Providing Of Mahkota Dewa Fruit Extract (*Phaleria Macrocarpa*) To Reduce Malondialdehyde Levels In The Blood Of White Rats (*Rattus Norvegicus*) Triggered By Excessive Physical Activity

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Abstract.

Anti-inflammatory, antioxidant, and apoptosis-modulating potential are just a few biological activities that have garnered much interest in natural food-derived components during the past two decades. Mahkota Dewa fruit (Phaleria macrocarpa) has several beneficial pharmacological activities. This study investigated whether Mahkota Dewa fruit extract (Phaleria macrocarpa) reduced malondialdehyde levels in blood samples of white rats (Rattus norvegicus) generated by excessive physical activity. The samples for this study were white rats (Rattus norvegicus) weighing 160-200 gr and 2-3 months old. The independent variable was the Mahkota Dewa fruit extract (Phaleria macrocarpa). The dependent variable was excessive physical activity-induced malondialdehyde levels in white rats (Rattus norvegicus). The average Malondialdehyde (MDA) levels show that the group given 5 ml of the Mahkota Dewa fruit extract (Phaleria macrocarpa) had tremendous success in lowering MDA levels compared to the other groups. The results of the observations and data analysis show that administration of the extract can reduce MDA levels significantly in male Wistar rats (Rattus norvegicus) because of too much exercise.

Keywords: *Phaleria macrocarpa, Malondialdehyde, Oxidative stress and Lipid peroxidation.*

I. INTRODUCTION

A healthy lifestyle includes eating well and exercising regularly. Physical activity improves health, life expectancy, and chronic illness risk [1]. This paradoxical phenomenon suggests that vigorous physical exertion can cause the development of hazardous chemicals. Exercise helps prevent, treat, and manage chronic diseases. Heavy exercise can cause cardiovascular events, especially in people with poor habitual physical activity or high pathological risk [2]. Excessive exercise increases energy needs and muscular activation. These modifications create free radicals [3].Lipid peroxidation is mediated by free radicals produced by cellular oxygen consumption [4]. Free radicals are produced during biological events that maintain metabolism and energy production [5]. Normal electron leakage into oxygen molecules from mitochondria and endoplasmic reticulum electron flow during oxidative respiration is the primary source of free radicals in cells. This converts superoxide anion into reactive oxygen hydrogen peroxide. In organisms with transition metal ions, hydrogen peroxide creates peroxyl radicals, the most reactive radicals. Free radicals' strong reactivity disrupts biomolecules like lipids, proteins, and nucleic acids, causing cellular, tissue, and organ damage when not removed from the environment [6].Extreme exercise raises oxygen consumption more than rest, exposing muscles to oxidative stress. The most important free radical species in living organisms are those generated by oxygen and nitrogen molecules, which are radical species [2], [5]. The subjects had a routine lifestyle yet balanced energy and vascular contributions. Extreme physical exertion significantly increases striated and smooth muscle oxygen consumption and ROS.

ROS from activity activates the body's antioxidant defense system to protect cells and tissues from free radicals. Oxidative stress is an imbalance between ROS and the antioxidant defense system [3].Oxidative stress is generated by an imbalance between cell and tissue ROS production and detoxification [7]–[10]. ROS are produced as a byproduct of oxygen metabolism and play several physiological roles, including cell signaling. However, environmental stressors (UV, ionizing radiation, pollutants, and heavy metals) and xenobiotics (antiblastic drugs) increase ROS production, causing an imbalance that damages

cells and tissues [11]. Lipid peroxidation indicates oxidative stress.Both enzymatic and non-enzymatic lipid peroxidation create lipid radicals from lipid molecules. Hydroxyl and hydroperoxyl radicals start oxidative chain reactions and lipid peroxidation [12], [13]. Membrane phospholipids with polyunsaturated fatty acids (PUFA) like arachidonic, linoleic, linolenic, eicosapentaenoic, and docosahexaenoic acids are most susceptible to peroxidation. Thus, ROS reacts with PUFA to deprotonate the double bond and introduce oxygen, forming lipid peroxide radicals that oxidize to lipid hydroperoxides. Lipid peroxidation damages membranes and creates secondary products. Damage to native lipid chains and lipid-lipid or lipid-protein cross-links can alter membrane function, biological systems, and enzymatic inactivation. The three-carbon compound malondialdehyde (MDA) is a secondary product and hallmark of lipid peroxidation produced by free radicals [3], [14]. Arachidonic acid and polyunsaturated fatty acids decompose to form MDA. Stable and membrane-permeable MDAs can carry signals.

MDA, a prominent oxidative stress marker, is hazardous and relevant to biological disorders.The best way to avoid lipid peroxidation and MDA damage is with antioxidants. Antioxidants prevent cell and tissue damage from reactive oxygen and nitrogen species [15]. Cells and tissues react to free radicals, activating prevention strategies, repair mechanisms, physical protection, and antioxidant defense [16]. The first line of defense against oxidative stress is antioxidants. Endogenous and exogenous antioxidant defenses exist. Endogenous antioxidant enzymes and non-enzymatic compounds are found in the cytoplasm and cell organelles. Fruits, cereals, coffee, tea, nuts, vegetables, and fruits contain exogenous antioxidants [16].Antioxidants reduce oxidative stress, DNA mutations, malignant transformation, and cell damage. Antioxidant reactions can reduce molecular oxygen, remove pro-oxidative metal ions, trap aggressive ROS like superoxide anion or hydrogen peroxide, remove chain-starting radicals like hydroxyl OH·, alkoxyl RO·, or peroxyl ROO·, break sequence radicals, or quench singlet oxygen (1O2) [16]–[19].SOD, GPx, catalase, albumin, transferrin, and metallothionein are high-molecular-weight antioxidants. Uric acid, ascorbic acid, lipoic acid, glutathione, ubiquinol, tocopherol/vitamin E, and flavonoids are low-molecular- In the last two decades, natural food-derived components have garnered attention for their anti-inflammatory, antioxidant, and anti-apoptotic properties. One is Mahkota Dewa fruit (*Phaleria macrocarpa*) [19]. The Thymelaceae family includes *Phaleria macrocarpa*, an important herb. Malaysia and Indonesia call it Mahkota Dewa. This plant is Papuan.

Flavonoids, polyphenols, saponins, tannins, and lignin were found in *Phaleria macrocarpa* leaves and fruit in previous phytochemistry studies. This chemical has chemopreventive and antioxidant properties like contemporary medicines [20].Mahkota Dewa (*Phaleria macrocarpa*) leaves and fruit contain antibacterial, antioxidant, anti-cancer, anti-proliferative, sexual enhancement, weight growth, and total cholesterol-lowering properties, according to various research. The fruit is traditionally used to treat type 2 diabetes. The fruit is nutritious [21].Based on the background above, researchers want to study how Mahkota Dewa fruit extract (*Phaleria macrocarpa*) reduces blood malondialdehyde levels in white rats (*Rattus norvegicus*) caused by excessive physical activity. Prior research supports this occurrence. Meiyanti et al. (2020) observed that Mahkota Dewa fruit extract is an antioxidant, especially on fruit. Other analyses indicated that *Phaleria macrocarpa* fruit peel extract has significant antioxidant activity [22]. This study investigated whether Mahkota Dewa fruit extract (*Phaleria macrocarpa*) reduced malondialdehyde levels in blood samples of white rats (*Rattus norvegicus*) generated by excessive physical activity.

II. METHODS

This study employs a genuine experimental design based on experimental quantitative research methods. A before-and-after test with a comparison group was chosen as the methodology [23]. White rats (*Rattus norvegicus*) were subjected to high levels of physical activity, and blood samples were collected to determine the efficacy of Mahkota Dewa fruit extract (*Phaleria macrocarpa*) in lowering malondialdehyde levels. Experimental variables are variables that are related and applied directly to find out what effect they have on specific symptoms [24]. There are two types of variables in this study: independent variables and dependent variables. Mahkota of Dewa Fruit Extract (*Phaleria macrocarpa*) was used as an independent variable. The levels of malondialdehyde produced by overtraining in white rats (*Rattus norvegicus*) served as

the dependent variable in this study. The samples for this study were white rats (*Rattus norvegicus*) weighing 160-200 grams and 2-3 months old.The tools used in this research include a rat cage, digital scale, blender, stirrer, rotary evaporator, porcelain cup, test tube, measuring flask, tub or bucket for swimming the rat, stopwatch, 3 ml, and 5 ml syringe, and glove, masks, blunt-tipped sonde syringes, blood capillary pipettes, spectrophotometer.The ingredients used include Mahkota Dewa fruit, 90% ethanol, 0.9% NaCl, MDA Assay Kit (contains glacial acetic acid, Trichloroacetic acid/TCA, and Thiobarbituric acid/TBA), distilled water, white rats, feed and drink mouse.

Research procedures acclimated test animals for seven days at the University of North Sumatra Faculty of Mathematics and Natural Sciences Animal House. Mice were given time, food, and drink (ad libitum) to adjust. Extraction of Mahkota Dewa Fruit Extract (*Phaleria macrocarpa*) involves three mass transfer steps: solvent penetration into the solid phase (internal transport), solute dissolution (solubility), and solute diffusion from the solid phase to the solvent. Then, a phytochemical test was performed to determine if the Mahkota Dewa fruit (*Phaleria macrocarpa*) extract could lower MDA levels in male Galuur Wistar rats (*Rattus norvegicus*) using the Tannin Content Test, Flavonoid Content Test, Alkoloid Content Test, Steroid Content Test/Terpenoids, and Saponin Content Test.Treatment Method This study required 20 white mice measuring 160-200 grams and aged 2-3 months, divided into four groups of 5 mice each, and treated for 14 days. White mice were fasted for ± 15 hours before blood samples were taken on day 15. Experimental blood MDA levels were measured using TBARs. The research data was analyzed using SPSS 25.0 for Windows. The Kolmogorov-Smirnov test ($p > 0.05$) assessed data normality. The significance between groups was tested using a one-way analysis of variance (One-way ANOVA) with a 95% confidence level ($p < 0.05$). The Post Hoc Test with LSD was used for further research.

III. RESULTS AND DISCUSSION

Result

This study used 20 160-200-gram white Wistar rats. Mahkota Dewa fruit extract (*Phaleria macrocarpa*) was tested for its ability to reduce malondialdehyde in male Wistar white rats—physical exercise preconditions mice for treatment. Swimming for one hour at 08.00-09.00 WIB was the morning physical exercise in this study. The treatment was conducted in a container with ±40 cm of water depth. Post-treatment, mice were dried for ±15 minutes and fed Mahkota Dewa fruit (*Phaleria macrocarpa*) extract orally with a probe, according to dose and group. Sonde is carefully placed in the stomach. After verifying that the sonde reached the belly, the extract is pushed in.

Table 1. Characteristics of Test Animals

Component	Group K	Group P1	Group P2	Group P3
Types of Rats		*Rattus norvegicus*		
Gender		Male		
General condition		White fur, healthy and active		
AVG Initial B/W (gr)	201	199	201	198
AVG Final B/W (gr)	183	180	182	181

Mouse body weight was measured on day one before treatment. Average mouse body weight was used as pre-test data. The 15th day following all treatments, the mice's body weight was weighed again to compare pre-and post-tests.The Mahkota Dewa fruit extract phytochemical test follows. Phytochemical tests were performed to determine if compounds in the Mahkota Dewa fruit (*Phaleria macrocarpa*) extract could reduce malondialdehyde levels in male Wistar rats (*Rattus norvegicus*) induced by 1 hour of swimming. The tests measure tannin, saponin, flavonoid, alkaloid, and steroid/terpenoid concentration.

Table 2. Phytochemical Test

Compound	Note
Flavonoid	+
Alkaloid	+
Saponin	+
Steroid	+
Tannin	+

The Mahkota Dewa fruit extract included secondary metabolites, according to phytochemical testing. These included flavonoids, steroids, saponins, alkaloids, and tannins. These chemicals will lower malondialdehyde levels in Wistar white rats (*Rattus norvegicus*) blood serum caused by excessive physical activity.Next, the researcher observed research implementation. Control mice were given distilled water, while animals given Mahkota Dewa fruit extract (*Phaleria macrocarpa*) at 3ml, 4ml, and 5ml doses had their blood serum malondialdehyde levels compared. The research was controlled so that all mice received the same treatment: extreme physical exercise, such as swimming for an hour, to weary them and cause oxidative stress.

Researchers encouraged mice to swim by placing a stick on their tails if they were stationary. A nearly drowned rat shows signs of fatigue.The research data was divided into pre-tests and post-tests on days 1 and 15. The retro-orbital plexus was used to draw blood from rats at the commencement of the study. The thiobarbituric acid (TBA) test method can measure malondialdehyde levels spectrophotometrically by peroxidizing polyunsaturated fatty acids (PUFA) to lipid peroxides, which decompose into malondialdehyde. Malondialdehyde and thiobarbituric acid (TBA) form a pink molecule that absorbs 532 nm light.Table 3 shows TBARs pre- and post-test MDA levels in white rats (Rattus novergicus). Pre- and post-test outcomes are defined. The control and treatment groups had different blood serum MDA levels, according to study group observations. From the table, treatment group III with a 5 ml dosage had the lowest post-test findings, averaging 2.35 nmol/ml.

Table 3. Blood Serum MDA Levels

No	Group	Repetition	Pre-test MDA level (nmol/ml)	Post-test MDA levels (nmol/ml)
1		1	1.13	6.98
2		2	1.14	7.07
3	Control	3	1.12	6.94
4		4	0.93	6.72
5		5	1.03	6.91
		Mean	1.07	6.92
6		1	0.97	4.72
7		2	1.02	4.83
8	Treatment I	3	1.13	4.57
9		4	1.14	4.98
10		5	1.11	4.67
		Mean	1.07	4.75
11		1	0.98	3.51
12		2	1.12	3.45
13	Treatment II	3	1.19	3.56
14		4	1.09	3.76
15		5	1.01	3.87
		Mean	1.07	3.63
16		1	0.93	2.36
17		2	0.98	2.44
18	Treatment III	3	1.16	2.19
19		4	1.17	2.53
20		5	1.16	2.23
		Mean	1.08	2.35

Table 3 shows that the control group, which exercised excessively and drank only distilled water, had a post-test MDA level of 6.92 nmol/ml. It outperforms the others. Post-test results for treatment group II with a dose of 3ml averaged 4.75 nmol/ml and 3.63 nmol/ml.

Table 4. Normality Test

Group	N	Sig
Control	5	.200
P-1	5	.200
P-2	5	.200
P-3	5	.200

The Kolmogorov-Smirnov Test was used to examine the data distribution, and the findings indicated that all groups were statistically significant at the 0.200 level. If the p-value is greater than 0.05, the data is

considered regularly distributed. As a result, we know that the data follows a normal distribution. Once it is shown that the data follows a normal distribution, the Levene test is used to check if all members of the study population are statistically equivalent.

Table 5. Homogeneity Test Results

Levene Static	**df1**	**df2**	**Sig**
.679	3	16	.645

Table 5 displays the results of the Levene test used to determine whether or not the data is homogeneous. The significance value in the probability column is 0.645. It can be concluded that the control group, treatment group-1, treatment group-2, and treatment group-3 all originate from populations with the same variance or that the two groups are homogeneous because the resulting significant probability value is greater than 0.05.

Table 6. One-Way Anova Test Results

	Sum of Squares	**df**	**Mean square**	**F**	**Sig**
Between Groups	56.452	3	.204	808.830	.000
Within Groups	.372	16	.023		
Total	56.824	19			

Table 6 demonstrates that the resulting significant value from the One-Way ANOVA test is less than 0.05 or 0.000. There is a statistically significant contrast between the control and treatment groups, as shown by these results. The average amounts of malondialdehyde (MDA) were compared across groups using a post hoc LSD test. Table 7 displays the outcomes of the post-hoc LSD test that was performed.

Table 7. LSD Post Hoc Test

	Experimental Group (I)	Experimental Group (J)	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval	
						Lower Bound	Upper Bound
LDL	Control (K)	Treatment P1	2.17000*	.09647	.000	1.9655	2.3745
		Treatment P2	3.29400*	.09647	.000	3.0895	3.4985
		Treatment P3	4.57400*	.09647	.000	4.3695	4.7785
	(P1)	Control (K)	-2.17000*	.09647	.000	-2.3745	-1.9655
		Treatment P2	1.12400*	.09647	.000	.9195	1.3285
		Treatment P3	2.40400*	.09647	.000	2.1995	2.6085
	(P2)	Control (K)	-3.29400*	.09647	.000	-3.4985	-3.0895
		Treatment P1	-1.12400*	.09647	.000	-1.3285	-.9195
		Treatment P3	1.28000*	.09647	.000	1.0755	1.4845
	(P3)	Control (K)	-4.57400*	.09647	.000	-4.7785	-4.3695
		Treatment P1	-2.40400*	.09647	.000	-2.6085	-2.1995
		Treatment P2	-1.28000*	.09647	.000	-1.4845	-1.0755

The LSD Post Hoc Test is used to compare groups for statistical significance. In this study, all groups differed significantly from one another, as evidenced by a p-value (less than 0.05) from the Post Hoc LSD test analysis.

Discussion

Mahkota Dewa (*Phaleria macrocarpa*) fruit extract was administered to male Wistar white rats (*Rattus norvegicus*) to see if it could lower their malondialdehyde (MDA) levels. Twenty Wistar white rats (*Rattus norvegicus*) were utilized in this study. Mice averaged 200 grams before the experiment was performed. The mice were weighed once more at the end of the trial on day 15, and the results showed that each group averaged 181.5g. From these data, we may infer that the mice lost an average of 18.5 g of body weight throughout the experiment.Male Wistar strain white rats (*Rattus norvegicus*) served as the test subjects. The rats were split into four groups: one received only distilled water as a placebo. In contrast, the other three received different concentrations of an extract of the Mahkota Dewa fruit (*Phaleria macrocarpa*). Three milliliters of Mahkota Dewa fruit extract (*Phaleria macrocarpa*) were given to the first treatment group, four milliliters to the second, and five milliliters to the third. After randomly assigning participants to one of four groups, the researchers conducted a series of tests using a range of interventions. The purpose of this study was to determine which dose of Mahkota Dewa fruit extract (*Phaleria macrocarpa*) was most efficient in decreasing MDA levels, which were generated by excessive physical activity in male Wistar white rats (*Rattus norvegicus*).

To be considered physical exercise, a person must use their skeletal muscles to create a movement that expends energy. To increase energy expenditure above basal levels and improve health, any activity in which skeletal muscles contract is considered physical exercise [3]. The prevention, treatment, and control of chronic diseases all depend on appropriate amounts of physical activity and exercise. Increased energy expenditure and robust activation of muscular tissue are two effects of strenuous physical activity. The byproduct of these alterations is free radicals [3].Lipid peroxidation is mediated by free radicals produced when cells use oxygen [25], [26]. Oxidative stress is a condition that develops when free radicals build up in the body. Lipid peroxidation is brought on by oxidative stress. Malondialdehyde (MDA) is the end product of lipid peroxidation in the membrane. Malondialdehyde (MDA) is a biomarker of oxidative stress and lipid peroxidation [14], [22]. It is a three-carbon molecule that is produced by free radicals. When there are lots of free radicals floating around, this is reflected in a high MDA level. Antioxidants are the most efficient and appropriate strategy for preventing lipid peroxidation and the damaging effects of MDA, while other methods exist. Reactive oxygen and nitrogen species can cause harm to cells and tissues, although antioxidants neutralize them [20]–[22]. The Mahkota Dewa fruit (*Phaleria macrocarpa*) is a plant that can be extracted and used as an antioxidant supplement. Due to its substance, researchers believe that consuming Mahkota Dewa fruit extract (*Phaleria macrocarpa*) can lower malondialdehyde levels.

Researchers hypothesized that the Mahkota Dewa fruit extract (*Phaleria macrocarpa*) could prevent the increase in malondialdehyde (MDA) that occurs when male Wistar white rats (*Rattus norvegicus*) swim for long periods.In this study, a 14-day trial period of observation yielded data that required processing and testing, necessitating multiple data analyses. The first step is a test for normalcy. Using the Kolmogorov-Smirnov test implemented in SPSS, we check the collected data for normality. Consequently, all groups' test data follows a normal distribution with a significance level 0.000. This suggests the data follows a normal distribution and represents the whole population.The homogeneity check comes next. This analysis needs to be performed to see if the research participants are representative of a population with consistent or typical variance. The collected results indicate a significance level of 0.645. When comparing the control group, treatment group 1, treatment group 2, and treatment group 3, the derived significant probability value is greater than 0.05, indicating that they all represent the same population. To determine the efficacy and significance of this data, the One-Way ANOVA test was applied due to its normal distribution and homogeneity.This test yields a significance level of 0.000 or higher (greater than 0.05). These results suggest that post hoc LSD testing is required because there are statistically significant differences between the control group, treatment groups 1 and 2, and treatment groups 2 and 3.The average amounts of malondialdehyde (MDA) were compared between the groups using a post hoc LSD test. In this study, all groups differed significantly from one another, as indicated by a Post Hoc LSD test significance value of 0.000 or less than 0.05.

Overall, this study demonstrates that high levels of exercise in each test group contributed to the reduction of MDA levels in mice. Average post-test findings illustrate the variation in MDA reduction. The average MDA concentration in the group that received only distilled water served as a control at 6.92 nmol/ml. The average value for Group 1 (which got 3 ml of Mahkota Dewa fruit extract, or *Phaleria macrocarpa*) was 4.75 nmol/ml. The average value for Group 2 with the 4 ml dose was 3.63 nmol/ml, Group 3 with the 2 ml dose was 2.35 nmol/ml, and Group 4 with the 2 ml dose was 2.35 nmol/ml. Malondialdehyde levels in male white rats (*Rattus norvegicus*) of the Wistar strain were lowered by both treatments. Still, the Mahkota Dewa (*Phaleria macrocarpa*) fruit extract at a dose of 5 ml was more effective.Mahkota Dewa Fruit Extract (*Phaleria macrocarpa*) was able to lower MDA levels in the trial group compared to the group that was given distilled water alone, according to the results. Mahkota Dewa fruit extract (*Phaleria macrocarpa*) contains tannins, alkaloids, steroids, triterpenoids, and flavonoids, all contributing to this effect. The antioxidant properties of these bioactive substances have been documented [20]–[22], [27]. Antioxidants assist the body to obtain more antioxidants to combat free radicals created by strenuous exercise. These results suggest that the Mahkota Dewa (*Phaleria macrocarpa*) fruit extract can mitigate the increase in malondialdehyde that is brought on by strenuous exercise in male Wistar white rats (*Rattus norvegicus*).

IV. CONCLUSION

Extensive studies on male Wistar white rats (*Rattus norvegicus*) indicate that MDA levels caused by prolonged swimming for 1 hour can be reduced by supplementing their diet with an extract from the fruit of the Mahkota Dewa (*Phaleria macrocarpa*). The significance level of the One-Way ANOVA test was either 0.000 or less than 0.05, proving this. It is clear from these results that the treatment group differs significantly from the control group. This study's Post Hoc LSD test analysis yielded a significance level of 0.000, or less than 0.05, indicating that there are statistically significant differences between the groups.

The average MDA levels show that the group given 5 ml of the Mahkota Dewa fruit extract (*Phaleria macrocarpa*) had tremendous success in lowering MDA levels compared to the other groups. The results of the observations and data analysis show that administration of the extract can reduce MDA levels significantly in male Wistar rats (*Rattus norvegicus*) because of too much exercise.Further research into the healing effects of Mahkota Dewa fruit extract (*Phaleria macrocarpa*) is warranted, as shown by the findings of the existing studies and trials. The extract of the Mahkota Dewa fruit (*Phaleria macrocarpa*) needs to be thoroughly evaluated for its substance composition, and novel functional food ingredients should be developed to be included in appealing products and tested on humans. SOD antioxidant levels should also be checked as a biomarker for the existence of free radicals.

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