MOLEKUL
eISSN: 2503-0310

Articles
https://doi.org/10.20884/1.jm.2026.21.2.19263

Nanoemulsion-Based Delivery of *Peronema canescens* Ethanol Leaf Extract Using Cinnamon Oil and Red Palm Oil: Physicochemical Characterization, Antioxidant Activity, and Immunomodulatory Potential

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Received January 14, 2026; **Accepted** June 11, 2026; **Available online** July 20, 2026

ABSTRACT. Natural plant extracts are widely recognized for their bioactive potential, yet their use is often hindered by poor physicochemical stability and limited oral absorption. *Peronema canescens* Jack. (Sungkai) leaves have traditionally been employed for their immunostimulatory and antioxidant effects, but their application in pharmaceutical formulations is restricted due to low solubility in water and instability in conventional preparations. This study focused on the development of a nanoemulsion-based delivery system for the ethanol extract of *P. canescens* leaves and evaluated its antioxidant and immunomodulatory properties. The nanoemulsions were formulated as oil-in-water systems and characterized for droplet size, uniformity, optical clarity, and physical stability. Antioxidant potential was measured using the DPPH radical scavenging assay, expressed as IC_{50}, while immunomodulatory effects were assessed in vivo through hematological parameters after oral administration. The SNEDDS formulations exhibited nanoscale droplets (40–59 nm), high transparency (82–98% transmittance), and stable physical properties. Extract-loaded formulations generally displayed strong antioxidant activity with IC_{50} values below 50 ppm, although the crude extract showed slightly superior radical scavenging. In vivo, the formulations containing *P. canescens* extract influenced total leukocyte counts to varying degrees, whereas unloaded formulations had negligible effects. Some formulations produced leukocyte levels comparable to or exceeding those of the crude extract and positive control, while hemoglobin, erythrocyte, and hematocrit levels remained within normal physiological ranges. These findings demonstrate that nanoemulsion-based systems can preserve the antioxidant activity of *P. canescens* leaf extract and modulate immune responses effectively in vivo. This approach offers a practical strategy to enhance the stability, consistency, and potential application of plant-derived bioactive compounds in nutraceutical and phytopharmaceutical development.

Keywords: antioxidant activity, immunomodulation, nanoemulsion, *Peronema canescens*.

INTRODUCTION

Peronema canescens Jack., commonly known as Sungkai, is a medicinal plant traditionally used in Southeast Asia for the management of febrile illnesses, including malaria, influenza-like conditions, and high fever. Recent scientific interest in Sungkai has intensified following evidence supporting its pharmacological relevance, particularly in immune-related applications. Phytochemical analyses have revealed that Sungkai leaves contain a wide spectrum of secondary metabolites, including flavonoids, phenolic compounds, alkaloids, tannins, and saponins, which are associated with antioxidant, anti-inflammatory, and immunomodulatory activities (Fikriansyah et al., 2023; Latief et al., 2024; Latief, et al., 2021; Latief, et al., 2021; Tarigan et al., 2023, 2025). Among these compounds, flavonoids and phenolics have been highlighted as key contributors to immune modulation through their ability to regulate oxidative stress and inflammatory signaling pathways (Jantan et al., 2015; Mamun et al., 2024).

Oxidative stress is a major contributor to immune system dysfunction and is characterized by an imbalance between the generation of reactive oxygen species (ROS) and endogenous antioxidant defenses (Pizzino et al., 2017). Excessive ROS production can impair immune cell function through lipid peroxidation, protein oxidation, and DNA damage, ultimately reducing immune responsiveness and increasing susceptibility to disease. Antioxidants play a critical role in maintaining immune homeostasis by neutralizing free radicals and preserving cellular redox balance (Snezhkina et al., 2020). Consequently, natural products that exhibit both antioxidant and immunomodulatory activities, such as Sungkai leaf extract, are considered promising candidates for the development of supportive immune therapies (Shalihin et al., 2024).

Despite its therapeutic potential, the clinical translation of Sungkai leaf extract is constrained by several physicochemical limitations inherent to herbal extracts. These include poor aqueous solubility, low chemical stability, and susceptibility to degradation during processing, storage, and gastrointestinal transit (Favaro-Trindade et al., 2020; Hussain et al., 2018). Such limitations often result in low oral bioavailability and inconsistent therapeutic outcomes, which hinder further pharmaceutical development (Zhuo et al., 2024). Addressing these challenges requires advanced drug delivery strategies capable of enhancing solubilization, protecting labile phytochemicals, and improving systemic absorption. Nanoemulsion-based drug delivery systems, particularly self-nanoemulsifying drug delivery systems (SNEDDS), have emerged as a promising approach to overcome these formulation barriers (Miksusanti et al., 2023; Montes et al., 2017). SNEDDS are isotropic mixtures of oils, surfactants, and co-surfactants that spontaneously form fine oil-in-water nanoemulsions upon exposure to gastrointestinal fluids. The formation of nanoscale droplets significantly increases interfacial surface area, enhances solubilization of lipophilic compounds, and promotes improved permeability and oral bioavailability (Kaur et al., 2024; Onoue et al., 2025; Zhuo et al., 2024). Considerable studies have demonstrated that nanoemulsion systems can enhance the physicochemical stability and biological efficacy of plant-derived bioactives, including improved antioxidant, anti-inflammatory, and immunomodulatory effects compared to conventional extract formulations (Saffari et al., 2025).

The selection of the oil phase plays a crucial role in determining the performance and functionality of nanoemulsion systems. Cinnamon oil has attracted considerable attention due to its intrinsic biological activities, including potent antioxidant, anti-inflammatory, antimicrobial, and immunomodulatory effects (Khedkar & Ahmad Khan, 2023). These activities are largely attributed to bioactive constituents such as cinnamaldehyde and other phenylpropanoids. Moreover, cinnamon oil has demonstrated favorable compatibility with nanoemulsion systems, contributing not only as a solubilizing agent but also as a functional excipient capable of synergistically enhancing therapeutic efficacy (Masyita et al., 2022).

In parallel, red palm oil represents a nutritionally and pharmacologically valuable lipid source, rich in natural antioxidants such as carotenoids, tocopherols, and tocotrienols (Gao et al., 2023). These compounds are known to exert strong antioxidant and immunoprotective effects, while also improving oxidative stability of lipid-based formulations. In addition, the favorable fatty acid composition of red palm oil enhances solubilization capacity for lipophilic bioactives and contributes to improved nanoemulsion stability (Madoromae & Lertcanawanichakul, 2025). The incorporation of red palm oil into nanoemulsion systems therefore offers dual benefits, acting both as a delivery vehicle and as an active contributor to antioxidant and immunomodulatory performance.

Previous studies have successfully demonstrated the application of nanoemulsion and SNEDDS formulations for various plant-derived extracts, resulting in enhanced physicochemical properties and improved biological activities. For example, nanoemulsified curcumin formulations have shown increased antimicrobial and antioxidant efficacy (Confessor et al., 2024), while nanoemulsified *Clinacanthus nutans* extracts exhibited synergistic anti-inflammatory and immunomodulatory effects in disease models (Pechroj et al., 2024). However, despite growing evidence supporting the advantages of nanoemulsion-based delivery systems, their application to *P. canescens* leaf extract remains largely unexplored. Furthermore, to the best of our knowledge, no studies have reported the development of a nanoemulsion system utilizing a combined cinnamon oil–red palm oil oil phase to simultaneously enhance delivery efficiency and contribute intrinsic antioxidant and immunomodulatory activities.

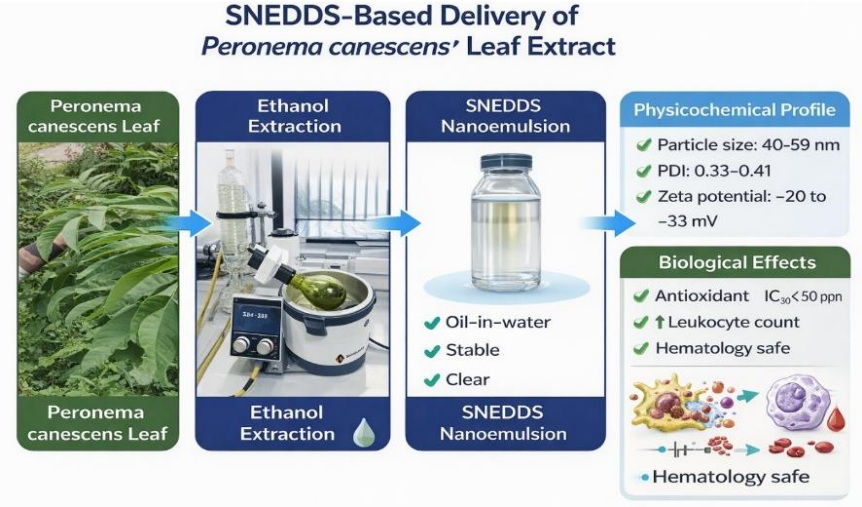

Figure 1. Graphical abstract

Therefore, a clear research gap exists in the development and systematic evaluation of a multifunctional nanoemulsion-based delivery system for Sungkai leaf extract that integrates bioactive oil components to achieve synergistic physicochemical and biological performance. Addressing this gap, the present study aims to develop and characterize a cinnamon oil–red palm oil nanoemulsion encapsulating *P. canescens* ethanol leaf extract, and to evaluate its physicochemical characteristics, antioxidant activity, and immunomodulatory potential. By integrating traditional medicinal knowledge with modern nano-based drug delivery technology, this study seeks to provide a scientifically validated platform for enhancing the therapeutic efficacy and translational potential of Sungkai-derived bioactive compounds.

EXPERIMENTAL SECTION

Materials

Sungkai (*P. canescens* Jack.) Leaf samples were collected from Senaung Village, Jambi Luar Kota District, Muaro Jambi Regency, Jambi Province in July 2023 and validated in the Department of Biology, Universitas Jambi. The scientific name of the plant was cross-referenced with http://www.theplantlist.org, accessed on August 30th, 2024. The plant material was authenticated prior to use. Analytical-grade solvents, including ethanol (70%), *n*-hexane, and ethyl acetate, were purchased from Merck KGaA (Darmstadt, Germany) and used for extraction and fractionation processes. Cinnamon oil (*Cinnamomum burmannii*) was purchased from CV. Atsiri Farmer Indonesia, while red palm oil (*Elaeis guineensis*) was obtained from CV. Salmira. Both oils were used as the oil phase in the self-nanoemulsifying drug delivery system (SNEDDS) formulation. Tween 80 (polysorbate 80) and polyethylene glycol 400 (PEG 400), both purchased from Merck KGaA (Darmstadt, Germany), were used as the surfactant and co-surfactant, respectively.

Sodium alginate, used as a biopolymer, was obtained from Sigma-Aldrich (St. Louis, MO, USA). Methylene blue dye was purchased from Merck KGaA (Darmstadt, Germany) and used for emulsion type determination. Deionized water was produced in-house, while aqua pro injection was obtained from Otsuka Pharmaceutical Co., Ltd. (Tokyo, Japan) and used for particle size and zeta potential analysis. Sodium carboxymethyl cellulose (Na-CMC), purchased from Brataco Chemical (Jakarta, Indonesia), was used as the vehicle for *in vivo* administration. For antioxidant activity evaluation, 2,2-diphenyl-1-picrylhydrazyl (DPPH) was obtained from Sigma-Aldrich (St. Louis, MO, USA). A commercial immunostimulant (Stimuno®; Dexa Medica, Bandung, Indonesia) was used as the positive control in the *in vivo* immunomodulatory study.

Animal experiment

BALB/c mice were obtained from the Department of Biology, University of Jambi. The animals weighed approximately 20–30 g and were about 10 weeks old. Prior to the experiment, the mice were acclimatized to the laboratory environment for 7 days to allow physiological adaptation and minimize stress during the experimental procedures. The animal study protocol was approved by the Research Ethics Commission, Faculty of Medicine, Andalas University (approval No. 526/UN.16.2/KEP-FK/2023) and was conducted in accordance with the National Guidelines and Ethical Standards for Health Research and Development issued by the National Health Research and Development Ethics Committee, Ministry of Health of the Republic of Indonesia. All efforts were made to minimize animal suffering and to reduce the number of animals used in the study. All mice were maintained under standardized housing conditions with a 12 h light/12 h dark cycle, temperature of 20–21 °C, and relative humidity of 45–70%, with food and water provided ad libitum. The test substance was administered orally once daily for 14 days according to the respective treatment group

Preparation and Extraction of *P. canescens* Leaf

Fresh Sungkai leaves were washed thoroughly with running water to remove adhering impurities, air-dried at room temperature away from direct sunlight, and milled into a fine powder (simplisia). The extraction was carried out using a maceration method with 70% ethanol as the solvent. The powdered leaves were soaked in ethanol at a sample-to-solvent ratio of 1:10 (w/v) for six days, with solvent replacement performed once during the extraction period to enhance extraction efficiency. The combined filtrates were collected and concentrated under reduced pressure using a rotary evaporator to obtain a viscous crude ethanol extract, which was then stored in airtight containers at 4 °C until further use.

Formulation of SNEDDS

The self-nanoemulsifying drug delivery system (SNEDDS) formulations were developed using Sungkai leaf ethanol extract as the active pharmaceutical ingredient. Cinnamon oil, either alone or in combination with red palm oil, was used as the oil phase. Tween 80 served as the surfactant, polyethylene glycol 400 (PEG 400) as the co-surfactant, and deionized water as the aqueous phase. Sodium alginate was incorporated as a biopolymer to enhance formulation stability and to modulate the viscosity of the nanoemulsion system.

A total of eight formulations (F1–F8) were prepared to evaluate the effects of extract concentration and oil phase composition on the physicochemical characteristics of the SNEDDS. Formulations F1–F4 were prepared without red palm oil, while formulations F5–F8 contained red palm oil at a fixed concentration of 0.5 g. Within each group, the amount

Table 1. Composition of the *P. canescens* leaf extract SNEDDS formulations

Component	F1	F2	F3	F4	F5	F6	F7	F8
Extract (mg)	260	400	530	-	260	400	530	-
Red Palm Oil	-	-	-	-	0.5 g	0.5 g	0.5 g	0.5 g
Cinnamon Oil	0.5 g	0.5 g	0.5 g	0.5 g	-	-	-	-
Tween 80	4.0 g	4.0 g	4.0 g	4.0 g	4.0 g	4.0 g	4.0 g	4.0 g
PEG 400	1.5 g	1.5 g	1.5 g	1.5 g	1.5 g	1.5 g	1.5 g	1.5 g
Sodium Alginate	5.0 g	5.0 g	5.0 g	5.0 g	5.0 g	5.0 g	5.0 g	5.0 g
Deionized Water	Add up to 100 mL							

of *P. canescens* leaf extract was varied to assess dose-dependent effects, whereas the concentrations of cinnamon oil, surfactant, co-surfactant, sodium alginate, and aqueous phase were kept constant, as summarized in **Table 1**.

The oil phase (cinnamon oil with or without red palm oil), surfactant (Tween 80), and co-surfactant (PEG 400) were first mixed until a clear and homogeneous isotropic mixture was obtained. Subsequently, the Sungkai leaf extract was incorporated into the mixture under continuous stirring. Deionized water was then added gradually to a final volume of 100 mL, allowing spontaneous formation of the nanoemulsion system. The resulting SNEDDS formulations were visually inspected for homogeneity and transparency and subsequently subjected to physicochemical characterization to evaluate their stability and suitability for oral administration.

The manufacturing process involved first dissolving the Sungkai extract in cinnamon oil to form a homogeneous mixture. This was followed by the addition of Tween 80 and PEG 400, which was stirred on a hot plate stirrer for one hour. Sodium alginate was then added, and the mixture was stirred for another hour without heat to form the primary emulsion. The final nanoemulsion was created by adding this primary emulsion dropwise into deionized water under constant stirring, followed by sonication for one hour to ensure uniform droplet size.

Physicochemical Characterization of SNEDDS

The physicochemical characterization of the SNEDDS formulations was conducted to evaluate their stability and suitability for oral delivery systems. Physical appearance and preliminary stability were assessed by visual inspection of clarity, color, odor, and the presence of any phase separation, as recommended for self-emulsifying systems (Pouton, 2006). Physical stability was further evaluated using a centrifugation test, in which each formulation was placed in centrifuge tubes and centrifuged at 4700 rpm for 30 min. Formulations that showed no phase separation, creaming, or cracking after centrifugation were considered physically stable, indicating resistance to gravitational stress during storage (Listyorini et al., 2018; Date et al., 2010).

The emulsion type of the formulations was determined using the methylene blue dye test. Methylene blue, a water-soluble dye, was added to each formulation; uniform dispersion of the dye throughout the system confirmed an oil-in-water (O/W) nanoemulsion, whereas localized dye aggregation indicated a water-in-oil (W/O) system. This method is widely used for rapid identification of the continuous phase in nanoemulsion systems (Talegaonkar et al., 2008). The clarity of the nanoemulsions was quantitatively evaluated by measuring percent transmittance using a UV–Vis-spectrophotometer at 650 nm, with deionized water as the blank. High transmittance values indicate small droplet size and good homogeneity of the nanoemulsion system (Agustin et al., 2025). The density of each SNEDDS formulation was determined using the pycnometer method by measuring the mass of a known volume of sample and expressing the results in g/mL. Density measurement provides supporting information related to formulation uniformity and reproducibility (Preeti et al., 2023).

Antioxidant Activity of SNEDDS Formulations

The antioxidant activity of the SNEDDS formulations was evaluated using the DPPH free radical scavenging assay. Appropriately diluted samples were mixed with freshly prepared DPPH solution in ethanol and incubated in the dark at room temperature. Absorbance was measured at 517 nm using a UV–Vis spectrophotometer. Radical scavenging activity was calculated relative to a DPPH control, and IC_{50} values were determined from dose–response curves as indicators of antioxidant potency (Agustin et al., 2025).

In Vivo Immunomodulatory Study

An *in vivo* immunomodulatory study was conducted using male mice (*Mus musculus*) to evaluate the effects of the SNEDDS formulations on hematological and immune-related parameters. The animals were randomly divided into six experimental groups (n = 5 per group): negative control (NC), receiving Na-CMC solution; positive control (PC), receiving a commercial immunostimulant (Stimuno); crude extract (CC), receiving a suspension of Sungkai ethanol extract; F1 and F5, receiving SNEDDS containing 260 mg extract; Formulation F2 and F6 receiving SNEDDS containing 400 mg extract; and F3

and F7, receiving SNEDDS containing 530 mg extract. The dose selection was based on preliminary formulation optimization and intended to evaluate a dose–response relationship.

All treatments were administered orally once daily for 14-consecutive days. At the end of the treatment period, blood samples were collected via cardiac puncture under appropriate anesthesia. Hematological analysis was performed to assess the immunomodulatory response, with total leukocyte count as the primary endpoint, as leukocytes represent a key indicator of systemic immune activation. In addition, secondary hematological parameters, including hemoglobin concentration, erythrocyte count, hematocrit, and platelet count, were evaluated to assess the safety of the formulations and their potential effects on hematopoietic function.

Total and differential blood cell parameters were analyzed using an automated hematology analyzer based on flow cytometry and impedance principles, which allows accurate quantification of leukocytes, erythrocytes, and platelets through cell size, granularity, and fluorescence characteristics. Hemoglobin concentration was determined photometrically following red blood cell lysis, in accordance with standard hematological methods. The integration of leukocyte profiling with erythrocyte- and platelet-related parameters enabled a comprehensive evaluation of immunostimulatory efficacy while simultaneously monitoring hematological safety (Sumadja et al., 2025).

Statistical Analysis

All quantitative data were expressed as mean ± standard error of the mean (SEM). Statistical significance between groups was determined using One-Way Analysis of Variance (ANOVA), with the significance level (α) set at 0.05.

RESULTS AND DISCUSSIONS

Physicochemical Characterization of SNEDDS

All SNEDDS formulations exhibited a clear and homogeneous appearance, indicating successful formation of nanoemulsion systems (**Table 2**). Formulations containing Sungkai leaf extract (F1-F3; F5-F7) showed a uniform yellow color and a characteristic odor of Sungkai combined with cinnamon oil, whereas the blank formulation (F4 and F8) was colorless with a cinnamon oil odor only. No phase separation, creaming, or cracking was observed in any formulation, demonstrating good physical stability of the SNEDDS systems (**Figure 2, Table 2**).

As shown in **Table 3**, all SNEDDS formulations were soluble in the methylene blue test, confirming the formation of oil-in-water (O/W) nanoemulsions. All formulations also remained physically stable without phase separation during the stability assessment. The extract-loaded formulations exhibited a yellow color, with color intensity increasing in proportion to extract concentration, whereas the blank formulation (F4 and F8) was colorless. All formulations presented a characteristic cinnamon oil odor, with an additional Sungkai aroma observed in F1 – F3 whereas formulations F5–F7 exhibited the characteristic aroma of Sungkai combined with red palm oil. The methylene blue dye test confirmed that all formulations formed oil-in-water (O/W) nanoemulsions. Moreover, all formulations remained physically stable, as evidenced by the absence of phase separation following centrifugation.

As summarized in **Table 4**, the formulations showed high optical clarity, with percent transmittance values ranging from 82.0 ± 0.41% to 98.0 ± 0.46%. The highest transmittance was observed in the blank formulations F4 and F8, at approximately 96% and 98%, respectively, while slightly lower values were recorded for extract-loaded formulations, reflecting the presence of dissolved phytoconstituents. The density of all formulations was comparable, ranging from 0.94 ± 0.12 to 1.04 ± 0.11 g/mL, indicating formulation uniformity. All formulations exhibited high optical clarity, confirming the formation of transparent oil-in-water systems.

Particle size analysis demonstrated that several SNEDDS formulations produced droplets within the nanoscale range. Formulations F1, F2, F3, and F7 exhibited mean particle sizes below 60 nm, with values of 50.87 ± 0.41, 40.13 ± 0.43, 58.47 ± 0.35, and 53.99 ± 0.34 nm, respectively. Formulations F5 and F6 showed larger droplet sizes of 68.87 ± 0.70 and 68.20 ± 0.76 nm, respectively, which remained within the sub-100 nm range. Particle size data were not applicable for formulations F4 and F8.

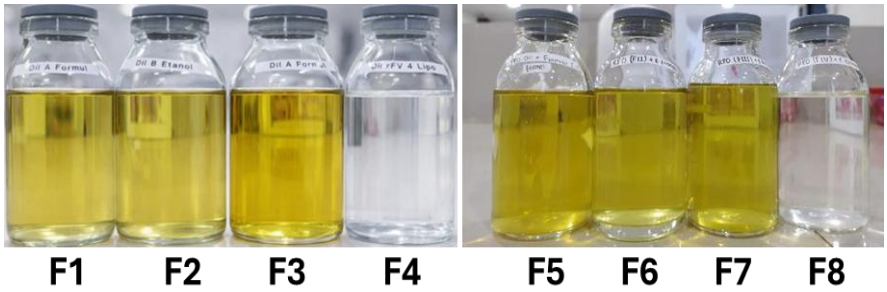

Figure 2. Representative photographs showing the physical appearance and visual stability of nanoemulsions obtained from eight different formulations.

Table 2. Physical appearance of nanoemulsion formula

Formulation	Parameters			
	Clarity	Color	Aroma	Phase
F1	Clear	Yellow	Characteristic Sungkai and cinnamon oil	Stable, no phase separation
F2	Clear	Yellow	Characteristic Sungkai and cinnamon oil	Stable, no phase separation
F3	Clear	Yellow	Characteristic Sungkai and cinnamon oil	Stable, no phase separation
F4	Clear	Colorless	Characteristic cinnamon oil	Stable, no phase separation
F5	Clear	Yellow	Characteristic Sungkai and red palm oil	Stable, no phase separation
F6	Clear	Yellow	Characteristic Sungkai and red palm oil	Stable, no phase separation
F7	Clear	Yellow	Characteristic Sungkai and red palm oil	Stable, no phase separation
F8	Clear	Colorless	Characteristic Red Palm Oil	Stable, no phase separation

Table 3. Emulsion type and physical stability

Formula	Solubility (Methylene blue)	Nanoemulsion Type
F1	Soluble	Oil in Water (O/W)
F2	Soluble	Oil in Water (O/W)
F3	Soluble	Oil in Water (O/W)
F4	Soluble	Oil in Water (O/W)
F5	Soluble	Oil in Water (O/W)
F6	Soluble	Oil in Water (O/W)
F7	Soluble	Oil in Water (O/W)
F8	Soluble	Oil in Water (O/W)

Table 4. Physicochemical characterization of SNEDDS formulations

Formula	Transmittance (%)	Density (g/mL)	Particle Size (nm)	Polydispersity Index (PDI)	Zeta Potential (mV)
F1	$88^{a} \pm 0.22$	$1.032^{a} \pm 0.05$	$50.87^{a} \pm 0.41$	$0.41^{a} \pm 0.06$	$(-)20.53^{c} \pm 0.07$
F2	$90^{a} \pm 0.32$	$1.033^{a} \pm 0.51$	$40.13^{b} \pm 0.43$	$0.33^{a} \pm 0.05$	$(-)33.57^{b} \pm 0.33$
F3	$84^{a} \pm 0.31$	$1.034^{a} \pm 0.04$	$58.47^{a} \pm 0.35$	$0.39^{a} \pm 0.03$	$(-)24.63^{c} \pm 0.92$
F4	$96^{a,b} \pm 0.52$	$1.034^{a} \pm 0.11$	N/A	N/A	N/A
F5	$87^{a} \pm 0.37$	$1.03^{a} \pm 0.46$	$68.8^{c} \pm 0.70$	$0.69^{ab} \pm 0.01$	$(-)27.4^{c} \pm 0.29$
F6	$86^{a} \pm 0.27$	$1.03^{a} \pm 0.51$	$68.2^{c} \pm 0.76$	$0.83^{b} \pm 0.11$	$(-)37.6^{a} \pm 0.17$
F7	$82^{a} \pm 0.41$	$1.03^{a} \pm 0.11$	$53.9^{a} \pm 0.34$	$0.49^{a} \pm 0.01$	$(-)33.1^{b} \pm 0.23$
F8	$98^{b} \pm 0.46$	$0.94^{a} \pm 0.12$	N/A	N/A	N/A

*Values are presented as mean ± SEM. Different superscript letters indicate significant differences among groups ($p < 0.05$).

The polydispersity index (PDI), which reflects the homogeneity of droplet size distribution, varied among formulations. F1, F2, F3, and F7 exhibited PDI values below 0.50, indicating relatively narrow and homogeneous size distributions. In contrast, higher PDI values were observed for F5 (0.69 ± 0.01) and F6 (0.83 ± 0.11), suggesting broader droplet size distributions. PDI values were not applicable for F4 and F8. In addition, zeta potential measurements showed that the SNEDDS formulations possessed negative surface charges, with values ranging from −20.53 ± 0.07 to −37.60 ± 0.17 mV. Among the formulations, F2 and F6 exhibited the highest absolute zeta potential values, whereas F1 and F3 showed moderately lower negative charges. Zeta potential data were not available for formulations F4 and F8. Overall, the results indicate that the SNEDDS formulations displayed acceptable optical clarity, nanoscale droplet size, and variable degrees of size homogeneity and surface charge, as summarized in **Table 4**.

Antioxidant Activity of Extract and SNEDDS Formulations

The antioxidant activity of Sungkai ethanol extract and the SNEDDS formulations was evaluated using the DPPH radical scavenging assay. The results are presented in Table 4. The crude ethanol extract exhibited an IC_{50} value of 27.91 ppm and was classified as having very strong antioxidant activity. Among the SNEDDS formulations, F1, F2, F3, F5, F6, and F7 showed IC_{50} values of 43.08, 39.41, 38.45, 31.29, 40.59, and 41.78 ppm, respectively, and were also categorized as very strong antioxidants (Nasri et al., 2025). Formulations F4 and F8 showed no detectable antioxidant activity, with IC_{50} values recorded as 0 ppm. Overall, the IC_{50} values of the extract-loaded SNEDDS formulations ranged from 31.29 to 43.08 ppm, while the crude extract showed a lower IC_{50} value than all nanoemulsion formulations. The antioxidant activity classification for each sample is summarized in **Table 5.**

The DPPH radical scavenging assay demonstrated that both the crude ethanol extract of Sungkai and most extract-loaded SNEDDS formulations exhibited very strong antioxidant activity. The crude extract showed the lowest IC_{50} value (27.91 ppm), indicating higher radical scavenging efficiency than all nanoemulsion formulations. This result is consistent with the direct availability of free phenolic and flavonoid compounds in the crude extract, which can readily interact with DPPH radicals in *in vitro* systems (Chaudhary et al., 2023).

Among the SNEDDS formulations, IC_{50} values ranged from 31.29 to 43.08 ppm. Formulation F5 exhibited the strongest antioxidant activity (31.29 ppm), followed by F3, F2, F6, F7, and F1. These findings indicate that incorporation of the Sungkai extract into the SNEDDS system was able to preserve substantial antioxidant capacity, although with a modest reduction relative to the crude extract. Such reductions have been widely reported in nanoemulsion-based systems and are often attributed to partial encapsulation of antioxidant compounds within lipid droplets, which may limit their immediate accessibility to DPPH radicals during *in vitro* evaluation (Inugala et al., 2015; Suryani et al., 2019).

Formulations F4 and F8 showed no detectable antioxidant activity, consistent with the absence or ineffective loading of the Sungkai extract. This observation confirms that the radical scavenging activity was primarily derived from extract-associated bioactive compounds rather than from the excipient system alone. Although cinnamon oil and red palm oil contain antioxidant constituents, their concentrations in the tested formulations were insufficient to produce measurable DPPH scavenging activity in the absence of the extract under the experimental conditions applied.

Variations in antioxidant activity among extract-loaded SNEDDS formulations suggest that formulation composition influenced the apparent radical scavenging efficiency. Notably, formulations containing red palm oil (F5–F7) tended to exhibit lower IC_{50} values than formulations without red palm oil at comparable extract levels, indicating a contributory role of red palm oil–associated antioxidants such as carotenoids and tocotrienols. Similar synergistic effects between lipid-based carriers and plant-derived antioxidants have been reported in nanoemulsion systems, where bioactive oils contribute to improved functional performance (Madoromae & Lertcanawanichakul, 2025). However, the non-uniform trend observed across formulations indicates that antioxidant activity depends on the combined effects of extract concentration, oil phase composition, and nanoemulsion structure.

Overall, the results demonstrate that the SNEDDS platform effectively maintained the antioxidant potential of *P. canescens* ethanol extract while providing the advantages of a lipid-based delivery system. Although the crude extract exhibited superior *in vitro* antioxidant activity, the preserved activity observed in the SNEDDS formulations supports their further investigation, particularly for *in vivo* applications where improved stability and delivery efficiency may compensate for minor reductions in *in vitro* radical scavenging performance.

Table 5. IC_{50} of antioxidant activity of SNEDDS formulations

Formula	IC_{50} (ppm)	Antioxidant category
F1	$43.08^{c} \pm 0.02$	Very strong
F2	$39.41^{c} \pm 0.03$	Very strong
F3	$38.45^{c} \pm 0.04$	Very strong
F4	0	ND (Not Detected)
F5	$31.29^{c} \pm 0.005$	Very strong
F6	$40.59^{c} \pm 0.003$	Very strong
F7	41.78 ± 0.025	Very strong
F8	0	ND (Not Detected)
Extract	$27.91^{c} \pm 0.004$	Very strong
Ascorbic acid	$11.046^{b} \pm 0.040$	Very strong

*Values are presented as mean ± SEM. Different superscript letters indicate significant differences among groups ($p < 0.05$).

Table 6. Blood biochemistry profile of mice treated with nanoemulsion formulations

Parameters	Treatments PC, Stimuno®	CE	F1	F2	F3	F4	F5	F6	F7	F8
Leukocyte Count ($10^3/\mu L$)	5.93^{d} ± 0.06	5.40^{a} ± 0.09	5.17^{a} ± 0.05	5.29^{a} ± 0.14	5.49^{a} ± 0.30	3.87^{b} ± 0.59	5.15^{a} ± 0.20	5.82^{ab} ± 0.60	7.08^{c} ± 1.39	3.86^{b} ± 1.02
Hemoglobin (g/dL)	13.5^{a} ± 0.06	12.1^{a} ± 0.06	13.8^{a} ± 0.05	13.8^{a} ± 0.14	14.3^{b} ± 0.30	12.9^{a} ± 0.59	13.56^{a} ± 0.26	15.1^{b} ± 0.49	11.12^{c} ± 0.47	12.75^{a} ± 0.05
Erythrocytes Count ($10^6/\mu L$)	8.57^{a} ± 0.06	8.69^{a} ± 0.045	8.2^{a} ± 0.05	8.98^{a} ± 0.14	8.65^{a} ± 0.30	8.92^{a} ± 0.59	8.5^{a} ± 0.40	9.06^{a} ± 0.355	8.25^{a} ± 0.05	8.94^{a} ± 0.28
Hematocrit Value (%)	37.9^{a} ± 0.06	36^{a} ± 0.055	40^{b} ± 0.05	42.8^{b} ± 0.14	42.1^{b} ± 0.30	39.9^{a} ± 0.59	34.33^{a} ± 8.72	37.36^{a} ± 1.38	27.9^{c} ± 4.12	39.1^{b} ± 3.25
Platelets Count ($10^3/\mu L$)	699^{a} ± 0.06	585^{b} ± 0.16	492^{c} ± 0.05	595^{b} ± 0.14	369^{d} ± 0.30	636^{a} ± 59.65	375.33^{e} ± 65.73	573^{b} ± 43.54	665^{a} ± 11.14	671^{a} ± 28.5

*Values are presented as mean ± SEM. Different superscript letters indicate significant differences among groups ($p < 0.05$).

In Vivo Immunomodulatory Activity

The immunomodulatory activity was evaluated *in vivo* by analyzing hematological parameters of mice after two weeks of oral administration. The parameters measured included total leukocyte count, hemoglobin level, erythrocyte count, hematocrit value, and platelet count. The results are summarized in **Table 6** and are presented as mean ± SEM. The positive control group (PC), treated with a commercial immunostimulant (Stimuno®), showed a total leukocyte count of 5.93 ± 0.06 $\times 10^3/\mu$L. The crude ethanol extract group (CE) exhibited a leukocyte count of 5.40 ± 0.09 $\times 10^3/\mu$L. Among the SNEDDS-treated groups, leukocyte counts were 5.17 ± 0.05, 5.29 ± 0.14, 5.49 ± 0.30, 3.87 ± 0.59, 5.15 ± 0.20, 5.82 ± 0.60, 7.08 ± 1.39, and 3.86 ± 1.02 $\times 10^3/\mu$L for formulations F1 to F8, respectively.

Hemoglobin levels across the treatment groups ranged from 11.12 ± 0.47 to 15.10 ± 0.49 g/dL. The erythrocyte counts varied between 8.06 ± 0.35 and 9.06 ± 0.55 $\times 10^6/\mu$L, while hematocrit values ranged from 27.9 ± 4.12% to 42.1 ± 3.99%. Platelet counts among the groups ranged from 369 ± 59.65 to 699 ± 0.06 $\times 10^3/\mu$L. Overall, differences were observed among treatment groups in total leukocyte count and platelet count, while hemoglobin concentration, erythrocyte count, and hematocrit values remained within comparable ranges across all groups, as detailed in **Table 6.**

The immunomodulatory effect of the SNEDDS formulations was primarily reflected by changes in total leukocyte count after two weeks of oral administration (**Table 6**). Variations in leukocyte responses across formulations F1–F8 indicate that both extract loading and formulation composition influenced the immunological outcome. The data, the positive control, exhibited a leukocyte count of 5.93 ± 0.06 $\times 10^3/\mu$L, confirming the validity of the experimental model, while the crude ethanol extract showed a comparable response (5.40 ± 0.09 $\times 10^3/\mu$L), supporting the intrinsic immunomodulatory potential of *P. canescens* leaf extract. Among the SNEDDS formulations, F1–F3 demonstrated a gradual increase in leukocyte count (5.17–5.49 $\times 10^3/\mu$L), indicating a formulation-dependent and extract-related trend within this group. In contrast, formulations F4 and F8 produced markedly lower leukocyte counts (3.87 ± 0.59 and 3.86 ± 1.02 $\times 10^3/\mu$L), consistent with the absence or ineffective loading of the extract. This confirms that the observed immunomodulatory response was primarily driven by the bioactive constituents of *P. canescens*, rather than by the nanoemulsion excipients alone.

Formulations containing red palm oil (F5–F7) exhibited varying effects on leukocyte counts. While F5 and F6 yielded leukocyte levels similar to the crude extract, F7 produced the highest leukocyte response among all treatments (7.08 ± 1.39 $\times 10^3/\mu$L), surpassing both the crude extract and the positive control. This pronounced effect in F7 may be attributed to several factors. First, the higher extract loading (530 mg) in combination with red palm oil likely enhanced the solubilization and intestinal absorption of bioactive compounds, facilitating more efficient systemic delivery. Nanoemulsion-based lipid carriers, such as those used in F7, are known to improve dispersion, protect labile compounds from degradation, and promote uptake via the lymphatic pathway, thereby amplifying immunomodulatory effects (Baral et al., 2023). Second, the bioactive components of red palm oil, particularly carotenoids and tocotrienols, possess potent antioxidant properties that can support hematopoietic function and leukocyte proliferation. By mitigating oxidative stress, these lipid antioxidants

may preserve immune cell viability and enhance functional responsiveness (Madoromae & Lertcanawanichakul, 2025). Additionally, the combination of cinnamon and red palm oil in F7 may provide synergistic effects, as cinnamon polyphenols have been shown to modulate immune signaling pathways, potentially further stimulating leukocyte production. Together, these factors suggest that F7's formulation—optimized for both extract content and lipid-mediated delivery—created a favorable environment for immune enhancement, explaining its superior leukocyte response compared with other formulations (Cao et al., 2008; Jimoh et al., 2024; Oguntibeju et al., 2009).

Importantly, hemoglobin levels, erythrocyte counts, and hematocrit values remained within physiological ranges across all groups, indicating that the immunomodulatory response was not accompanied by disruption of erythropoiesis. Similar selectivity toward leukocyte modulation without hematological toxicity has been reported for nanoemulsified herbal extracts in previous *in vivo* studies (Pechroj et al., 2024). Platelet counts showed moderate variation among formulations but were not suppressed, suggesting maintenance of hematological homeostasis, consistent with reports on antioxidant-mediated protection of hematopoietic function (Preeti et al., 2023).

Overall, the findings demonstrate that SNEDDS formulations containing *P. canescens* ethanol extract (F1–F3 and F5–F7) were capable of modulating leukocyte levels to different extents, whereas formulations lacking effective extract loading showed no immunostimulatory response. The pronounced effect observed with F7, together with the more controlled responses of F1–F3, indicates that extract presence and formulation composition are critical determinants of immunomodulatory performance, supporting further refinement of SNEDDS-based delivery systems for *P. canescens*.

CONCLUSIONS

This study demonstrated that a nanoemulsion-based delivery system for *P. canescens* leaf ethanol extract can be successfully formulated with acceptable physicochemical characteristics while preserving strong antioxidant activity. The SNEDDS formulations containing the extract were able to modulate leukocyte levels *in vivo* to varying extents, whereas formulations lacking effective extract loading showed no immunomodulatory response, and erythrocyte-related parameters remained within normal physiological ranges. These findings indicate that nanoemulsion-based delivery systems represent a promising approach for improving the consistency and biological performance of *P. canescens* leaf extract and support further investigation toward its development as a nutraceutical or phytopharmaceutical agent.

REFERENCES

Agustin, P., Ihsan, M., Lestari, A., & Tarigan, I. L. (*2025*). Formulation of nanoemulsion based Sungkai leaves extract (*P.* canescens Jack) and Cinnamon oil (*Cinnamomum burmannii* (Nees & T Nees) Blume) as an antioxidant and skin protection factors (SPF) Agent. *Chimica et Natura Acta*, *13*(1), 49–65. https://doi.org/10.24198/cna.v13.n1.55234

Baral, K. C., Lee, S. H., Song, J. G., Jeong, S. H., & Han, H.-K. (2023). Improved therapeutic efficacy of MT102, a new anti-inflammatory agent, via a self-microemulsifying drug delivery system, in ulcerative colitis mice. *Pharmaceutics*, *15*(12). https://doi.org/10.3390/ pharmaceutics 15122720

Cao, H., Urban, J. F., & Anderson, R. A. (2008). Cinnamon polyphenol extract affects immune responses by regulating anti- and proinflammatory and glucose transporter gene expression in mouse macrophages. *The Journal of Nutrition*, *138*(5), 833–840. https://doi.org/ https://doi.org/10.1093/jn/138.5.833

Chaudhary, P., Janmeda, P., Docea, A. O., Yeskaliyeva, B., Abdull Razis, A. F., Modu, B., Calina, D., & Sharifi-Rad, J. (2023). Oxidative stress, free radicals and antioxidants: potential crosstalk in the pathophysiology of human diseases. *Frontiers in Chemistry*, *11*, 1158198. https://doi.org/10.3389/fchem.2023.1158198

Confessor, M. V. A., Agreles, M. A. A., Campos, L. A. de A., Silva Neto, A. F., Borges, J. C., Martins, R. M., Scavuzzi, A. M. L., Lopes, A. C. S., Kretzschmar, E. A. de M., & Cavalcanti, I. M. F. (2024). Olive oil nanoemulsion containing curcumin: antimicrobial agent against multidrug-resistant bacteria. *Applied Microbiology and Biotechnology*, *108*(1), 241. https://doi.org/10.1007/s00253-024-13057-x

Favaro-Trindade, C. S., Patel, B., Silva, M. P., Comunian, T. A., Federici, E., Jones, O. G., & Campanella, O. H. (2020). Microencapsulation as a tool to producing an extruded functional food. *Lwt*, *128*, 109433. https://doi.org/10.1016/j.lwt.2020.109433

Fikriansyah, M., Nelson, Latief, M., & Tarigan, I. L. (2023). Anticancer activities of seven Peronemins (A2, A3, B1, B2, B3, C1, and D1) from *Peronema canescens* Jack: A prediction studies. *Chempublish Journal*, *7*(1), 54–63. https://doi.org/10.22437/chp.v7i1.23726

Gao, Z., Zhu, Y., Jin, J., Jin, Q., & Wang, X. (2023). Chemical–physical properties of red palm oils and their application in the manufacture of aerated emulsions with improved whipping capabilities. *Foods*, *12*(21). https://doi.org/10.3390/foods12213933

Hussain, S. A., Hameed, A., Nazir, Y., Naz, T., Wu, Y., Suleria, H. A. R., & Song, Y. (2018).

Microencapsulation and the characterization of polyherbal formulation (PHF) rich in natural polyphenolic compounds. *Nutrients*, *10*(7). https://doi.org/10.3390/nu10070843

Inugala, S., Eedara, B. B., Sunkavalli, S., Dhurke, R., Kandadi, P., Jukanti, R., & Bandari, S. (2015). Solid self-nanoemulsifying drug delivery system (S-SNEDDS) of darunavir for improved dissolution and oral bioavailability: In vitro and in vivo evaluation. *European Journal of Pharmaceutical Sciences*, *74*, 1–10. https://doi.org/10.1016/j.ejps.2015.03.024

Jantan, I., Ahmad, W., & Bukhari, S. N. A. (2015). Plant-derived immunomodulators: An insight on their preclinical evaluation and clinical trials. *Frontiers in Plant Science*, *6*(AUG), 1–18. https://doi.org/10.3389/fpls.2015.00655

Jimoh, O. A., Ayodele, A. D., Ojo, O. A., Okin-Aminu, H. O., & Olarotimi, O. J. (2024). Effects of turmeric, ginger, cinnamon, and garlic essential oils on HSP70, NFκB, oxidative DNA damage, inflammatory cytokines, and oxidative markers in broiler chickens. *Translational Animal Science*, *8*. https://doi.org/10.1093/tas/txae127

Kaur, G., Panigrahi, C., Agarwal, S., Khuntia, A., & Sahoo, M. (2024). Recent trends and advancements in nanoemulsions: Production methods, functional properties, applications in food sector, safety and toxicological effects. *Food Physics*, *1*, 100024. https://doi.org/10.1016/j.foodp.2024.100024

Khedkar, S., & Ahmad Khan, M. (2023). Aqueous extract of Cinnamon (*Cinnamomum* spp.): role in cancer and inflammation. *Evidence-Based Complementary and Alternative Medicine*, *2023*. https://doi.org/10.1155/2023/5467342

Latief, M., Arum, D., Nurjannah, S., Tarigan, I. L., Khatib, A., & Yusnaidar. (2024). LC-MS based metabolite profiling of ethanol extract from the Sungkai (*Peronema canescens* Jack) and in silico prediction of antidiabetic activity with α-glucosidase. *Molekul*, *19*(3), 455–462. https://doi.org/10.20884/1.jm.2024.19.3.8806

Latief, M., Fisesa, A. T., Sari, P. M., & Tarigan, I. L. (2021). Anti-inflammatory activity of Sungkai leaves (*Peronema canescens* Jack) ethanol in carregeenan induced mice. *Jurnal Farmasi Sains dan Praktis*, *7*(2), 2579–4558.

Latief, M., Sari, P. M., Fatwa, L. T., Tarigan, I. L., & Rupasinghe, H. P. V. (2021). Antidiabetic activity of Sungkai (*Peronema canescens* Jack) leaves ethanol extract on the male mice induced alloxan monohydrate. *Pharmacology and Clinical Pharmacy Research, 6*(2). https://doi.org/10.15416/pcpr.v4i3.31666

Madoromae, H., & Lertcanawanichakul, M. (2025). Red palm oil: Nutritional composition, bioactive properties, and potential applications in health and cosmetics: A narrative review. *Molecules*, *30*(22). https://doi.org/10.3390/molecules30224402

Mamun, M. A. Al, Rakib, A., Mandal, M., Kumar, S., Singla, B., & Singh, U. P. (2024). Polyphenols: Role in modulating immune function and obesity. *Biomolecules*, *14*(2). https://doi.org/10.3390/biom14020221

Masyita, A., Mustika Sari, R., Dwi Astuti, A., Yasir, B., Rahma Rumata, N., Emran, T. Bin, Nainu, F., & Simal-Gandara, J. (2022). Terpenes and terpenoids as main bioactive compounds of essential oils, their roles in human health and potential application as natural food preservatives. *Food Chemistry: X*, *13*, 100217. https://doi.org/10.1016/j.fochx.2022.100217

Miksusanti, A. E. F., & Bihurinin, A. H. B. (2023). Optimization of tween 80 and PEG-400 concentration in Indonesian virgin coconut oil nanoemulsion as antibacterial against *Staphylococcus aureus*. *Sains Malaysiana*, *52*(4), 1259–1272. https://doi.org/10.17576/JSM-2023-5204-17

Montes O. A. J. M., Candal, R. J., & Herrera, M. L. (2017). Nanoemulsions: stability and physical properties. *Current Opinion in Food Science*, *16*, 1–6. https://doi.org/10.1016/j.cofs.2017.06.003

Nasri, N., Kaban, V. E., Rani, Z., Suci, N., Tania, G., & Ferendina, I. (2025). Potential antioxidant and antibacterial activity of curry leaf ethanol extract (*Murraya koenigii*) against *Propionibacterium acnes*. *Journal of Pharmaceutical and Sciences*, *8*(4), 2398–2408. https://doi.org/10.36490/journal-jps.com.v8i4.881

Oguntibeju, O. O., Esterhuyse, A. J., & Truter, E. J. (2009). Red palm oil: nutritional, physiological and therapeutic roles in improving human wellbeing and quality of life. *British Journal of Biomedical Science*, *66*(4), 216–222. https://doi.org/10.1080/09674845.2009.11730279

Onoue, S., Yamada, K., & Sato, H. (2025). Advanced oral drug delivery systems: Current challenges and emerging technologies. *Acta Pharmaceutica Sinica B*. https://doi.org/ https://doi.org/10.1016/j.apsb.2025.11.036

Pechroj, S., Kaewkod, T., Sattayawat, P., Inta, A., Suriyaprom, S., Yata, T., Tragoolpua, Y., & Promputtha, I. (2024). Multifunctional nanoemulsified *Clinacanthus nutans* extract: synergistic anti-pathogenic, anti-biofilm, anti-inflammatory, and metabolic modulation effects against Periodontitis. *Biology*, *13*(10). https://doi.org/10.3390/biology13100815

Pizzino, G., Irrera, N., Cucinotta, M., Pallio, G., Mannino, F., Arcoraci, V., Squadrito, F., Altavilla, D., & Bitto, A. (2017). Oxidative stress:

Harms and benefits for human health. *Oxidative Medicine and Cellular Longevity*, *2017*. https://doi.org/10.1155/2017/841676 3

Preeti, S. S., Malik, R., Bhatia, S., Al Harrasi, A., Rani, C., Saharan, R., Kumar, S., Geeta, & Sehrawat, R. (2023). Nanoemulsion: An emerging novel technology for improving the bioavailability of drugs. *Scientifica*, *2023*, 6640103. https://doi.org/10.1155/2023/ 6640103

Saffari, I., Chaleshtori, R. S., Mirzaei, H., & Taghizadeh, M. (2025). Enhanced properties and biological activities of *Heracleum persicum* extract via nanoemulsification and nanoencapsulation: anti-listeria effects, cytotoxicity, and applications in traditional cheese. *Journal of Food Processing and Preservation*, *2025*(1). https://doi.org/10.1155/jfpp/5727548

Shalihin, M. I., Khatib, A., Yusnaidar, Y., Lasmana, I., & Latief, M. (2024). An in - vogue plant, *Peronema canescens* Jack : traditional uses and scientific evidence of its bioactivities. *Discover Plants*. https://doi.org/10.1007/s44372-024-00048-5

Snezhkina, A. V., Kudryavtseva, A. V., Kardymon, O. L., Savvateeva, M. V., Melnikova, N. V., Krasnov, G. S., & Dmitriev, A. A. (2020). ROS generation and antioxidant defense systems in normal and malignant cells. *Oxidative Medicine and Cellular Longevity*, *2019*. https://doi.org/10.1155/2019/6175804

Sumadja, W. A., Filawati, F., Ramadhan, I. I., Rahmasari, N., & Tarigan, I. L. (2025). Phytogenic feed additive derived from *Peronema canescens* leaves: Bioactive profile, effects on broiler growth, carcass yield, blood biochemistry, and molecular interactions. *Open Veterinary Journal*, *15*(9), 4617–4634. https://doi.org/10.5455/OVJ.2025.v15.i9.67

Suryani, Z. W. O. S., Sahumena, M. H., Adawia, S., Wahyuni, R., Adjeng, A. N. T., Nisa, M., Kasmawati, H., Ihsan, S., Ruslin, & Aswan, M. (2019). Preparation and characterization of self-nanoemulsifying drug delivery system (SNEDDS) from *Moringa oleifera* L.and *Cassia alata* L. leaves extracts. *AIP Conference Proceedings*, *2199*. https://doi.org/10.1063/1.5141325

Talegaonkar, S., Azeem, A., Ahmad, F. J., Khar, R. K., Pathan, S. A., & Khan, Z. I. (2008). Microemulsions: a novel approach to enhanced drug delivery. *Recent Patents on Drug Delivery & Formulation*, *2*(3), 238–257. https://doi.org/10.2174/187221108786241679

Tarigan, I. L., Farah, F., Puspitasari, R. D., Saharin, S. M., & Latief, M. (2025). Formulation and characterization of microencapsules containing ethanol extract of Sungkai leaves (*Peronema canescens* Jack). *Chempublish Journal*, *9*(1), 100–119. https://doi.org/https://doi.org/10.22437/chp.v9i1.43042

Tarigan, I. L., Triani, A. A., & Latief, M. (2023). Antidiabetic activity of the methanol fraction of Sungkai leaves (*Peronema canescens* Jack). *The Journal of Pure and Applied Chemistry Research*, *12*(2), 117–127. https://doi.org/10.21776/ub.jpacr.2023.012.02.699

Zhuo, Y., Zhao, Y.-G., & Zhang, Y. (2024). Enhancing drug solubility, bioavailability, and targeted therapeutic applications through magnetic nanoparticles. *Molecules*, *29*(20). https://doi.org/10.3390/molecules29204854