Sinteza eISSN : 2797-8133
Jurnal Farmasi Klinis dan Sains Bahan Alam
Vol.5, No.2, Agustus 2025, Hal. 92-101

Bioactive Compound Profiling of Ethyl Acetate Fraction from Oil Palm (Elaeis guineensis Jacq.) Leaves using Liquid Chromatography High Resolution Mass Spectrometry (LC-HRMS)

Deni Setiawan[1]*, Samsul Hadi[1], Nur Mahdi[1], Nurul Mardiati[1], Normaidah[2], Nabila Hadiah Akbar[2], Muhammad Rasyid Ridha[3], Fitri Apriliany[4]
[1] Department of Pharmacy, Faculty of Mathematics and Natural Sciences, Lambung Mangkurat University Banjarbaru, South Kalimantan, Indonesia
[2] Pharmacist Professional Study, Faculty of Mathematics and Science, Lambung Mangkurat University. Banjarbaru, Indonesia.
[3] Research Organization for Health, National Research and Innovation Agency, Republic of Indonesia. Bogor, Indonesia
[4] Department of Pharmacy, Faculty of Health, Bumigora University Mataram, Indonesia

**Corresponding author: Deni Setiawan email:deni.setiawan@ulm.ac.id*

Submitted: 04-05-2025 *Revised:* 17-06-2025 *Accepted:* 18-06-2025
DOI: 10.29408/sinteza.v5i2.30147

ABSTRACT

Oil palm leaves could yield various health benefits, potentially leading to innovative applications in natural remedies, supplements, and dietary products. Targeted extraction and sophisticated analytical methods have become necessary for investigating bioactive compounds in plant materials. The combination of liquid chromatography and high-resolution mass spectrometry (LC–HRMS) makes for a potent technique for analyzing a wide range of metabolites, allowing for the precise and sensitive identification of various plant compounds. This investigation aimed to examine the active compounds in the ethyl acetate fraction of *Elaeis guineensis* leaves using LC–HRMS to identify potential new avenues for drug research. The simplicia was extracted by completely immersing 500 g of granules in acetone for three days. The crude extract was fractionated with n-hexane, ethyl acetate, and n-butanol solvents to separate components according to their polarity. The ethyl acetate part was analyzed using LC–HRMS with specific settings, including a temperature of 30°C and a gas flow rate of 11.01 L/min. The extract yield from dense oil palm leaves was 32.5 g, equivalent to 6.5%. Subsequently, the components were separated by fractionating the complete yield. The n-hexane fraction yield was 7.085 g or 21.83%, the ethyl acetate fraction yield was 3.38 g or 10.4%, the n-butanol fraction yield was 8.84 g or 27.2%, and the remaining fraction yield was 3.93 g or 12.1%. In conclusion, oil palm leaves are a prospective source of zingerol compounds, suggesting potential to be used as an alternative to rhizomes.

Keywords: Oil palm leave, *Elaeis guineensis* Jacq., LC-HRMS, Zingerol,

INTRODUCTION

Oil palm (*Elaeis guineensis* Jacq.) is widely cultivated in tropical regions, particularly in Southeast Asia, due to its economic importance as a major source of edible oil and industrial raw materials (Alhaji et al., 2024). While most studies and applications have focused on the oil derived from the fruits and kernels, the leaves of oil palm remain an underutilized by-product despite abundant availability in plantations (Abogunrin-Olafisoye et al., 2024). Recent studies have shown that oil palm leaves contain useful compounds like flavonoids, phenolic acids, and other substances that may help with health issues, unveiling their roles in protecting the body as antioxidants, reducing inflammation, fighting germs, and preventing cancer (Mohamed, 2014). There has been evidence that oil palm leaves could be harnessed for various health benefits, potentially leading to innovative uses in food products, supplements, and natural remedies (Lau et al., 2024). Further research into their

nutritional value and therapeutic properties may pave the way for new applications, enhancing the sustainability and profitability of oil palm cultivation (Nabila et al., 2023). Our previous study indicated that the ethanol extract of oil palm leaves contains tannins, saponins, flavonoids, and alkaloids that have larvicidal activity (Setiawan et al., 2025). Other studies also showed the same contents, in addition to analgesic activity in mice induced by acetic acid (Zulfansyah et al., 2023).

The exploration of bioactive compounds in plant materials often requires targeted extraction and advanced analytical techniques. Solvent partitioning plays a crucial role in fractionating complex plant matrices to enrich specific groups of compounds, whereas identification of fractions could be conducted through a combination of chromatographic and spectroscopic techniques (Gil-Martín et al., 2022). Ethyl acetate, a moderately polar solvent, is commonly used to extract phenolic and flavonoid-rich fractions, which are known to harbor significant biological activity (Susanti et al., 2024). However, comprehensive profiling of these fractions in oil palm leaves remains limited. Liquid chromatography combined with high-resolution mass spectrometry (LC-HRMS) is a powerful method for studying many different metabolites, enabling the detection of various plant chemicals with great sensitivity and accuracy (Anagnostopoulou et al., 2025). This technique allows for precise mass detection, structural elucidation, and tentative identification of unknown compounds, making it ideal for phytochemical profiling of complex plant extracts (Altemimi et al., 2017). Because more and more people have taken interest in using agricultural leftovers and there is a rising need for new natural substances in medicine and health products, it is important to thoroughly analyze the plant chemicals in the ethyl acetate fraction from oil palm leaves. Therefore, it was the aim of this study to examine the active compounds in the ethyl acetate fraction of oil palm (*Elaeis guineensis*) leaves using LC–HRMS to discover possible new options for drug research. By identifying and characterizing these compounds, we hope to uncover novel therapeutic agents that can be developed into effective treatments. Additionally, it is expected that this research could contribute to sustainable practices by promoting the utilization of by-products from oil palm cultivation.

METHODS

Materials and Instruments

Oil palm leaves were taken from Kuranji District, Tanah Bumbu Regency, South Kalimantan. The materials used were acetone (*Merck*, Germany), ethyl acetate (*Merck*, Germany), n-hexane (*Merck*, Germany), acetonitrile (*Merck*, Germany), buffer acetate, and aquadest. The instruments used were an analytical balance (*Ohaus*, USA), a macerator, a rotary evaporator (*B-ONE*, Chinese), and an instrument for conducting LC–HRMS (Liquid Chromatography–High-Resolution Mass Spectrometry) (*Thermo*, USA).

Procedures

Sample extraction

Some oil palm leaf samples were cleaned by rinsing with running water and were carefully inspected for any contaminants. After rinsing, the plant samples were sliced and dried in an oven at 40°C for three hours. Sample standardization was carried out based on specific criteria. Simplicia extraction was conducted by completely immersing 500 g of powder in acetone. The mixture was stirred every six hours, and the solvent was changed every 24 hours three times. The liquid extract was evaporated in a rotary evaporator, and the water bath was maintained at 50°C until the weight reached a stable state.

Fractionation

Crude extract was fractionated with n-hexane, ethyl acetate, and n-butanol solvents to separate components based on their polarity. N-hexane is a non-polar solvent that primarily extracts lipophilic (non-polar) compounds such as fatty acids and terpenoids. Ethyl acetate is a semi-polar solvent that is effective for extracting moderately polar compounds like flavonoids, alkaloids, or phenolic acids. n-Butanol is a polar solvent that targets more

hydrophilic (polar) compounds such as glycosides and polar phenolics. Thick extract was weighed and dissolved in distilled water with a 1:50 extract-to-water ratio, which was modified from a previous method (Ikhwan Rizki et al., 2022). The solution was then subjected to liquid-liquid fractionation with n-hexane with a ratio of extract solution to n-hexane of 1:10. The bottom layer was fractionated again, and the top layer was collected as the n-hexane liquid fraction. n-hexane was added repeatedly until it was clear. The bottom layer was fractionated again with ethyl acetate with a ratio of 1:10. The bottom layer was fractionated repeatedly with ethyl acetate, and the top layer was collected as the ethyl acetate fraction. The repetition was continued until the top layer became clear. The bottom layer was fractionated again with n-butanol with a ratio of 1:10. The bottom layer was fractionated repeatedly with n-butanol, and the top layer was collected as the n-butanol fraction. The repetition was continued until the top layer became clear. The bottom layer was separated and became the residual fraction or water fraction. The n-hexane, ethyl acetate, n-butanol, and water fractions were collected and dried using a rotary evaporator. After drying, they were weighed, and each percentage of yield was calculated.

LC-HRMS Analysis

LC–HRMS analysis was performed on the ethyl acetate fraction using specific settings, including a gas temperature of 30°C, a gas flow of 11.01 L/min, a nebulizer pressure of 40 psi, a VCap of 3,500 V, a fragmentor voltage of 175 V, a skimmer voltage of 65.0 V, and an octopole RF peak of 750 V. The elution solvent comprised acetonitrile, 5 mM acetate buffer, and air, with a flow rate of 1.5 mL/min. The elution gradient commenced at 5% acetonitrile for 0.1 minutes, increased to 30% acetonitrile over 10 minutes, reached 80% acetonitrile at 32 minutes, and finally returned to the original conditions. The column temperature was consistently maintained at 30°C throughout the operation. The diode flow detector cell routed the column elution to the Q-TOF high-resolution mass spectrometer, equipped with an electrospray interface (Aryal et al., 2021).

Data Analysis

The raw data from LC–HRMS was analyzed using MZmine 2, and chemical identification was carried out with Mestre Nova 12.0 by referencing the PubChem, Dictionary of Natural Products 2, ChemSpider, and METLIN databases.

RESULTS AND DISCUSSION

Extraction and Fractionation

After extraction, a water bath at 50°C evaporated the filtrate, yielding a concentrated extract with a consistent weight. The yield of the extract from thick oil palm leaves was 32.5 g or 6.5%, lower than the 7.2% ethanol extract yield obtained in our previous study. This discrepancy might be attributable to variations in the extraction methods or the specific conditions under which the leaves were processed. Further investigation into the solvent properties and extraction times could help optimize the yield for future studies (Duan et al., 2024). The entire yield was then fractionated to separate the components. The yield of the n-hexane fraction was 7.085 g or 21.83%, the yield of the ethyl acetate fraction was 3.38 g or 10.4%, the yield of the n-butanol fraction was 8.84 g or 27.2%, and the yield of the remaining fraction was 3.93 g or 12.1%. These results indicate a successful separation of the components, highlighting the efficiency of the fractionation process. Further analysis of each fraction could provide insights into their potential applications and overall purity.

LC-HRMS Result

LC–HRMS is typically conducted to provide detailed information about the composition and structure of complex mixtures. Researchers can identify and quantify various compounds using high-resolution mass spectrometry, leading to a deeper understanding of chemical interactions and potential applications in pharmaceuticals and environmental science (Hulleman et al., 2023). This advanced technique allows for detecting

trace levels of substances, making it invaluable for studies in metabolomics and proteomics. Additionally, its ability to analyze samples with minimal preparation enhances the efficiency of research and development processes across multiple disciplines. High-resolution mass spectrometry can also be combined with other analytical techniques, like chromatography, to yield even more thorough information about the makeup of the sample (Morlock, 2021). This better equips scientiests in addressing challenges in drug development and environmental monitoring, ultimately contributing to advancements that benefit society as a whole.

Zingerol, as a primary compound (Table 1), has been extensively studied for its pharmacological activity, which involves anti-inflammatory and antioxidant properties. Researchers are exploring its effectiveness in various therapeutic applications, particularly in managing arthritis and chronic pain. These studies suggest that zingerol may play an essential role in developing natural treatments for these conditions, potentially offering safer alternatives to conventional therapies (Ahmad et al., 2018). As research continues to uncover its full benefits, zingerol may become a valuable addition to holistic health practices. Practitioners increasingly incorporate it into dietary supplements and health products, aiming to harness its properties for better patient outcomes. As public interest in natural health solutions increases, zingerol's popularity is likely to increase, leading to further exploration of its uses in preventive and therapeutic contexts. Rhizomes like ginger contain abundant amounts of zingerol. As more people seek alternatives to traditional medicines, integrating compounds such as zingerol into mainstream healthcare could transform patient care significantly (Sharma et al., 2023). This shift may inspire healthcare providers to consider natural compounds alongside conventional treatments, thereby encouraging a more holistic approach to treatment.

Some other identified components are echinenone, mitragynine, and lupeol. Researchers have examined these chemicals for their diverse biological activity and potential health advantages. They have been persistently investigating their functions in traditional medicine and their applications in contemporary pharmacology. As understanding of these chemicals advances, interest in their potential in support of novel therapeutic techniques is increasing. Current research seeks to elucidate their mechanisms of action and assess their effectiveness in addressing various health issues. Echinenone, mitragynine, and lupeol have each been integral to ancient medicinal practices globally. Echinenone, a carotenoid present in some algae, has been historically employed for its antioxidant characteristics, whereas mitragynine (Setiawansyah et al., 2024), extracted from the kratom tree, has been utilized in Southeast Asia as analgesic and stimulant (Cinosi et al., 2015). Lupeol, a triterpene in numerous fruits, is esteemed in Ayurvedic medicine for its anti-inflammatory and analgesic properties (Dalimunthe et al., 2024). Each of these substances embodies a profound legacy of herbal treatments transmitted through the centuries, illustrating the varied methodologies of health and wellness across distinct cultural contexts.

Table 1. LC-HRMS data obtained from the ethyl acetate fraction detailing the identities of 20 compounds as major compounds.

Comp. No	Compound Name	*m/z*1	Retention Time (min)	[M − H]−	Area (Max)	Compound CID
1	Zingerol	195,10952	6,013	C11 H16 O3	1409066007	7733
2	4-({[4-(3-ethyl-7-morpholin-4-yl-3H-[1,2,3] triazolo[4,5-d]pyrimidin-5-yl)phenyl]carbamoyl}amino)-N-(2-pyridin-2-ylethyl)benzamide	591,26714	15,021	C31 H32 N10 O3	1129773970	44819375
3	1-(3-{[5-Carbamoyl-4-ethyl-6-(4-nitro-phenyl)-2-oxo-3,6-dihydro-2H-pyrimidine-1-carbonyl]-amino}-propyl)-4-phenyl-piperidine-4-carboxylic acid methyl ester	591,26714	14,821	C30 H36 N6 O7	973471625,9	9916549
4	Echinenone	549,41649	17,408	C40 H54 O	972658147,9	5281236
5	N-tert-butoxycarbonyl-L-tryptophyl-glycyl-L-alpha-aspartyl-L-phenylalaninamide	621,27745	15,752	C31 H38 N6 O8	623930694,6	44376687
6	Linalyl Propionate	209,16159	7,631	C13 H22 O2	456659505,8	62328
7	Mitragynine	397,21962	8,499	C23 H30 N2 O4	390329239,7	3034396
8	(1R,2S,5S,10S,14R,15R,23R)-N-benzyl-1,2,8,8,15,22,22-heptamethyl-19,20-diazahexacyclo [12.11.0.02,11.05,10.015,23.017,21] pentacosa-11,17(21),18-triene-5-carboxamide	566,41881	17,332	C38 H53 N3 O	333234359,5	127032735
9	Lupeol	425,38534	18,731	C30 H50 O	331930100,7	259846
10	3-BHA	179,11463	9,059	C11 H16 O2	323147794,8	8456
11	N-[(2S)-1-[[(2S)-5-(diaminomethylideneamino)-1-[[(2S)-1-[4-(diaminomethy lideneamino) butylamino]-1-oxo-3-(4-phenylphenyl)propan-2-yl]amino]-1-oxopentan-2-yl]amino]-1-oxo-3-(4-phenylphenyl)propan-2-yl]decanamide	885,5584	22,283	C51 H70 N10 O4	299149497,6	122696354
12	benzyl N-[4-[[5-cyano-4-(3-hydroxy-3-methylazetidin-1-yl) pyrimidin-2-yl] amino] cyclohexyl]-N-[5-(2-methoxypyrimidin-5-yl) pyrimidin-2-yl] carbamate	621,27745	15,526	C32 H34 N10 O4	252040040,2	153347599
13	2-Amino-1,3,4-octadecanetriol	316,29207	9,899	C18 H39 N O3	219541955,7	122121

14	(3β,24R,24′R)-fucosterol epoxide	427,36443	19,076	C29 H48 O2	179201784,8	2723897
15	(2R,5S)-2-[[bis(4-methoxyphenyl)-phenylmethoxy] methyl]-5-[4-[[bis[(1-octyltriazol-4-yl) methyl] amino] methyl] triazol-1-yl] oxolan-3-ol	901,55309	21,639	C51 H70 N10 O5	172122433,3	166480337
16	3,5,5-trimethyl-4-[3-[3,4,5-trihydroxy-6-(hydroxymethyl) oxan-2-yl] oxybutyl] cyclohex-2-en-1-one	371,21413	6,412	C19 H32 O7	157858984,6	14135394
17	dibutyl (Z)-but-2-enedioate	227,13591	8,29	C12 H20 O4	143346444,2	5271569
18	p-cymene; 1-methyl-4-propan-2-ylbenzene	133,10936	7,631	C10 H14	123339639	7463
19	5-Benzyldihydro-2(3H)-furanone	175,08338	0,886	C11 H12 O2	109143263,2	15717
20	β-Ionone	191,15112	6,412	C13 H20 O	104986141,5	638014

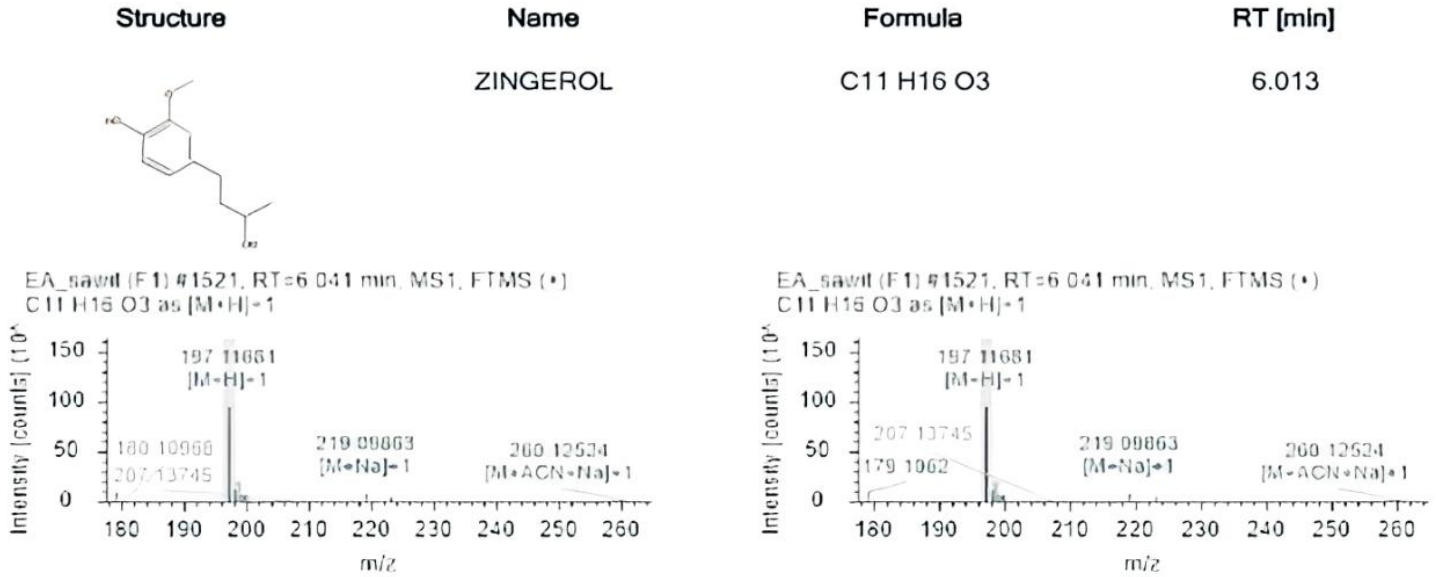

Figure 1. Structure and chromatogram of Zingerol

Zingerol demonstrates significant therapeutic potential through its diverse bioactivities, particularly through its anti-inflammatory and antioxidant properties. Its anti-inflammatory mechanisms, including the inhibition of pro-inflammatory cytokines and COX-2 enzymes, make it a promising avenue to treating chronic conditions such as rheumatoid arthritis, inflammatory bowel disease, and Alzheimer's disease (Gupta et al., 2025). Additionally, its antioxidant activity positions it as a valuable agent against oxidative-stress-related disorders, including cardiovascular diseases, diabetes, and neurodegenerative conditions, through its ability to neutralize reactive oxygen species (ROS) and enhance endogenous antioxidant defenses(Jomova et al., 2023). The compound's anticancer properties are equally noteworthy, as it can induce apoptosis, inhibit angiogenesis, and suppress metastasis in cancer cells, potentially complementing existing chemotherapeutic agents or serving as standalone treatments, similar to other natural compounds, like curcumin and resveratrol (Cui et al., 2025).

The development of zingerol as a therapeutic agent can be advanced through several strategic approaches, including structure–activity relationship (SAR) analysis to optimize its pharmacokinetic properties and the exploration of combination therapies. SAR studies could guide the rational design of derivatives with enhanced potency and selectivity by modifying hydroxyl or alkyl groups to improve solubility, stability, and bioavailability (Ait Lahcen et al., 2024). Meanwhile, combination therapy investigations, particularly with anti-inflammatory drugs or chemotherapeutic agents, could yield synergistic effects while reducing adverse effects. To establish zingerol as a viable medicinal agent, comprehensive preclinical studies focusing on pharmacokinetics, toxicity, and efficacy in relevant disease models are essential, followed by clinical trials to evaluate its safety and efficacy in humans, and ultimately by working toward regulatory approval.

CONCLUSION

Oil palm leaves provide a promising source of Zingerol components, as they include the principal constituent zingerol, which can serve as an alternative to rhizomes. Its potential effects in reducing oxidative stress may support cardiovascular health and enhance immune function.

ACKNOWLEDGEMENT

In order to conduct this research, the authors would like to thank Universitas Lambung Mangkurat.

REFERENCES

Abogunrin-Olafisoye, O. B., Adeyi, O., Adeyi, A. J., & Oke, E. O. (2024). Sustainable utilization of oil palm residues and waste in nigeria: practices, prospects, and environmental considerations. *Waste Management Bulletin*, *2*(1), 214–228. https://doi.org/10.1016/j.wmb.2024.01.011

Ahmad, B., Rehman, M. U., Amin, I., Mir, M. ur R., Ahmad, S. B., Farooq, A., Muzamil, S., Hussain, I., Masoodi, M., & Fatima, B. (2018). Zingerone (4-(4-hydroxy-3-methylphenyl) butan-2-one) protects against alloxan-induced diabetes via alleviation of oxidative stress and inflammation: Probable role of NF-kB activation. Saudi Pharmaceutical Journal, 26(8), 1137–1145. https://doi.org/10.1016/j.jsps.2018.07.001

Ait Lahcen, N., Liman, W., Oubahmane, M., Hdoufane, I., Habibi, Y., Alanazi, A. S., Alanazi, M. M., Delaite, C., Maatallah, M., & Cherqaoui, D. (2024). Drug design of new anti-EBOV inhibitors: QSAR, homology modeling, molecular docking and molecular dynamics studies. *Arabian Journal of Chemistry*, *17*(9), 1–13. https://doi.org/10.1016/j.arabjc.2024.105870

Alhaji, A. M., Almeida, E. S., Carneiro, C. R., da Silva, C. A. S., Monteiro, S., & Coimbra, J. S. dos R. (2024). Palm Oil (Elaeis guineensis): A Journey through Sustainability, Processing, and Utilization. *Foods*, *13*(17), 2814. https://doi.org/10.3390/foods13172814

Altemimi, A., Lakhssassi, N., Baharlouei, A., Watson, D. G., & Lightfoot, D. A. (2017). Phytochemicals: Extraction, isolation, and identification of bioactive compounds from plant extracts. *Plants*, *6*(4). https://doi.org/10.3390/plants6040042

Anagnostopoulou, K., Alampanos, V., Evgenidou, E., & Lambropoulou, D. A. (2025). Liquid chromatography-high resolution mass spectrometry based analysis of persistent mobile organic compounds in aqueous samples: Method development and optimization. *Green Analytical Chemistry*, *12*, 100214. https://doi.org/10.1016/j.greeac.2025.100214

Aryal, B., Adhikari, B., Aryal, N., Bhattarai, B. R., Khadayat, K., & Parajuli, N. (2021). LC-HRMS Profiling and Antidiabetic, Antioxidant, and Antibacterial Activities of Acacia catechu (L.f.) Willd. *BioMed Research International*, *2021*(11), 1. https://doi.org/10.1155/2021/7588711

Cinosi, E., Martinotti, G., Simonato, P., Singh, D., Demetrovics, Z., Roman-Urrestarazu, A., Bersani, F. S., Vicknasingam, B., Piazzon, G., Li, J. H., Yu, W. J., Kapitány-Fövény, M., Farkas, J., Di Giannantonio, M., & Corazza, O. (2015). Following “the Roots” of Kratom (Mitragyna speciosa): The Evolution of an Enhancer from a Traditional Use to Increase Work and Productivity in Southeast Asia to a Recreational Psychoactive Drug in Western Countries. *BioMed Research International*, *2015*. https://doi.org/10.1155/2015/968786

Cui, D., Zhang, C., Zhang, L., Zheng, J., Wang, J., He, L., Jin, H., Kang, Q., Zhang, Y., Li, N., Sun, Z., Zheng, W., Wei, J., Zhang, S., Feng, Y., Tan, W., & Zhong, Z. (2025). Natural anti-cancer products: insights from herbal medicine. *Chinese Medicine (United Kingdom)*, *20*(1), 1–91. https://doi.org/10.1186/s13020-025-01124-y

Dalimunthe, A., Carensia Gunawan, M., Dhiya Utari, Z., Dinata, M. R., Halim, P., Estherina S. Pakpahan, N., Sitohang, A. I., Sukarno, M. A., Yuandani, Harahap, Y., Setyowati, E. P., Park, M. N., Yusoff, S. D., Zainalabidin, S., Prananda, A. T., Mahadi, M. K., Kim, B., Harahap, U., & Syahputra, R. A. (2024). In-depth analysis of lupeol: delving into the diverse pharmacological profile. In *Frontiers in Pharmacology* (Vol. 15). Frontiers Media SA. https://doi.org/10.3389/fphar.2024.1461478

Duan, X., Subbiah, V., Agar, O. T., Barrow, C. J., Ashokkumar, M., Dunshea, F. R., & Suleria, H. A. R. (2024). Optimizing extraction methods by a comprehensive experimental approach and characterizing polyphenol compositions of Ecklonia radiata. *Food Chemistry*, *455*, 1. https://doi.org/10.1016/j.foodchem.2024.139926

Gil-Martín, E., Forbes-Hernández, T., Romero, A., Cianciosi, D., Giampieri, F., & Battino, M. (2022). Influence of the extraction method on the recovery of bioactive phenolic compounds from food industry by-products. In *Food Chemistry* (Vol. 378). Elsevier Ltd. https://doi.org/10.1016/j.foodchem.2021.131918

Gupta, J., Sharma, B., Sorout, R., Singh, R. G., Ittishree, & Sharma, M. C. (2025). Ginger (Zingiber officinale) in traditional Chinese medicine: A comprehensive review of its anti-inflammatory properties and clinical applications. *Pharmacological Research - Modern Chinese Medicine*, *14*(1), 1–11. https://doi.org/10.1016/j.prmcm.2024.100561

Hulleman, T., Turkina, V., O’Brien, J. W., Chojnacka, A., Thomas, K. V., & Samanipour, S. (2023). Critical Assessment of the Chemical Space Covered by LC-HRMS Non-Targeted Analysis. In *Environmental Science and Technology* (Vol. 57,

Issue 38, pp. 14101–14112). American Chemical Society. https://doi.org/10.1021/acs.est.3c03606

Ikhwan Rizki, M., Khumaira Sari, A., Kartika, D., Khairunnisa, A., Normaidah, dan, & Penelitian, A. (2022). Penetapan Kadar Fenolik Total dan Uji Aktivitas Antioksidan Fraksi dari Ekstrak Etanol Daun Cempedak (Artocarpus integer) dengan Metode DPPH. *MPI (Media Pharmaceutica Indonesiana) ¿*, *4*(2), 168–178.

Jomova, K., Raptova, R., Alomar, S. Y., Alwasel, S. H., Nepovimova, E., Kuca, K., & Valko, M. (2023). Reactive oxygen species, toxicity, oxidative stress, and antioxidants: chronic diseases and aging. *Archives of Toxicology*, *97*(10), 2499–2574. https://doi.org/10.1007/s00204-023-03562-9

Lau, G. W., King, P. J. H., Chubo, J. K., King, I. C., Ong, K. H., Ismail, Z., Robin, T., & Shamsi, I. H. (2024). The Potential Benefits of Palm Oil Waste-Derived Compost in Embracing the Circular Economy. *Agronomy*, *14*(11). https://doi.org/10.3390/agronomy14112517

Luo, X., Li, J., Cen, Z., Feng, G., Hong, M., Huang, L., & Long, Q. (2025). Exploring the therapeutic potential of lupeol: A review of its mechanisms, clinical applications, and advances in bioavailability enhancement. *Food and Chemical Toxicology*, *196*, 115193. https://doi.org/10.1016/J.FCT.2024.115193

Mohamed, S. (2014). Oil Palm Leaf: A New Functional Food Ingredient for Health and Disease Prevention. *Journal of Food Processing & Technology*, *05*(02), 1–6. https://doi.org/10.4172/2157-7110.1000300

Morlock, G. E. (2021). High-performance thin-layer chromatography combined with effect-directed assays and high-resolution mass spectrometry as an emerging hyphenated technology: A tutorial review. *Analytica Chimica Acta*, *1180*. https://doi.org/10.1016/j.aca.2021.338644

Nabila, R., Hidayat, W., Haryanto, A., Hasanudin, U., Iryani, D. A., Lee, S., Kim, S., Kim, S., Chun, D., Choi, H., Im, H., Lim, J., Kim, K., Jun, D., Moon, J., & Yoo, J. (2023). Oil palm biomass in Indonesia: Thermochemical upgrading and its utilization. *Renewable and Sustainable Energy Reviews*, *176*, 1–23. https://doi.org/10.1016/j.rser.2023.113193

Setiawan, D., Hadi, S., Shindi P, M. R., Mahdi, N., & Rinda, R. P. (2025). EFFECTIVENESS TEST OF OIL PALM LEAF EXTRACT (Elaeis guineensis Jacq.) AS A MOSQUITO BIOLARVACIDE Aedes aegypti. *Jurnal Farmasi Sains Dan Praktis (JFSP)*, *11*(1), 11–17. https://doi.org/10.31603/pharmacy.v%vi%i.10275

Setiawansyah, A., Susanti, G., Hidayati, N., Gemantari, B. M., Alrayan, R., Hadi, I., Luthfiana, D., & Hasanah, N. (2024). Telaah Potensi Antivirus Mitraginin terhadap Protease 3CLpro SARS-CoV-2 dengan Pendekatan Molecular Docking. *Sinteza*, *4*(2), 65–73. https://doi.org/10.29408/sinteza.v4i2.25634

Sharma, S., Shukla, M. K., Sharma, K. C., Tirath, Kumar, L., Anal, J. M. H., Upadhyay, S. K., Bhattacharyya, S., & Kumar, D. (2023). Revisiting the therapeutic potential of gingerols against different pharmacological activities. *Naunyn-Schmiedeberg's Archives of Pharmacology*, *396*(4), 633–647. https://doi.org/10.1007/s00210-022-02372-7

Susanti, I., Pratiwi, R., Rosandi, Y., & Hasanah, A. N. (2024). Separation Methods of Phenolic Compounds from Plant Extract as Antioxidant Agents Candidate. *Plants*, *13*(7), 1. https://doi.org/10.3390/plants13070965

Tsai, F. S., Lin, L. W., & Wu, C. R. (2016). Lupeol and its role in chronic diseases. In *Advances in Experimental Medicine and Biology* (Vol. 929, pp. 145–175). Springer New York LLC. https://doi.org/10.1007/978-3-319-41342-6_7

Wang, H., Chen, Y., Wang, L., Liu, Q., Yang, S., & Wang, C. (2023). Advancing herbal medicine: enhancing product quality and safety through robust quality control

practices. *Frontiers in Pharmacology*, *14*. https://doi.org/10.3389/fphar.2023.1265178

Zhu, W., Huang, L., Cheng, H., Li, N., Zhang, B., Dai, W., Wu, X., Zhang, D., Feng, W., Li, S., & Xu, H. (2024). GABA and its receptors' mechanisms in the treatment of insomnia. In *Heliyon* (Vol. 10, Issue 23). Elsevier Ltd. https://doi.org/10.1016/j.heliyon.2024.e40665

Zulfansyah, R., Mahdi, N., & Hamiddani S., R. (2023). Uji Efek Analgetik Ekstrak Etanol 96% Daun Kelapa Sawit (Elaeis Guineensis Jacq) Terhadap Mencit (Mus Musculus) Yang Di Induksi Asam Asetat. *Jurnal Ilmiah Ibnu Sina (JIIS): Ilmu Farmasi Dan Kesehatan*, *8*(2), 297–306. https://doi.org/10.36387/jiis.v8i2.1485