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Spirost: An Anti-Inflammatory Compound Isolated from *Cocos nucifera* L. Solid Endosperm

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Abstract

This study aims to determine the content of active compounds in *Cocos nucifera* L. endosperm solid using the GC-MS method. Sampling of *Cocos nucifera* L. endosperm solid was located in Lolak District, Bolaang Mongondow Regency, North Sulawesi Province. Extraction process and analysis of active compounds using Gas *Chromatography - Mass Spectrometry* (GC-MS) was conducted at the Integrated Research and Testing Laboratory of Gadjah Mada University (LPPT UGM). Analysis by Gas Chromatography-Mass Spectrometry (GC-MS) of solid powder of *Cocos nucifera* L. endosperm produced Spirost-8-en-11-one, 3-hydroxy-, (3ß,5a,14ß,20ß,22ß,25R)- as a bioactive compound that can be developed as an anti-inflammatory.

Keywords: Spirost; Endosperm *of Cocos nucifera* L.; GC-MS; Anti-inflammatory

INTRODUCTION

The biological constituents of *Cocos nucifera* L. possess multiple therapeutic agents that contribute significantly to human health [1]. Both the aqueous endosperm (commonly referred to as coconut water) and the solid endosperm (coconut meat) exhibit pronounced antioxidant, antibacterial, and anti-inflammatory activities. These components are also rich sources of vital micronutrients, such as vitamins and minerals, in addition to bioactive fatty acids [2]. The fatty acid profile of coconut meat demonstrates potent antifungal and antiviral effects, thereby supporting the enhancement of the immune response. Owing to these properties, *Cocos nucifera* has been extensively employed in culinary practices and is traditionally regarded as a medicinal resource in the treatment of various disorders, such as urolithiasis, diabetes mellitus, hyperlipidemia, and obesity [3]. *Cocos nucifera* is recognized for its diverse pharmacological activities, which are supported by the presence of bioactive constituents with significant therapeutic potential. It has been shown to exert analgesic effects by mitigating nociceptive responses, and to possess antiarthritic properties through the modulation of joint

inflammation [4]. The species exhibits antibacterial and antimicrobial activities that inhibit the proliferation of pathogenic microorganisms [5]. The antipyretic activity of *Cocos nucifera* contributes to the modulation of elevated body temperature associated with febrile states. Its anthelmintic efficacy facilitates the elimination of gastrointestinal helminths, thereby supporting intestinal health. The plant also exhibits antidiarrheal properties, which contribute to the reestablishment of gastrointestinal equilibrium by regulating intestinal motility and minimizing fluid loss. In addition, *Cocos nucifera* has been shown to possess hypoglycemic and antihypertensive activities, as evidenced by its capacity to reduce circulating glucose levels and lower systemic arterial pressure [6]. The antioxidant and anti-inflammatory mechanisms of the plant further enhance its capacity to protect against cellular oxidative stress and inflammatory pathologies. Finally, the cardioprotective effects of *Cocos nucifera* promote the maintenance of cardiovascular integrity and overall cardiac function [7].

Diosgenin, a bioactive steroidal sapogenin predominantly found in the species of the *Dioscorea* genus, has demonstrated substantial potential for pharmaceutical development. This compound has been associated with a broad range of pharmacodynamic activities, including antineoplastic, immunoregulatory, anti-inflammatory, and antithrombotic effects [8]. Among these, its antineoplastic efficacy and underlying molecular mechanisms have been comprehensively investigated, thereby providing a robust foundation for its application in oncological therapeutics. However, the clinical utility of diosgenin remains constrained by its poor gastrointestinal absorption and inherently low systemic bioavailability, which markedly compromises its pharmacological effectiveness [9].

Current approaches aimed at improving the aqueous solubility of diosgenin primarily focus on structural modification during the early stages of rational drug design. Structural derivatives of diosgenin have demonstrated the capacity to enhance both its pharmacological efficacy and hydrophilic properties, thereby increasing its systemic bioavailability [10]. These findings underscore the potential for further advancement in drug development, and they highlight the necessity of in-depth investigations into the conformational dynamics and interaction profiles of its analogues. Moreover, diosgenin represents a pivotal intermediate in the synthesis of steroid-based pharmaceuticals, which emphasizes the importance of continued research on its structural modification to yield novel synthetic compounds with superior therapeutic effectiveness and diminished toxicological risk [11].

The primary aim of the present investigation is to characterize the bioactive constituents contained within the solid endosperm powder of *Cocos nucifera* L. The analysis conducted through gas chromatography–mass spectrometry provides a foundational reference for the prospective formulation of standardized pharmaceutical raw materials.

MATERIALS AND METHODS

Sample origin

The solid endosperm of *Cocos nucifera* L. was collected from specimens located in Lolak District, Bolaang Mongondow Regency, within the North Sulawesi Province of Indonesia in October 2024. The extraction procedures and subsequent quantification of bioactive compounds were conducted utilizing gas chromatography–mass spectrometry at the Integrated Research and Testing Laboratory of Gadjah Mada University (UGM University).

Material preparation

The present study utilized a range of laboratory instruments and analytical equipment, including a laboratory blender (model 8010 BU), glass beakers, stainless steel spatulas, pipettes, aluminum foil, plastic film, filter paper, and glass funnels. In addition, a rotary evaporator system comprising the Buchi Rotavapor R-300, Buchi Recirculating Chiller F-305, and Buchi Vacuum Pump V-300 was employed. An analytical balance (Sartorius), centrifuge, vortex mixer, and gas chromatography spectrometry system (Agilent 5977B GC/MSD) were also incorporated to facilitate sample preparation and compound analysis. The primary materials used in the experimental procedures consisted of solid endosperm powder derived from *Cocos nucifera* L. and methanol (MeOH) as the extraction solvent.

Preparation and Making Simple

The extraction procedure employed in this study was adapted from the methodology reported by Nurholis's research (2023) [12]. A powder-to-solvent ratio of 1 to 10 was utilized, wherein each sample consisted of 20 grams of *Cocos nucifera* L. endosperm powder dissolved in 200 milliliters of methanol within a glass beaker. The beaker was subsequently covered with aluminum foil and its opening sealed using plastic film to minimize solvent evaporation. Maceration was performed for 24 hours in a dark environment at ambient temperature to facilitate compound extraction. Following maceration, the mixture was subjected to filtration using filter paper and a glass funnel. The resulting filtrate was concentrated using a rotary evaporator at a temperature not exceeding 54 degrees Celsius in order to obtain a viscous extract. The concentrate was vortexed for 10 seconds to ensure homogenization and then centrifuged for one minute at 6000 revolutions per minute to achieve phase separation into the pellet and supernatant. The pellet fraction was transferred into a 1.5 milliliter vial for subsequent analysis using gas chromatography–mass spectrometry.

Compound Analysis Using GC-MS

The obtained specimens were subjected to Gas Chromatography–Mass Spectrometry (GC–MS) analysis, adhering strictly to a rigorously validated acquisition methodology. The mass spectrometer's transfer line and ion source temperatures were consistently maintained at 250 degrees Celsius. Injection parameters included a syringe with a total capacity of 10,000 microliters, a sample vial depth of 27,000 millimeters, and a wash solvent depth of 40,000 millimeters. Rinsing was executed with a volume of 1,000 microliters, while solvent aspiration involved a draw rate of 2,000 microliters per second to reach a volume of 3,000 microliters, repeated across five consecutive cycles. The needle inserted the sample at a velocity of 20,000 millimeters per second, with air bubble elimination conducted at a rate of 5,000 microliters per second and a dwell time of 2,000 seconds between strokes. A 1,000-microliter aliquot was introduced into the GC–MS system. Upon thermal equilibration, the injector was activated to follow a predefined temperature gradient. Initially, the sample was held at 70 degrees Celsius for two minutes to ensure complete volatilization. The resultant vapor was carried by helium gas at a constant flow rate of 1 milliliter per minute in a splitless injection mode into the chromatographic column. The column oven temperature program began at 70 degrees Celsius, increased at a rate of 5 degrees Celsius per minute to 200 degrees Celsius, then continued with a ramp of 10 degrees Celsius per minute to a final temperature of 250 degrees Celsius, which was sustained for ten minutes. Compounds were resolved within the column based on their differential affinities to the mobile phase, consisting of helium, and the stationary phase. Subsequently, the eluted analytes

were transmitted to the mass spectrometer for characterization via their mass-to-charge (m/z) ratios. The chromatographic and spectral data were subsequently exported for further detailed analysis [13].

Data analysis

Gas Chromatography–Mass Spectrometry (GC–MS) analysis yields chromatographic profiles characterized by discrete peaks, each corresponding to an individual molecular entity. In this investigation, only compounds exhibiting a similarity index equal to or greater than eighty percent were considered for definitive identification [14]. This threshold is consistent with established analytical protocols, wherein compounds displaying similarity indices below eighty percent are typically regarded as unidentified substances, as referenced in prior studies. A higher similarity index, approaching a value of one hundred percent, indicates a substantial concordance between the fragmentation pattern of the analyte and that of the standard reference compound contained within the spectral database [15]. The similarity index serves a pivotal function in the accurate elucidation of chemical structures, as it quantifies the degree of alignment between the mass spectral data of the analyte and the corresponding reference spectra. Identification of the detected compounds was performed through comparative analysis of the acquired spectra with those archived in the W12N20 MAIN.L spectral database, integrated within the MassHunter analytical platform. The outcomes of this study will be systematically presented in tabular form, encompassing compound classification, known biological activities, and potential pharmaceutical applications, all of which are substantiated by a comprehensive literature evaluation.

RESULTS AND DISCUSSION

Based on the analytical results obtained from the Gas Chromatography–Mass Spectrometry (GC–MS) examination of the solid endosperm of *Cocos nucifera* L., peaks were identified. These peaks represent the presence of various organic compounds and secondary metabolites within the sample. The corresponding gas chromatogram, which depicts the chemical composition of the solid endosperm powder of the solid endosperm of *Cocos nucifera* L, is presented in Figure 1.

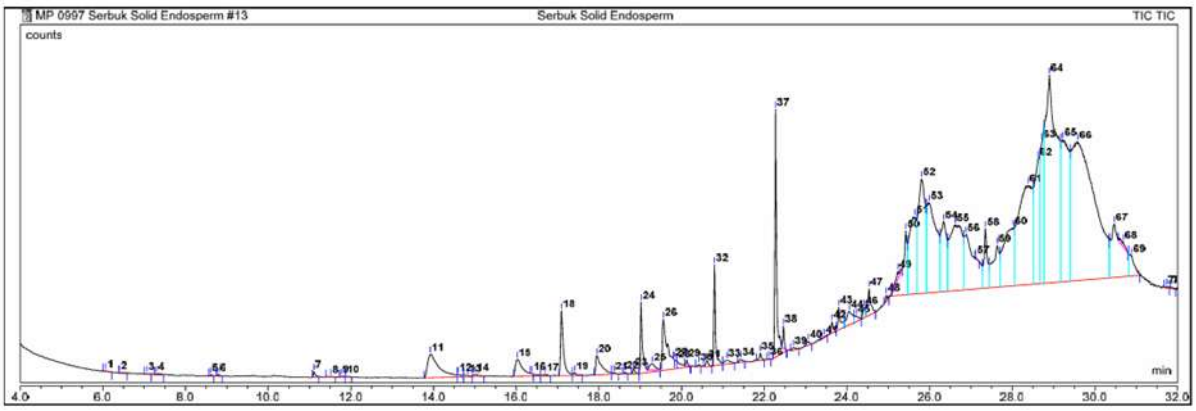


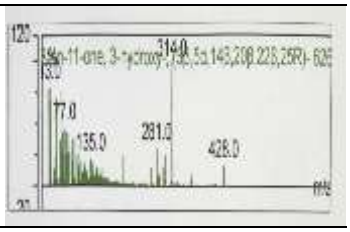
Figure 1. Chromatogram results GC-MS analysis of Solid Endosperm *Cocos nucifera* L.

Figure 1 presents the gas chromatographic profile used for the identification of bioactive constituents within the solid endosperm of *Cocos nucifera* L. The identification of chemical compounds was achieved by correlating the obtained mass spectral fragments, base peak intensity, retention time, and similarity index with reference spectra archived in the MainLib database, as documented in the

literature [16],[18]. A similarity index threshold of not less than eighty percent, as outlined in Table 1, was established as the minimum requirement for assigning definitive compound identity. As an illustrative case, peak number forty-seven, eluting at a retention time of 23.45 minutes and exhibiting a molecular mass of 428, was identified as Spirost-8-en-11-one, 3-hydroxy-, (3ß,5a,14ß,20ß,22ß,25R)-, with a calculated relative abundance of twenty percent.

According to the data presented in Table 1, one of the identified compounds exhibiting anti-inflammatory bioactivity was detected at peak number forty-seven. This compound demonstrated a retention time of 23.45 minutes and accounted for twenty-one percent of the total chromatographic area. The chemical entity associated with this peak was identified as spirost, a compound recognized for its anti-inflammatory properties. Further structural characterization and molecular confirmation of spirost, along with other bioactive constituents, are detailed in Table 2. This table provides compound information based on molecular structure as obtained from the National Center for Biotechnology Information (2025) through the PubChem Compound Summary database.

Table 1. Compound identified based on GC-MS of solid endosperm powder *of C. nucifera*

Peak	(tR)	Compound Name	Area (%)	Molecular Weight (gr/mol)	Molecular Formula	Mainlib
47	23.45	Spirost-8-en-11-one, 3-hydroxy-, (3ß,5a,14ß,20ß,22ß,25R)-	21	428	C27H40O4	

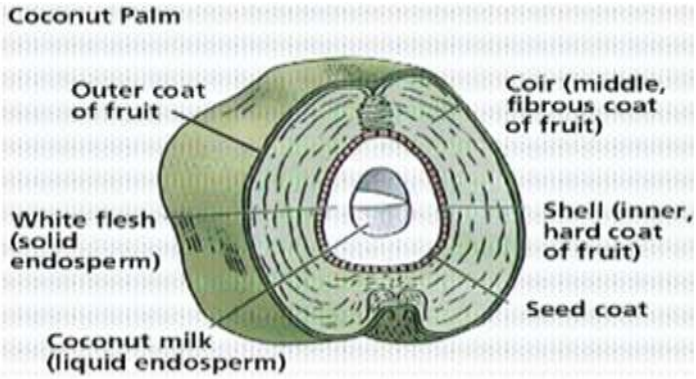


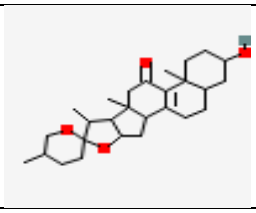
Figure 2. *Structure of a Coconut fruit*
Source: Nwankwojike, *et al*. (2012)

Table 2 presents the molecular characterization of bioactive compounds identified in the solid endosperm of *Cocos nucifera* L., with data sourced from the PubChem Compound Summary provided by the National Center for Biotechnology Information (2025). The compound listed, Spirost-8-en-11-one, 3-hydroxy-, (3ß,5a,14ß,20ß,22ß,25R)-, was observed at a retention time of 24.53 minutes, with a molecular formula of $C_{27}H_{40}O_4$ and a molecular weight of 428 grams per mole.

Spirost is a fundamental structural motif found within various classes of

steroidal compounds, notably within steroidal sapogenins such as diosgenin. In this context, spirost denotes a characteristic ring system consisting of a fused polycyclic core with attached carbon side chains, which imparts distinct physicochemical and biological properties to the molecule. Diosgenin, chemically referred to as 25R-spirost-5-en-3β-ol, serves as a prototypical example and is primarily derived from Dioscorea opposita. Diosgenin has been widely studied for its diverse pharmacological activities, including anti-inflammatory, anticancer, antithrombotic, and immunomodulatory effects. Moreover, it represents a critical intermediate in the semi-synthetic production of steroidal pharmaceuticals[19],[22]. Structural modifications of diosgenin and related spirost-based molecules have been shown to enhance their solubility, dissolution rates, and overall pharmacodynamic properties. The identification of spirost-related structures in *Cocos nucifera* L. underscores its potential as a source of biologically active steroidal compounds with therapeutic relevance.

Table 2. Compounds identified in the *Cocos nucifera* L. endosperm solid powder based on molecular structure from National Center for Biotechnology Information (2025). PubChem Compound Summary

No.	Organic compounds	Retention Time (Minutes)	Chemical Formula	Molecular Weight (g/mol)	Structure
1	Spirost-8-en-11-one, 3-hydroxy-, (3ß,5a,14ß,20ß,22ß,25R)-	24.53	$C_{27}H_{40}O_4$	428	

The present study examines the synthetic pathways and pharmacological attributes of diosgenin and its structural derivatives, intending to provide precise and comprehensive insights that may facilitate the advancement and practical application of diosgenin in pharmaceutical development. The enhancement of its therapeutic potential relies significantly on such investigations.

Diosgenin serves as a fundamental precursor in the synthesis of glucocorticoid-based pharmaceuticals. Compounds such as prednisone, prednisolone, dexamethasone, betamethasone, methylprednisolone, and hydrocortisone are derived from diosgenin through a range of chemical and biotechnological processes, including microbial fermentation [23].

In its pure form, diosgenin appears as a white, needle-like crystalline substance or a fine, light-colored powder. It represents the pharmacologically active constituent in traditional Chinese medicine-derived steroidal saponins and is commonly sourced from legumes and species of *Dioscorea*. Diosgenin is widely recognized as a critical intermediate in the semi-synthetic production of numerous steroidal pharmaceuticals, including contraceptive agents and steroid hormones [24].

Diosgenin exhibits a broad spectrum of pharmacological activities, including antitumor, anti-inflammatory, and hypolipidemic effects. Additionally, it demonstrates neuroimmunomodulatory and behavior-enhancing properties to neurological disorders, such as Alzheimer's disease [14].

The solubility and physicochemical properties of diosgenin have been enhanced through the conjugation of various amino acids at the C-3 hydroxyl position. This structural modification capitalizes on the

intrinsic neuroprotective potential of amino acids, leading to the synthesis of multiple diosgenin–amino acid conjugates. Evaluation of these derivatives indicated that most compounds exhibited improved pharmacological efficacy in comparison to the parent molecule. Notably, the derivative 3β-(L-isoleucine)-diosgenin demonstrated dual functionality in neurological contexts, exerting both neuroprotective and angiogenic effects. The complete synthetic methodology for these compounds is described in detail in reference [25].

A series of diosgenin-derived compounds was synthesized to develop new therapeutic agents possessing anticancer and anti-inflammatory properties. Among the synthesized derivatives, the diosgenyl ester of 6-aminohexanoic acid exhibited the most potent anticancer activity and is regarded as a promising candidate for anticancer drug development. This compound was synthesized through the reaction of 6-aminohexanoic acid with di-tert-butyl dicarbonate in a solvent system composed of acetone and water, with triethylamine serving as a catalytic base. In addition, the diosgenyl salicylate conjugate, prepared by esterifying diosgenin with 2-acetoxybenzoyl chloride in the presence of pyridine, exhibited the most significant anti-inflammatory activity among the evaluated compounds.

Rheumatoid arthritis is a prevalent chronic autoimmune disease characterized by complex pathological mechanisms, most notably synovial membrane inflammation that progressively leads to the degradation of articular cartilage and subchondral bone. In advanced stages, this condition frequently results in a diminished range of joint mobility. Recent investigations have elucidated the immunomodulatory role of diosgenin in regulating inflammatory processes. Diosgenin demonstrates immunosuppressive activity by modulating immune cell responses and related signaling pathways in collagen-induced arthritis models in mice. In particular, Wang and colleagues reported that diosgenin influences $CD4^+$ T cell differentiation by suppressing the proliferation of T helper 1 and T helper 17 cells while enhancing the activity of T helper 2 cells.

Further experimental evidence suggests that diosgenin modulates the expression of vascular endothelial growth factor in murine synovial cells through the inhibition of two subunits of activator protein-1, thereby attenuating both angiogenic and inflammatory responses associated with rheumatoid arthritis. In addition, diosgenin has been shown to inhibit pro-inflammatory mediator expression stimulated by interleukin-1 beta. It significantly suppresses the production of nitric oxide and prostaglandin E2, as well as the expression levels of inducible nitric oxide synthase and cyclooxygenase-2 proteins in human chondrocytes. This suppression also extends to the inhibition of interleukin-1 beta-induced degradation of IκBα in human chondrocytes derived from osteoarthritic tissue. Moreover, recent findings have demonstrated that diosgenin inhibits the proliferation and migration of rheumatoid arthritis synoviocytes and mitigates their inflammatory activity by downregulating the expression of phosphodiesterase type 3B [26].

CONCLUSION

Gas Chromatography–Mass Spectrometry analysis of the solid endosperm of *Cocos nucifera* L. revealed the presence of Spirost-8-en-11-one, 3-hydroxy-, (3β,5α,14β,20β,22β,25R)- as a bioactive constituent with promising potential for anti-inflammatory therapeutic development. This compound was identified at peak number forty-seven in the chromatographic profile, exhibiting a retention time of 23.45 minutes and accounting for twenty-one percent of the total peak area. Its molecular characteristics include a molecular formula of $C_{27}H_{40}O_4$

and a molecular mass of 428 g/mol. The identification was confirmed by achieving a similarity index of no less than eighty percent when compared with reference spectra from the MainLib database.

REFERENCES

[1] P. P. S. Beegum *et al.*, "Perspectives on the cardioprotective, neuroprotective and anti-obesity functions of coconut (*Cocos nucifera* L.)," *Food Biosci.*, vol. 58, p. 103756, 2024, doi: https://doi.org/10.1016/j.fbio.2024.103756.

[2] P. D. Hamilton, K. T. Charles, A. M. Bih Loh, N. N. Aristide Loïc, K. Germain, and F. Elie, "Physicochemical, nutritional, antioxidant properties and stability monitoring of coconut (Cocos nucifera L.) water from two localities in Cameroon," *Heliyon*, vol. 10, no. 23, p. e40712, 2024, doi: https://doi.org/10.1016/j.heliyon.2024.e40712.

[3] A.-M. Liao *et al.*, "Synthesis, anticancer activity and potential application of diosgenin modified cancer chemotherapeutic agent cytarabine," *Food Chem. Toxicol.*, vol. 148, p. 111920, 2021, doi: https://doi.org/10.1016/j.fct.2020.111920.

[4] P. Marasri, S. Sookkhee, P. Wanachantararak, and D. Owittayakul, "Anti-Inflammatory Activity and Wound Healing Ability of Coconut Oil Mouthwash on Gingival Fibroblast Cell In Vitro," *Nat. Life Sci. Commun.*, vol. 23, Sep. 2024, doi: 10.12982/NLSC.2024.059.

[5] Y. S., V. Sundaram, and R. Shanmugam, "In-vitro screening of bio-potency of Cocos nucifera haustorium and its efficacy against HepG2 cell line," *J. Exp. Biol. Agric. Sci.*, vol. 13, pp. 151–162, May 2025, doi: 10.18006/2025.13(2).151.162.

[6] O. L. Erukainure and C. I. Chukwuma, "Coconut (Cocos nucifera (L.)) Water Improves Glucose Uptake with Concomitant Modulation of Antioxidant and Purinergic Activities in Isolated Rat Psoas Muscles," *Plants*, vol. 13, no. 5. 2024, doi: 10.3390/plants13050665.

[7] Y. S., V. Sundaram, and R. Shanmugam, "A comparative mini review of the phytochemicals and biological properties of haustorium and endosperm of Cocos nucifera," *J. Exp. Biol. Agric. Sci.*, vol. 13, pp. 125–136, May 2025, doi: 10.18006/2025.13(2).125.136.

[8] Rizwan ur-Rehman, Sania Riaz, Misha Arooj, Saleha Khan, Urwa Tariq, and Maliha Fatima, "Diosgenin: A Potential Therapeutic Phytocompound for the Management of Atherosclerosis and Other Physiological Disorders," *Nat. Prod. Commun.*, vol. 19, no. 12, p. 1934578X241301228, Dec. 2024, doi: 10.1177/1934578X241301228.

[9] P. Gu *et al.*, "Network pharmacology-based investigation of the pharmacological mechanisms of diosgenin in nonalcoholic steatohepatitis," *Sci. Rep.*, vol. 15, Mar. 2025, doi: 10.1038/s41598-025-95154-z.

[10] R. Fan *et al.*, "Recent advances in chemical synthesis, biocatalysis, and biological evaluation of diosgenin derivatives – A review," *Steroids*, vol. 180, p. 108991, Feb. 2022, doi: 10.1016/j.steroids.2022.108991.

[11] N. HUANG, D. YU, J. WU, and X. DU, "Diosgenin: an important natural pharmaceutical active ingredient," *Food Sci. Technol.*, vol. 42, Dec. 2021, doi: 10.1590/fst.94521.

[12] W. Nurcholis, N. Marliani, R.

Asyhar, and M. Minarni, "Optimized Solvents for the Maceration of Phenolic Antioxidants from Curcuma xanthorrhiza Rhizome using a Simplex Centroid Design," *J. Pharm. Bioallied Sci.*, vol. 15, p. 35, Apr. 2023, doi: 10.4103/jpbs.jpbs_185_23.

[13] Z. Chen *et al.*, "Diosgenin inhibited the expression of TAZ in hepatocellular carcinoma," *Biochem. Biophys. Res. Commun.*, vol. 503, no. 3, pp. 1181–1185, 2018, doi: https://doi.org/10.1016/j.bbrc.2018.07.022.

[14] Y. Qi *et al.*, "Neuroprotective Effect of Dioscin on the Aging Brain," *Molecules*, vol. 24, no. 7. 2019, doi: 10.3390/molecules24071247.

[15] W.-L. Liao *et al.*, "Induction of G2/M Phase Arrest by Diosgenin via Activation of Chk1 Kinase and Cdc25C Regulatory Pathways to Promote Apoptosis in Human Breast Cancer Cells," *International Journal of Molecular Sciences*, vol. 21, no. 1. 2020, doi: 10.3390/ijms21010172.

[16] F. J. Paat, H. Wahyuni, N. O. Sapii, S. Tumbelaka, J. F. Watung, and S. Wantasen, "Analysis of biopesticide active compounds in Barringtonia asiatica L. Kurz using the GC-MS method," *IOP Conf. Ser. Earth Environ. Sci.*, vol. 1302, no. 1, p. 12009, 2024, doi: 10.1088/1755-1315/1302/1/012009.

[17] T. Kaunang *et al.*, "Are probiotics beneficial for obese patients with major depressive disorder? Opinion for future implications and strategies," *Front. Nutr.*, vol. 10, May 2023, doi: 10.3389/fnut.2023.1205434.

[18] N. Pathak *et al.*, "Bivalent furostene carbamates as antiproliferative and antiinflammatory agents," *J. Steroid Biochem. Mol. Biol.*, vol. 194, p. 105457, 2019, doi: https://doi.org/10.1016/j.jsbmb.2019.105457.

[19] S.-Q. Zhang, Y.-X. Song, W.-X. Zhang, M.-J. Chen, and S.-L. Man, "Research on anti-tumor natural product diosgenin," *Zhongguo Zhong Yao Za Zhi*, vol. 46, pp. 4360–4366, Sep. 2021, doi: 10.19540/j.cnki.cjcmm.20210610.701.

[20] D. Wankhar, S. Bhagavatheeswaran, V. Ramachandran, S. Sambantham, and A. Balakrishnan, "Exploring the anti-angiogenic properties of diosgenin saponin from Trigonella graecum (fenugreek): A study on Zebrafish embryos," *Natl. J. Physiol. Pharm. Pharmacol.*, p. 1, Jan. 2024, doi: 10.5455/njppp.2024.14.020962024190 32024.

[21] M. Vengaimaran, D. Kalaiyarasi, and S. Mirunalini, "Evaluating in-vitro antioxidant and in-silico anti-inflammatory potential of Diosgenin," *Res. J. Biotechnol.*, vol. 17, pp. 111–118, Dec. 2021, doi: 10.25303/1701rjbt111118.

[22] X.-B. Wu *et al.*, "Anti-apoptotic Effects of Diosgenin on Ovariectomized Hearts," *Steroids*, vol. 179, p. 108980, Feb. 2022, doi: 10.1016/j.steroids.2022.108980.

[23] I. Herráiz, "Chemical Pathways of Corticosteroids, Industrial Synthesis from Sapogenins," in *Methods in Molecular Biology*, vol. 1645, 2017, pp. 15–27.

[24] H. Syahputra, M. Masfria, M. Amana, and M. Rivai, "Isolation and identification of diosgenin and flavonoids compound from ethanol extract of Dioscorea hispida Dennst. tuber," *Indones. J. Pharm. Clin. Res.*, vol. 7, pp. 7–15, Nov. 2024, doi: 10.32734/idjpcr.v7i1.15994.

[25] D. Cai *et al.*, "Design, Synthesis and Biological Evaluation of Diosgenin-

Amino Acid Derivatives with Dual Functions of Neuroprotection and Angiogenesis," *Molecules*, vol. 24, no. 22. 2019, doi: 10.3390/molecules24224025.

[26] R. Yang *et al.*, "Dioscin relieves endotoxemia induced acute neuro-inflammation and protects neurogenesis via improving 5-HT metabolism," *Sci. Rep..*, vol. 7, no. 1, p. 40035, 2017, doi: 10.1038/srep40035.

[27] Nwankwojike, O. Onuba, U. Ogbonna. Development of a Coconut Dehusking Machine for Rural Small-Scale Farm Holders (2012). International Journal of Innovative Technology & Creative Engineering.Vol 2. No. 3 March 2012.