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Profile of F2-Isoprostane Level After 5-Day Administration of Robusta Coffee at a Steady State Dose in Subjects Performing Physical Exercise

Perfil del nivel de F2-isoprostano tras 5 días de administración de café robusta en dosis estables en sujetos que realizan ejercicio físico

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Abstract This study aims to analyze the effect of robusta Dampit coffee on F2-isoprostane levels influenced by ROS due to excessive exercise. This study was an experimental study with a pre- and post-test control group design with coffee administration. The total sample was 18 untrained or sedentary male, divided into two groups: coffee group (COF, n=9) and control/placebo group (PLB, n=9). The COF group was given 2 cups of filtered coffee a day (100 ml/cup) at 12-hour intervals for 5 days. Both groups performed physical exercise with a step test on day 6. Blood samples were collected pre and two hours post exercise. F2-isoprostane concentration was analyzed using the F2-isoprostane biomarker and ELISA to measure the level of lipid peroxidation. Results showed a decrease in F2-isoprostane levels in both COF (pre: 1531.57±278.13 pg/mL; post: 1367.6±230.24 pg/mL; p=0.110) and PLB (pre: 1716.65±501.19 pg/mL; post: 1600.02±500.59 pg/mL; p=0.139) groups with a greater decrease in the COF group. However, this reduction was not significantly different between groups (p=0.734). Although not significantly different, exercising participants tended to have lower F2-isoprostane levels after consuming robusta coffee for five days at a steady state dose. Therefore, further investigation is needed to ascertain the physiological consequences of coffee administration over a longer period of time and its effect on recovery speed.

Keywords: coffee, exercise, lipid peroxidation, and F2-isoprostane

Resumen Este estudio tiene como objetivo analizar el efecto del café robusta Dampit sobre los niveles de F2-isoprostano influenciados por ROS debido al ejercicio excesivo. Este estudio fue un estudio experimental con un diseño de grupo de control pre y post prueba con administración de café. La muestra total fue de 18 varones no entrenados o sedentarios, divididos en dos grupos: grupo café (COF, n=9) y grupo control/placebo (PLB, n=9). El grupo COF recibió 2 tazas de café filtrado al día (100 ml/taza) a intervalos de 12 horas durante 5 días. Ambos grupos realizaron ejercicio físico con una prueba de pasos el día 6. Se recogieron muestras de sangre antes y dos horas después del ejercicio. Se analizó la concentración de F2-isoprostano mediante el biomarcador F2-isoprostano y ELISA para medir el nivel de peroxidación lipídica. Los resultados mostraron una disminución de los niveles de F2-isoprostano en ambos grupos COF (pre: 1531.57±278.13 pg/mL; post: 1367.6±230.24 pg/mL; p=0.110) y PLB (pre: 1716.65±501.19 pg/mL; post: 1600.02±500.59 pg/mL; p=0.139) con una mayor disminución en el grupo COF. Sin embargo, esta reducción no fue significativamente diferente entre los grupos (p=0.734). Aunque no fueron significativamente diferentes, los participantes que hacían ejercicio tendían a tener niveles más bajos de F2-isoprostano después de consumir café robusto durante cinco días a una dosis de estado estacionario. Por lo tanto, es necesario seguir investigando para determinar las consecuencias fisiológicas de la administración de café durante un periodo de tiempo más largo y su efecto en la velocidad de recuperación.

Palabras clave: café, ejercicio, peroxidación lipídica y F2-isoprostano

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Introduction

Exercise or physical training can have both positive and negative effects, depending on the amount and intensity of the activity, especially for untrained people (Jesus et al., 2019; Devi et al., 2023). According to Irwadi et al. (2018), oxidative stress is known to be caused by strenuous activity and intense exercise. Strenuous and excessive exercise will increase reactive oxygen species (ROS) and lead to the development of oxidative stress in untrained individuals (Darbandi et al., 2018). To counteract the excessive increase in ROS and prevent oxidative stress, the body needs endogenous antioxidants and exogenous antioxidants (López et al., 2022). Some exogenous antioxidants that are often used include Vitamin E, Vitamin C, and various herbal plants such as chia seed and coffee (Martini et al., 2016; Amer et al., 2017; Irwadi et al., 2018; Trisnadi et al., 2023)

To determine the level of oxidative stress after heavy physical exercise, it can be analyzed through lipid peroxidation products in the form of F2-isoprostane (Milne, 2017). The increase in the amount of ROS during excessive physical exercise is due to the high intensity of physical exercise that requires increased energy generation and muscle contraction, both of which are sources of ROS production (Gomes et al., 2012; Sakellariou et al., 2014). It is known that during heavy exercise, the body requires 10-15 times more oxygen because there is an increase in metabolism to meet the energy needs of contracting muscles (Sánchez et al., 2008; Kurkcu et al., 2010; Kusnanik et al., 2023). NADPH oxidase and xanthine oxidase, both of which have side products in the form of superoxide, a radical catalyzing the increased oxygen demand that occurs when muscles contract (Kim et al., 2017; Bouviere et al, 2021)

Both Arabica coffee and Robusta coffee are popular varieties of coffee, but Robusta coffee is known to have higher levels of phenols and total antioxidants than Arabica coffee (Hasbullah et al., 2021). The most prevalent

substances found in coffee are polyphenols, which are chlorogenic acids, esters of caffeic acid and quinic acid, which act as hydrogen donors in free radical molecules as part of their antioxidant function (Liang & Kitts, 2014; Tewabe B, 2015). In studies using flavonoids, which also belong to the group of polyphenols in lemons and chia seeds, were found to have meaningful results in antioxidant benefits (Ayubi et al., 2024; Trisnadi et al., 2023; Król et al., 2020). Therefore, coffees that have polyphenol content have an equal chance of meaningful results.

Dampit robusta coffee is one of the robusta coffee varieties originating from East Java, Indonesia. Despite extensive research on coffee's antioxidant qualities, little is known about non-exercisers daily coffee drinking habits. In addition, there isn't a lot of study on daily coffee intake that takes into account steady state concentration calculations that account for half-life, bioavailability, clearance, and coffee consumption intervals (Smy, et al., 2020). Coffee has been demonstrated to significantly reduce oxidative stress in several studies when consumed daily and followed by exercise (Viana et al., 2012; Jówko et al., 2011). However, there hasn't been any research up to this point that examines the role of daily coffee drinking in preventing an increase in oxidative stress in males who aren't used to exercising by taking steady state levels into account.

Material & Method

Study Design

This study was experimental research with randomized pre and post-test control group design. There were 2 groups in this study the control or placebo group (PLB) and the experimental group (COF).

Participants

This study was conducted on 18 men with the following criteria: (i) aged between 20 - 30 years; (ii) having a sedentary lifestyle or never exercised before; (iii) not habitually consuming coffee; (iv) having a normal body mass index (18.5 - 22.9 kg/m^2); (v) willing to sign an informed consent form to be included in this study. Exclusion criteria in this study were subjects who had a history of health problems such as high blood pressure, heart attack, or GERD, as well as subjects who had experienced side effects from drinking coffee such as nausea or dizziness. The ethics committee of the Faculty of Medicine, Universitas Airlangga has approved this study (67/EC/KEPK/FKUA/2023).

Exercise protocol

The YMCA step test was the exercise used in this study. Both groups were instructed to warm up independently for 60 seconds before performing the exercise. The YMCA step up and down bench exercise using a bench with a height of 30 cm was performed for 3 minutes or until fatigue, as well as maintaining the specified heart rate of 120 bpm (Kieu et al., 2020).

Coffee Intervention

To obtain the highest level of polyphenols from the coffee, Dampit Robusta coffee beans are roasted at a low roasting rate (Bobková et al., 2020). After grinding to a medium level (not too fine or coarse), the coffee is prepared using the Vietnamese drip technique with 100 ml of hot water heated to about 90°C to brew the coffee (Muzykiewicz et al., 2021). The COF group consumed coffee twice a day (12-hour interval) for 5 days. To achieve a dose of 300 mg of caffeine in a day, coffee was consumed at a dose of 14.6 grams per serving brewed with 100 ml of water, then allowed to stand for a while to obtain a steady state concentration (Kolahdouzan & Hamadeh, 2017). The formula listed below was used to determine the steady state concentration (Wadhwa RR, 2023):

$$(\text{SSC}) = \frac{(Dose\ per\ interval\ x\ bioavailability\ x\ t)}{(Clearance + bioavailability\ x\ t)}$$

$$300 = \frac{(Y\ x\ 0{,}95\ x\ 720)}{(0{,}8+0{,}95+720)}$$

Y = 293,45 mg kaf (2% grams of coffee)

Y= 14.6 grams of coffee/intake

F2-Isoprostane Analysis

The amount of lipid peroxidation determined by blood serum F2-isoprostane was included in the study results. Blood sampling was performed before and two hours after exercise, Blood serum was taken before exercise to determine F2-isoprostane levels before exercise. Blood was taken 2 hours after exercise referring to studies conducted by Janicka et al., (2010) and Ostrom et al. (2021) where there was an increase in F2-isoprostane levels at the highest 2 hours after exercise (Figure 1). Blood was drawn as much as 5.5 mL through the antecubital vein to analyze the concentration of F2-isoprostane by using isoprostane ELISA BT LAB Bioassay Technology Laboratory Cat. No. E1251Hu.

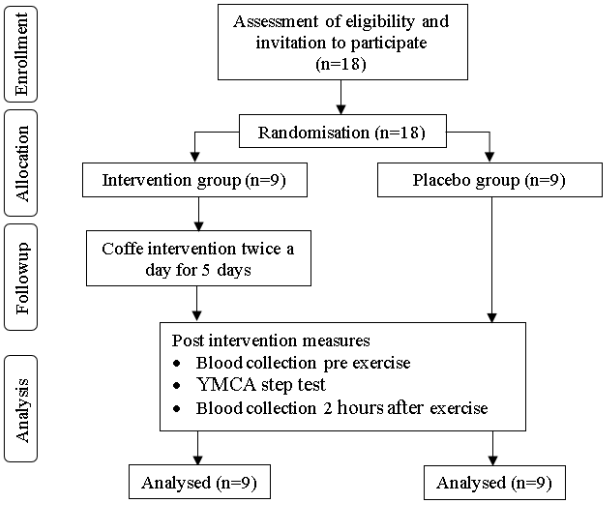

Figure 1. flow chart of the study protocol

Statistical Analysis

The data results were analyzed using Software Statistical Packet for Social Science (SPSS) and analyzed descriptively

to determine the mean and standard deviation of each variable measurement result, then normality and homogeneity tests were carried out. The concentration of F2-isoprostanes was not normally distributed while the data on subject characteristics were known to be normally distributed and homogeneous. The Wilcoxon test was performed to determine if there was a difference in F2-isoprostanes concentration before and after the intervention in the same group. The Mann Whitney test was used to analyze differences between groups with a 95% significance level.f

Result

The results showed that there was no difference in characteristics between the COF group and the PLB group ($p>0.05$) as shown in Table 1.

Table 1.
Baseline Characteristic

Variable	COF Mean±SD	PLB Mean±SD	p-value
Age (year)	22.4 ± 2.87	22.1 ± 2.51	0.807
Height (cm)	170.1 ± 5.61	168.7 ± 7.46	0.642
Weight (Kg)	61.13 ± 7.74	63.74 ± 7.83	0.465
BMI (kg/m^2)	21.12 ± 2.26	22.36 ± 2.27	0.239
SBP (mmHg)	127.67 ± 5.59	129.11 ± 15.47	0.798
DBP (mmHg)	81.33 ± 6.87	77.33 ± 7.38	0.252
SpO2 (%)	98.33 ± 1.32	98.33 ± 0.87	0.649
Blood Glucose (mg/dL)	83.00 ± 15.40	90.67 + 14.93	0.300
Uric Acid (mg/dL)	4.12 ± 0.68	4.57 ± 1.46	0.437

Note: SD – Standard Deviation BMI – Body Mass Index, SBP – Systolic Blood Pressure, DBP – Diastolic Blood Pressure – the independent test was used for statistical analysis

Based on Table 2, both groups experienced a decrease in F2-isoprostane levels after exercise. The COF group decreased from 1531.57±278.13 pg/mL to 1367.60±230.24 pg/mL, while the PLB group decreased from 1716.65±501.19 pg/mL to 1600±500.59 pg/mL. Delta F2-isoprostane in the COF group decreased greater (-163.94 ± 247.53) than the PLB group (-116.97±322.89). However, the delta F2-isoprostane between the COF and PLB groups was not significantly different p=0.734 (Figure 2).

We estimated the effect size based on each group's mean pre-post difference (delta). Effect size was calculated using Cohen's formula, the calculation results showed that the effect size obtained was small at 0.163 ($d < 0.2$). This indicates that coffee consumption has a low effect on changes in F2-isoprostane concentration during physical exercise.

Table 2.
F2-Isoprostane Concentration Changes

F2-Isoprostane (pg/mL)	Pre-test (mean±SD)	Post-test (mean±SD)	Delta (mean±SD)	p-value
PLB	1716.65±501.19	1600.02±500.59	-116.97±322.89	0.139
COF	1531.57±278.13	1367.6±230.24	-163.94±247.53	0.110
p-value	0.508	0.453		

The Wilcoxon that was used for comparing data between pre & post within a group. The mann Whitney u test was used for comparing data between groups.

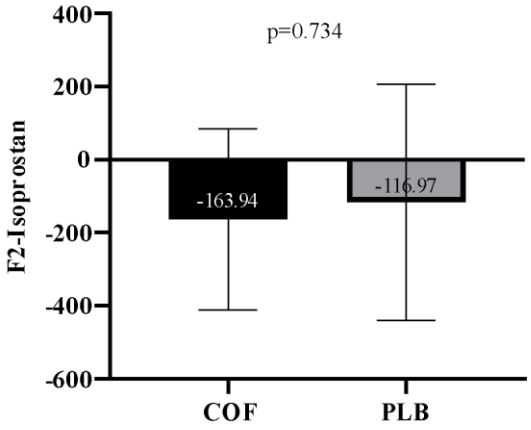

Figure 2. The changing of F2-isoprostane concentration

Discussion

This study aimed to confirm that the ROS formation process and the effects of coffee consumption were solely due to the study intervention and not due to activities performed outside the study. The study subjects were untrained men who did not have the habit of consuming coffee, then the subjects were given the intervention of consuming coffee and doing physical exercise. Each subject has nearly the same distribution of characteristics, but what is concerning is that each subject's average age and BMI level are the same. If either of these factors is too high, free radicals can be said to be produced if there is obesity or an age that is too old (Rodríguez-Hernández et al., 2013; Devi et al., 2023). According to data from WHO 2018, the normal BMI varies from 18.5-24.9 kg/m2. This is significant because the energy production pathway, where ROS are produced, includes by-products in the form of free radicals, can be used to forecast the risk of energy metabolism problems.

In an effort to provide more significant results than earlier studies, this research tests a consumption strategy that takes the steady state of the substances consumed into account. 20 persons were split into two groups, 10 of whom consumed placebo coffee and 10 of whom saw a decline; the delta in the coffee group was larger than the delta in the placebo group. People drink a lot of coffee, and experts recommend it because of its high antioxidant content. This study looked at the effects of recurrent coffee consumption on lipid peroxidation or other signs of oxidative stress in healthy, untrained men. The content's primary focus was on polyphenols, which are the antioxidants in coffee with the greatest components and take the form of chlorogenic acid (Liang & Kitts, 2014).

Research on the relationship between coffee consumption and lipid peroxidation was carried out using many acute and chronic consumption methods. The acute consumption study in healthy subjects conducted by Ochiai et al. (2015) found that there were no major changes in oxidative stress biomarkers, although the biomarkers were different using either MDA or F2-isoprostane. In contrast

to chronic studies in healthy subjects conducted by Corrêa et al. (2012) and Mišík et al. (2010), it was found that coffee consumption had little effect on changes in lipid peroxidation, although there was a tendency to decrease lipid peroxidation in the coffee group. Following coffee consumption, residual chlorogenic acid can also be found in urine and plasma, this occurs because chlorogenic acid is efficiently hydrolyzed by colonic microflora and converted to quinic acid, then decarboxylated to benzoic acid. (Choudhury et al., 1999; Olthof et al., 2003; Gonthier et al., 2003; Socała et al., 2021). In other research, it was found that chlorogenic acid is quickly metabolized in the liver and absorbed through the digestive tract, so the effect is that if the distance between consumption and increased ROS is far apart, the effect will not work as well (Mišík et al., 2010).

This study obtained results of changes that were not significant but the decrease was greater in the coffee group than the control group, it is possible that the intervention time and/or the amount of coffee consumed was not enough to induce significant changes in the F2-isoprostane lipid peroxidation parameters, even after considering the steady state phase of coffee, research that obtained significant effects was obtained in subjects who were accustomed to consuming coffee, and were given a very large amount of coffee, 1200 ml of filtered coffee (Kempf et al., 2010). In another study with trained human subjects, the administration of antioxidants after exercise for a period of 70 days had effective results in reducing the oxidative effect parameters of exercise (López et al., 2022). A study with rat subjects treated with the intervention of consuming 4 cups of coffee a day for 21 days with exercise had significant results. (Viana et al., 2012). Apart from that, it is believed that the consuming process to reach steady state is too quick, falling short of the necessary 5 to 7 days. According to research by Ochiai et al. (2014) and Corrêa et al. (2012), the performance of polyphenols consumed in the form of brewed filter coffee is shown to increase total antioxidant levels in the body but not to prevent increased ROS. However, research Ochiai et al. (2015) stated that polyphenols can play a role in suppressing the lipid peroxidation pathway after consumption or for a brief period of time. In the meantime, research that combines coffee consumption and exercise, in the form of mice that are given exercise and coffee consumption every day, demonstrates that coffee consumption has a considerable impact (Viana et al.,2012). Because the increase in ROS brought on by exercise activates the Nrf2/antioxidant response element pathway, which affects the expression of genes encoding endogenous antioxidant enzymes, these findings point to a process of adaptation of physical exercise to the antioxidant response in the body (Shaposhnikov et al., 2018; Corrêa et al., 2012).

Our research has two drawbacks. It had a limited sample size, compared solely coffee and a placebo, and did not alter the coffee dose. As a supporting element in the oxidative stress process, total antioxidant levels were not assessed in this study; instead, only the products of lipid peroxidation were measured.

Conclusion

F2-isoprostane levels were not significantly impacted by coffee drinking. This occurs when there is a mismatch between the amount of coffee consumed and the amount of physical activity required. However, more investigation into larger doses of coffee consumption is required by examining the mechanism of lipid peroxidation and boosting the body's total antioxidant levels.

In subjects who exercise, consuming robusta coffee for five days at a steady state dose has the potential to lower F2-isoprostane levels. However, more study is required to demonstrate the physiological benefits of coffee consumption by giving it for longer periods of time or at higher doses. In addition, research is required to identify the precise pathways.

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