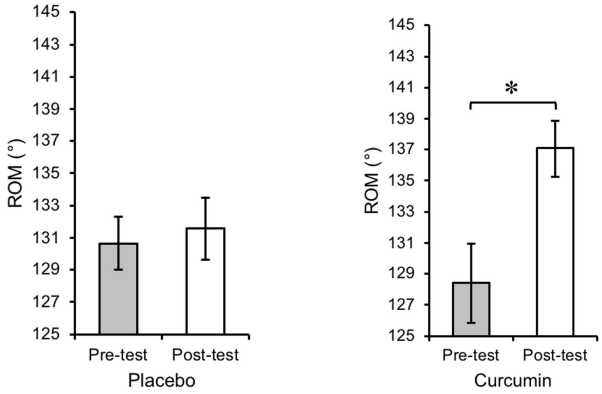

Figure 3. The group given curcumin during EIMD was able to increase ROM significantly (*p<0.05) compared to the placebo group. Data are presented as Mean Std Error. P-value was obtained by using the Pairet t-test to compare the pre-test and post-test of each group.

Table 5.
Results of ROM t-test

Different Test Method	Group	P-value
Pairet t-test	Placebo (pre-test and post-test)	0.508
	Curcumin (pre-test and post-test)	0,001*
Independent t-test	Delta placebo and curcumin	0,048**

Information:
* There was a significant difference in the Pairet t-test (p <0.05)
** There is a significant difference in the Independent t-test (p <0.05)

Discussion

The aim of this study was to prove the effect of curcu-

min on pain intensity and ROM during EIMD. Our results showed that the placebo group did not significantly reduce pain intensity and increase ROM during EIMD, while the group given curcumin at a dose of 400 mg significantly decreased pain intensity and increased ROM during EIMD.

In the case of EIMD, a histological study showed that neutrophils enter the muscle and accumulate in the damaged area from 1 to 24 hours after exercise (Paulsen *et al.*, 2010). In addition, EIMD is characterized by muscle ultrastructural disturbances that increase the release of inflammatory cytokines by macrophages (Nanavati *et al.*, 2022). Neutrophils and pro-inflammatory cytokines that interact with each other aim to control the pro-inflammatory response when muscle damage occurs (Hody *et al.*, 2019). On the other hand, when pro-inflammatory cytokines increase, macrophages also release anti-inflammatory cytokines that contribute to muscle recovery and regeneration (Nonnenmacher and Hiller, 2018). We believe that the main cause of muscle soreness is the uncontrolled increase in pro-inflammatory cytokines such as TNF-a and IL-6 during EIMD and then decreased ROM for several days after exercise. Our previous study has reported that supplementation with omega 3 which is known for its anti-inflammatory properties can reduce TNF-a levels after weight training. In this regard, curcumin is also one of the natural ingredients that have anti-inflammatory activity. A recent literature study reported that curcumin given at doses (>180 mg/day) was able to suppress the secretion of pro-inflammatory cytokines such as IL-1, IL-6, IL-8, IL-17, and TNF-a (Peng *et al.*, 2021; Ayubi *et al.*, 2023). Supported by a clinical trial that has proven that curcumin is able to reduce inflammatory mediators (Chen *et al.*, 2018; Chowdhury *et al.*, 2019).

We think that reducing pain intensity and increasing ROM is necessary to support body functions. One study reported that ROM was correlated with tissue hardness and decreased muscle strength was correlated with increased pain intensity (Konrad *et al.*, 2022)**.** Accelerating recovery after EIMD can maximize the value of exercise related to hypertrophy and increased muscle strength. On the other hand, the limitations of our study have not carried out an analysis of muscle strength. We strongly recommend further research to analyze the effects of curcumin on muscle strength. Thus, our study was aimed at adult males. We hereby report that administration of curcumin during EIMD is highly recommended to reduce pain intensity and increase ROM.

Conclusion

Administration of curcumin at a dose of 400 mg during EIMD was able to reduce pain intensity and increase ROM during EIMD. Since pain intensity and ROM are very necessary for supporting body functions, we highly recommend the use of curcumin which has many positive benefits for sports activists to support physical performance.

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