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Curcumin reduce creatine kinase (CK) levels without decreasing malondialdehyde (MDA) levels after 24 hours of high-intensity physical exercise

La curcumina reduce los niveles de creatina quinasa (CK) sin disminuir los niveles de malondialdehído (MDA) después de 24 horas de ejercicio físico de alta intensidad

*Nining Widyah Kusnanik, *Novadri Ayubi, **Lilik Herawati, *Tutur Jatmiko, ***Abd. Muin, ****Stephen P. Bird
*Universitas Negeri Surabaya (Indonesia), **Universitas Airlangga, (Indonesia), ***Shanghai University of Sport (China), ****University of Southern Queensland (Australia)

Abstract. This study aims to analyze the effect of curcumin on serum levels of creatine kinase (CK) and malondialdehyde (MDA) after 24 hours of high-intensity physical exercise. This experimental study used a pre and post-control group design. A total of 18 healthy men with an average age of 23 years participated in this study. Subjects were selected using a random sampling technique and then the subjects were divided into 2 groups, namely the group given a placebo and the group given curcumin at a dose of 400 mg. On the first day, all subjects took data on the characteristics of the research subjects, and 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. On the second day, after 24 hours, all subjects took pre-test data samples to measure serum CK and MDA levels, then the intervention was given based on their respective groups. On the third day, after 24 hours, all subjects took post-test blood samples to measure CK and MDA serum levels. Blood samples were analyzed in the laboratory using the ELISA method. The results of this study reported that the group given a placebo did not significantly reduce serum CK levels, while the group with curcumin at a dose of 400 mg could significantly reduce CK levels ($p<0.05$). Furthermore, there was no significant decrease in serum MDA levels in the placebo group or the curcumin group ($p>0.05$). It can be concluded that the administration of curcumin after 24 hours after high-intensity weight training was able to reduce serum CK levels without a decrease in MDA serum levels. Since the decrease in serum CK levels is an essential part of recovery during muscle damage. Therefore, curcumin is recommended to be taken after 24 hours after exercise to speed up recovery.
Keywords: Curcumin; creatine kinase; malondialdehyde; muscle damage; free radicals; physical training

Resumen. Este estudio tiene como objetivo analizar el efecto de la curcumina sobre los niveles séricos de creatina quinasa (CK) y malondialdehído (MDA) después de 24 horas de ejercicio físico de alta intensidad. Este estudio experimental utilizó un diseño de grupo de control previo y posterior. En este estudio participaron un total de 18 hombres sanos con una edad promedio de 23 años. Los sujetos fueron seleccionados utilizando una técnica de muestreo aleatorio y luego los sujetos fueron divididos en 2 grupos, a saber, el grupo que recibió un placebo y el grupo que recibió curcumina en una dosis de 400 mg. El primer día, todos los sujetos tomaron datos sobre las características de los sujetos de investigación, y luego los sujetos realizaron el ejercicio físico de alta intensidad en forma de ejercicios de escuadra y prensa de piernas con una intensidad de 80-90% de la capacidad máxima. En el segundo día, después de 24 horas, todos los sujetos tomaron muestras de datos previos a la prueba para medir los niveles séricos de CK y MDA, luego se administró la intervención en función de sus respectivos grupos. El tercer día, después de 24 horas, todos los sujetos tomaron muestras de sangre posteriores a la prueba para medir los niveles séricos de CK y MDA. Las muestras de sangre se analizaron en el laboratorio mediante el método ELISA. Los resultados de este estudio informaron que el grupo que recibió un placebo no redujo significativamente los niveles séricos de CK, mientras que el grupo con curcumina en una dosis de 400 mg pudo reducir significativamente los niveles de CK ($p<0.05$). Además, no hubo una disminución significativa en los niveles séricos de MDA en el grupo de placebo o el grupo de curcumina ($p>0.05$). Se puede concluir que la administración de curcumina después de 24 horas del entrenamiento con pesas de alta intensidad fue capaz de reducir los niveles séricos de CK sin una disminución de los niveles séricos de MDA. Dado que la disminución en suero, el nivel de CK es una parte esencial de la recuperación durante el daño muscular. Por lo tanto, se recomienda tomar curcumina después de 24 horas después del ejercicio para acelerar la recuperación.
Palabras clave: Curcumina; creatina quinasa; malondialdehído; daño muscular; radicales libres; entrenamiento físico

Fecha recepción: 31-10-22. Fecha de aceptación: 16-03-23
Nining Widyah Kusnanik
niningwidyah@unesa.ac.id

Introduction

High-intensity physical exercise such as resistance training, especially with eccentric movements, will cause metabolic stress in the form of energy deficiency and muscle damage (Harty et al. 2019). Muscle damage caused by exercise or Exercise-Induced Muscle Damage (EIMD) is characterized by the onset of muscle pain (Casanova et al. 2018). Thus, the resulting muscle soreness can limit performance after a training session (Owens et al. 2019; Viribay et al. 2020; Xin and Eshaghi 2021; Romero-Parra et al. 2021). Several studies explain that pain occurs due to an uncontrolled inflammatory process during exercise-induced muscle damage (Dupuy et al. 2018). Creatine Kinase (CK) is believed to be a biomarker of muscle damage (Esteves-Lima et al. 2020; Oosthuyse and Bosch 2017).

In addition, physical exercise triggers a 10-fold increase in oxygen consumption for rest (Powers, Radak, and Ji 2016). As a result of metabolic processes, cells will produce free radicals or reactive oxygen species (ROS). Free radicals are characterized by increased levels of malondialdehyde (MDA) (Morales and Munné-Bosch 2019). In addition to aerobic exercise which generally triggers free radicals, an anaerobic exercise involving less oxygen circulation can also cause oxidative stress that triggers the increased production of free radicals through the xanthine oxidase and NADPH oxidase pathways, ischemia-reperfusion, increased purine oxidation, damage to iron-containing proteins impaired Ca2+ homeostasis, and catecholamines autoxidation (N Ayubi et al. 2022). Increased production of free radicals will also cause muscle damage (Morales and Munné-Bosch 2019).

In most cases, inflammation peaks 24 hours after a training session (Chang et al. 2021; Muljadi et al. 2021; Hung 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) (Kyriakidou et al. 2021). Post-exercise NSAID administration is a wrong alternative in pain management, this is because NSAIDs have a disturbing effect on muscle growth responses that have an impact on muscle hypertrophy and strength. As a result, giving NSAIDs will actually negate the results of the exercise performed (Duman et al. 2021). In addition, the increase in free radicals can cause degenerative diseases such as cancer, diabetes mellitus, and atherosclerosis which are the causes of heart disease (Singh, Devi, and Gollen 2015; Maritim, Sanders, and Watkins 2003). It is estimated that as many as 17 million people worldwide die each year from degenerative diseases. Several countries in the world, such as Brazil, Canada, China, India, Nigeria, Pakistan, Russia, United Kingdom, and Tanzania, have an incidence of death from degenerative diseases reaching 80% (Powers, Radak, and Ji 2016).

Alternative solutions need to be found to solve this problem. One of the natural ingredients that are easily found is curcumin. Curcumin is well known for its anti-inflammatory properties. Curcumin is able to inhibit inflammation through modulation of Nuclear Factor-Kappa B (NF-B) signaling and blockade of pro-inflammatory cytokine signals by activating protein responses in the muscle thereby accelerating recovery from exercise-induced muscle damage (Gallego-Selles et al. 2022). In addition, curcumin is also known for its anti-oxidants, on the other hand, curcumin plays a role in suppressing pro-oxidant activity by increasing heme oxygenase 1 (HO-1) and glutathione peroxidase (GPx) genes (Iova et al. 2021). Curcumin has been used extensively to increase endurance and VO2Max (Salehi et al. 2021). Curcumin has also been used in the world of medicine and health to accelerate wound healing (Alqahtani et al. 2020). Until now, curcumin has not been reported to reduce CK as a biomarker of muscle damage, and MDA as a biomarker of oxidative stress after 24 hours of high-intensity physical exercise.

This study aimed to analyze the effect of curcumin on serum levels of CK and MDA after 24 hours of high-intensity physical exercise.

Methods

Study Design

This experimental research used a pre and post-control group design. The research subjects were selected using random sampling technique with lottery paper to divide the subjects into 2 groups, namely the control group that received placebo and the treatment group that received curcumin.

Subjects

A total of 18 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 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 the study. The dropout criteria in this study were consuming coffee, consuming foods containing turmeric, and consuming drinks containing vitamin C. The research subjects received instructions about the research procedure and gave written consent.

Subjects Calculation

The calculation of the subject size in this study uses the following subject size formula (Higgins & Kleinbaum, 1985):

$$n = \frac{1}{1-f} \text{ x } \frac{2(Z\alpha + Z\beta)^2 . SD^2}{(Xc - Xt)^2}$$

$$n = \frac{1}{1-0{,}1} \text{ x } \frac{2(1{,}96 + 1{,}28)^2 . 1{,}21^2}{(4{,}81 - 3{,}04)^2}$$

$$n = 1{,}11 \text{ x } \frac{30{,}74}{3{,}13}$$

n = 9 People

Based on the results of the calculations above, it shows that the size of the research subjects for each group is 9 people, so that the total number of subjects is 19 people for 2 groups.

Procedure

1. Initially, we prepared administration such as ethical feasibility permits, research 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 (Novadri Ayubi et al. 2023).
4. 1 day before the study was conducted, the subjects were informed to get enough rest and not eat breakfast in the morning to ensure that their bodies were in the same condition during exercise.
5. On the first day, in the morning to be precise, all subjects collected data on the characteristics of the research subjects, then the subjects performed high-intensity

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physical exercises in the form of squad exercises and leg presses with an intensity of 80-90% of their maximum ability. Prior to the exercise the subject was given an energy drink.

6. On the second day, after 24 hours of doing the exercises, all subjects were taken pretest blood samples to measure serum CK and MDA levels, then given intervention based on their respective groups.

7. On the third day, after 24 hours of curcumin intervention, all subjects took post-test blood samples to measure serum CK and MDA levels.

8. Blood samples were analyzed in the laboratory using the ELISA method with the catalog number Human CK ELISA kit E2090Hu and Human MDA ELISA kit E1371Hu.

9. In The final stage of this research, the data is analyzed and the report is prepared as the responsibility of the researcher.

CONSORT flowchart

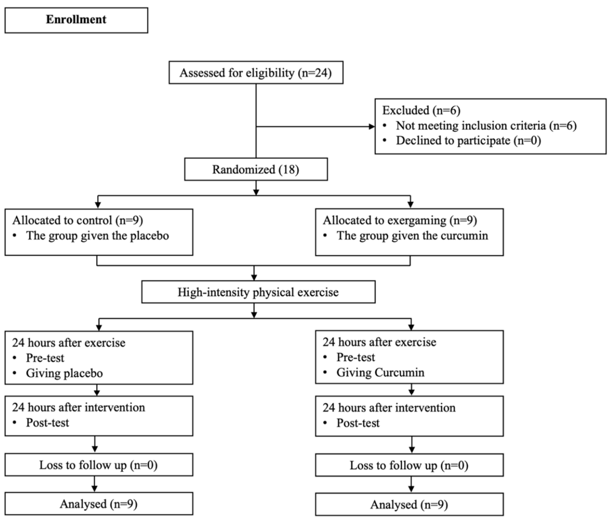

Figure 1. The CONSORT flowchart

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, but if the data were not normally distributed, the difference was performed using the Wilcoxon signed-rank test.

Ethics

This research has been approved by the ethics committee of Universitas Airlangga with ethics number 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	n	x̄±SD	Shapiro-Wilk	p-value
Age	Placebo	9	23.11±1.69	0.001	0.944
	Curcumin	9	23.22±1.78	0.946	
Height	Placebo	9	166.83±4.51	0.544	0.501
	Curcumin	9	168.22±4.03	0.222	
Weight	Placebo	9	67.27±7.30	0.798	0.127
	Curcumin	9	60.83±9.52	0.702	
BMI	Placebo	9	23.80±3.01	0.905	0.079
	Curcumin	9	21.15±.2.95	0.414	
Body temperature	Placebo	9	36.57±0.28	0.024	0.634
	Curcumin	9	36.57±0.41	0.684	
Systolic	Placebo	9	122.88±6.05	0.843	0.314
	Curcumin	9	119.11±9.06	0.976	
Diastolic	Placebo	9	74.77±3.86	0.715	0.392
	Curcumin	9	71.11±11.90	0.497	
Pulse	Placebo	9	85.11±5.60	0.048	0.260
	Curcumin	9	88.44±6.55	0.373	

In the t-test there is no significant difference in the characteristics of each group (p≥0.05).

Curcumin lowers serum CK levels

Based on the normality test in Table 2, the data on serum CK levels were normally distributed (p>0.05).

Table 2.
Normality test results for CK serum levels

Data	Group	Shapiro-Wilk	
		n	P
CK (*Pre-test*)	Placebo	9	0.173
	Curcumin	9	0.788
CK (*Post-test*)	Placebo	9	0.664
	Curcumin	9	0.144

The results of the analysis of CK exclamation levels between pre-test and post-test administration of curcumin in each group are presented in Figure 2.

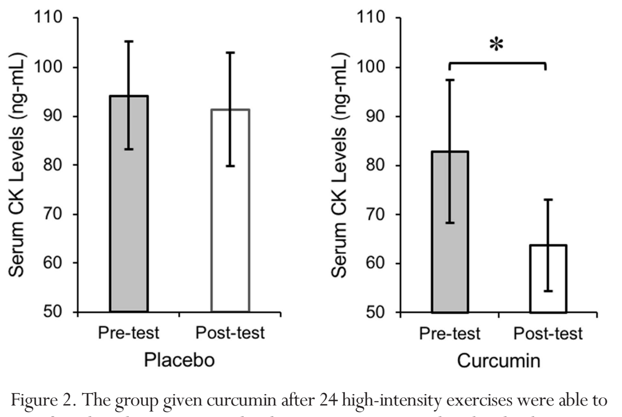

Figure 2. The group given curcumin after 24 high-intensity exercises were able to significantly reduce serum CK levels (*p<0.05) compared to the placebo group. Data are presented as Mean Std Error. P-value was obtained by using paired t-test to compare the pre-test and post-test of each group.

Curcumin does not increase serum MDA levels

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

The results of the analysis of serum MDA levels between the pre-test and post-test of curcumin administration after 24 hours of high-intensity physical exercise in each group are presented in Figure 3.

Table 4.
Normality test results for MDA serum levels

Data	Group	Shapiro-Wilk	
		n	P
MDA (*Pre-test*)	Placobo	9	0,293
	Curcumin	9	0.376
MDA (*Post-test*)	Placobo	9	0.190
	Curcumin	9	0.077

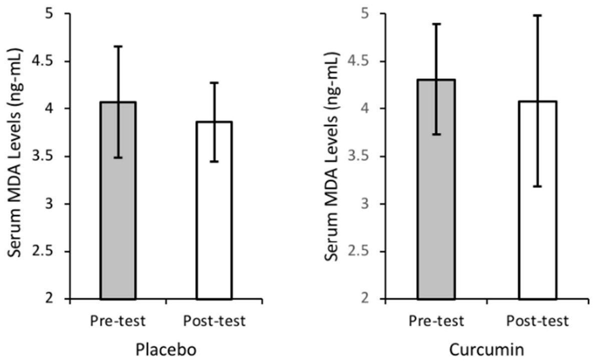

Figure 3. Intervention after 24 hours of high-intensity physical exercise had no significant effect (p>0.05) on serum MDA levels in each group. Data are presented as Mean Std Error. P-value is obtained by using the Pairet t-test to compare the pre-test and post-test of each group.

Discussion

The purpose of this study was to determine the effect of curcumin on serum levels of CK and MDA after 24 hours of high-intensity physical exercise. The results of our study showed that the group given a placebo did not significantly reduce serum CK levels after 24 hours of high-intensity physical exercise, while the group with curcumin at a dose of 400 mg could significantly reduce CK levels after 24 hours of high-intensity physical exercise. Our research findings answer and confirm a literature study reported that curcumin has a positive effect on the inflammatory response and muscle damage (Dias et al. 2021; Novadri Ayubi et al. 2023). Although there was a decrease in serum CK levels which is a marker of muscle damage, we did not find a significant decrease in serum MDA levels in the placebo group or the curcumin group. We expected the finding that there was no decrease in MDA serum levels because it was not certain that the administration of curcumin 24 hours after physical exercise with pain intensity was able to reduce MDA serum levels. We support the theory that after 24 hours of high-intensity physical exercise there is a peak in the inflammatory response and muscle damage (Askenase and Sansing 2016). Our previous study also reported that omega-3 administration was able to reduce serum TNF-a levels and pain intensity after 24 hours of weight training (Novadri Ayubi et al. 2023). In our study, it appears that curcumin causes different responses in serum CK levels and serum MDA levels. One study reported that MDA levels increased 5 minutes after the end of a training session (Bouzid et al. 2015). Given that curcumin also has antioxidant activity, from this study we support that curcumin may be more effectively taken 5 minutes after the end of a training session so as to reduce serum MDA levels.

In summary, the new findings in this study reported that curcumin at a dose of 400 mg/day was able to reduce serum CK levels without decreasing serum MDA levels after 24 hours of high-intensity physical exercise. The weakness of our research may be the limited number of samples. In future research, it is hoped to analyze more samples and analyze other biomarkers of oxidative stress such as protein carbonyl (PC).

Conclusion

Administration of curcumin after 24 hours of high-intensity weight training was able to reduce serum CK levels without a decrease in MDA serum levels. Since the decrease in serum CK levels is an essential part of recovery during muscle damage. Therefore, curcumin is highly recommended to be consumed after 24 hours after exercise to speed up recovery.

Acknowledgements

The authors would like to thanks to Rector Universitas Negeri Surabaya and PNBP Unesa 2022 for supporting research grant.

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