

# EFFECTS OF THE ADMINISTRATION OF BREWED ROBUSTA COFFEE LEAVES ON TOTAL ANTIOXIDANT STATUS IN RATS WITH HIGH-FAT, HIGHFRUCTOSE DIET-INDUCED METABOLIC SYNDROME

*by* Gemala Anjani

---

**Submission date:** 02-Dec-2022 11:34AM (UTC+0700)

**Submission ID:** 1968937183

**File name:** OF\_THE\_ADMINISTRATION\_OF\_BREWED\_ROBUSTA\_COT\_-\_Gemala\_Anjani.pdf (281.37K)

**Word count:** 5025

**Character count:** 26556



## EFFECTS OF THE ADMINISTRATION OF BREWED ROBUSTA COFFEE LEAVES ON TOTAL ANTIOXIDANT STATUS IN RATS WITH HIGH-FAT, HIGH-FRUCTOSE DIET-INDUCED METABOLIC SYNDROME

Nurmasari Widyastuti, Gemala Anjani, Vita Gustin Almira, Suci Eka Putri, Amali Rica Pratiwi

### ABSTRACT

Robusta coffee (*Coffea canephora*) leaves contain phytochemical compounds and have antioxidant and anti-diabetic effects. This study investigated the effect of brewed Robusta coffee leaves on the total antioxidant status in metabolic syndrome rats. Metabolic syndrome in rats was induced by high-fat-fructose diet containing pork oil (20%), cholesterol (1.5%), cholic acid (0.5%), standard feed (80%), and fructose (1 mL per 200 g BW). The animals were categorized into normal control group (K1), metabolic syndrome control group without treatment (K2), mangiferin treatment group (X1), brewed Robusta coffee leaves 0.09 g per 200 BW group (X2), brewed Robusta coffee leaves 0.18 g per 200 BW group (X3), and brewed Robusta coffee leaves 0.36 g per 200 BW group (X4). Each dose of the coffee leaves was brewed with 3.6 mL of water at 70 °C for 10 min. The intervention was administered for 28 days. There was a significant increase in the total antioxidant status ( $p < 0.000$ ) in all the groups. In conclusion, the administration of brewed Robusta coffee leaves increased the total antioxidant status in metabolic syndrome rats.

**Keywords:** metabolic syndrome; Robusta coffee leaves; total antioxidant

### INTRODUCTION

Metabolic syndrome is a cluster of metabolic disorders characterized by hyperglycemia, hypertension, obesity, low high-density lipoprotein (HDL), and hypertriglyceridemia (Srikanthan et al., 2016). Obesity and insulin resistance are the known risk factors for metabolic syndrome. The prevalence of metabolic syndrome has been increasing every year. From 2009 to 2013, the prevalence of metabolic syndrome increased from 28.84% to 30.52% in adults >30 years of age in Korea (Lee et al., 2018). In Indonesia, its prevalence by the province in 1995 – 2007 was about 21.66%, with the highest prevalence noticed in Jakarta (Herningtyas and Ng, 2019).

The main mechanism of obesity and insulin resistance is oxidative stress (Hurrell and Hsu, 2017; Marseglia et al., 2015), which damages both insulin secretion by the pancreatic  $\beta$ -cells and glucose transport in the muscle and adipose tissues (Marseglia et al., 2015). Oxidative stress is caused by increases in lipid peroxide, malondialdehyde (MDA), carbonyl protein, and oxide xanthine activity because of an imbalance between free radicals and antioxidants (Mancini et al., 2015; Tangvarasittichai, 2015). The body has natural defenses in the form of antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx). Besides, consumption of a diet high in antioxidants

provides defence against oxidative stress (de Souza Cardoso et al., 2018). Robusta coffee leaves are consumed by the people of West Sumatra, Indonesia, as a healthy beverage (Rasyid, Sanjaya and Zulharmita, 2013). These leaves contain caffeine, chlorogenic acid, flavonoid, and mangiferin, which have antioxidant and anti-diabetic properties (Chen, Ma and Kitts, 2018).

In this study, we evaluated the effect of administration of brewed Robusta coffee leaves processed using the Japanese style green tea process (JGTP) (Chen, Ma and Kitts, 2018) and mangiferin on the total antioxidant status in a rat model of high-fat-fructose diet (HFFD)-induced metabolic syndrome.

### Scientific hypothesis

Brewed Robusta coffee leaves increase the total antioxidant status in rats with metabolic syndrome.

### MATERIAL AND METHODOLOGY

This study is included in the research project Study of The Administration of Brewed Robusta Coffee Leaves for Metabolic Response In Vivo in Metabolic Syndrome supported by funding received from Faculty of Medicine, Universitas Diponegoro 2019.

### The processing of Robusta coffee leaves using JGTP

Robusta coffee leaves were picked from 2<sup>nd</sup>, 3<sup>rd</sup>, and 4<sup>th</sup> leaves of each branch of Robusta coffee plants. Leaves were sorted and then blanched for 75 s. They were then dipped in water and placed in a sealer for  $\pm 15$  min to separate the leaves from the midrib. Next, the leaves were crushed using a crushing-tearing-curling machine 3 times. Finally, the leaves were dried for 4–5 h in a rack drier machine at 80 °C. The dried leaves were stored in airtight containers. The process was carried out in a mini-processing green tea processing laboratory at The Tea Quality Processing & Testing Laboratory in The Tea and Quinine Research Center Gambung, Bandung, Indonesia.

### Animal treatments

Six-week-old male Wistar rats ( $n = 36$ ), each weighing 150–200 g, were acquired from the Centre for Food and Nutrition of Universitas Gadjah Mada, Yogyakarta-Indonesia. The animals were provided standard feed of Comfeed II at 20 g per rat per day and water ad libitum. Body weight gain was recorded weekly and the remaining food was weighed daily. The experiments were approved by The Ethical Committee of Medical Research of Faculty of Medicine, Universitas Diponegoro (No. 16/EC/H/FK-UNDIP/III/2019), Indonesia. Rats were randomly divided into six groups ( $n = 6$  per group): healthy control (K1), metabolic syndrome without treatment (K2), mangiferin 20 mg.kg<sup>-1</sup> BW (X1), brewed Robusta coffee leaves 0.09 g per 200 g BW (X2), brewed Robusta coffee leaves 0.18 g per 200 g BW (X3), and brewed Robusta coffee leaves 0.36 g per 200 g BW (X4) groups. All animals, except the K1 group animals, were fed a HFFD for 14 days. This diet contained pork oil (20%), cholesterol (1.5%), cholic acid (0.5%), and standard feed (80%) and was administered orally, while fructose 1 mL per 200g BW was administered by sonde. Metabolic syndrome was defined when the rats had fasting blood glucose  $\geq 110$  mg.dL<sup>-1</sup>, triglycerides  $>150$  mg.dL<sup>-1</sup>, and HDL  $<40$  mg.dL<sup>-1</sup>.

Brewed Robusta coffee leaves were administered daily through a gastric sonde. The doses were brewed in 3.6 mL of water at 70 °C for 10 min. Mangiferin was dissolved in 3.6 mL of water and administered through a gastric sonde. The intervention was performed for 28 days.

### Blood sample analyses

Fasting blood glucose, triglyceride, and HDL measurements as criteria of metabolic syndrome were performed after 14 days of HFFD administration. Fasting blood glucose, triglyceride, and HDL were analysed by GOD-PAP, GPO, and CHOD-PAP methods respectively. Measurement of total antioxidant status was performed before intervention and at the end of intervention. Total antioxidant status was analysed by ABTS method. Blood sampling to analyze fasting blood glucose, triglyceride, HDL, and total antioxidant status through plexus retroorbital. Blood serum was analyzed in the Centre for Food and Nutrition of Universitas Gadjah Mada Yogyakarta-Indonesia.

### Statistical analysis

Statistical analyses were performed using the IBM SPSS Statistic 22 software. Data are presented as mean  $\pm$ SD or median. Paired *t*-test and one-way analysis of variance were used for parametric results; differences between the groups were evaluated using the *post-hoc* test. Wilcoxon, Kruskal-Wallis, or Mann-Whitney test was used, as appropriate, for non-parametric results.

### RESULTS AND DISCUSSION

Oxidative stress occurs when more oxidizing species are produced than the amount of antioxidants present in the body (Morillas-Ruiz and Hernández-Sánchez, 2015). Insufficient antioxidant levels in the body could be overcome by dietary antioxidants (Mironczuk-Chodakowska, Witkowska and Zujko, 2018; Yadav et al., 2016).

In this study, body weight of the animals significantly increased after treatment in all the groups ( $p < 0.05$ ). The X2 group ( $34.33 \pm 1.03$  g) experienced the highest weight gain after the administration of brewed Robusta coffee leaves compared to other treatment groups (Table 1). The X1 group ( $22.00$  ( $22.00 - 26.00$ ) g) also experienced weight gain. The weight gain was the highest in the K2 group ( $43.50 \pm 1.64$  g). The body weight between all groups significantly different before and after treatment (Table 2). Statistically, the body weight in the X4 group was not significantly different from that in the K1 group, as well as the body weight in the X3 group was not significantly different from that in the X4 group. This indicated that the increase in body weight in the X3 group was similar to that in the K1 group.

HFFD administration in rats has been known to cause weight gain and increases in blood glucose, triglyceride, LDL, and cholesterol levels (Nugroho et al., 2012). In this study, rats were administered HFFD for 14 days to achieve metabolic syndrome. In a previous study, HFFD administration caused hyperglycemia and dyslipidemia (Octavia, Djamiatun and Suci, 2017). In another study, a high-fat diet increased fasting blood glucose and a high-fructose diet increased triglyceride levels in rats (Huang et al., 2004). The administration of a high-fat diet increased reactive oxygen species (ROS) and decreased antioxidant enzyme activity (Du et al., 2012; Sreekumar et al., 2002). A high-fructose dietary induces oxidative stress by decreasing the antioxidant defense system (Zhang, Jiao and Kong, 2017).

Rats achieved metabolic syndrome condition with fasting blood glucose ( $131.14 \pm 2.13 - 132.70 \pm 1.48$  mg.dL<sup>-1</sup>), triglycerides ( $153.49 \pm 1.96 - 157.18 \pm 4.88$  mg.dL<sup>-1</sup>), and HDL ( $24.59 \pm 1.99 - 26.22 \pm 1.69$  mg.dL<sup>-1</sup>) as seen in Table 3. Fasting blood glucose and triglyceride levels in the K2, X1, X2, X3, and X4 groups were increased compared to those in the K1 group. Meanwhile, HDL level in the K2, X1, X2, X3, and X4 groups was decreased compared to that in the K1 group.

**Table 1** The Average Body Weight Before and After Treatment.

Groups	Body Weight (g)		$\Delta$	<i>p</i>	<i>P</i>
	Pre Mean $\pm$ SD	Post Mean $\pm$ SD			
K1 (n=6)	183.00 $\pm$ 2.82	208.50 $\pm$ 3.27	25.50 $\pm$ 1.37	0.000 <sup>a*</sup>	0.000 <sup>c*</sup>
K2 (n=6)	195.83 $\pm$ 2.04	239.33 $\pm$ 2.16	43.50 $\pm$ 1.64	0.000 <sup>a*</sup>	
X1 (n=6)	197.50 $\pm$ 5.68	220.50 $\pm$ 5.95	22.00 (22.00 – 26.00) <sup>d</sup>	0.024 <sup>b*</sup>	
X2 (n=6)	196.50 $\pm$ 3.78	230.83 $\pm$ 3.37	34.33 $\pm$ 1.03	0.000 <sup>a*</sup>	0.000 <sup>a*</sup>
X3 (n=6)	198.33 $\pm$ 4.67	226.83 $\pm$ 4.99	28.50 $\pm$ 1.87	0.000 <sup>a*</sup>	
X4 (n=6)	201.67 $\pm$ 3.32	228.17 $\pm$ 4.70	26.50 $\pm$ 1.87	0.000 <sup>a*</sup>	

Note: normal control group (K1); metabolic syndrome control group without treatment (K2); mangiferin treatment group (X1); brewed Robusta coffee leaves 0.09 g/200BW group (X2); brewed Robusta coffee leaves 0.18 g/200BW group (X3); brewed Robusta coffee leaves 0.36 g/200BW group (X4); a\* = paired t-test  $p < 0.05$  = significantly different; b\* = Wilcoxon test  $p < 0.05$  = significantly different; c\* = kruskal-wallis test  $p < 0.05$  = significantly different; d = abnormal distribution data, displayed in median (min-max).

**Table 2** Mann-Whitney Test Results for Weight Change Before and After Treatment.

Groups	$\Delta$ BW (g) Mean $\pm$ SD	<i>p</i> Value					
		K1	K2	X1	X2	X3	X4
K1	25.50 $\pm$ 1.37	-	0.004 <sup>*</sup>	0.026 <sup>*</sup>	0.004 <sup>*</sup>	0.019 <sup>*</sup>	0.219
K2	43.50 $\pm$ 1.64	-	-	0.003 <sup>*</sup>	0.004 <sup>*</sup>	0.004 <sup>*</sup>	0.004 <sup>*</sup>
X1	22.00 (22.00 – 26.00)	-	-	-	0.003 <sup>*</sup>	0.004 <sup>*</sup>	0.011 <sup>*</sup>
X2	34.33 $\pm$ 1.03	-	-	-	-	0.004 <sup>*</sup>	0.004 <sup>*</sup>
X3	28.50 $\pm$ 1.87	-	-	-	-	-	0.122
X4	26.50 $\pm$ 1.87	-	-	-	-	-	-

Note: normal control group (K1); metabolic syndrome control group without treatment (K2); mangiferin treatment group (X1); brewed Robusta coffee leaves 0.09 g/200BW group (X2); brewed Robusta coffee leaves 0.18 g/200BW group (X3); brewed Robusta coffee leaves 0.36 g/200BW group (X4); \* $p < 0.05$  = significantly different.

**Table 3** Fasting Blood Glucose, Triglyceride and HDL Level After Administration of HFFD.

Groups	Fasting blood glucose (mg/dl)	Triglyceride (mg/dL)	HDL (mg/dL)
	Mean $\pm$ SD	Mean $\pm$ SD	Mean $\pm$ SD
K1 (n = 6)	71.29 $\pm$ 1.53	68.77 $\pm$ 5.97	86.36 $\pm$ 2.28
K2 (n = 6)	132.70 $\pm$ 1.48	157.18 $\pm$ 4.88	25.05 $\pm$ 1.84
X1 (n = 6)	131.81 $\pm$ 1.88	153.75 $\pm$ 3.11	26.22 $\pm$ 1.69
X2 (n = 6)	131.56 $\pm$ 2.57	156.12 $\pm$ 2.48	26.22 $\pm$ 1.30
X3 (n = 6)	131.14 $\pm$ 2.13	153.49 $\pm$ 1.96	26.22 $\pm$ 2.15
X4 (n = 6)	132.53 $\pm$ 2.36	156.12 $\pm$ 2.77	24.59 $\pm$ 1.99

Note: normal control group (K1); metabolic syndrome control group without treatment (K2); mangiferin treatment group (X1); brewed Robusta coffee leaves 0.09 g/200 BW group (X2); brewed Robusta coffee leaves 0.18 g/200 BW group (X3); brewed Robusta coffee leaves 0.36 g/200 BW group (X4).

Compared to the baseline level, a significant difference in TAS levels was found after the administration of brewed Robusta coffee leaves and mangiferin in the K1 ( $p = 0.010$ ), X1 ( $p = 0.000$ ), X2 ( $p = 0.027$ ), X3 ( $p = 0.027$ ), and X4 ( $p = 0.000$ ) groups. Meanwhile, there was no significant difference in TAS in the K2 group ( $p = 0.063$ ) before and after treatment. Significantly increased TAS levels were found in the X2, X3, and X4 groups, implying that three doses of brewed Robusta coffee leaves could significantly increase TAS levels in rats with metabolic syndrome (Table 4).

After the administration of brewed Robusta coffee leaves, the TAS increased in the treatment groups. The higher the doses administered, the greater was the increase in the

TAS in the metabolic syndrome rats. Rats administered mangiferin also experienced an increase in the TAS. This may be attributed to the presence of phytochemical contents, such as mangiferin, flavonoids, chlorogenic acid, and caffeine, in brewed Robusta coffee leaves. The processing of Robusta coffee leaves by the JGTP method contributes to the retention of more number of phytochemical components (Chen, Ma and Kitts, 2018). In previous study, the extract of Robusta coffee leaves has high antioxidant activity. It is equivalent to the content of phenolic components in the leaves. The phenolic components contained in leaves contributes significantly to antioxidant capacity (Kristiningrum, Cahyanti and Wulandari 2017).



Table 4 Total Antioxidant Status Before and After Treatment.

Group	TAS level (mmol/L)		30 Δ Mean ±SD	P	p
	Pre Mean ±SD	Post Mean ±SD			
K1 (n=6)	2.25 ±0.17	2.06 ±0.90	-0.19 ±0.11	0.010 <sup>a*</sup>	0.000 <sup>c*</sup>
K2 (n=6)	0.29 (0.15 – 0.44) <sup>d</sup>	0.22 (0.15 – 0.29) <sup>d</sup>	-0.14 (-0.15 – 0.00)	0.063 <sup>b*</sup>	
X1 (n=6)	0.29 ±0.12	1.54 ±0.20	1.24 ±0.20	0.000 <sup>a*</sup>	
X2 (n=6)	0.26 ±0.10	0.66 ±0.15	0.44 (0.29 – 0.45)	0.027 <sup>b*</sup>	
X3 (n=6)	0.26 ±0.10	1.31 ±0.22	0.74 (0.73 – 1.03)	0.027 <sup>b*</sup>	
X4 (n=6)	0.26 ±0.10	1.37 ±0.20	1.10 ±1.18	0.000 <sup>a*</sup>	

Note: The rats were classified into the following groups: normal control group (K1); metabolic syndrome control group without treatment (K2); mangiferin treatment group (X1); brewed Robusta coffee leaves 0.09 g/200 BW group (X2); brewed Robusta coffee leaves 0.18 g/200 BW group (X3); brewed Robusta coffee leaves 0.36 g/200 BW group (X4).

a\* = paired *t*-test  $p < 0.05$  = significantly different; b\* = Wilcoxon test  $p < 0.05$  = significantly different; c\* = Kruskal-Wallis test  $p < 0.05$  = significantly different; d = abnormal distribution data, displayed in median (min-max).

The phytochemical caffeine primarily contributes in improving the antioxidant status. The antioxidant effect of caffeine is exerted by scavenging the hydroxyl radicals (Yamagata, 2018). Caffeine directly inhibits lipid peroxidation and has a high inhibitor level against radical formation. This compound can also reduce oxidative stress and ROS, as well as protect antioxidant system (Jeska-Skowron et al., 2016; Tellone et al., 2015). The administration of caffeine at 30 and 100 mg.kg<sup>-1</sup> reduces lipid peroxidation and increases antioxidant enzyme activity (Demirtaş et al., 2012). Consumption of caffeine 5 mg.kg<sup>-1</sup> body weight per day in 2 doses daily can reduce MDA and elevate the total antioxidant capacity (Metro et al., 2017).

Chlorogenic acid also acts as an antioxidant. It donates hydrogen atoms to reduce free radicals and inhibits oxidation reactions. It also oxidizes phenoxyl radicals and stabilizes them through resonance stabilization (Liang and Kitts, 2016). Chlorogenic acid at 5 mg.kg<sup>-1</sup> for 45 days causes a decrease in lipid oxidation and an increase in antioxidant endogenous enzymes in diabetic rats (Pari, Karthikesan and Menon, 2010). High chlorogenic acid shows a high level of efficiency in scavenging DPPH radicals and converting Fe<sup>3+</sup> to Fe<sup>2+</sup>. This compound shows antioxidant activity by donating hydrogen to free radicals (Liang and Kitts, 2014; Wu, 2007). 5-O-caffeoylquinic acid (5-CQA) is a subclass of chlorogenic acid that has a strong hydroxyl radical scavenger activity with a constant scavenger rate HO of  $7.73 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}$  (Liang and Kitts, 2014).

Flavonoids are part of antioxidants that contribute to the high antioxidant capacity and are present in fruits and vegetables. High flavonoid intake is associated with high plasma levels of total antioxidant capacity (Alipour, Rashidkhani and Edalati, 2016). Intake of flavonoids, such as flavan-3-ols, flavonols, and anthocyanins, decreases dyslipidemia, induces antioxidant capacity, and prevents insulin resistance in diabetic patients (Yamagata, 2019). Patients with type 2 diabetes administered flavonoid-enriched chocolate at 27 g per day for a year reduced insulin resistance and improved insulin sensitivity (Curtis et al., 2012). The administration of the flavonoid

quercetin at 15 mg per kg per day for 4 weeks decreased lipid peroxidation and increased antioxidant enzyme activity in diabetic rats (Coskun et al., 2005). Mangiferin is a xanthone that is found in high levels in several parts of the mango. It is also found in Arabica coffee leaves and is thought to be found in Robusta coffee leaves (Chen, 2019). Mangiferin confers its antioxidant effects by having a high iron-chelating ability (Imran et al., 2017). The administration of mangiferin at 50 and 100 mg.kg<sup>-1</sup> reduces MDA levels in plasma and cardiac tissues and increases the level of SOD in cardiac tissues (Arozal et al., 2015). In previous study, mangiferin at the dose of 10 mg.dL<sup>-1</sup> and 20 mg.dL<sup>-1</sup> in diabetic rats increased antioxidant defense mechanism, such as SOD and catalase (Muruganandan et al., 2002). Mangiferin at 40 mg per kg per day significantly reduced blood glucose levels and increased plasma insulin levels and antioxidant enzymes, such as SOD, catalase, and glutathione peroxidase. Mangiferin from *Salacia chinensis* prevents oxidative stress and protects pancreatic β-cells in rats with streptozotocin-induced diabetes (Sellamuthu et al., 2013).

## CONCLUSION

The administration of brewed Robusta coffee leaves processed by the JGTP method increases TAS in rats with HFFD metabolic syndrome. The intervention of brewed Robusta coffee leaves with a dose of 0.36 g per 200 BW is the most effective dose in increasing TAS levels.

## REFERENCES

- Alipour, B., Rashidkhani, B., Edalati, S. 2016. Dietary flavonoid intake, total antioxidant capacity and lipid oxidative damage: A cross-sectional study of Iranian women. *Nutrition*, vol. 32, no. 5, p. 566-572. <https://doi.org/10.1016/j.nut.2015.11.011>
- Arozal, W., Suyatna, F. D., Juniantito, V., Rosdiana, D. S., Amurugam, S., Aulia, R., Monayo, E. R., Siswandi, R. 2015. The Effects of Mangiferin (*Mangifera indica* L.) in Doxorubicin-induced Cardiotoxicity in Rats. *Drug Research*, vol. 65, no. 11, p. 574-580. <https://doi.org/10.1055/s-0034-1394457>
- Coskun, O., Kanter, M., Korkmaz, A., Oter, S. 2005. Quercetin, a flavonoid antioxidant, prevents and protects

- streptozotocin-induced oxidative stress and  $\beta$ -cell damage in rat pancreas. *Pharmacological Research*, vol. 51, no. 2, p. 117-123. <https://doi.org/10.1016/j.phrs.2004.06.002>
- Curtis, P. J., Sampson, M., Potter, J., Dhatriya, K., Kroon, P. A., Cassidy, A. 2012. Chronic Ingestion of Flavan-3-ols and Isoflavones Improves Insulin Sensitivity and Lipoprotein Status and Attenuates Estimated 10-Year CVD Risk in Medicated Postmenopausal Women With Type 2 Diabetes: A 1-year, double-blind, randomized, controlled trial. *Diabetes Care*, vol. 35, no. 2, p. 226-232. <https://doi.org/10.2337/dc11-1443>
- de Souza Cardoso, J., Oliveira, P. S., Bona, N. P., Vasconcellos, F. A., Baldissarelli, J., Vizzotto, M., Pereira Soares, M. S., Ramos, V. P., Spanevello, R. M., Lencina, C. L., Tavares, R. G., Stefanello, F. M. 2018. Antioxidant, antihyperglycemic, and antidiabetic effects of Brazilian-native fruit extracts in an animal model of insulin resistance. *Redox Report*, vol. 23, no. 1, p. 41-46. <https://doi.org/10.1080/13510002.2017.1375709>
- Demirtaş, C., Ofuoglu, E., Hussein, A., Pasaoglu, H. 2012. Effects of Caffeine on Oxidant-Antioxidant Mechanisms in the Rat Liver. *Gazi Medical Journal*, vol. 23, no. 1, p. 13-18. <https://doi.org/10.5152/gmj.2012.04>
- Du, Z., Yang, Y., Hu, Y., Sun, Y., Zhang, S., Peng, W., Zhong, Y., Huang, X., Kong, W. 2012. A long-term high-fat diet increases oxidative stress, mitochondrial damage and apoptosis in the inner ear of d-galactose-induced aging rats. *Hearing Research*, vol. 287, no. 1-2, p. 15-24. <https://doi.org/10.1016/j.heares.2012.04.012>
- Herningtyas, E. H., Ng, T. S. 2019. Prevalence and distribution of metabolic syndrome and its components among provinces and ethnic groups in Indonesia. *BMC Public Health*, vol. 19, 12 p. <https://doi.org/10.1186/s12889-019-6711-7>
- Huang, B.-W., Chiang, M.-T., Yao, H.-T., Chiang, W. 2004. The effect of high-fat and high-fructose diets on glucose tolerance and plasma lipid and leptin levels in rats. *Diabetes, Obesity and Metabolism*, vol. 6, no. 2, p. 120-126. <https://doi.org/10.1111/j.1462-8902.2004.00323.x>
- Hurrell, S., Hsu, W. H. 2017. The etiology of oxidative stress in insulin resistance. *Biomedical Journal*, vol. 40, no. 5, p. 257-262. <https://doi.org/10.1016/j.bj.2017.06.007>
- Chen, X. 2019. A review on coffee leaves: Phytochemicals, bioactivities and applications. *Critical Reviews in Food Science and Nutrition*, vol. 59, no. 6, p. 1008-1025. <https://doi.org/10.1080/10408398.2018.1546667>
- Chen, X.-M., Ma, Z., Kitts, D. D. 2018. Effects of processing method and age of leaves on phytochemical profiles and bioactivity of coffee leaves. *Food Chemistry*, vol. 249, p. 143-153. <https://doi.org/10.1016/j.foodchem.2017.12.073>
- Imran, M., Arshad, M. S., Butt, M. S., Kwon, J.-H., Arshad, M. U., Sultan, M. T. 2017. Mangiferin: a natural miracle bioactive compound against lifestyle related disorders. *Lipids in Health and Disease*, vol. 16, 17 p. <https://doi.org/10.1186/s12944-017-0449-y>
- Jeszka-Skowron, M., Sentkowska, A., Pyrzyńska, K., De Peña, M. P. 2016. Chlorogenic acids, caffeine content and antioxidant properties of green coffee extracts: influence of green coffee bean preparation. *European Food Research and Technology*, vol. 242, p. 1403-1409. <https://doi.org/10.1007/s00217-016-2643-y>
- Kristiningrum, N., Cahyanti, Y. N., Wulandari, L. 2017. Determination of Total Phenolic Content And Antioxidant Activity In Methanolic Extract of Robusta and Arabica Coffee Leaves. *UNEJ E-Proceeding*, p. 96-99. Available at: <https://jurnal.unej.ac.id/index.php/prosiding/article/view/3901>
- Lee, S. E., Han, K., Kang, Y. M., Kim, S.-O., Cho, Y. K., Ko, K. S., Park, J.-Y., Lee, K.-U., Koh, E. H. 2018. Trends in the prevalence of metabolic syndrome and its components in South Korea: Findings from the Korean National Health Insurance Service Database (2009-2013). *PLOS ONE*, vol. 13, no. 3, e0194490. <https://doi.org/10.1371/journal.pone.0194490>
- Liang, N., Kitts, D. D. 2014. Antioxidant Property of Coffee Components: Assessment of Methods that Define Mechanisms of Action. *Molecules*, vol. 19, no. 11, p. 19180-19208. <https://doi.org/10.3390/molecules191119180>
- Liang, N., Kitts, D. D. 2016. Role of Chlorogenic Acids in Controlling Oxidative and Inflammatory Stress Conditions. *Nutrients*, vol. 8, no. 1, 20 p. <https://doi.org/10.3390/nu8010016>
- Mancini, A., Martorana, G. E., Magini, M., Festa, R., Raimondo, S., Silvestrini, A., Nicolotti, N., Mordente, A., Mele, M. C., Donato Miggiano, G. A., Meucci, E. 2015. Oxidative stress and metabolic syndrome: Effects of a natural antioxidants enriched diet on insulin resistance. *Clinical Nutrition ESPEN*, vol. 10, no. 2, p. e52-e60. <https://doi.org/10.1016/j.clnesp.2014.11.002>
- Marseglia, L., Manti, S., D'Angelo, G., Nicotera, A., Parisi, E., Di Rosa, G., Gitto, E., Arrigo, T. 2015. Oxidative Stress in Obesity: A Critical Component in Human Diseases. *International Journal of Molecular Sciences*, vol. 16, no. 1, p. 378-400. <https://doi.org/10.3390/ijms16010378>
- Metro, D., Cernaro, V., Santoro, D., Papa, M., Buemi, M., Benvenaga, S., Manasseri, L. 2017. Beneficial effects of oral pure caffeine on oxidative stress. *Journal of Clinical & Translational Endocrinology*, vol. 10, p. 22-27. <https://doi.org/10.1016/j.jcte.2017.10.001>
- Mironczuk-Chodakowska, I., Witkowska, A. M., Zujko, M. E. 2018. Endogenous non-enzymatic antioxidants in the human body. *Advances in Medical Sciences*, vol. 63, no. 1, p. 68-78. <https://doi.org/10.1016/j.advms.2017.05.005>
- Morillas-Ruiz, J. M., Hernández-Sánchez, P. 2015. Oxidative Stress and Antioxidant Defenses Induced by Physical Exercise. In Gowder, S. J. T., *Basic Principles and Clinical Significance of Oxidative Stress*. London, UK : IntechOpen. ISBN: 978-953-51-2200-5. <https://doi.org/10.5772/61547>
- Muruganandan, S., Gupta, S., Kataria, M., Lal, J., Gupta, P. K. 2002. Mangiferin Protects Streptozotocin-induced Oxidative Damage to Cardiac and Renal Tissues in Rats. *Toxicology*, vol. 176, no. 3, p. 165-173. [https://doi.org/10.1016/S0300-483X\(02\)00069-0](https://doi.org/10.1016/S0300-483X(02)00069-0)
- Nugroho, A. E., Andrie, M., Warditani, N. K., Siswanto, E., Pramono, S., Lukitaningsih, E. 2012. Antidiabetic and antihyperlipidemic effect of Andrographis paniculata (Burm. f.) Nees and andrographolide in high-fructose-fat-fed rats. *Indian Journal of Pharmacology*, vol. 44, no. 3, p. 377-381. <https://doi.org/10.4103/0253-7613.96343>
- Octavia, Z. F., Djamiatun, K., Suci, N. 2017. Pengaruh pemberian yogurt sinbiotik tepung pisang tanduk terhadap profil lipid tikus sindrom metabolik (The effect of synbiotic yogurt of tanduk banana flour in lipid profile of metabolic syndrome rats). *Jurnal Gizi Klinik Indonesia*, vol. 13, no. 4, p. 159-169. In Indonesian <https://doi.org/10.22146/jgk.19369>
- Pari, L., Karthikesan, K., Menon, V. P. 2010. Comparative and combined effect of chlorogenic acid and tetrahydrocurcumin on antioxidant disparities in chemical induced experimental diabetes. *Molecular and Cellular*

Biochemistry, vol. 341, p. 109-117.  
<https://doi.org/10.1007/s11010-010-0442-5>

Rasyid, R., Sanjaya, W. F., Zulhamita. 2013. Penetapan Kadar Kofein Daun Kopi Kawa (*Coffea Robusta*, Lind) (The determination of caffeine on leaves Kawa Coffee (*Coffea Robusta*, Lind)). *Jurnal Farmasi Higea*, vol. 5, no. 2, p. 137-143. In Indonesian

Sellamuthu, P. S., Arulselvan, P., Muniappan, B. P., Fakurazi, S., Kandasamy, M. 2013. Mangiferin from *Salacia chinensis* Prevents Oxidative Stress and Protects Pancreatic  $\beta$ -Cells in Streptozotocin-Induced Diabetic Rats. *Journal of Medicinal Food*, vol. 16, no. 8, p. 719-727.  
<https://doi.org/10.1089/jmf.2012.2480>

Sreekumar, R., Unnikrishnan, J., Fu, A., Nygren, J., Short, K. R., Schimke, J., Barazzoni, R., Sreekumaran Nair, K. 2002. Impact of high-fat diet and antioxidant supplement on mitochondrial functions and gene transcripts in rat muscle. *American Journal of Physiology, Endocrinology and Metabolism*, vol. 282, no. 5, p. E1055-E1061.  
<https://doi.org/10.1152/ajpendo.00554.2001>

Srikanthan, K., Feyh, A., Visweshwar, H., Shapiro, J. I., Sodhi, K. 2016. Systematic Review of Metabolic Syndrome Biomarkers: A Panel for Early Detection, Management, and Risk Stratification in the West Virginian Population. *International Journal of Medical Sciences*, vol. 13, no. 1, p. 25-38. <https://doi.org/10.7150/ijms.13800>

Tangvarasittichai, S. 2015. Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World Journal of Diabetes*, vol. 6, no. 3, p. 456-480.  
<https://doi.org/10.4239/wjdv6.i3.456>

Tellone, E., Galtieri, A., Giardina, B., Russo, A., Bellocco, E., Barreca, D., Ficarra, S. 2015. Antioxidant Activity of Caffeine: A Focus on Human Red Blood Cells and Correlations with Several Neurodegenerative Disorders. In Preedy, V. R. *Coffee in Health and Disease Prevention*. London, UK : Academic Press, p. 835-842.  
<https://doi.org/10.1016/B978-0-12-409517-5.00092-9>

Wu, L. 2007. Effect of chlorogenic acid on antioxidant activity of Flos Lonicerae extracts. *Journal of Zhejiang University SCIENCE B*, vol. 8, p. 673-679.  
<https://doi.org/10.1631/jzus.2007.B0673>

Yadav, A., Kumari, R., Yadav, A., Mishra, J. P., Srivastava, S., Prabha, S. 2016. Antioxidants and its functions in human body - A Review. *Research in Environment and Life Sciences*, vol. 9, no. 11, p. 1328-1331.

Yamagata, K. 2018. Do Coffee Polyphenols Have a Preventive Action on Metabolic Syndrome Associated Endothelial Dysfunctions? An Assessment of the Current Evidence. *Antioxidants*, vol. 7, no. 2, 18 p.  
<https://doi.org/10.3390/antiox7020026>

Yamagata, K. 2019. Metabolic Syndrome: Preventive Effects of Dietary Flavonoids. In *Studies in Natural Products Chemistry*. Amsterdam, Netherland : Elsevier, vol. 60, p. 1-28. <https://doi.org/10.1016/B978-0-444-64181-6.00001-2>

Zhang, D.-M., Jiao, R.-Q., Kong, L.-D. 2017. High Dietary Fructose: Direct or Indirect Dangerous Factors Disturbing Tissue and Organ Functions. *Nutrients*, vol. 9, no. 4, 335 p.  
<https://doi.org/10.3390/nu9040335>

#### Acknowledgments:

This study was supported by Research and Development (RPP) from the Faculty of Medicine, Universitas Diponegoro.

#### Contact address:

\*Nurmasari Widyastuti, Universitas Diponegoro, Faculty of Medicine, Department of Nutrition Science, Jl. Prof H. Soedarto, SH, Tembalang, 50275, Semarang, Indonesia, Tel.: +6281575897167,

E-mail: [widystutinurmasari@gmail.com](mailto:widystutinurmasari@gmail.com)

ORCID: <https://orcid.org/0000-0003-2964-2632>

Gemala Anjani, Universitas Diponegoro, Faculty of Medicine, Department of Nutrition Science, Jl. Prof H. Soedarto, SH, Tembalang, 50275, Semarang, Indonesia, Tel.: +6281285376785,

E-mail: [gemaanjani@gmail.com](mailto:gemaanjani@gmail.com)

ORCID: <https://orcid.org/0000-0002-7774-7693>

Vita Gustin Almira, Universitas Diponegoro, Faculty of Medicine, Department of Nutrition Science, Jl. Prof H. Soedarto, SH, Tembalang, 50275, Semarang, Indonesia, Tel.: +62896702780780,

E-mail: [vitagalmira@gmail.com](mailto:vitagalmira@gmail.com)

ORCID: <https://orcid.org/0000-0003-0432-9084>

Suci Eka Putri, Universitas Diponegoro, Faculty of Medicine, Department of Nutrition Science, Jl. Prof H. Soedarto, SH, Tembalang, 50275, Semarang, Indonesia, Tel.: +6282391182648,

E-mail: [suciekaputri08@gmail.com](mailto:suciekaputri08@gmail.com)

ORCID: <https://orcid.org/0000-0002-2706-2733>

Amali Rica Pratiwi, Universitas Diponegoro, Faculty of Medicine, Department of Nutrition Science, Jl. Prof H. Soedarto, SH, Tembalang, 50275, Semarang, Indonesia, Tel.: +6281232256199,

E-mail: [amalinicapradiwi212@gmail.com](mailto:amalinicapradiwi212@gmail.com)

ORCID: <https://orcid.org/0000-0003-1293-2174>

Corresponding author: \*



# EFFECTS OF THE ADMINISTRATION OF BREWED ROBUSTA COFFEE LEAVES ON TOTAL ANTIOXIDANT STATUS IN RATS WITH HIGH-FAT, HIGHFRUCTOSE DIET-INDUCED METABOLIC SYNDROME

## ORIGINALITY REPORT

15%

SIMILARITY INDEX

9%

INTERNET SOURCES

11%

PUBLICATIONS

2%

STUDENT PAPERS

## PRIMARY SOURCES

1	lipidworld.biomedcentral.com Internet Source	1 %
2	"Abstracts", Diabetologia, 1997 Publication	1 %
3	www.science.gov Internet Source	1 %
4	ijpronline.com Internet Source	1 %
5	www.karger.com Internet Source	1 %
6	scialert.net Internet Source	1 %
7	Yuka Miyajima, Makoto Nodera, Shuichi Adachi. "Determination of Zinc Sufficiency via the Direct Assessment of Fingertip Blood Samples", Research Square Platform LLC, 2022	1 %



8	Kazuo Yamagata. "Metabolic Syndrome: Preventive Effects of Dietary Flavonoids", Elsevier BV, 2019 Publication	1 %
9	docplayer.net Internet Source	1 %
10	Dorota Woźniak, Izabela Nawrot-Hadzik, Weronika Kozłowska, Sylwester Ślusarczyk, Adam Matkowski. "Chapter 23-1 Caffeoylquinic Acids", Springer Science and Business Media LLC, 2020 Publication	1 %
11	www.mdpi.com Internet Source	1 %
12	Seulbi Lee, Hyesook Park, Soontae Kim, Eun-Kyung Lee, Jiyoung Lee, Young Sun Hong, Eunhee Ha. "Fine particulate matter and incidence of metabolic syndrome in non-CVD patients: A nationwide population-based cohort study", International Journal of Hygiene and Environmental Health, 2019 Publication	<1 %
13	biochemia.wp.uph.edu.pl Internet Source	<1 %
14	revistas.uptc.edu.co Internet Source	<1 %

15 Muhammad Imran, Muhammad Sajid Arshad, Masood Sadiq Butt, Joong-Ho Kwon, Muhammad Umair Arshad, Muhammad Tauseef Sultan. "Mangiferin: a natural miracle bioactive compound against lifestyle related disorders", Lipids in Health and Disease, 2017  
Publication

---

16 Submitted to University of Edinburgh  
Student Paper

---

17 [www.frontiersin.org](http://www.frontiersin.org)  
Internet Source

---

18 Submitted to Universitas Dian Nuswantoro  
Student Paper

---

19 [repository-tnmgrmu.ac.in](http://repository-tnmgrmu.ac.in)  
Internet Source

---

20 Beitolah Alipour, Bahram Rashidkhani, Sareh Edalati. "Dietary flavonoid intake, total antioxidant capacity and lipid oxidative damage: A cross-sectional study of Iranian women", Nutrition, 2016  
Publication

---

21 [libres.uncg.edu](http://libres.uncg.edu)  
Internet Source

---

22 Igor Moraes Mariano, Victor Hugo de Freitas, Juliene Gonçalves Costa Dechichi, Jaqueline Pontes Batista et al. "Isoflavone did not

promote additional effects on heart rate variability of post-menopausal women submitted to combined exercise training: A clinical, controlled, randomized, double-blind study", Applied Physiology, Nutrition, and Metabolism, 2019

Publication

---

23

Leszek Dobrowolski, Bozena Badzyńska, Monika Grzelec-Mojzesowicz, Janusz Sadowski. "Renal Vascular Effects of Frusemide in the Rat: Influence of Salt Loading and the Role of Angiotensin II", Experimental Physiology, 2001

<1 %

Publication

---

24

SAMIRA SALEH, NABILA EL-MARAGHY, ENJI REDA, WALEED BARAKAT. "Modulation of Diabetes and Dyslipidemia in Diabetic Insulin-Resistant Rats by Mangiferin: Role of Adiponectin and TNF- $\alpha$ ", Anais da Academia Brasileira de Ciências, 2014

<1 %

Publication

---

25

Jian Wang, G. Mazza. "Effects of Anthocyanins and Other Phenolic Compounds on the Production of Tumor Necrosis Factor  $\alpha$  in LPS/IFN- $\gamma$ -Activated RAW 264.7 Macrophages", Journal of Agricultural and Food Chemistry, 2002

<1 %

Publication

---

26 Jong Sam Lee, Clinton R. Bruce, Lawrence L. Spriet, John A. Hawley. "Interaction of Diet and Training on Endurance Performance in Rats", Experimental Physiology, 2001

Publication

<1 %

27 Rosa Cinzia Borrelli, Attilio Visconti, Carmela Mennella, Monica Anese, Vincenzo Fogliano. "Chemical Characterization and Antioxidant Properties of Coffee Melanoidins", Journal of Agricultural and Food Chemistry, 2002

Publication

<1 %

28 Subramoniam, Appian. "References", Plants with Anti-Diabetes Mellitus Properties, 2016.

Publication

<1 %

29 journals.plos.org

Internet Source

<1 %

30 uwspace.uwaterloo.ca

Internet Source

<1 %

31 www.hindawi.com

Internet Source

<1 %

32 www.irispublishers.com

Internet Source

<1 %

Exclude quotes On

Exclude matches Off

Exclude bibliography On



# EFFECTS OF THE ADMINISTRATION OF BREWED ROBUSTA COFFEE LEAVES ON TOTAL ANTIOXIDANT STATUS IN RATS WITH HIGH-FAT, HIGHFRUCTOSE DIET-INDUCED METABOLIC SYNDROME

GRADEMARK REPORT

FINAL GRADE

/0

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6