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The Effect of Green Coffee on Blood Pressure, Liver and Kidney Functions in Obese Model Rats

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Abstract

BACKGROUND: The effect of green coffee (GC) on blood pressure (BP) is still debated, but GC is thought to improve liver and kidney function.

AIM: This study aimed to analyze the effect of the GC intervention on BP, liver, and kidney functions in obese model rats.

METHODS: The research was a pre-clinical trial of pretest-posttest with control group design. Animals were divided into four groups: obese rats (G1), obese rats and GC (G2), obese rats and physical exercise (PE) (G3), and a combination of interventions (PE+GC) (G4). Data analysis used an independent sample t-test and analysis of variance; ($p < 0.05$).

RESULTS: There was a different effect of the GC, PE, and PE+GC intervention on BP (186.50 ± 3.45 vs. 91.33 ± 1.96 p = 0.001*; 189.17 ± 2.93 vs. 119.50 ± 3.73 p = 0.001*; 191.8 3 ± 2.64 vs. 98.83 ± 3.76 p = 0.001*) in obese rats. There was a significant difference in Serum Glutamic Oxaloacetic Transaminase (SGOT) (p=0.001*), Serum Glutamic Pyruvic Transaminase (SGPT) (p = 0.001*), Blood urea nitrogen (BUN) (p = 0.001*), and Creatinine (p = 0.001*) before and after the intervention in the three groups (G2, G3, and G4). SGOT, SGPT, and Creatinine levels decreased significantly after PE, GC, and PE+GC intervention. On the other hand, BUN levels decreased significantly after GC and its combination intervention. Meanwhile, in the control group and the intervention of PE, it increased significantly.

CONCLUSIONS: GC is more effective in lowering BP without causing impaired liver and kidney function in obese rats.

Introduction

The prevalence of coffee drinkers is increasing worldwide: Africa, Europe, America, and Asia [1]. More than 89% of the world's adult population consumes coffee [2]. Finland and Norway are the highest coffee-consuming countries globally, reaching 9.6 and 7.2 kg per capita per year [3]. The US's average caffeine consumption of coffee is 2-3 cups of coffee a day or the equivalent of 180–190 mg of caffeine [1]. Meanwhile, coffee consumption in Indonesia increases by 7.5% annually [4].

Epidemiological data show that coffee is one of the most consumed beverages globally as an energy drink, functional food, supplement, and medicine [5], [6], [7]. More than 80% of the world's population consumes herbal medicines or food supplements to improve their health; however, improper consumption can affect impaired liver and kidney function [8]. Green coffee (GC) has long been reported to be used as a health beverage [9]. Research has reported the benefits of GC as a beverage that positively affects health, such as weight loss, lowering the risk, or inhibiting the development of chronic diseases, including cancer, metabolic syndrome, and hypertension [10]. GC also has benefits for controlling and preventing metabolic syndrome, including hypertension and obesity [9], [11].

Obesity is a critical health issue that contributes to various diseases that can be life-threatening [12]. Obesity is comorbid for some chronic diseases such as Type 2 diabetes, dyslipidemia, respiratory disorders, and hypertension [12], [13]. Obesity is positively related to high blood pressure (BP), and decreased BP is associated with weight loss [14], [15]. Epidemiological studies have shown that body mass index (BMI) and waist circumference are closely related to the incidence of hypertension [14], BMI has a positive correlation with BP [16].

The etiology of hypertension is varied, consisting of genetics, unhealthy lifestyles that trigger overweight, obesity, blood sugar disorders, and many other factors [15]. Hypertension is a lifelong disease that can increase the risk of death due to complications of heart and blood vessel disease. Therefore, it is necessary to control BP by consuming anti-hypertensive

drugs and lifestyle modifications such as exercise and consuming healthy foods or drinks that have anti-hypertensive effects [17].

Coffee is one of the popular drinks consumed for its health effects [18]. The phytochemical content of various types of coffee, such as GC (unroasted), Arabica, and Robusta coffee (roasted), is different [18]. Coffee contains anti-inflammatory, anticancer, antifibrotic, and antioxidant [18]. Robusta coffee contains twice as much caffeine as Arabica coffee (1.7–4.0 and 0.8–1.4% caffeine) [4]. GC contains a number of chemical compounds such as caffeine, antioxidants, minerals, carbohydrates, protein, trigonelline, chlorogenic acid (CGA), glycosides, and volatile components [19]. The roasting process affects the active phytochemical content of coffee, reduces caffeine and CGA levels; therefore, the CGA content in GC is higher than roasted coffee (Arabica and Robusta) [20], [21].

GC has been reported to function for BP regulation and has anti-hypertensive activity [5]. The effect of GC consumption on BP is still a debate among scientists [5]. Empirical evidence shows that regular consumption of GC does not increase the risk of hypertension [5]. The antioxidant content of the GC extract is reported as a hypotensive effect in rats [10]. CGA in GC is higher than Arabica and Robusta coffee, causing the hypotensive effect of GC [22]. The CGA is a potent antioxidant that plays a role in regulating BP, controlling blood, including blood sugar [23]. Empirical evidence shows that GC extract has an antihypertensive effect in rats and humans with spontaneous hypertension [5].

GC contains various active phytochemicals that are thought to affect kidney health, including methylxanthines, dietary fiber, kahweol, trigonelline, cafestol, and diterpenes [9]. Methylxanthines is one of the caffeine that affects BP, and it is reported that the caffeine content varies in each type of coffee. Analysis of 14 related research on coffee shows that the caffeine content in every 250 ml is 13–73 mg. [24]. The highest levels of cafestol and kahweol were found in French and Turkish coffee, around 6.5–11.9 mg per cup; on the other hand, the lowest content was in filter coffee of 0.1-0.5 mg per cup [24].

There are indications that GC is protective against various organs such as cells, kidneys, and liver [25]. A research result states that GC antioxidants have a renoprotective effect in patients with nephrotoxicity [25]. Aforesaid diterpenes are one type of antioxidant that is predicted to have a protective effect on the liver [26]. The higher polyphenol content in GC increases the popularity of GC consumption among the public [27]. In addition, the antioxidant content in Robusta coffee is higher than Arabica coffee [27]. This study analyzed the effect of GC powder, physical training, and its combination (GC and physical training) on BP, liver, and kidney function. They were assessed by measuring the levels of Serum Glutamic Oxaloacetic Transaminase (SGOT), Serum Glutamic Pyruvic Transaminase (SGPT), Blood urea nitrogen (BUN), and Creatinine in obese rats.

Methods

Study design and animals

This type of research is experimental with pretest-posttest design with control group design. Subject inclusion criteria were white rats, male, Wistar strain, 2–3 months old, and healthy. Exclusion criteria: there are anatomical abnormalities. The total number of rats was 24, divided into four groups, and each group consisted of 6 rats. Group 1 (G1) was the group that was induced obesity without intervention (as the control group); Group 2 (G2) was a group of obese rats with PE intervention (as a positive control); Group 3 (G3) a group of obese rats with GC intervention; and Group 4 (G4) was a group of obese rats with a combination intervention (PE and GC).

Intervention

Rats were made obese by feeding a high-fat diet until the Lee index reached more than 300 g/cm and approximately 4 weeks. Treatment in this study consisted of GC and physical exercise (PE). The type of GC was a finely ground GC with a dose of 400 mg/kg BW or equivalent to 7.2 mg/200 g BW/day. This dose calculation is based on the conversion of the human dose to the experimental animal dose using a comparison of the body surface area of the experimental animal following the dose calculation conversion table refer to the conversion table of Laurence and Bacharach, 1964). The dose of coffee consumption in humans 70 kg is 400 mg/kg BW converted to rats weighing 200 g. The dose was 400 × 0.018 (conversion factor according to the table Laurence and Bacharach, 1964) [28] = 7.2 mg/200 g BW/day. GC was brewed by boiling water, allowed to cool (around 10–15 min), then given to rats by infusion. GC was given every day, once a day, every morning (between 08.00 and 09.00 a.m.) for 4 weeks. PE given is swimming, 30 min/day, 3 times a week, for 4 weeks.

BP measurement and blood analysis

The BP measured was systolic BP using a sphygmomanometer, measured twice before (pretest data) and after the intervention (posttest data). BP measurements for pretest and posttest data were carried out 2 times, then divided by 2, to obtain the mean value. Blood samples were taken through the orbital plexus, as much as 1–2 cc. Blood sampling was carried

out in the morning between 07.00 and 08.00 a.m., twice (before and after intervention). SGOT and SGPT examinations were conducted using the photometric method. Meanwhile, BUN level was measured using an enzymatic method (glutamate dehydrogenase), and creatinine level was measured by colorimetric method.

Ethical approval

All procedures in this study have received research permits and ethical approval from the medical research ethics committee number 234/EA/FK-RSUDZA/2021.

Statistical analysis

Data analysis used an independent sample t-test with a significance level of 95% ($p < 0.05$). This analysis aimed to determine the effect of the GC intervention on BP variables, SGOT, SGPT, Creatinine, and BUN values that were assessed by assessing the difference between the pretest and posttest scores. Independent sample t-test aimed to analyze the difference in pretest and post-test data for each group (G1, G2, G3, and G4). The difference in numbers shows the difference between the pretest-posttest values in each group. If the difference in numbers is $p < 0.05$, GC therapy may affect the research variables (BP, SGOT, SGPT, urea, Creatinine).

Results

Characteristics of animal models

The obesity indicator used for experimental animals was the Lee index. It was based on the results of body weight measurement (g) divided by naso-anal length (cm), which are then put into the BMI formula according to Lee (Lee index). The indicator of obesity based on the Lee index is more than 300 g/cm. The results of the Lee index examination can be seen in Table 1. It shows that all animal models have an index of >300 g/cm.

Table 1: Lee index description of each rat for each group

Code	Lee Index (g/cm)			
	G1	G2	G3	G4
1	329.02	331.41	326.11	320.51
2	327.13	326.01	321.25	327.36
3	321.14	328.78	324.27	324.79
4	329.56	328.14	328.98	326.41
5	328.52	328.02	329.92	324.55
6	330.38	329.78	326.50	326.07

The effect of the GC intervention, physical training, and its combination on BP

The description of BP before and after the intervention is shown in Table 2. The independent sample t-test analysis results showed no difference in BP before and after giving GC to obese rats ($p = 0.078$). On the other hand, there was a difference in the BP means before and after the intervention group of obese rats with physical training intervention ($p = 0.001$), coffee intervention (0.001), and combined physical training and GC interventions (0.001). These results indicate that physical training, GC, and combined physical training and GC interventions could reduce the BP in obese rats. The mean difference between pre-test and post-test BP showed that the difference in BP in the GC intervention group was more than in the G2 and G4 groups (95 mmHg, 70 mmHg, and 93 mmHg). These results indicate that GC effectively lowers BP in obese rats.

Table 2: The difference in blood pressure before and after the intervention in each group

Variable	Group	Data	n	Mean ± SD	p-value
BP (mmHg)	G1	Pretest	6	190.67 ± 7.61	0.078
		Posttest	6	198.0 ± 05.09	
	G2	Pretest	6	189.17 ± 2.93	0.001*
		Posttest	6	119.50 ± 3.73	
	G3	Pretest	6	186.50 ± 3.45	0.001*
		Posttest	6	91.33 ± 1.96	
	G4	Pretest	6	191.83 ± 2.64	0.001*
		Posttest	6	98.83 ± 3.76	

The effect of the GC intervention, physical training, and its combination on liver function

The effect of coffee consumption on liver function can be seen based on blood SGOT and SGPT levels, as shown in Table 3. The results of these measurements indicate that there is a significant difference in the levels of SGOT ($p < 0.05$) and SGPT ($p < 0.05$) in the groups receiving intervention with physical training, GC, and combination therapy (coffee and physical training) compared to the control group ($p > 0.05$). These results indicate that physiological doses of GC have no negative effect on liver function.

Table 3: Differences in SGOT and SGPT levels before and after intervention in each group

Variable	Group	Data	n	Mean ± SD	p-value
SGOT (U/L)	G1	Pretest	6	77.76 ± 1.21	0.187
		Posttest	6	78.81 ± 1.36	
	G2	Pretest	6	77.35 ± 2.01	0.001*
		Posttest	6	58.36 ± 0.36	
	G3	Pretest	6	76.38 ± 1.05	0.001*
		Posttest	6	38.35 ± 0.43	
	G4	Pretest	6	75.98 ± 1.49	0.001*
		Posttest	6	47.79 ± 1.43	
SGPT (U/L)	G1	Pretest	6	37.38 ± 1.68	0.303*
		Posttest	6	38.35 ± 1.41	
	G2	Pretest	6	37.78 ± 1.12	0.001*
		Posttest	6	30.51 ± 0.36	
	G3	Pretest	6	37.95 ± 1.46	0.001*
		Posttest	6	20.47 ± 0.36	
	G4	Pretest	6	37.95 ± 1.13	0.001*
		Posttest	6	24.11 ± 0.58	

The effect of the GC intervention, physical training, and its combination on kidney function

The effect of GC on kidney function can be analyzed based on BUN and creatinine levels, as shown in Table 4. The results of independent sample t-test analysis showed that there was a significant difference

Table 4: Differences in blood urea nitrogen and creatinine levels before and after intervention in each group

Variable	Group	Data	n	Mean ± SD	p-value
Blood urea nitrogen (mg/dl)	G1	Pretest	6	41.40 ± 0.83	0.001*
		Posttest	6	50.95 ± 0.99	
	G2	Pretest	6	41.51 ± 1.13	0.001*
		Posttest	6	47.23 ± 0.58	
	G3	Pretest	6	41.24 ± 0.98	0.001*
		Posttest	6	13.57 ± 0.92	
	G4	Pretest	6	43.61 ± 1.32	0.001*
		Posttest	6	23.19 ± 1.22	
Creatinine (mg/dl)	G1	Pretest	6	3.27 ± 0.03	0.133
		Posttest	6	3.31 ± 0.04	
	G2	Pretest	6	3.26 ± 0.05	0.001*
		Posttest	6	2.96 ± 0.05	
	G3	Pretest	6	3.21 ± 0.05	0.001*
		Posttest	6	0.89 ± 0.01	
	G4	Pretest	6	3.36 ± 0.06	0.001*
		Posttest	6	1.26 ± 0.07	

in creatinine levels before and after intervention with GC (p = 0.001*), physical training (p = 0.001*), and their combination (p = 0.001*). Compared to the control group (p = 0.133), there were differences in levels of BUN before and after intervention in all groups (p < 0.05). The BUN levels increased significantly in the control and physical training intervention groups. In contrast, after the intervention with GC and the combination of interventions, BUN levels decreased significantly. These results indicate that the physiological dose of GC does not affect kidney function.

The analysis of variance (ANOVA) in Table 5 shows significant differences in the variables BP, SGOT, SGPT, BUN, and Creatinine after the intervention. These results also showed that the mean BP reduction was most significant in the PE intervention group (95.17 mmHg), followed by the GC+PE intervention group (93 mmHg) and the GC intervention group (69.67 mmHg). The results of the ANOVA analysis to assess the effect of the intervention on liver function showed that the average decrease in SGOT and SGPT levels was in the PE intervention group (38.03 U/L and 17.48 U/L), followed by the GC+PE intervention group (28.19 U/L and 13.84). U/L), and GC intervention group (18.99 U/L and 7.27 U/L). The effect of the intervention on kidney function indicated that the PE intervention had more effect on decreasing BUN and creatinine levels than the GC intervention (27.67 mg/dl and 2.32 mg/dl vs. –5.72 mg/dl and 0.3 mg/dl). On the other hand, it was found that BUN levels increased in the GC intervention group. This result still needs to be investigated further, especially the long-term effects of GC consumption. Although the results show that GC lowers BP, it does not affect liver and kidney function.

Table 5: Differences in BP, SGOT, SGPT, BUN, and Creatinine before and after intervention between group

Variable	Intervention	Group				p-value
		G1	G2	G3	G4	
BP	Before	190.67 ± 7.61	189.17 ± 2.93	186.50 ± 3.45	191.83 ± 2.64	0.001
(mmHg)	After	198.0 ± 05.09	119.50 ± 3.73	91.33 ± 1.96	98.83 ± 3.76	
SGOT	Before	77.76 ± 1.21	77.35 ± 2.01	76.38 ± 1.05	75.98 ± 1.49	0.001
(U/L)	After	78.81 ± 1.36	58.36 ± 0.36	38.35 ± 0.43	47.79 ± 1.43	
SGPT	Before	37.38 ± 1.68	37.78 ± 1.12	37.95 ± 1.46	37.95 ± 1.13	0.001
(U/L)	After	38.35 ± 1.41	30.51 ± 0.36	20.47 ± 0.36	24.11 ± 0.58	
BUN	Before	41.40 ± 0.83	41.51 ± 1.13	41.24 ± 0.98	43.61 ± 1.32	0.001
(mg/dl)	After	50.95 ± 0.99	47.23 ± 0.58	13.57 ± 0.92	23.19 ± 1.22	
Creatinine	Before	3.27 ± 0.03	3.26 ± 0.05	3.21 ± 0.05	3.36 ± 0.06	0.001
(mg/dl)	After	3.31 ± 0.04	2.96 ± 0.05	0.89 ± 0.01	1.26 ± 0.07	

The results of this study illustrate that PE intervention is more effective in reducing BP, improving liver and kidney function, but further research and long-term intervention are needed.

Discussion

This research shows that the GC intervention affected the BP in obese rats. GC has been reported to lower BP in rats with spontaneous hypertension and humans with mild hypertension [29]. Research conducted on human subjects also shows that giving GC extract at a dose of 500 mg/day had reduced systolic and diastolic BP accompanied by an increase in nitric oxide (NO) levels [30]. CGA is a potent polyphenol compound from GC that works as an antioxidant that can lower BP because GC has anti-hypertensive activity [30]. CGA is a potent antioxidant that has an anti-hypertensive effect [29]. CGA also affects increasing the elasticity of blood vessels [30]. Orlistat content in GC helps lower BP [23]. Ferulic acid has also been shown to lower BP by stimulating bioavailability and the production of vasodilators such as NO [29]. CGA in GC has a protective effect on vascular endothelium, stimulates the production of NO release from vascular endothelial cells, inhibits the secretion of homocysteine levels in plasma, reduces free radicals by inhibiting the activity of the enzyme NAD(P)H oxidase, and also inhibits angiotensin-converting enzyme [31].

Another study found that giving GC bean extract for 6 weeks did not reduce heart rate and BP. It even tended to increase BP slightly in normotensive women [32]. Exercise for 6 weeks lowers BP by increasing the bioavailability of NO, lowering peripheral vascular resistance, and decreasing sympathetic nervous system activity [32]. We also found that physical training (swimming) in obese rats could lower BP.

Obesity is one of the causes of hepatic injury. The benefits of coffee on liver disease have been reported by several studies [31]. The study results indicated that the GC intervention did not decrease kidney and liver function in obese rats because coffee has hepatoprotective properties. The results of the study state that consumption of coffee 2 cups/day can reduce the risk of liver cancer by 40% compared to those who do not consume coffee [31]. It was found that GC intervention decreased SGOT and SGPT levels in obese rats. In contrast, the opposite result was reported that long-term coffee consumption (more than 30 years) of 2 cups of coffee/day in humans could decrease liver function by increasing the SGOT and SGPT levels. This is because liver enzymes are targets of coffee caffeine. However, the mechanism is unclear because there are many influencing factors,

and further research is needed [33]. Coffee has a protective effect on liver fibrosis in non-alcoholic fatty liver disease patients. However, it is still necessary to study the threshold for the hepatoprotective effect of coffee [34]. CGA and caffeine in coffee act as antioxidants and anti-inflammatory and prevent cell apoptosis [31].

Caffeine, phenolic, and melanoidins compounds in GC have hepatoprotective activity [35]. Caffeine plays a role in inhibiting hepatic fibrogenesis through downregulation of connective tissue growth factor production and upregulation of PPARγ receptors. Meanwhile, phenolics and melanoidins have antioxidant activity that prevents hepatic tissue damage [35].

This study reported that GC did not decrease kidney function in obese rats. Coffee consumption reduces the risk of chronic kidney disease [36]. Another study also reported that GC extract therapy at a dose of 1000 mg/kg BW/day was not toxic to the liver and kidneys. This can be seen from liver and heart function biomarkers, for example, the unchanged levels of aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, and kidney function (BUN, Creatinine, and uric acid) [7]. CGA in GC has antioxidant activity that improves kidney function [37]. CGA also has a renal protective effect by inhibiting the production of oxidative stress, anti-inflammatory, inhibiting cell apoptosis in the liver tubules, and inhibiting the regulation of the transcription factor p53 [38]. The recommended consumption of coffee caffeine that is beneficial for improving health is around 300 and 400 mg/day or the equivalent of 3-4 cups of coffee per day; on the other hand, coffee consumption exceeding the recommended dose will have a negative effect on health [1].

Limitations of the study

In this study, only a single dose of GC was used. It should be intervened by using several doses, including the maximum dose. The maximum dose will describe the negative effects of coffee consumption on BP, kidney function, and liver function.

Conclusions

A single daily dose of GC did not increase BP in obese model rats and had no negative effect on liver and kidney functions. Therefore, GC has the potential to be developed as a healthy drink because it is safe for daily consumption. However, further research using a clinical trial is needed. To conclude, coffee could be used as a standardized herbal medicine to treat various diseases, including controlling BP.

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