



Effectiveness of Oral Providing of Ajwa Date Fruit Extract on Malondialdehyde and Superoxide Dismutase Levels of White Rats Induced by Excessive Physical Activity

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Abstract

Natural food ingredients are becoming increasingly popular as a treatment. According to studies and investigations, experts increasingly turn to natural remedies to treat disease, including date fruit extract (*Phoenix dactylifera*). This study tested the effectiveness of oral date palm fruit extract (*Phoenix dactylifera*) in reducing blood malondialdehyde levels in white rats (*Rattus norvegicus*) induced by excessive physical activity and increasing blood levels. Intense physical exercise increases white rat blood superoxide dismutase. This research is a laboratory experimental research or an actual experiment. The research design used a pre-test and post-test with a control group design to analyze the effectiveness of oral administration of date palm (*Phoenix dactylifera*) extract on the MDA and SOD levels of white rat (*Rattus norvegicus*) samples induced by excessive physical activity. The results of date fruit extract (*Phoenix dactylifera*) at 5 ml were more effective at reducing MDA and increasing SOD levels in white mice induced by excessive physical activity than at 3 and 4 ml. The experimental group treated with date fruit extract (*Phoenix dactylifera*) had lower MDA and higher SOD levels than the group given distilled water. Date fruit extract (*Phoenix dactylifera*) contains flavonoids and tannins. Some bioactive substances are antioxidants. Antioxidants can assist the body fight free radicals from excessive physical exertion.

Introduction

Natural food ingredients are becoming increasingly popular as a treatment. According to studies and investigations, experts increasingly turn to natural remedies to treat disease, including date fruit extract (*Phoenix dactylifera*). This study tested the effectiveness of oral date palm fruit extract (*Phoenix dactylifera*) in reducing blood malondialdehyde levels in white rats (*Rattus norvegicus*) induced by excessive physical activity and increasing blood levels. Intense physical exercise increases white rat blood superoxide dismutase. This research is a laboratory experimental research or an actual experiment. The research design used a pre-test and post-test with a control group design to analyze the effectiveness of oral administration of date palm (*Phoenix dactylifera*) extract on the MDA and SOD levels of white rat (*Rattus norvegicus*) samples induced by excessive physical activity. The results of date fruit extract (*Phoenix dactylifera*) at 5 ml were more effective at reducing MDA and increasing SOD levels in white mice induced by excessive physical activity than at 3 and 4 ml. The experimental group treated with date fruit extract (*Phoenix dactylifera*) had lower MDA and higher SOD levels than the group given distilled water. Date fruit extract (*Phoenix dactylifera*) contains

flavonoids and tannins. Some bioactive substances are antioxidants. Antioxidants can assist the body fight free radicals from excessive physical exertion.

Methods

This research is laboratory or actual experiments (Notoatmodjo, 2022). The research design used a pre-test and post-test with a control group design to analyze the effectiveness of oral administration of date palm (*Phoenix dactylifera*) extract on the MDA and SOD levels of white rat (*Rattus norvegicus*) samples induced by excessive physical activity. This sample study used Wistar strain adult male white rats (*Rattus norvegicus*) measuring 160-200 grams, 2-3 months old, and healthy, as shown by active mobility and no physical deformities.

A variable is any measurable or calculable attribute, number, or quantity (Suwarno & Nugroho, 2023). This study uses independent and dependent variables. This study's independent variable was oral date palm fruit extract (*Phoenix dactylifera*). After intense physical activity, this study measured malondialdehyde and superoxide dismutase levels in male Wistar rats (*Rattus norvegicus*). 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 gloves, masks, blunt-tipped sonde syringes, blood capillary pipettes, and spectrophotometer. Meanwhile, the materials used include dates, 90% ethanol, 0.9% NaCl, MDA Assay Kit, SOD Assay Kit, distilled water, male white rats, rat food, and drink.

Research Procedures began with the acclimatization of test animals at the Animal House, Faculty of Mathematics and Natural Sciences, Medan State University for one week. Then, make a date extract. After feeding date extract to 20 adult Wistar male white rats weighing 160-200 grams and 2-3 months old, divided into four groups of 5 rats each, and treated for 14 days between groups:

Control group (P-0): mice swam till near drowning \pm 1 hour/day and received distilled water/day/tail for 14 days. In Treatment Group-1 (P-1), mice swam for \pm 1 hour/day and orally administered 3 ml of date fruit extract/day/head via stomach probe for 14 days. In Treatment Group-2 (P-2), mice swam for \pm 1 hour/day and were orally administered 4 ml of date fruit extract/day/head via stomach probe for 14 days. In Treatment Group-3 (P-3), mice swam for \pm 1 hour/day and orally administered 5 ml of date fruit extract/day/head via stomach probe for 14 days.

Because white Wistar rats' stomach volumes were anticipated to be 3-5 ml orally, this study used 3 ml, 4 ml, and 5 ml date extract dosages. Next, white mice were fasted for \pm 15 hours before blood samples were obtained on day 15. Tail vein blood was collected from rats. K3 EDTA vaculabs gathered blood. Plasma was obtained by centrifuging blood at 3500 rpm for 10 minutes. The plasma is micropipetted. Plasma is received in a microtube for MDA and SOD testing. The TBARs method measured blood MDA levels in experimental samples by reacting blood plasma with 20% TCA, 1% TBA, and 50% glacial acetic acid.

TBA is mixed with 50% glacial acetic acid to provide an acidic state, and TBA can bind MDA to produce a colored product that can be measured by spectrophotometry. TCA and TBA with glacial acetic acid were combined with plasma samples. Next, the incubation was done in a 95°C water bath for 45 minutes till the temperature dropped. Plasma was centrifuged for 15 minutes at 1000 rpm. The material was placed in a buffet to measure absorption with a UV-Vis Spectrophotometer at 532.2 nm. The MDA concentration was calculated by plotting the absorbance data into the manual kit's MDA measurement method.

A SOD kit measures SOD levels as follows:

Begin with a sample tube (1 ml reagent 1 and 100 μ l sample) and a control tube (1 ml reagent and 100 μ l aquabides). Add 0.1 ml each of reagents 2, 3, and 4 to the first tube. After incubating

for 40 minutes at 37°C in a vortex mixer, two cc of chromogenic agent was added to the tube. The solution was returned to the vortex mixer for 10 minutes at room temperature, zeroed with aquabides, and each tube's OD at 550 nm with a 1 cm cuvette. Plotting the absorption data into the SOD measurement formula yielded the sample SOD concentration in percent. MDA levels were evaluated using SPSS. 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.

Result and Discussion

Phytochemical Test Results of Date Fruit Extract

Table 1. Phytochemical Test Results for PRP (Platelet-Rich Plasma)

Compound	Procedure	Result	Note
Flavonoids	Mg HCL Concentrated	Orange	+
Saponins	Aquades	There is no foam	-
Tannin	FeCl ₃	Blackish green	+
Alkaloids	Reagen Wagner	No sediment	-
Steroids	Sulfuric acid	There is no red color	-

Date palm extract included only flavonoids and tannins, according to phytochemical testing. Saponin, alkaloids, and steroid metabolites were absent. Due to their antioxidant properties, date palm extract phytochemicals can be utilized as medicines.

MDA and SOD Observation Results

The average levels of MDA and SOD in the treatment group given date extract at a dose of 3 ml, 4 ml, and 5 ml, and the control group measured from the first to the last day (day 14) are shown in Table 1.2.

Table 2. Average MDA and SOD Levels

Group	Sample	MDA	SOD
		(nmol/ml)	(%)
Control (P0)	1	15.21	25.45
	2	14.38	27.27
	3	15.49	30.91
	4	15.91	34.55
	5	15.55	29.09
Mean		15.31	29.45
SD		0.58	3.50
Treatment I (P1)	1	12.71	43.64
	2	14.07	38.18
	3	13.79	50.91
	4	13.23	47.27
	5	13.89	34.55
Mean		13.54	42.91
SD		0.56	6.63
Treatment II (P2)	1	11.97	52.73
	2	14.51	43.64
	3	12.36	47.27
	4	11.76	56.36
	5	12.37	50.91

Mean		12.59	50.18
SD		1.10	4.91
Treatment III (P3)	1	13.35	69.09
	2	10.78	65.45
	3	9.95	56.36
	4	9.08	52.73
	5	12.18	60.00
Mean		11.07	60.73
SD		1.71	6.63

Table 2 shows that the P0 control group received just distilled water and intensive physical activity and had the highest average MDA levels (15.31 ± 0.58 nmol/ml). In the group given increased exercise and 3ml of Ajwa date fruit extract (P1), the average MDA level was 13.54 ± 0.56 . Excess training and 4ml Ajwa date fruit extract (P2) led to an intermediate MDA level of 12.59 ± 1.10 in the P2 group. MDA levels were lowest in the excessive exercise group administered 5ml Ajwa date fruit extract (P3), with an average of 11.07 ± 1.71 .

Table 2 above shows that the P0 control group received just distilled water and excessive physical activity and had the lowest average SOD levels (29.45 ± 3.50 nmol/ml). In the group given increased exercise and 3ml of Ajwa date fruit extract (P1), the average SOD percentage was 42.91 ± 6.63 . Given increased activity and 4ml Ajwa date fruit extract (P2), the average SOD percentage was 50.18 ± 4.91 in the P2 group. SOD levels were highest in the group with excessive exercise and 5ml Ajwa date fruit extract (P3), averaging 60.73 ± 6.63 .

Description of Normality Test

Table 3. MDA Level Data Normality Test Results

Group	Statistics	Significance
Control (K)	0,912	0,477
Treatment 1 (P1)	0,904	0,431
Treatment 2 (P2)	0,868	0,257
Treatment 3 (P3)	0,972	0,887

The table above, which was checked for normality using SPSS, shows that the control and treatment groups for MDA level had significant values. Where the significance value (p) in the Shapiro-Wilk Test is the value that exceeds the standard margin of $p > 0.05$, 0.477 for the control group given only heavy physical activity (P0), 0.431 for the group given heavy physical activity and a dose of date palm fruit extract 3 ml (P1), 0.257 for the group given heavy physical activity and 4 ml date extract (P2), and 0.887 for the group given heavy physical activity and 5 ml date fruit. The Shapiro-Wilk normality test showed that all research groups' MDA levels were regularly distributed. Data is generally distributed if the p-value is > 0.05 and not customarily distributed if $p < 0.05$ (Ghozali, 2018).

Table 4. Normality Test Results for SOD Level Data

Group	Statistics	Significance
Control (K)	0,979	0,928
Treatment 1 (P1)	0,971	0,883
Treatment 2 (P2)	0,990	0,979
Treatment 3 (P3)	0,971	0,884

According to Table 4, a normality test using SPSS demonstrates that the control and treatment groups have significant MDA percentage values. The significance value (p) in the Shapiro-Wilk Test is the value that exceeds the standard margin of $p > 0.05$, which is 0.928 for the control

group given only heavy physical activity (P0), 0.883 for the group given heavy physical activity and 3 ml date palm fruit extract (P1), 0.979 for the group given heavy physical activity and 4 ml date extract (P2), and 0.884 for the group given heavy physical activity and 5 ml date fruit. The Shapiro-Wilk normality test showed that all research groups' SOD percentages were regularly distributed.

Description of Data Homogeneity Test Between Groups

After 14 days of severe physical activity, the One-Way ANOVA Test examined MDA levels in groups P0, P1, P2, and P3 for homogeneity. Results indicate a non-uniform variance of 0.023 ($p < 0.05$) in data from research variables for the control group (P0), groups P1, P2, and P3.

Table 5. Results of Test of Homogeneity of Variances MDA Levels

Category	Statistic Levene	Significance
Mean	4,194	0,023
Median	2,626	0,086
Trimmed Mean	4,082	0,025

Table 5 shows the ANOVA test results (attached) to determine if the four research or observation groups have different MDA levels. Using table data in the "Sig." The p-value is 0.000. H_0 is rejected at the actual level = 0.05 because the four groups have significantly different average MDA levels. Next, the One-Way ANOVA assessment was used to assess for homogeneity the percentage of SOD levels in groups P0, P1, P2, and P3 after 14 days of severe physical exercise. The control group (P0), group P1, group P2, and group P3 have uniform data variance from study variables, 0.380 ($p > 0.05$). Table 6 shows the data.

Table 6. Results of Test of Homogeneity of Variances SOD Levels

Category	Statistic Levene	Significance
Mean	1,096	0,380
Median	0,826	0,499
Trimmed Mean	1,093	0,381

Table 6 shows the ANOVA test results (attached) to determine if the four study or observation groups have different SOD percentages. Using table data in the "Sig." The p-value is 0.000. Since H_0 is rejected at the actual level = 0.05, the four groups' average (mean) SOD levels differ significantly.

Advanced Test Description Post Hoc Test

Table 7. Post Hoc Bonferroni Test Results for MDA Levels

Multiple Comparisons							
Dependent Variable: Length Wound							
(I) Group	(J) Treatment	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval		
					Lower Bound	Upper Bound	
Bonferroni	Control	1 st	1.77000	.63509	.079	-.1406	3.6806
		2 nd	2.91400*	.63509	.002	1.0034	4.8246
		3 rd	4.24000*	.63509	.000	2.3294	6.1506
	Treatment 1	Control	-1.77000	.63509	.079	-3.6806	.1406
		2 nd	1.14400	.63509	.543	-.7666	3.0546
		3 rd	2.47000*	.63509	.008	.5594	4.3806
		Control	-2.91400*	.63509	.002	-4.8246	-1.0034

Treatment 2	1 st	-1.14400	.63509	.543	-3.0546	.7666
	3 rd	1.32600	.63509	.319	-.5846	3.2366
Treatment 3	Control	-4.24000*	.63509	.000	-6.1506	-2.3294
	1 st	-2.47000*	.63509	.008	-4.3806	-.5594
	2 nd	-1.32600	.63509	.319	-3.2366	.5846
*. The mean difference is significant at the 0.05 level.						

Further Bonferroni Post Hoc Test findings are in Table 7. Comparing group I and group J shows that the average MDA levels in the Wistar strain of white rats (*Rattus norvegicus*) differ, as indicated by an asterisk "*": between group P0 and groups P2 and P3, between group P1 and group P3, and between-group P2 and groups P1 and P3. Comparisons between groups without the "*" indicate close average MDA levels. From Table 8, the results of further tests using the Post Hoc Bonferroni Test on the percentage of SOD levels, the comparison of group I and group J shows that almost all of the comparisons between groups show a difference in the average "a" e of SOD levels in the Wistar strain of white rats (*Rattus norvegicus*), which are marked with an asterisk "*", except for comparisons between group P1 and group P2, between group P2 and groups P1 and P Therefore, the comparison between groups where no "*" stars were identified in the test results shows no difference or is almost close. Group Bonferroni Post Hoc Testing was done using SPSS for Windows.

Table 8. Post Hoc Bonferroni Test Results for SDO Levels

Multiple Comparisons							
Dependent Variable: Length Wound							
(I) Group	(J) Treatment	Mean Difference (I-J)	Std. Error	Sig.	95% Confidence Interval		
					Lower Bound	Upper Bound	
Bonferroni	Control	1 st	-13.45600*	3.52524	.009	-24.0611	-2.8509
		2 nd	-20.72800*	3.52524	.000	-31.3331	-10.1229
		3 rd	-31.27200*	3.52524	.000	-41.8771	-20.6669
	Treatment 1	Control	13.45600*	3.52524	.009	2.8509	24.0611
		2 nd	-7.27200	3.52524	.334	-17.8771	3.3331
		3 rd	-17.81600*	3.52524	.001	-28.4211	-7.2109
	Treatment 2	Control	20.72800*	3.52524	.000	10.1229	31.3331
		1 st	7.27200	3.52524	.334	-3.3331	17.8771
		3 rd	-10.54400	3.52524	.052	-21.1491	.0611
	Treatment 3	Control	31.27200*	3.52524	.000	20.6669	41.8771
		1 st	17.81600*	3.52524	.001	7.2109	28.4211
		2 nd	10.54400	3.52524	.052	-.0611	21.1491
*. The mean difference is significant at the 0.05 level.							

After severe physical activity, oral Ajwa date fruit extract (*Phoenix dactylifera*) is tested for its effects on MDA and SOD levels in white rats (*Rattus norvegicus*). This study tested 20 Wistar white rats (*Rattus norvegicus*). Mouse weight averaged 189 grams before the test. After 15 days, the mice were weighed again and averaged 181g. These results show that the mice lost 18 grams following the study.

Male Wistar strain white rats (*Rattus norvegicus*) were given excessive physical activity with swimming treatment and grouped into four groups: one control group received only distilled water, the other three received Ajwa date fruit extract (*Phoenix dactylifera*) with three dose variations. The first group received 3ml of Ajwa date fruit extract (*Phoenix dactylifera*), the

second 4ml, and the last 5ml. The researchers evaluated four groups with different therapies. The goal was to determine whether the Ajwa date fruit extract (*Phoenix dactylifera*) dose reduced MDA. It increased SOD in male Wistar white rats (*Rattus norvegicus*) produced by excessive physical activity.

Any physical movement caused by skeletal muscle contraction boosts energy expenditure and enhances health (Biswas, 2021; Rodrigues et al., 2019; Tamariz-Ellemann et al., 2023; Virani et al., 2020). Exercise helps prevent, treat, and manage chronic diseases. Heavy exercise can cause health problems. Excessive exercise increases energy needs and muscular activation. These modifications create free radicals. Oxidative stress occurs from free radical buildup. Oxidative stress peroxidizes lipids (Coskun et al., 2005; Kruk et al., 2022; Newsholme et al., 2019; Verhaegen et al., 2022). MDA is produced via membrane lipid peroxidation. Every morning for 14 days, mice were subjected to extreme physical activity by swimming in a tub or bucket until they nearly drowned (± 1 hour). Mice were dried with a towel and rested for ± 1 hour after severe physical activity.

Due to an imbalance between antioxidants and pro-oxidants, hyperoxidative environments increase MDA expression. So, antioxidants are needed to correct this imbalance (Akbari et al., 2022; Verhaegen et al., 2022). Enzymatic endogenous antioxidants, including SOD, GPx, and catalase, are also present in the body. Antioxidants from outside the body are needed to balance oxidants because the body has limited antioxidants. Ajwa dates (*Phoenix dactylifera*) contain antioxidants. Researchers believe Ajwa date fruit extract (*Phoenix dactylifera*) can lower MDA and raise SOD due to its substance. To test this hypothesis, researchers used Ajwa date fruit extract (*Phoenix dactylifera*) to reduce MDA levels and increase SOD levels in male Wistar white rats (*Rattus norvegicus*) induced by excessive swimming (Boudghane et al., 2023; Kharal et al., 2023).

This research's 14-day observation trial yielded data that needed processing and testing, requiring various data analyses. The first test is normalcy. SPSS uses the Shapiro-Wilk test to check data normality. All test groups had typically distributed data with p values > 0.05 for MDA and SOD levels. Thus, the data is regularly distributed or represents the population. The homogeneity test follows. The research subjects' population variance must be tested to determine their homogeneity. The results indicate a 0.023 or $p < 0.05$ significance for the average MDA level observation. Since the significant probability value is less than 0.05, the control group treatment groups I, II, and III are not homogeneous or from the same population.

Testing the homogeneity of average SOD levels yielded a value of 0.380 or $p < 0.05$. As the significant probability value is greater than 0.05, the control group treatment groups I, II, and III are homogeneous or from the same population. This study found that excessive physical exercise in each trial group decreased MDA levels in mice. The average post-test data show MDA levels falling differently. On average, the control group given distilled water had 15.31 nmol/ml MDA. I received 3 ml of Ajwa date fruit extract in the treatment group and averaged 13.54 nmol/ml. Group II at 4 ml had an average value of 12.39 nmol/ml, and group III at 5 ml had 11.07 nmol/ml. This comparison shows that Ajwa date fruit extract (*Phoenix dactylifera*) at 5 ml reduces MDA levels generated by excessive physical activity in male Wistar white rats (*Rattus norvegicus*).

Based on the results, all trial groups of mice administered Ajwa date fruit extract (*Phoenix dactylifera*) after severe physical exercise had higher SOD levels. Differences in average post-test values show increased SOD levels. SOD averaged 29.25% in the distilled water control group. I received 3 ml of Ajwa date fruit extract in the treatment group and scored 42.91%. Treatment group II with 4ml scored 50.18%, and treatment group III with 5ml scored 60.73%. This comparison shows that Ajwa date fruit extract (*Phoenix dactylifera*) at 5 ml increases SOD

levels in male Wistar white rats (*Rattus norvegicus*) generated by excessive physical activity better.

The experimental group treated with Ajwa date fruit extract (*Phoenix dactylifera*) had lower MDA and higher SOD levels than the group given distilled water. Ajwa date fruit extract (*Phoenix dactylifera*) contains flavonoids and tannins. Some bioactive substances are antioxidants (Akbari et al., 2022; Duke et al., 2022; Kharal et al., 2023). Antioxidants can assist the body fight free radicals from excessive physical exertion. According to these findings, Ajwa date fruit extract (*Phoenix dactylifera*) reduces MDA and increases SOD in male Wistar white rats (*Rattus norvegicus*) after extreme physical activity. This study's smaller sample size of 20 white mice or five mice/group may affect the outcomes. The number of samples utilized affects research because it reduces generalization errors.

Conclusion

According to phytochemical studies, Ajwa date fruit extract (*Phoenix dactylifera*) included flavonoids and tannins. Therefore, Ajwa date fruit extract contains phytochemicals with potent antioxidant properties that can be employed as therapeutic components. Then, the control group (P0) had considerably different average MDA and SOD levels than the treatment groups P1, P2, and P3. The control group (P0) does not contain active compounds that can reduce MDA and increase SOD after heavy activity. In this study, Ajwa date fruit extract (*Phoenix dactylifera*) at 5 ml was more effective at lowering MDA and increasing SOD levels in white mice induced by excessive physical activity than at 3 and 4 ml.

Future research should compare Ajwa date fruit extract (*Phoenix dactylifera*) dosages with the positive control group and other characteristics. Further research is needed on the usefulness of Ajwa date fruit extract (*Phoenix dactylifera*) in lowering MDA and raising SOD, which is safer for people. A full test of the substance composition of Ajwa date fruit (*Phoenix dactylifera*) extract is essential to inventing functional food ingredients that can be put into an attractive product and tested on humans.

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References

- Akbari, B., Baghaei-Yazdi, N., Bahmaie, M., & Mahdavi Abhari, F. (2022). The role of plant-derived natural antioxidants in reduction of oxidative stress. *BioFactors*, 48(3), 611–633. <https://doi.org/10.1002/biof.1831>
- Bencivenga, D., Arcadio, F., Piccirillo, A., Annunziata, M., Della Ragione, F., Cennamo, N., Borriello, A., Zeni, L., & Guida, L. (2023). Plasmonic optical fiber biosensor development for point-of-care detection of malondialdehyde as a biomarker of oxidative stress. *Free Radical Biology and Medicine*, 199(February), 177–188. <https://doi.org/10.1016/j.freeradbiomed.2023.02.020>
- Biswas, G. (2021). *Review of Forensic Medicine and Toxicology: Including Clinical and Pathological Aspects; As Per the Competency Based Medical Education Guidelines of NMC* (5th ed.). New Dehli: Jaypee Brothers Medical Pub.
- Boudghane, L. C., Bouabdellah, N., Bouanane, S., Ahmed, F. Z. B., Laroussi, M. A., Bendiaf, Y., Nas, F., & Merzouk, H. (2023). Phytochemical, antioxidant, and antimicrobial attributes of different extracts of seeds: the Algerian variety of dates' Deglet Nour' (*Phoenix dactylifera* L.). *Vegetos*, 36(2), 559–565. <https://doi.org/10.1007/s42535->

- Coskun, O., Kanter, M., Korkmaz, A., & Oter, S. (2005). Quercetin, a flavonoid antioxidant, prevents and protects streptozotocin-induced oxidative stress and β -cell damage in rat pancreas. *Pharmacological Research*, 51(2), 117–123. <https://doi.org/10.1016/j.phrs.2004.06.002>
- Duke, J. A., Bogenschutz-Godwin, M. J., DuCellier, J., Duke, P.-A. K., & Kumar, R. (2022). *Handbook of Medicinal Herbs Second Edition* (Kindle Edi, Vol. 5, Issue 1). Florida: CRC Press. <https://doi.org/10.1097/00004850-199001000-00014>
- El Assar, M., Álvarez-Bustos, A., Sosa, P., Angulo, J., & Rodríguez-Mañas, L. (2022). Effect of Physical Activity/Exercise on Oxidative Stress and Inflammation in Muscle and Vascular Aging. *International Journal of Molecular Sciences*, 23(15). <https://doi.org/10.3390/ijms23158713>
- Fang, X., Ardehali, H., Min, J., & Wang, F. (2023). The molecular and metabolic landscape of iron and ferroptosis in cardiovascular disease. *Nature Reviews Cardiology*, 20(1), 7–23. <https://doi.org/10.1038/s41569-022-00735-4>
- Franklin, B. A., Eijsvogels, T. M. H., Pandey, A., Quindry, J., & Toth, P. P. (2022). Physical activity, cardiorespiratory fitness, and cardiovascular health: A clinical practice statement of the American Society for Preventive Cardiology Part II: Physical activity, cardiorespiratory fitness, minimum and goal intensities for exercise training, prescriptive methods, and special patient populations. *American Journal of Preventive Cardiology*, 12(September), 100425. <https://doi.org/10.1016/j.ajpc.2022.100425>
- Ghozali, I. (2018). Aplikasi Analisis Multivariate dengan Program IBM SPSS 25. In *Badan Penerbit Universitas Diponegoro*.
- Kharal, S., Siddique, F., Arshad, M., Iftikhar, K., Akhtar, M. T., Qadir, R., Sameeh, M. Y., Mustaqeem, M., Zhuang, J., & Xia, L. (2023). Assessment of phytochemicals, antioxidant properties, and in vivo antidiarrheal activity of date palm (*Phoenix dactylifera* L.). *International Journal of Food Properties*, 26(1), 2243–2255. <https://doi.org/10.1080/10942912.2023.2244684>
- Kruk, J., Aboul-Enein, B. H., Duchnik, E., & Marchlewicz, M. (2022). Antioxidative properties of phenolic compounds and their effect on oxidative stress induced by severe physical exercise. *Journal of Physiological Sciences*, 72(1), 1–24. <https://doi.org/10.1186/s12576-022-00845-1>
- Mostafa, H., Airouyuwa, J. O., & Maqsood, S. (2022). A novel strategy for producing nanoparticles from date seeds and enhancing their phenolic content and antioxidant properties using ultrasound-assisted extraction: A multivariate based optimization study. *Ultrasonics Sonochemistry*, 87(December 2021), 106017. <https://doi.org/10.1016/j.ultsonch.2022.106017>
- Newsholme, P., Keane, K. N., Carlessi, R., & Cruzat, V. (2019). Oxidative stress pathways in pancreatic β -cells and insulin-sensitive cells and tissues: Importance to cell metabolism, function, and dysfunction. *American Journal of Physiology - Cell Physiology*, 317(3), C420–C433. <https://doi.org/10.1152/ajpcell.00141.2019>
- Notoatmodjo, S. (2022). *Metodologi Penelitian Kesehatan* (3rd ed.). Jakarta: Rineka Cipta.
- Polidori, M. C., & Mecocci, P. (2022). Modeling the dynamics of energy imbalance: The free radical theory of aging and frailty revisited. *Free Radical Biology and Medicine*, 181(December 2021), 235–240. <https://doi.org/10.1016/j.freeradbiomed.2022.02.009>
- Qiu, Y., Fernández-García, B., Lehmann, H. I., Li, G., Kroemer, G., López-Otín, C., & Xiao,

- J. (2023). Exercise sustains the hallmarks of health. *Journal of Sport and Health Science*, 12(1), 8–35. <https://doi.org/10.1016/j.jshs.2022.10.003>
- Rodrigues, M., Kosaric, N., Bonham, C. A., & Gurtner, G. C. (2019). Wound healing: A cellular perspective. *Physiological Reviews*, 99(1), 665–706. <https://doi.org/10.1152/physrev.00067.2017>
- Rustanti, N., Nafsih, V. Z., Avisha, R. N., Kurniawati, D. M., Purwanti, R., Nissa, C., Wijayanti, H. S., & Afifah, D. N. (2019). Pengaruh yoghurt dan soyghurt kayu manis (*Cinnamomum burmannii*) terhadap kadar glukosa darah, insulin serum, dan malondialdehyde tikus pra sindrom metabolik. *Jurnal Gizi Indonesia*, 8(1), 60–68. <https://doi.org/10.14710/jgi.8.1.60-68>
- Silina, E. V., Stupin, V. A., Abramov, I. S., Bolevich, S. B., Deshpande, G., Achar, R. R., & Sinelnikova, T. G. (2022). Oxidative Stress and Free Radical Processes in Tumor and Non-Tumor Obstructive Jaundice: Influence of Disease Duration, Severity and Surgical Treatment on Outcomes. *Pathophysiology*, 29(1), 32–51. <https://doi.org/10.3390/pathophysiology29010005>
- Suwarno, B., & Nugroho, A. (2023). *Kumpulan Variabel-Variabel Penelitian Manajemen Pemasaran (Definisi & Artikel Publikasi)* (1st ed.). Bogor: Halaman Moeka Publishing.
- Tamariz-Elleemann, A., Wickham, K. A., Nørregaard, L. B., Gliemann, L., & Hellsten, Y. (2023). The time is now: regular exercise maintains vascular health in ageing women. *Journal of Physiology*, 601(11), 2085–2098. <https://doi.org/10.1113/JP282896>
- Verhaegen, D., Smits, K., Osório, N., & Caseiro, A. (2022). Oxidative Stress in Relation to Aging and Exercise. *Encyclopedia*, 2(3), 1545–1558. <https://doi.org/10.3390/encyclopedia2030105>
- Virani, S. S., Alonso, A., Benjamin, E. J., Bittencourt, M. S., Callaway, C. W., Carson, A. P., Chamberlain, A. M., Chang, A. R., Cheng, S., Delling, F. N., Djousse, L., Elkind, M. S. V., Ferguson, J. F., Fornage, M., Khan, S. S., Kissela, B. M., Knutson, K. L., Kwan, T. W., Lackland, D. T., ... Tsao, C. W. (2020). Heart disease and stroke statistics—2020 update a report from the American Heart Association. In *Circulation* (Vol. 141, Issue 9). <https://doi.org/10.1161/CIR.0000000000000757>