BIOLOGY, MEDICINE, & NATURAL PRODUCT CHEMISTRY ISSN 2089-6514 (paper)
Volume 14, Number 2, October 2025 | Pages: 1171-1176 | DOI: 10.14421/biomedich.2025.142.1171-1176 ISSN 2540-9328 (online)

Fragrant Pandan (*Pandanus ammaryllifolius*) Leaves Ethanol Extract as an Enhancer of Endogenous Antioxidant Defence under High-Fat Diet Conditions

Ni Made Wiasty Sukanty[1]*, Laksmi Nur Fajriani[1], I Putu Bayu Agus Saputra[2], Iptan Ariki[1], I Ketut Agus Yura Aditya[3], Angeline Devon Venansius[1]

[1]Undergraduate Nutrition Study Program, Faculty of Health, Universitas Bumigora, Indonesia.
[2]Medical Education Study Program, Faculty of Medicine, Universitas Pendidikan Ganesha, Indonesia.
[3]Undergraduate Pharmacy Study Program, Faculty of Health, Universitas Bumigora, Indonesia.

Corresponding author*
nimadewiastysukanty@gmail.com

Manuscript received: 06 October, 2025. Revision accepted: 29 November 2025, 2025. Published: 04 December, 2025.

Abstract

Excessive fat consumption, especially saturated and trans fatty acids, plays a significant role in metabolic disorders such as obesity, dyslipidemia, and cardiovascular disease through increased oxidative stress. Malondialdehyde (MDA), the end product of lipid peroxidation, serves as a biomarker of oxidative damage, whereas indirect bilirubin acts as an endogenous antioxidant. This study aimed to evaluate the effect of fragrant pandan leaves ethanol extract (FPLEE) in reducing MDA levels and modulating indirect bilirubin activity in rats fed a high-fat diet (HFD). The experimental method used 24 male *Rattus norvegicus* divided into six treatment groups: normal control (NC), positive control (C+), negative control (C-), and three FPLEE treatment groups with different doses (8, 16, and 32 mg/200 g BW/day). Administration was carried out for 14 days after 14 days of HFD induction. MDA levels were measured using the ELISA method, while total bilirubin and direct bilirubin were measured using spectrophotometry to determine indirect bilirubin levels. Statistical analysis was performed using one-way ANOVA and the post hoc Bonferroni test. The results showed that there were no significant differences in MDA levels between groups, although the C+ group fed a HFD showed a tendency toward increased MDA. Indirect bilirubin levels increased significantly in the low-dose FPLEE group (8 mg/200 g BW/day), indicating increased endogenous antioxidant activity, while higher doses did not. Thus, FPLEE has the potential to be an effective natural phytopharmaceutical agent in enhancing the body's antioxidant defence against oxidative stress caused by excessive fat consumption, especially at low doses.

Keywords: antioxidants; cholesterol; maceration; oxidative stress; *Pandanus ammaryllifolius*.

Abbreviations: Malondialdehyde (MDA), Deoxyribonucleic Acid (DNA), Ribonucleic Acid (RNA), Reactive Oxygen Species (ROS) , Fragrant Pandan Leaves Ethanol Extract (FPLEE), Body Weight (BW), High-Fat Diet (HFD), Propylthiouracil (PTU), Carboxymethyl Cellulose (CMC), Standard Diet (SD), propylthiouracil (PTU), Carboxymethyl Cellulose (CMC), Enzyme-Linked Immunosorbent Assay (ELISA), Statistical Package for the Social Sciences (SPSS), Superoxide Dismutase (SOD), Glutathione Peroxidase (GPx), Catalase (CAT), Heme Oxygenase-1 (HO-1), Nuclear Factor Erythroid 2-Related Factor 2 (Nrf2), Kelch-Like ECH-Associated Protein 1 (Keap1), Uridine Diphosphate (UDP), UDP glucuronosyltransferase family 1 member A1 (UGT1A1).

INTRODUCTION

Excessive fat consumption, particularly from saturated and trans fatty acids, is a significant contributing factor to metabolic disorders such as obesity, dyslipidemia, atherosclerosis, and cardiovascular disease. Long-term high-fat diets increase lipid accumulation, triggering protein carbonylation and lipid peroxidation, which in turn increase free radical formation and reduce antioxidant defences, ultimately leading to oxidative stress (Jiang, Shuai; Liu, 2021). Malondialdehyde (MDA), the end product of lipid peroxidation, can interact with proteins, Deoxyribonucleic Acid (DNA), and Ribonucleic Acid (RNA). MDA's interaction with these macromolecules can disrupt cellular metabolism, making it often used as a biochemical marker to assess the level of oxidative damage. Elevated MDA levels indicate cell membrane damage due to an imbalance between free radicals and the body's antioxidant capacity (Juan, de la Lastra, Plou, & Pérez-Lebeña, 2021).

The body has natural defence mechanisms against free radicals through both enzymatic and non-enzymatic antioxidant systems. One important non-enzymatic endogenous antioxidant is indirect bilirubin, a heme degradation product capable of neutralising free radicals (Xiao, Xiong, Li, Chen, & Li, 2023). Bilirubin's antioxidant properties stem from its chemical structure, which comprises four pyrrole rings, long conjugated

double bonds, and reactive hydrogen atoms. Bilirubin can interact with electrons in oxygen-free radicals, thereby neutralising Reactive Oxygen Species (ROS) and preventing oxidation (Boriskina et al., 2024). However, under conditions of chronic oxidative stress due to high-fat consumption, the endogenous antioxidant defence capacity is often reduced, so support from exogenous antioxidant sources is needed (Obeagu & Obeagu, 2024).

Pharmacologically, simvastatin is widely used to lower blood lipid levels and prevent complications of atherosclerosis. This drug is effective in suppressing cholesterol synthesis, but its use is often associated with side effects such as myopathy, liver dysfunction, and discomfort in some patients (Ruscica, Ferri, Banach, Sirtori, & Corsini, 2022; Zhang, Halmos, & Westerterp, 2023). These side effects have prompted the need to explore safer, natural alternatives for controlling lipid levels and addressing oxidative stress. One potential candidate that is gaining attention is the use of local herbal plants with high antioxidant activity (Bareetseng, 2022).

Pandanus amaryllifolius is a local plant rich in bioactive compounds, including flavonoids, polyphenols, and alkaloids. The fragrant pandan leaves ethanol extract (FPLEE) possesses optimal biological potential due to its high content of phenolic and flavonoid compounds. These compounds are known to have antioxidant properties that can help protect the body from the effects of oxidative stress by inhibiting free radicals (Padhi, Gupta, Saraugi, Sehrawat, & Routray, 2024). With its potential biological activity, FPLEE has the potential to be developed as a safer, natural alternative to conventional therapies, such as simvastatin, particularly in efforts to improve lipid profiles and control oxidative stress.

This study aimed to investigate the effects of pandan leaf extract on reducing MDA levels and modulating indirect bilirubin activity resulting from excessive fat consumption. The results are expected to provide a scientific basis for the development of pandan leaf extract as a potential phytopharmaceutical candidate for preventing degenerative diseases associated with oxidative stress.

MATERIALS AND METHODS

Study area

This research has received approval from the Research Ethics Committee with the number 057/EC-04/FK-06/UNIZAR/VI/2025. This research is a quantitative experimental study using a posttest-only control group design. This research was carried out in three stages, namely: the first stage was the preparation of FPLEE using the maceration method at the Chemistry Laboratory of the University of Mataram; the second stage was the administration of treatment to test animals carried out at the Pharmaceutical Research and Development Laboratory from July to August 2025; and the third stage included the measurement of MDA, total bilirubin, and direct bilirubin levels. MDA levels were measured using the sandwich Enzyme-Linked Immunosorbent Assay (ELISA) method, while total bilirubin and direct bilirubin levels were measured using the spectrophotometric method. The indirect bilirubin value was obtained from the difference between total bilirubin and direct bilirubin levels. The subjects in this study were 24 male white rats (*Rattus norvegicus*) aged 2–3 months and weighing 150–250 grams. The rats were randomly divided into six groups: normal control (NC), positive control (C+), negative control (C-), and three treatment groups (T1, T2, and T3).

Procedures

The process of making FPLEE

The production of FPLEE was carried out using the maceration method. This maceration method began by washing fresh fragrant pandan leaves with running water to remove dirt, followed by air-drying for approximately two weeks until the leaves are dehydrated. Afterwards, the dried leaves were cut into small pieces and ground into a powder using a blender. The dry powder was then soaked in 96% ethanol at a ratio of 1 kg of powder to 6 L of solvent and left to stand for three days. After the soaking process was complete, the solution was filtered using filter paper to separate the filtrate from the dregs. The resulting filtrate was then evaporated using a rotary evaporator at 50°C to separate the solvent and produce a thick fragrant pandan leaf extract (Sukanty, Ariani, & Yunita, 2024).

The process of making the FPLEE suspension

The FPLEE dosage given to each treatment group was 8 mg/200 g BW/day for T1, 16 mg/200 g body weight/day for T2, and 32 mg/200 g BW/day for T3 (Sukanty et al., 2024). The FPLEE suspension was made using a 1% CMC solution as the solvent. To achieve these doses, the suspension concentrations were 120 mg/30 mL for T1, 240 mg/30 mL for T2, and 480 mg/30 mL for T3. The suspension was administered orally using a probe, at a volume of 2 mL/200 g BW/day, so that each mouse received the appropriate dose for its treatment group. The FPLEE suspension was stored in a dark glass bottle at approximately 20°C to maintain stability and prevent degradation of the active compound due to light exposure.

The process of making a High-Fat Diet (HFD)

The HFD was made by mixing 5 g of 65% sucrose, 10 grams of lard, 83 g of duck egg yolk, 1.5 g of cholesterol powder, and 0.5 g of propylthiouracil (PTU). All ingredients were thoroughly mixed and stirred until a homogeneous mixture is achieved. The HFD was

administered orally at a dose of 2 mL/200 g BW/day for 14 days (Yang et al., 2019).

The process of making the simvastatin suspension
A 1% Carboxymethyl Cellulose (CMC) solution was prepared by mixing 1 gram of CMC with 100 mL of warm water and stirring until completely dissolved. Then, 10.3 mg of simvastatin was dissolved in 100 mL of CMC solution. The simvastatin suspension was administered orally to mice using a tube at a dose of 0.206 mg/200 g BW/day.

The treatment of experimental rats
The rats underwent a seven-day adaptation period, receiving a standard diet (SD) and ad libitum access to drinking water. After the adaptation period, the rats were randomly divided into six groups: NC, C-, C+, and three treatment groups (T1, T2, and T3). All groups, except NC, were fed a HFD for 14 days. After the induction period, the C- was given simvastatin, while the C+ continued to receive the HFD. The T1, T2, and T3 were each given FPLEE at concentrations of 8 mg/200 g BW/day, 16 mg/200 g BW/day, and 32 mg/200 g BW/day for 14 days. After all treatments were completed, the rats were euthanised, and the blood was collected via cardiac puncture for biochemical analysis.

Table 1. The treatment of experimental animals.

Group	Days 1-14	Days 15-28
NC	SD	SD
C+	SD and HFD	SD and HFD
C-	SD and HFD	SD and 0.206 mg/200 g BW/day of simvastatin
T1	SD and HFD	SD and 8 mg/200 g BW/day of FPLEE
T2	SD and HFD	SD and 16 mg/200 g BW/day of FPLEE
T3	SD and HFD	SD and 32 mg/200 g BW/day of FPLEE

The measurement of total bilirubin, direct bilirubin, indirect bilirubin, and MDA levels
The sample used for the test parameters was blood serum. Total and direct bilirubin levels were measured using spectrophotometry, and the results of both parameters were used to calculate indirect bilirubin by dividing the total and direct bilirubin levels. MDA levels were analysed using the sandwich ELISA method.

Data analysis
Data from indirect bilirubin and MDA measurements were analysed using Statistical Package for the Social Sciences (SPSS) version 23 software. The analysis began with normality and homogeneity tests to ensure the data met the requirements for parametric analysis. Next, a One-Way ANOVA test was performed to examine differences between groups, followed by a Bonferroni Post Hoc test to identify groups with significant differences. All analyses were performed at a 5% significance level ($\alpha = 0.05$) or a 95% confidence level.

RESULTS AND DISCUSSION

Result
This study aimed to investigate the effect of FPLEE on indirect bilirubin and MDA levels in rats fed a high-fat diet. Indirect bilirubin was used as an indicator of endogenous antioxidant activity, while MDA levels reflected the level of oxidative stress due to lipid peroxidation.

Table 2. One-Way ANOVA test results on indirect bilirubin and MDA levels.

Group	Indirect Bilirubin			MDA		
	Mean ± SD (mg/dL)	F	p	Mean ± SD (mmol/mL)	F	p
NC	0.0225 ± 0.01258	11.508	0.000**	2.2075 ± 0.18661	0.752	0.595
C+	0.0375 ± 0.02217			2.1275 ± 0.19103		
C-	0.0250 ± 0.01915			2.0150 ± 0.30161		
T1	0.1600 ± 0.04082			1.9700 ± 0.08165		
T2	0.0425 ± 0.04573			2.0425 ± 0.20630		
T3	0.0375 ± 0.03096			2.0625 ± 0.13574		

**p < 0.01

The results of the analysis of indirect bilirubin levels in Table 2 show a statistically significant difference between groups ($F = 11.508$; $p = 0.000$, $p < 0.01$). The C+ group (high-fat feed) showed an increase in indirect bilirubin levels compared to the NC, although the increase was not very striking. The most significant

increase was observed in T1 (8 mg/200 g BW/day), with an average indirect bilirubin level of 0.1600 ± 0.04082 mg/dL, which was higher than in the other groups. In contrast, the C- and T3 exhibited bilirubin levels comparable to the control value, indicating a dose-response difference.

In the MDA parameter, no significant differences were found between treatment groups (F = 0.752; p = 0.595). However, descriptively, the C+ showed the highest MDA levels (2.1275 ± 0.19103 mmol/mL), indicating oxidative stress associated with high fat consumption. The C- had the lowest MDA value (1.0150 ± 0.30161 mmol/mL), followed by T1 (1.9700 ± 0.08165 mmol/mL). In contrast, MDA levels in T2 and T3 tended to remain high and approached those of the C+, indicating that a consistent decrease in MDA had not occurred at any dose of FPLEE.

Table 3. Bonferroni post hoc analysis of indirect bilirubin levels.

Group		p
NC	C+	1.000
	C-	1.000
	T1	0.000**
	T2	1.000
	T3	1.000
C+	C-	1.000
	T1	0.000**
	T2	1.000
	T3	1.000
C-	T1	0.000**
	T2	1.000
	T3	1.000
T1	T2	0.001**
	T3	0.000**
T2	T3	1.000

**p < 0.01

Bonferroni post hoc analysis of indirect bilirubin levels in Table 3 reveals that the administration of FPLEE at a dose of 8 mg/200 g BW/day (group T1) resulted in a significant difference compared to the other groups. Specifically, indirect bilirubin levels in group T1 were significantly higher than those in the NC, C+, C-, T2, and T3, which received higher doses of FPLEE (16 mg/200 g BW/day and 32 mg/200 g BW/day). In contrast, there were no significant differences between groups NC, C+, C-, T2, and T3, indicating that only the 8 mg/200 g BW/day dose of FPLEE significantly increased indirect bilirubin levels. These results indicate that low doses of FPLEE have a more optimal stimulatory effect on endogenous antioxidant activity than higher doses, which is likely due to a non-linear biological response to increasing doses of FPLEE.

Discussion

The body is equipped with endogenous antioxidant systems, including enzymes and non-enzymes. Enzymatic antioxidant systems include superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT), which play a crucial role in neutralising ROS from an early stage (Irato & Santovito, 2021). An example of a non-enzymatic antioxidant system is bilirubin, which acts as a complement to other antioxidants (He et al., 2025).

In this study, indirect bilirubin levels showed varying responses across treatment groups. In the NC and C+ groups fed only an HFD, indirect bilirubin levels did not differ significantly. The indirect bilirubin result is consistent with the results of MDA as a biomarker of oxidative stress, which also showed no differences between the groups. Enzymatic defence mechanisms may contribute to the absence of differences in MDA levels between groups in this study, indicating that the body's enzymatic antioxidant system likely works effectively in addressing oxidative stress. In contrast, indirect bilirubin in this group acts as a complement to other antioxidants (He et al., 2025; Lankin, Tikhaze, & Melkumyants, 2023). This phenomenon may also occur due to the role of bioactive compounds in pandan leaves, such as flavonoids and alkaloids. Flavonoids contain hydroxyl groups that stabilise and inhibit the production of free radicals. Flavonoids also act as bidentate ligands, chelating redox-active metals and enhancing the activity of antioxidant enzymes, such as those that scavenge vitamin E radicals (Jomova et al., 2025).

In the C- that received HFD and simvastatin treatment, indirect bilirubin levels were also not different from those in NC. Simvastatin is known to have pleiotropic effects in the form of antioxidant activity and endothelial protection, which include increasing the expression of endogenous antioxidant enzymes and reducing ROS production. Furthermore, simvastatin can affect bilirubin metabolism by increasing the expression of Heme Oxygenase-1 (HO-1), an enzyme that catalyses the degradation of endogenous iron protoporphyrin heme into biliverdin, ferrous iron, and carbon monoxide. The formed biliverdin is reduced by biliverdin reductase to bilirubin (Consoli, Sorrenti, Grosso, & Vanella, 2021; Zhu et al., 2024). Thus, simvastatin supports the production of indirect bilirubin as an antioxidant. However, MDA levels were not significantly different across groups, indicating that severe oxidative stress requiring antioxidant system compensation was not present. Consequently, indirect bilirubin levels as an antioxidant did not increase drastically even though simvastatin was administered to the C-. The low concentration of ROS suggests a physiological role for ROS in redox regulation, such as regulating cell function by modifying the activity of enzymes and transcription factors (Amponsah-Offeh, Diaba-Nuhoho, Speier, & Morawietz, 2023; Lennicke & Cocheme, 2021).

Interestingly, in the treatment group with FPLEE, especially T1, there was an increase in indirect bilirubin levels compared to the control group. In relation to bilirubin, flavonoids can activate the nuclear factor erythroid 2-related factor 2 (Nrf2) signal transduction

pathway, where the bond between Kelch-like ECH-associated protein 1 (Keap1) and Nrf2 is broken, causing the translocation of Nrf2 from the cytosol to the nucleus to induce the transcription of genes containing antioxidant response elements, such as HO-1, so that the production of indirect bilirubin increases (Moratilla-Rivera, Sánchez, Valdés-González, & Gómez-Serranillos, 2023; Sang et al., 2025). In addition to this mechanism, flavonoids also inhibit Uridine Diphosphate (UDP) glucuronosyltransferase family 1 member A1 (UGT1A1), an enzyme that conjugates indirect bilirubin with glucuronic acid to become direct bilirubin (Žiberna, Jenko-Pražnikar, & Petelin, 2021). The increase in indirect bilirubin in T1 reflects the body's adaptive response to exposure to phytochemical compounds, in which endogenous antioxidant capacity is strengthened through increased reserves of indirect bilirubin as a non-enzymatic antioxidant that complements the work of other antioxidants (He et al., 2025).

However, in groups T2 (16 mg/200 g BW/day) and T3 (32 mg/200 g BW/day), indirect bilirubin levels did not increase. It may be explained by a possible dose effect, where higher flavonoid concentrations actually suppress indirect bilirubin concentrations. Although the exact mechanism of flavonoids in reducing bilirubin levels is not yet fully understood, the dual effects of flavonoids may explain this phenomenon. In addition to being antioxidants, flavonoids can act as prooxidants, where the flavonoid catechol ring can oxidise low-molecular-weight antioxidants (Jomova et al., 2025). Bilirubin is a low-molecular-weight antioxidant (Boriskina et al., 2024). Oxidation of indirect bilirubin decreases indirect bilirubin levels and increases biliverdin levels (Žiberna et al., 2021). It may be the underlying cause of low bilirubin concentrations in T2 and T3.

CONCLUSIONS

The results of this study indicate that although HFD did not significantly affect MDA levels, administration of FPLEE, especially at low doses (8 mg/200 g BW/day), was able to increase indirect bilirubin levels as part of the body's defence mechanism against ROS exposure. This increase indicates endogenous antioxidant activity that is preventive and adaptive. These findings support the potential of pandan wangi as a promising phytotherapeutic agent in efforts to prevent oxidative damage due to free radical exposure.

Acknowledgements: The author would like to thank the Ministry of Higher Education, Science, and Technology of the Republic Indonesia (Kemdiktisaintek), Bumigora University, and all colleagues who helped in carrying out this research.

Authors' Contributions

Ni Made Wiasty Sukanty contributed to determining the research topic, creating the FPLEE, analyzing the research data, and drafting the research article. Laksmi Nur Fajriani was involved in the creation of the FPLEE and HFD. Agus Saputra monitored the rat care, euthanized the rats, and collected blood samples. Iptan Ariki, I Ketut Agus Yura Aditya, and Angeline Devon Venansius were involved in the rat care and treatment. All authors have read and approved the final version of the manuscript.

Competing Interests: The authors declare that there are no competing interests.

Funding: This research was funded by the Ministry of Higher Education, Science, and Technology of the Republic Indonesia (Kemdiktisaintek) through the Research and Community Service (BIMA) Program in 2025.

REFERENCES

Amponsah-Offeh, M., Diaba-Nuhoho, P., Speier, S., & Morawietz, H. (2023). Oxidative Stress, Antioxidants and Hypertension. *Antioxidants*, *12*(281), 1–22. https://doi.org/10.3390/antiox12020281

Bareetseng, S. (2022). The Worldwide Herbal Market: Trends and Opportunities. *Journal of Biomedical Research & Environmental Sciences*, *3*(5), 575–584. https://doi.org/10.37871/jbres1482

Boriskina, O. S., Eliseeva, T. I., Tush, E. V., Soodaeva, S. K., Khramova, R. N., Khristianovich, E. A., … Kubysheva, N. I. (2024). Bronchial Asthma and Bilirubin. *Opera Medica et Physiologica*, *11*(1), 115–122. https://doi.org/10.24412/2500-2295-2024-1-115-122

Consoli, V., Sorrenti, V., Grosso, S., & Vanella, L. (2021). Heme Oxygenase-1 Signaling and Redox Homeostasis in Physiopathological Conditions. *Biomolecules*, *11*(589), 1–23. https://doi.org/10.3390/biom11040589

He, M., Lin, X., Zheng, Y., Liang, Q., Li, M., Qiang, W., … Shi, B. (2025). Indirect bilirubin is inversely associated with diabetic retinopathy risk and is a potential predictive biomarker. *World Journal of Diabetes*, *16*(9), 1–12. https://doi.org/10.4239/wjd.v16.i9.110590

Irato, P., & Santovito, G. (2021). Enzymatic and Non-Enzymatic Molecules with Antioxidant Function. *Antioxidants*, *10*(579), 1–4. https://doi.org/10.3390/antiox10040579

Jiang, Shuai; Liu, H. L. C. (2021). Dietary Regulation of Oxidative Stress in Chronic Metabolic Diseases. *Foods*, *10*(1854), 1–18.

Jomova, K., Alomar, S. Y., Valko, R., Liska, J., Nepovimova, E., Kuca, K., & Valko, M. (2025). Flavonoids and their role in oxidative stress, inflammation, and human diseases. *Chemico-Biological Interactions*, *413*, 1–44. https://doi.org/10.1016/j.cbi.2025.111489

Juan, C. A., de la Lastra, J. M. P., Plou, F. J., & Pérez-Lebeña, E. (2021). The Chemistry of Reactive Oxygen Species (ROS) Revisited: Outlining Their Role in Biological Macromolecules (DNA, Lipids and Proteins) and Induced Pathologies.

International Journal of Molecular Sciences, *22*(4642), 1–21. https://doi.org/10.3390/ijms22094642

Lankin, V. Z., Tikhaze, A. K., & Melkumyants, A. M. (2023). Malondialdehyde as an Important Key Factor of Molecular Mechanisms of Vascular Wall Damage under Heart Diseases Development. *International Journal of Molecular Sciences*, *24*(128), 1–13. https://doi.org/10.3390/ijms24010128

Lennicke, C., & Cocheme, H. M. (2021). Redox metabolism: ROS as specific molecular regulators of cell signaling and function. *Molecular Cell*, *81*(18), 3691–3707. https://doi.org/10.1016/j.molcel.2021.08.018

Moratilla-Rivera, I., Sánchez, M., Valdés-González, J. A., & Gómez-Serranillos, M. P. (2023). Natural Products as Modulators of Nrf2 Signaling Pathway in Neuroprotection. *International Journal of Molecular Sciences*, *24*(3748), 1–26. https://doi.org/10.3390/ijms24043748

Obeagu, E. I., & Obeagu, G. U. (2024). Antioxidants and the Prevention of Neonatal Jaundice: A Narrative Review. *International Journal of Medical Sciences and Pharma Research*, *10*(4), 28–34. https://doi.org/10.22270/ijmspr.v10i4.120

Padhi, S., Gupta, K. K., Saraugi, S. S., Sehrawat, R., & Routray, W. (2024). Comparative analysis of non-thermal technologies and solvent systems for the extraction and characterization of phytochemicals and antioxidants in Pandanus amaryllifolius. *Chemical Engineering Research and Design*, *210*, 212–229. https://doi.org/10.1016/j.cherd.2024.08.036

Ruscica, M., Ferri, N., Banach, M., Sirtori, C. R., & Corsini, A. (2022). Side effects of statins: from pathophysiology and epidemiology to diagnostic and therapeutic implications. *Cardiovascular Research*, *118*(17), 3288–3304. https://doi.org/10.1093/cvr/cvac020

Sang, Y., Huang, W., Lin, J., Yang, L., Zhou, Y., Yu, C., … Kong, X. (2025). Fluorinated sulfonamide-flavonoid derivatives as novel Keap1-Nrf2 inhibitors: Potent induction of cytoprotective gene HO-1 in vivo. *European Journal of Medicinal Chemistry*, *291*. https://doi.org/10.1016/j.ejmech.2025.117650

Sukanty, N. M. W., Ariani, F., & Yunita, L. (2024). The Effectiveness of Fragrant Pandan Leaves Ethanol Extract in Reducing Cholesterol Levels In High-Fat Diet-Induced Rats. *Biology, Medicine, & Natural Product Chemistry*, *13*(2), 505–509. https://doi.org/10.14421/biomedich.2024.132.505-509

Xiao, W., Xiong, Y., Li, Y., Chen, Z., & Li, H. (2023). Non-Enzymatically Colorimetric Bilirubin Sensing Based on the Catalytic Structure Disruption of Gold Nanocages. *Sensors*, *23*(2969), 1–13. https://doi.org/10.3390/s23062969

Yang, R., Wang, C., Ye, H., Gao, F., Cheng, J., Zhang, T., & Guo, M. (2019). Effects of feeding hyperlipidemia rats with symbiotic oat-based frozen yogurt on serum triglycerides and cholesterol. *Food Science and Nutrition*, *7*(3), 1096–1103. https://doi.org/10.1002/fsn3.949

Zhang, H., Halmos, B., & Westerterp, M. (2023). Statins for ACTA2 mutation-driven atherosclerosis? *Europan Heart Journal*, *44*(29), 2727–2729. https://doi.org/10.1093/eurheartj/ehad364

Zhu, Y., Li, D., Li, J., Wang, Y., Chen, Z., Lv, Q., … Zhang, W. (2024). Association of elevated baseline bilirubin caused by preadmission statin use with cardiovascular prognosis in patients undergoing elective percutaneous coronary intervention. *Scientific Reports*, *14*(1), 1–10. https://doi.org/10.1038/s41598-024-71497-x

Žiberna, L., Jenko-Pražnikar, Z., & Petelin, A. (2021). Serum Bilirubin Levels in Overweight and Obese Individuals: The Importance of Anti-Inflammatory and Antioxidant Responses. *Antioxidants*, *10*(9), 1–16. https://doi.org/10.3390/antiox10091352