The effect of coffee consumption on the tnf-α level after submaximal exercise

El efecto del consumo de café en los niveles de tnf-α tras el ejercicio submáximo

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Abstract

Introduction: Exercise has become a lifestyle choice for many individuals seeking to maintain their health and reduce the risk of various diseases. However, exercising at a certain intensity requires significant energy expenditure and can lead to micro-damage in the muscles, which can be detected through several biomarkers, including levels of Tumor Necrosis Factor Alpha (TNF-α). This condition may adversely affect physical performance, leading some individuals to take supplements as a preventive measure. Additionally, post-workout caffeine consumption has gained popularity, particularly in the form of caffeinated drinks, in an effort to enhance physical fitness and productivity. Nevertheless, there is limited comprehensive research on the mechanisms by which caffeine affects post-exercise recovery.
Objective: This study aims to investigate changes in TNF-α levels following coffee consumption and submaximal exercise.
Methodology: This quantitative quasi-experimental study employed a single-blind design. Twenty adult men (ages 19–29) were divided into a control (CON) group and an experimental (EXP) group. The EXP group consumed Robusta coffee for five days before the exercise intervention, while the CON group received a placebo on the same days. All participants underwent submaximal exercise using the Young Men's Christian Association (YMCA) step test method. Two hours after this intervention, blood samples were collected for TNF-α measurement.
Results: TNF-α levels were lower in the intervention group (88.17 n/L) than in the control group (121.44 n/L), although the difference was not statistically significant.
Conclusions: Coffee consumption may help reduce TNF-α and regulate inflammation after submaximal exercise.

Keywords

TNF-α; Robusta Coffee; Submaximal Exercise; anti-inflammatory.

Resumen

Introducción: El ejercicio se ha convertido en una opción de estilo de vida para muchos individuos que buscan mantener su salud y reducir el riesgo de diversas enfermedades. Sin embargo, hacer ejercicio a cierta intensidad requiere un gasto energético importante y puede provocar microdaños en los músculos, que pueden detectarse a través de varios biomarcadores, entre ellos los niveles de Factor de Necrosis Tumoral Alfa (TNF-α). Esta condición puede afectar negativamente al rendimiento físico, lo que lleva a algunas personas a tomar suplementos como medida preventiva. Además, el consumo de cafeína después del entrenamiento ha ganado popularidad, sobre todo en forma de bebidas con cafeína, en un esfuerzo por mejorar la forma física y la productividad. Sin embargo, la investigación exhaustiva sobre los mecanismos por los que la cafeína afecta a la recuperación tras el ejercicio es limitada.
Objetivo: Este estudio pretende investigar los cambios en los niveles del Factor de Necrosis Tumoral Alfa (TNF-α) tras el consumo de café y el ejercicio submáximo.
Metodología: Este estudio cuantitativo cuasi-experimental empleó un diseño simple ciego. Veinte hombres adultos (19-29 años) se dividieron en un grupo de control (CON) y un grupo experimental (EXP). El grupo EXP consumió café Robusta durante cinco días antes de la intervención de ejercicio, mientras que el grupo CON recibió un placebo los mismos días. Todos los participantes se sometieron a ejercicio submáximo utilizando el método de prueba de pasos de la Asociación Cristiana de Jóvenes (YMCA). Dos horas después de esta intervención, se recogieron muestras de sangre para medir el TNF-α.
Resultados: Los niveles de TNF-α fueron más bajos en el grupo de intervención (88,17 n/L) que en el grupo control (121,44 n/L), aunque la diferencia no fue estadísticamente significativa.
Conclusiones: El consumo de café puede ayudar a reducir el TNF-α y regular la inflamación después del ejercicio submáximo.

Palabras clave

TNF-α; café Robusta; ejercicio submáximo; antiinflamatorio.

Introduction

Physical exercise has recently become a necessity and a lifestyle for most people, significantly increasing after the COVID-19 pandemic several years ago. An appropriate amount of physical exercise can enhance health and lower mortality rates by decreasing the risk of chronic diseases such as heart disease, hypertension, and diabetes mellitus (Posadzki et al., 2020; Usmani et al., 2023). On the other hand, submaximal exercise can lead to inflammation due to micro-tears in the muscles, which are characterized by structural changes (Stožer et al., 2020).

Inflammation is the body's physical defense response to infection or irritation caused by physical trauma or chemical reactions (Favier & Nikovics, 2023; Park et al., 2022). Various biomarkers involved in the inflammatory process can be evaluated in the bloodstream, including acute phase proteins such as pro-inflammatory cytokines like Tumor Necrosis Factor Alpha (TNF-α), interleukins 1β, 6, 8, 10, and 12 (Menzel et al., 2021; Stožer et al., 2020). TNF-α has several functions, including enhancing and expediting pro-thrombotic activity, modulating macrophage responses, and stimulating growth factors and other cytokines that play a role in muscle remodeling following damaging exercise. (Stožer et al., 2020; Supit et al., 2015).

This condition can indirectly lead to a decrease in physical performance, prompting athletes and sports enthusiasts to widely adopt supplements such as caffeine as a preventive measure (Jiménez et al., 2021; O'Connor et al., 2022; Peeling et al., 2018). The consumption of caffeinated drinks, has become a common practice among individuals seeking to enhance their physical fitness and productivity (Fischer et al., 2019; Ungvari & Kunutsor, 2024). However, it is important to recognize that the effects of caffeine can vary significantly among individuals, influenced by factors such as dosage, physiological characteristics, and genetic predispositions (Loureiro et al., 2021). Previous studies have reported inconsistent effects of caffeine on performance, leaving the overall impact still unclear (Filip et al., 2020; Loureiro et al., 2021; Naulleau et al., 2022).

Robusta coffee, which is grown in the Indonesian city of Dampit, contains several active compounds, including caffeine, chlorogenic acid (CGA), trigonelline, diterpenes, and melanoids (Makiso et al., 2024). These active ingredients can influence adenosine receptor antagonism, which affects the role of methylxanthine in mobilizing intercellular calcium and stimulating the accumulation of cyclic adenosine monophosphate (cAMP). This process subsequently leads to the synthesis and release of hormones such as catecholamines within the central nervous system (Barcelos et al., 2020; Fiani et al., 2021; Ribeiro & Sebastião, 2010). Increased levels of cAMP have been shown to reduce TNF-α levels and inhibit the oxidative response of neutrophils (Aronoff et al., 2006; Lin et al., 2005). Consequently, variations in cAMP concentration resulting from caffeine consumption can influence the inflammatory state (Rodas et al., 2020; Tavares et al., 2020). However, there have been few studies that analyze in detail the effects of caffeine from coffee consumption on post-exercise conditions. Therefore, this study aims to investigate changes in TNF-α levels following coffee consumption and submaximal exercise.

Method

Research Design

This study is a quantitative quasi-experimental investigation employing a single-blind experimental design. It has been approved by the Ethics Commission of the Faculty of Medicine, Universitas Airlangga, under approval number 67/EC/KEPK/FKUA/2023. The sample size calculation is based on the formula established by Higgins and Kleinbaum (1985) and previous research conducted by Rodas (Rodas et al., 2020). Participant were recruited through social media networks. A total of 20 male participants, aged 19–29 years, who were physically active and met the inclusion criteria were enrolled in the study. The inclusion criteria required participants to have a normal body mass index (BMI), normal oxygen saturation levels, and stable blood pressure and heart rate. Exclusion criteria included a history of heart or lung disease, chronic gastritis, or regular medication use. All participants provided written informed consent before the study. They were then divided into two groups: the experimental group (EXP), which received Robusta coffee sourced from Dampit, Malang City, Indonesia (n=10), and the control group

(CON), which received a placebo consisting of coffee-flavored water (n=10). Blood samples were collected from each participant following the treatment period for both groups.

Coffee Consumption

Before performing submaximal exercise, the experimental group (EXP) underwent a five days conditioning phase, during which they consumed a minimum dose of Robusta coffee. This process aimed to provide a protective effect and ensure steady-state coffee levels in the body (Grgic et al., 2018), The steady-state concentration was calculated using the following formulation:

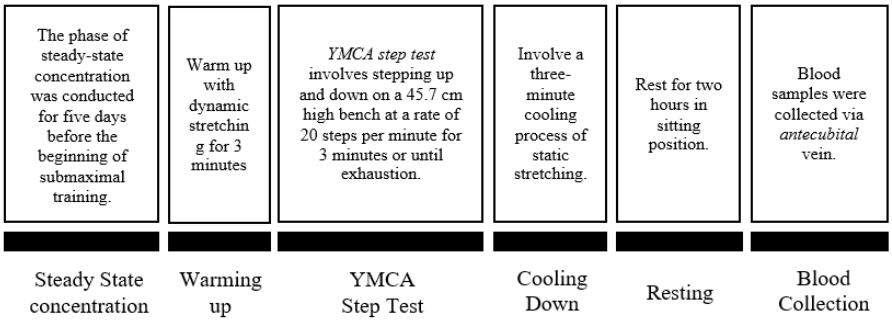
steady state concentration	= (dose per-interval x bioavailability x t)
	(clearance + bioavailability x t)
300	= (y x 0,95 x 720)
	(0,8 + 0,95 x 720)
y	= 293,45 kaf (2% grams of coffee)
y	= 14,6 grams of coffe/intake

To achieve elevated concentrations of caffeine and trigonelline in Robusta coffee beans, a slow roasting process. The beans are subsequently milled to a texture that is neither too coarse nor too fine. To provide a protective effect on the coffee, a steady-state concentration phase was established by consuming 14.6 grams of Robusta coffee. This coffee was brewed with 100 ml of hot water at a temperature of 90ºC and filtered using Kova coffee filter paper V60. Participants consumed the brewed coffee twice daily at 7 am and 7 pm for five consecutive days, ensuring regular caffeine intake at 12-hour intervals.

Submaximal Exercise Protocol

Throughout the submaximal training phase, all participants began with a 3-minute dynamic warm-up, incorporating a series of dynamic stretching techniques in accordance with the YMCA step test protocol. Following the warm-up, both the intervention (EXP) and control (CON) groups performed the submaximal YMCA step test. The test involved ascending and descending a 45.7 cm (18-inch) high bench at a standardized cadence of 20 steps per minute for a total duration of 3 minutes or until the participant reached a state of fatigue. To ensure consistency, each participant used a metronome set at 120 beats per minute to maintain the prescribed stepping rhythm (Howatson & Van Someren, 2008). Figure 1 illustrates the research process.

Figure 1 Illustrates the research process.



Rate Analysis of TNF-α

Blood samples were obtained from the antecubital vein of all participants exactly two hours after completing the YMCA step test to assess the acute inflammatory response to exercise. This time frame was selected based on prior literature indicating that TNF-α and IL-1 levels peak within a few hours due to cytokine-mediated inflammatory processes (Laake *et al*., 2014).

A total volume of 5.5 mL of blood was drawn from each participant using a sterile syringe and transferred into EDTA-coated tubes to prevent coagulation. TNF-α concentrations were quantified using the Human Enzyme-Linked Immunosorbent Assay (ELISA) method, a highly sensitive and specific technique for detecting cytokine levels in biological samples.

Data Analysis

To evaluate the effects of coffee consumption on exercise-induced inflammation, TNF-α levels were compared between the experimental and control groups using appropriate statistical analyses. Data were tested for normality and analyzed using independent t-tests, depending on the distribution of the variables. The significance level was set at $p < 0.05$.

Results

The findings of this study indicate that the characteristics of the respondents, including age, height, weight, and BMI, follow a normal distribution, as presented in Table 1. The Shapiro-Wilk test results in Table 1 confirm that the data follow a normal distribution ($p > 0.05$).

Table 1. Characteristics of Respondent

Variable	EXP	CON	P value
	Mean ± SD	Mean ± SD	
Age (years)	22.40 ± 2.87	21.7 ± 2.66	0.58
Height (cm)	1.69 ± 0.61	1.68 ± 0.05	0.85
Weight (kg)	61.18 ± 7.80	62.67 ± 5.95	0.77
BMI (kg/m^2)	21.12 ± 2.26	21.75 ± 1.83	0.50

Description: Data are presented with mean ± SD; EXP (experiment group); CON (control group; BMI (body mass index).

The comparative results of TNF-α levels between the intervention group and the control group following submaximal exercise are presented in Table 2. The TNF-α level in the intervention group was 88.17 n/L, while in the control group, it was 121.44 n/L. The Mann-Whitney test was utilized to assess the differences in this investigation, and the results did not reveal a statistically significant difference ($p>0.05$).

Table 2. Concentration Rate of TNF-α

Variable	EXP	CON	P value
	Mean ± SD	Mean ± SD	
TNF-α	88.17 ± 17.23	121.44 ± 131.85	0.45

Description: Data are presented with mean ± SD; EXP (experiment group); CON (control group); TNF-α (Tumor Necrosis Factor Alfa). P-value are obtained by independent t-test.

Discussion

TNF-α is a pro-inflammatory cytokine that plays a crucial role in the body's inflammatory response. Elevated inflammation levels can further amplify TNF-α activity, contributing to the regulation of molecular and cellular pathways involved in tissue repair. This process is typically accompanied by the dilation of venules and arterioles, increased vascular permeability, and enhanced blood flow, all of which facilitate leukocyte infiltration into the affected tissue. Additionally, inflammatory cells release soluble mediators, including various pro-inflammatory cytokines such as TNF-α (Barcelos *et al.*, 2020).

In this study, participants in the intervention group who consumed Robusta coffee exhibited a lower TNF-α concentration (88.17 n/L) compared to the control group receiving a placebo (121.44 n/L). Although this finding suggests a potential anti-inflammatory effect of Robusta coffee, the difference

between the two groups was not statistically significant. These differences in TNF-α levels align with previous research that suggests a potential link between caffeine and TNF-α reduction (Barcelos et al., 2020; Rodas et al., 2020). The decrease in TNF-α levels in the EXP group may be attributed to various molecular mechanisms. Previous studies have shown that polyphenol extracts from Robusta coffee beans can effectively inhibit TNF-α production in neutrophil cells stimulated with lipopolysaccharide (LPS). The most significant reduction was observed at a 12.5% concentration of polyphenol extract, suggesting a potential anti-inflammatory effect through TNF-α modulation (Ermawati et al., 2018). On the other hand, caffeine in coffee has been scientifically demonstrated to suppress the synthesis of specific inflammatory molecules, such as TNF-α, by enhancing cAMP production.

According to Park et al. (2018), cAMP functions as a second messenger molecule that induces cellular pathways leading to suppression TNF-α in cells. This effect occurs because caffeine inhibits phosphodiesterase (PDE) enzymes, which are responsible for cAMP degradation. By preventing cAMP breakdown, caffeine increases intracellular cAMP levels, thereby amplifying its signaling effects and contributing to its anti-inflammatory properties (Boswell-Smith et al., 2006). In previous research reported that coffee consumption had a positive effect on increasing measured inflammatory parameters. However, substantial changes were observed in participants who consumed more than 200 ml of coffee per day compared to the control group, who did not consume coffee (Zampelas *et al.,* 2004).

In addition, the consumption of coffee has been found to inhibit the nuclear factor-kappa B (NF-κB) pathway, a key regulator of DNA transcription involved in the modulation of cytokine and chemokine expression (Loftfield *et al.,* 2015). This inhibitory effect is partly attributed to compounds like pyrocatechol, which is produced during the roasting process. By suppressing NF-κB activation, these compounds reduce the expression of inflammation-related transcription factors, ultimately leading to decreased production of pro-inflammatory mediators such as TNF-α (Murata et al., 2023). This suggests that coffee consumption may play a protective role in mitigating inflammation through the modulation of key cellular signaling pathways.

Future research should focus on determining the optimal coffee consumption levels needed to achieve anti-inflammatory effects while considering individual variations in metabolism and sensitivity to caffeine. Moreover, further studies with larger sample sizes and longer intervention periods are necessary to explore the long-term effects of coffee-derived polyphenols and their potential synergistic interactions with other bioactive compounds.

Conclusions

The conclusion of this research indicates that consuming Robusta coffee after submaximal exercise can reduce TNF-α levels. While the intervention group exhibited lower TNF-α concentrations compared to the control group, the difference was not statistically significant. However, existing literature suggests that bioactive compounds in coffee, including polyphenols and caffeine, may contribute to TNF-α modulation through various molecular pathways, such as cAMP signaling and NF-κB inhibition. These mechanisms highlight the potential role of coffee in regulating inflammatory responses.

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