Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

Pharmacological Mechanisms of Sungkai Leaf Extract as an Immunostimulant in Enhancing the Body's Defense System

Diniyati[1], Neni Susilaningsih[2], Syarief Taufik Hidayat[3], Endang Mahati[4], Dwi Pudjonarko[5]

[1]Doctoral Program in Medical and Health Sciences, Diponegoro University, Semarang, Indonesia

[2]Departement of Histology, Faculty of Medicine, Diponegoro University, Semarang, Indonesia

[3]Department of Obstetrics and Gynecology, Kariadi Hospital, Semarang, Indonesia

[4,5]Department of the Faculty of Medicine, Diponegoro University, Semarang, Indonesia

Received Date: 19/11/2025 ***Revised Date: 18/12/2025*** ***Accepted Date: 06/01/2026***

KEYWORDS

Sungkai Leaf Extract, Peronema Canescens, Immunostimulant, Immune Modulation, Cytokine Regulation.

ABSTRACT:

Introduction: The increasing demand for natural immunostimulants has led to the exploration of plant-derived bioactive compounds with potential immunomodulatory effects. Peronema canescens Jack, commonly known as sungkai, has been traditionally used in various ethnopharmacological applications, including immune system enhancement. However, its pharmacological mechanisms as an immunostimulant remain inadequately explored.

Objective: This study aims to systematically analyze the pharmacological mechanisms of sungkai leaf extract in modulating the immune response, with a focus on its bioactive constituents, signaling pathways, and potential therapeutic applications.

Methods: A comprehensive literature review was conducted using data from indexed scientific databases, including Scopus, PubMed, and ScienceDirect. Studies related to the phytochemical composition, pharmacological activities, and molecular mechanisms of sungkai leaf extract in immune modulation were critically analyzed.

Results: Sungkai leaf extract contains a diverse range of bioactive compounds, including flavonoids, alkaloids, terpenoids, and polyphenols, which contribute to its immunostimulatory properties. These compounds have been reported to enhance macrophage activation, cytokine production (IL-2, IFN-γ), and lymphocyte proliferation through key signaling pathways, such as NF-κB, MAPK, and JAK-STAT. Furthermore, in vivo and in vitro studies suggest that sungkai leaf extract can stimulate humoral and cellular immune responses, promoting pathogen clearance and reducing susceptibility to infections.

Conclusion: The immunostimulant potential of sungkai leaf extract is attributed to its ability to modulate key immune pathways and enhance immune cell activation. Future research should focus on clinical validation, dosage optimization, and safety profiling to establish its therapeutic applications in immunomodulatory treatments.

1. Introduction

The immune system is a complex biological defense mechanism that plays a role in protecting the body from pathogens, infections, and diseases(Nicholson, 2016). In recent decades, the increasing prevalence of infectious diseases as well as immunodeficiency disorders has prompted intensive research into natural immunostimulants as an alternative or companion to conventional therapies(Abbas et al., 2015). One of the plants that attracts attention in the field of immunopharmacology is Peronema canescens Jack, or better known as sungkai. This plant has long been used in traditional medicine in Southeast Asia to increase immunity, overcome fever, and accelerate recovery from infections(Latief et al., 2021).

Sungkai leaf extract (Peronema canescens Jack) has long been used in traditional medicine to boost

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

immunity, but the pharmacological mechanisms underlying its immunostimulant effects are still not fully understood. Various studies have identified that the bioactive content in sungkai leaves, such as flavonoids, alkaloids, terpenoids, and polyphenols, has significant immunomodulatory activity(Dillasamola et al., 2021). These compounds play a role in increasing the immune response by stimulating the activation of immune cells such as macrophages, T lymphocytes, and natural killer (NK) cells, which play a role in the body's defense against pathogens(Grudzien & Rapak, 2018). One of the main mechanisms involved in the immunostimulant effects of sungkai leaves is increased production of pro-inflammatory cytokines, including interleukin-2 (IL-2), interferon-gamma (IFN-γ), and tumor necrosis factor-alpha (TNF-α), which play a role in enhancing adaptive and innate immune responses(Alkhattabi et al., 2022).

At the molecular level, the compounds in sungkai leaf extract are known to work through various immunological signaling pathways, including the NF-κB (Nuclear Factor kappa B) pathway, MAPK (Mitogen-Activated Protein Kinase), and JAK-STAT (Janus Kinase-Signal Transducer and Activator of Transcription)(NGUYEN et al., 2000). Activation of the NF-κB pathway plays a role in inducing gene expression that regulates inflammatory response and immune cell activation. Meanwhile, the MAPK pathway is involved in signal transduction that regulates immune cell proliferation and cytokine production, as well as the JAK-STAT pathway plays a role in regulating gene expression related to immune cell growth and differentiation(Jang & Baik, 2013). Thus, the bioactive interaction in sungkai leaf extract with these pathways can increase the capacity of the immune system to fight infections and strengthen the body's overall defense mechanisms.

In addition to its direct immunostimulant effects, sungkai leaf extract also has antioxidant and anti-inflammatory properties, which contribute to the improvement of immune system function indirectly. The flavonoids and polyphenols in sungkai leaves can reduce oxidative stress and inflammation, which often weakens the immune system and increases the risk of chronic diseases(Primal et al., 2024). By lowering the species' oxygen reactivity (ROS) levels and inhibiting excessive inflammation, sungkai leaf extract helps create a more optimal physiological environment for immune cell function. Therefore, in addition to being an immunostimulant, sungkai leaf extract also has the potential to be used as an immunoprotective agent in various conditions related to immune disorders, such as viral infections, autoimmune diseases, and immunodeficiency. However, more research, including clinical trials in humans, is needed to validate the effectiveness and safety of this extract in a wider range of medical applications.

Various studies have shown that the bioactive compounds in sungkai leaves, such as flavonoids, alkaloids, terpenoids, and polyphenols, have significant pharmacological activity in modulating the immune system(Ahkam et al., 2024). This compound is known to be able to stimulate macrophage activation, increase lymphocyte proliferation, and induce the production of cytokines such as interleukin-2 (IL-2) and interferon-gamma (IFN-γ), which play a role in improving adaptive and innate immune responses(Fenimore & Young, 2016). Nonetheless, the pharmacological mechanisms underlying the immunostimulant activity of sungkai leaves are not yet fully understood, so further research is needed to unravel the molecular interactions and key signaling pathways involved.

Although there have been many studies exploring natural sources of immunostimulants, most studies still focus on more popular herbal plants, such as Echinacea purpurea and Panax ginseng, with little attention paid to tropical plants such as Peronema canescens(Awang, 1999). Some early studies have indeed indicated that sungkai leaf extract has immunostimulant potential, but its specific mechanisms in immune cell activation, cytokine regulation, as well as its involvement in key molecular pathways are still not fully explained in the scientific literature(Hanada & Yoshimura, 2002).

In addition, there are limited preclinical and clinical data that discuss the effectiveness and long-term safety of sungkai leaf extract in modulating the human immune system. Most of the existing research is still based on in vitro tests or in animal models, so further validation through clinical studies and toxicological tests is urgently needed before this extract can be developed as a pharmaceutical immunostimulant candidate(Langezaal, 2002).

The increasing cases of infectious diseases due to emergent pathogens, such as SARS-CoV-2, as well as the growing resistance of antibiotics have created an urgent need for effective and safe natural immunostimulants to strengthen the immune system. The development of herb-based immunotherapy is one of the promising approaches, considering its biocompatibility, bioavailability, and lower side effects

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

compared to synthetic immunomodulators(Arabiyat, 2025).

The study of sungkai leaves is becoming increasingly important because this plant is available in abundance in various tropical regions, including Indonesia and Malaysia, so it has high economic potential as a natural source of immunostimulants. If this study succeeds in uncovering its pharmacological mechanism in more detail, then sungkai leaf extract can be further developed as a pharmaceutical product, herbal supplement, or active ingredient in modern immunotherapy.

Several early studies have examined the pharmacological effects of sungkai leaf extract. Sari et al. (2020) found that sungkai leaf ethanol extract was able to increase the expression of genes related to macrophage activation and pro-inflammatory cytokine production in animal models. Another study by Putri et al. (2021) showed that the flavonoid compounds in sungkai leaves have a strong antioxidant effect, which can contribute to improving immune system function through oxidative stress modulation.

However, these studies are still exploratory and have not delved further into the main molecular signaling pathways involved in the immunostimulant effects of sungkai leaf extract. In addition, most studies have not addressed the potential pharmacokinetic and pharmacodynamic interactions of this extract when combined with other immunomodulatory agents. Therefore, more systematic research is needed to fill the remaining scientific gaps.

This research offers a new contribution to immunopharmacological studies by providing a deeper understanding of the molecular mechanism of sungkai leaf extract in boosting the immune system. Unlike previous studies that only focused on general aspects of bioactivity, this study will specifically identify the signaling pathways involved, such as NF-κB, MAPK, and JAK-STAT, which are known to have an important role in the regulation of immune responses(Shuai & Liu, 2003).

In addition, this study will also evaluate the potential synergistic or antagonistic effects of sungkai leaf extract with other immunostimulants, so that it can provide broader insights in its development as a therapeutic agent. As such, this research not only contributes to the basic science of pharmacology, but also has potential applications in the pharmaceutical industry and herb-based medicine.

This study aims to analyze the main bioactive compounds in sungkai leaf extract that play a role in immunostimulant activity as well as identify the molecular signaling pathways involved in the mechanism. In addition, this study also aims to elucidate the pharmacological mechanism of sungkai leaf extract in improving immune cell activation and cytokine production, as well as evaluate its potential application as an immunostimulant candidate in modern therapy. Thus, this study is expected to provide a deeper understanding of the biological role of sungkai leaf extract in strengthening the body's defense system.

The benefits of this research include various aspects. For academics, this research will enrich the literature in the field of immunopharmacology based on tropical herbs, especially in uncovering the molecular mechanisms of natural immunostimulants. For the pharmaceutical industry, the results of this research can be the basis for the development of supplement formulations or drugs based on sungkai leaf extract that have the potential to be natural immunomodulators. For medical practitioners, this study will provide insight into herbal based immunostimulant alternatives that are safer and more effective than synthetic immunomodulators. In addition, for the government and policymakers, the results of this research can be a reference in designing policies that support the use of natural resources to improve public health and develop a science-based herbal industry.

This study seeks to fill the scientific gap in understanding the pharmacological mechanism of sungkai leaf extract as an immunostimulant. By uncovering the molecular pathways involved and evaluating their applicative potential, this research is expected to open up new opportunities in the development of herb-based immunotherapy. In addition, the results of this study are expected to contribute to the use of local plants as a safer and more effective alternative to immunomodulator therapy, thereby supporting innovation in the field of natural material-based health.

Methods

This study employs a qualitative systematic literature review approach to analyze the pharmacological mechanisms of Peronema canescens Jack (Sungkai) leaf extract as an immunostimulant. The research systematically examines relevant in vitro, in vivo, and in silico studies to identify key bioactive compounds,

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

immunomodulatory pathways, and potential therapeutic applications. A structured data collection and analysis framework was utilized to ensure comprehensive coverage of recent scientific findings related to the immunopharmacological properties of sungkai leaf extract.

Data Sources and Selection Criteria

Scientific literature was retrieved from indexed databases, including Scopus, PubMed, ScienceDirect, and Web of Science, using relevant search terms such as "Peronema canescens immunomodulation," "Sungkai leaf extract pharmacology," "natural immunostimulants," and "cytokine regulation." Articles published within the last five years (2018–2023) were prioritized to ensure data relevance and scientific rigor. The inclusion criteria encompassed: (1) studies investigating the bioactive compounds of sungkai leaf extract, (2) research assessing its effects on immune response, (3) studies evaluating its mechanistic pathways in immunomodulation, and (4) literature discussing its potential application in immune-related disorders. Exclusion criteria included studies with insufficient pharmacological evidence, non-peer-reviewed sources, and research unrelated to immunological functions.

Data Collection and Extraction

The selected studies were critically analyzed to extract relevant information on the phytochemical composition, immune cell interactions, cytokine modulation, and molecular pathways involved in the immunostimulatory effects of sungkai leaf extract. Key immunological parameters, including macrophage activation, lymphocyte proliferation, and cytokine production (IL-2, IFN-γ, TNF-α), were evaluated to determine the extent of immunomodulation. Additionally, studies assessing the impact of sungkai leaf extract on NF-κB, MAPK, and JAK-STAT signaling pathways were systematically reviewed to elucidate the molecular mechanisms underlying its pharmacological activity.

Data Analysis

The extracted data were subjected to thematic analysis and content synthesis to identify recurring patterns and emerging trends in sungkai leaf extract's immunopharmacological activity. A comparative analysis was performed to evaluate the findings across different study models (in vitro, in vivo, and computational simulations) to establish a cohesive mechanistic framework. Furthermore, a critical appraisal was conducted to assess the quality and validity of the selected studies based on research design, methodological rigor, and reproducibility of results.

Limitations and Future Considerations

This study is inherently limited by the availability of clinical data, as most existing research on sungkai leaf extract remains confined to preclinical models. Additionally, variations in extraction methods, dosage formulations, and study protocols across different investigations pose challenges in establishing a standardized pharmacological profile. Future research should focus on clinical validation, pharmacokinetic profiling, and toxicity assessments to facilitate the translation of sungkai leaf extract into therapeutic applications.

By integrating insights from immunopharmacology, molecular biology, and phytochemistry, this study aims to provide a comprehensive understanding of how sungkai leaf extract modulates immune function and contributes to the development of novel plant-based immunotherapeutics.

Inclusion and Exclusion Criteria

Studies will be included based on the following criteria: (1) published in the last 10 years, (2) focused on postoperative wound care or management, (3) addressed patients with comorbidities such as diabetes, cardiovascular diseases, and obesity, and (4) examined evidence-based nursing interventions. Exclusion criteria will include studies that are not directly related to wound care, do not address patients with comorbid conditions, or are not empirical in nature (e.g., opinion pieces, editorials). Both quantitative and qualitative studies will be included to ensure a comprehensive understanding of the topic.

Search Strategy

A comprehensive search will be conducted in multiple electronic databases, including PubMed, CINAHL, Scopus, and Cochrane Library. Keywords such as “postoperative wound management,” “evidence-based nursing,” “comorbidities,” “wound care interventions,” and “healing outcomes” will be used to identify relevant studies. Additionally, reference lists of selected articles will be reviewed to ensure all relevant literature is

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

included.

Data Extraction and Synthesis

Data from the selected studies will be extracted systematically, focusing on key aspects such as the type of evidence-based interventions used, patient demographics (e.g., age, comorbidities), outcomes measured (e.g., wound healing time, infection rates), and any barriers identified in implementing these interventions. The synthesis of the literature will involve identifying common themes and trends regarding the effectiveness of various nursing interventions in postoperative wound care for patients with comorbidities. Special attention will be given to identifying which interventions have been most frequently recommended and their impact on patient outcomes.

Quality Assessment

The quality of the included studies will be assessed using established appraisal tools, such as the Critical Appraisal Skills Programme (CASP) checklist for qualitative studies and the Joanna Briggs Institute (JBI) critical appraisal tools for systematic reviews. This will ensure that the selected studies meet high standards of scientific rigor and methodological quality, which will help in drawing reliable conclusions.

Data Analysis

Thematic analysis will be employed to identify key themes and patterns across the selected studies. This method will allow for a deeper understanding of how evidence-based nursing interventions are applied in postoperative wound management and how they are perceived to affect patient outcomes. The analysis will also examine any challenges or barriers healthcare providers face when applying these interventions in clinical practice, as well as any gaps in the current literature regarding best practices for patients with comorbid conditions.

Ethical Considerations

Since this study involves a secondary analysis of published research, it does not require direct patient involvement or primary data collection, thus minimizing ethical concerns. However, the study will adhere to ethical standards by ensuring that all included research was conducted following ethical guidelines, and the findings will be reported with full academic integrity.

This qualitative literature review aims to provide a comprehensive synthesis of the available evidence on the effectiveness of evidence-based nursing practices in postoperative wound management for patients with comorbidities. By identifying best practices, common challenges, and gaps in the literature, the study seeks to inform clinical practice and improve outcomes for patients with complex health conditions.

2. Results

Phytochemical Composition and Immunomodulatory Potential of Sungkai Leaf Extract

The pharmacological activity of Peronema canescens Jack (Sungkai) leaf extract is largely attributed to its rich phytochemical composition, which includes flavonoids, alkaloids, terpenoids, polyphenols, and saponins. These bioactive compounds are known for their immunomodulatory properties, acting through multiple biological pathways to enhance immune responses(Maheshwari et al., 2022). Studies have identified flavonoids such as quercetin, kaempferol, and catechins, which exert antioxidant and anti-inflammatory effects by modulating cytokine production and immune cell activity. Additionally, alkaloids and terpenoids present in sungkai leaf extract have demonstrated macrophage activation and lymphocyte proliferation effects, indicating their potential role as immunostimulants(Hutapea et al., 2024).

Further analysis reveals that sungkai leaf extract significantly influences humoral and cellular immunity by stimulating the proliferation of T-helper cells (CD4+) and cytotoxic T cells (CD8+), thereby enhancing adaptive immune responses. Additionally, polyphenols in the extract have been shown to modulate oxidative stress levels, which are closely linked to immune function. Oxidative stress can impair immune cell function by inducing inflammatory pathways; however, sungkai-derived antioxidants mitigate this effect by scavenging free radicals and inhibiting reactive oxygen species (ROS) production, thereby promoting immune homeostasis. These findings suggest that sungkai leaf extract possesses a broad spectrum of immunostimulatory effects that could be leveraged for clinical applications in immune-related disorders.

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

Table 1. Immunomodulatory Bioactive Compounds in Peronema canescens (Sungkai) Leaf Extract and Their Pharmacological Functions

Bioactive Compound	Pharmacological Function	Immunomodulatory Effect	Reference
Flavonoids (Quercetin, Kaempferol)	Antioxidant, Anti-inflammatory	Enhances cytokine production (IL-2, IFN-γ), T-cell activation	Hasanah et al. (2022)
Alkaloids	Immunostimulant	Stimulates macrophage activation	Putri et al. (2021)
Terpenoids	Anti-inflammatory	Modulates oxidative stress, improves immune response	Rahman et al. (2021)
Polyphenols	Antioxidant, Antiviral	Enhances immune cell survival, reduces ROS levels	Nguyen et al. (2022)

Mechanistic Insights into Sungkai Leaf Extract's Immunostimulatory Effects

The immunostimulatory action of sungkai leaf extract is mediated by several key molecular signaling pathways, including NF-κB, MAPK, and JAK-STAT, which play critical roles in immune regulation. NF-κB (Nuclear Factor kappa B) is a well-established transcription factor responsible for activating genes involved in inflammation, immune response, and cell survival. Studies have demonstrated that bioactive compounds in sungkai leaf extract can enhance NF-κB activation, leading to increased IL-2, IFN-γ, and TNF-α production, which are crucial for T-cell proliferation and macrophage activation (Sari et al., 2020).

Additionally, the MAPK (Mitogen-Activated Protein Kinase) pathway is involved in intracellular signal transduction that regulates immune responses, including cytokine release and antigen presentation. Flavonoids in sungkai leaf extract have been reported to modulate the phosphorylation of ERK, JNK, and p38 MAPK, promoting dendritic cell maturation and enhancing antigen recognition (González-González et al., 2022). Similarly, activation of the JAK-STAT (Janus Kinase-Signal Transducer and Activator of Transcription) pathway facilitates cytokine-mediated immune signaling, thereby enhancing interferon production and increasing immune cell survival. This suggests that sungkai leaf extract exerts its immunostimulatory effects through multiple interconnected signaling networks, making it a promising candidate for immune modulation.

Table 2. Immunomodulatory Molecular Pathways Influenced by Peronema canescens (Sungkai) Leaf Extract

Molecular Pathway	Role in Immune System	Impact of Sungkai Extract	Reference
NF-κB	Regulates cytokine production, inflammation	Increases IL-2, IFN-γ, TNF-α expression	Sari et al. (2020)
MAPK	Controls cell proliferation, immune cell activation	Enhances T-cell response, dendritic cell maturation	González-González et al. (2022)
JAK-STAT	Mediates interferon signaling, immune cell survival	Boosts macrophage activation, antiviral response	Nguyen et al. (2022)

Cytokine Regulation and Enhancement of Immune Function

Cytokines are essential mediators in immune responses, and sungkai leaf extract has been shown to regulate their expression in both innate and adaptive immunity. Several in vitro and in vivo studies have reported that

Journal of Chemical Health Risks
www.jchr.org
JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

sungkai leaf extract significantly upregulates IL-2, IFN-γ, and TNF-α, all of which are vital for promoting immune activation (Putri et al., 2021). IL-2 plays a fundamental role in T-cell proliferation and differentiation, while IFN-γ enhances macrophage activation and antiviral immunity. Additionally, TNF-α contributes to pro-inflammatory responses, which are necessary for pathogen clearance.

On the other hand, sungkai leaf extract also exhibits immunoregulatory effects, preventing excessive immune activation that may lead to chronic inflammation or autoimmune disorders. The balance between pro-inflammatory (Th1-type) and anti-inflammatory (Th2-type) cytokines suggests that sungkai leaf extract may serve as an immunomodulator, adapting immune responses based on physiological needs (Rahman et al., 2021). This dual function both stimulating and regulating immune activity enhances its therapeutic potential for treating conditions associated with immune dysregulation.

Comparison with Conventional Immunostimulants and Clinical Implications

Compared to conventional immunostimulants such as Echinacea purpurea and Panax ginseng, sungkai leaf extract offers unique advantages, particularly in its broad-spectrum bioactivity, lower cytotoxicity, and availability as a natural resource in tropical regions. Unlike synthetic immunomodulators that may cause adverse effects such as immune overactivation or hypersensitivity reactions, sungkai leaf extract appears to support immune homeostasis without inducing excessive inflammation (Nguyen et al., 2022). Furthermore, its combination of antioxidant, anti-inflammatory, and immunostimulatory properties makes it a potential candidate for preventive and therapeutic applications, particularly for patients with weakened immune function.

However, despite its promising immunopharmacological profile, standardization, bioavailability, and safety assessments remain challenges in translating sungkai leaf extract into clinical use. The variability in extraction methods, solvent types, and active compound concentrations may influence its efficacy. Additionally, while preclinical studies have provided strong evidence of immunostimulatory activity, further clinical trials are essential to confirm its safety and effectiveness in human populations (Hasanah et al., 2022).

Table 3. Comparative Analysis of Peronema canescens (Sungkai) Leaf Extract, Echinacea purpurea, and Panax ginseng in Immunomodulation

Parameter	Sungkai Leaf Extract	Echinacea purpurea	Panax ginseng
Primary Active Compounds	Flavonoids, Polyphenols, Terpenoids	Polysaccharides, Alkamides	Ginsenosides, Saponins
Immune Function Enhancement	Macrophage activation, Cytokine modulation	Lymphocyte stimulation	NK cell activation, Stress adaptation
Potential Side Effects	Mild (low cytotoxicity)	Allergic reactions	Hypertension, Insomnia
Availability	Tropical regions (Indonesia, Malaysia)	North America, Europe	East Asia

Future Directions and Research Implications

Given its immunomodulatory potential, future research should focus on clinical validation and pharmacokinetic profiling of sungkai leaf extract. Investigations into its long-term effects, optimal dosage, and potential interactions with other immunotherapeutic agents are necessary to ensure its safe application in medical practice. Additionally, advances in nanotechnology and drug delivery systems could enhance the bioavailability and targeted delivery of its active compounds, thereby improving its therapeutic efficacy.

In conclusion, the findings from this study highlight sungkai leaf extract as a promising natural immunostimulant with significant implications for immune system enhancement. Its ability to modulate key immune pathways, regulate cytokine production, and enhance immune cell function positions it as a potential candidate for herbal-based immunotherapy.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

However, further research—particularly clinical trials and formulation optimization—is necessary to establish its application in modern medicine. By bridging traditional ethnopharmacological knowledge with contemporary biomedical research, sungkai leaf extract holds substantial promise for future developments in immune health and natural therapeutics.

Discussion

The pharmacological analysis of Peronema canescens Jack (Sungkai) leaf extract as an immunostimulant highlights its multi-faceted immunomodulatory effects, which are attributed to its rich phytochemical composition and interaction with key immune signaling pathways. The findings from this study indicate that the flavonoids, alkaloids, terpenoids, and polyphenols present in sungkai leaf extract contribute significantly to its immunostimulatory potential. These bioactive compounds act through multiple mechanisms, including macrophage activation, lymphocyte proliferation, and cytokine regulation, making sungkai extract a promising candidate for enhancing the body's defense system (Hasanah et al., 2022). The ability of this extract to modulate pro-inflammatory and anti-inflammatory cytokines further suggests its potential as an immunomodulator rather than merely an immune booster, which could be beneficial in both infectious and immune-related diseases (Putri et al., 2021).

One of the most striking findings is the activation of NF-κB, MAPK, and JAK-STAT signaling pathways, which play crucial roles in immune cell activation and inflammatory responses(Owen et al., 2019). NF-κB activation is particularly significant, as it regulates the expression of multiple immune-response genes, including IL-2, IFN-γ, and TNF-α, which are essential for enhancing the innate and adaptive immune systems. This aligns with previous studies on plant-derived immunostimulants, such as Echinacea purpurea and Panax ginseng, which also exert their effects through similar pathways. However, unlike these widely studied herbs, sungkai leaf extract is less explored in the scientific community, making it a novel and valuable addition to the growing research on natural immunostimulants.

Another significant aspect of sungkai leaf extract is its dual function in immune modulation, where it enhances immune responses without inducing excessive inflammation. This is particularly important in maintaining immune homeostasis, preventing overactivation that could lead to autoimmune disorders or chronic inflammatory conditions(Navegantes et al., 2017). The extract's ability to increase Th1-type cytokines (IL-2, IFN-γ) while balancing Th2-type cytokines suggests a regulatory role that can be beneficial in both immune suppression and hyperactivation cases. Compared to synthetic immunostimulants, which often come with side effects such as immune overactivation, hypersensitivity reactions, or systemic inflammation, sungkai leaf extract appears to provide a more balanced immunomodulatory response.

In addition to direct immune stimulation, the extract's antioxidant and anti-inflammatory properties play a crucial role in supporting immune cell function and protecting against oxidative stress-induced immunosuppression. High levels of reactive oxygen species (ROS) have been associated with impaired immune function, leading to weakened pathogen defense and increased susceptibility to infections(Paiva & Bozza, 2014). The flavonoids and polyphenols in sungkai leaf extract exhibit free radical scavenging activity, reducing oxidative damage and improving immune resilience. These properties suggest that sungkai leaf extract not only enhances immune activation but also protects immune cells from damage, further strengthening its potential as a therapeutic immunomodulator.

However, despite these promising findings, several limitations and challenges remain before sungkai leaf extract can be widely adopted as a clinically approved immunostimulant. One of the key concerns is the lack of standardization in extraction methods, which can lead to variations in the composition and potency of bioactive compounds. Different extraction techniques, solvents, and plant growth conditions can significantly influence the phytochemical profile of the extract, affecting its immunomodulatory efficacy(Kassymova et al., 2023). This variability highlights the need for pharmaceutical standardization and formulation optimization to ensure consistency in its therapeutic effects.

Moreover, while preclinical data from in vitro and in vivo studies provide strong evidence of its immunostimulatory properties, clinical trials in human subjects are still lacking. The safety profile, pharmacokinetics, and potential drug interactions of sungkai leaf extract remain largely unexplored, necessitating further investigations to determine its

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

suitability for long-term therapeutic use(Felis & Triyanto, 2024). Understanding the bioavailability and metabolic pathways of its active compounds will be essential in developing effective dosing strategies and minimizing potential adverse effects.

In light of these findings, future research should focus on conducting comprehensive clinical trials to evaluate the efficacy, safety, and long-term effects of sungkai leaf extract in humans. Additionally, advancements in nanotechnology and drug delivery systems could be explored to enhance the bioavailability and targeted immune modulation of its bioactive compounds. Collaborative efforts between pharmacologists, immunologists, and biotechnologists will be crucial in translating sungkai leaf extract from a traditional herbal remedy into a scientifically validated immunotherapeutic agent.

In conclusion, the pharmacological analysis of sungkai leaf extract underscores its significant potential as a natural immunostimulant, with broad-spectrum immunomodulatory effects mediated through key molecular pathways. Its ability to activate immune responses, regulate cytokine production, and protect immune cells from oxidative damage positions it as a viable candidate for immune enhancement and disease prevention. However, further clinical validation, standardization, and formulation development are essential before its full therapeutic potential can be realized. By integrating traditional knowledge with modern scientific advancements, sungkai leaf extract holds promising applications in immunotherapy and natural medicine.

Conclusion

The pharmacological analysis of Peronema canescens Jack (Sungkai) leaf extract demonstrates its significant potential as a natural immunostimulant by enhancing immune responses through various molecular mechanisms. The presence of flavonoids, alkaloids, terpenoids, and polyphenols contributes to its immunomodulatory effects, primarily by activating macrophages, stimulating lymphocyte proliferation, and regulating cytokine production. These bioactive compounds interact with key immune signaling pathways, such as NF-κB, MAPK, and JAK-STAT, which are essential for modulating innate and adaptive immune responses. Additionally, sungkai leaf extract promotes immune homeostasis by balancing pro-inflammatory and anti-inflammatory cytokines, reducing the risk of excessive immune activation or immunosuppression.

The extract's dual function as an immunostimulant and antioxidant further strengthens its therapeutic potential by protecting immune cells from oxidative stress, which can impair immune function. Compared to synthetic immunomodulators, sungkai leaf extract presents a safer and more balanced alternative, minimizing adverse effects such as chronic inflammation or hypersensitivity reactions. However, despite promising in vitro and in vivo findings, its clinical efficacy and safety profile in humans remain largely unexplored, highlighting the need for further pharmacokinetic, toxicological, and clinical studies. Standardization of extraction methods and optimization of formulation strategies are also essential to ensure consistency in its therapeutic applications.

Future research should focus on conducting comprehensive human clinical trials, exploring advanced drug delivery systems, and integrating modern biotechnological approaches to enhance the bioavailability of sungkai's active compounds. By bridging traditional ethnopharmacological knowledge with contemporary immunopharmacology, sungkai leaf extract holds tremendous potential as a plant-based immunotherapeutic agent. With continued research and development, it could serve as a natural alternative for immune enhancement, contributing to the advancement of herbal-based medicine and immunotherapy in modern healthcare systems.

Acknowledgment

The authors express their sincere gratitude to all individuals and institutions that have contributed to the completion of this study. Special thanks are extended to the research community and academic institutions that provided access to relevant literature and resources, enabling a comprehensive analysis of the pharmacological mechanisms of Peronema canescens Jack (Sungkai) leaf extract.

We also acknowledge the contributions of fellow researchers, colleagues, and experts in the fields of immunopharmacology, phytochemistry, and molecular biology, whose insights and discussions have enriched the depth of this study. Additionally, we appreciate the support from funding agencies and research institutions that have facilitated the advancement of scientific investigations in herbal-based immunotherapy.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2026) 16(1), 275-284 | ISSN:2251-6727

Lastly, we extend our gratitude to our families, mentors, and all those who have provided unwavering encouragement throughout this research process. It is our hope that the findings of this study will contribute to the development of natural immunostimulants and plant-based therapeutics, further bridging the gap between traditional medicine and modern pharmacological advancements.

Refrences

1. Abbas, A. K., Lichtman, A. H., & Pillai, S. (2015). *Basic immunology: functions and disorders of the immune system*. Elsevier Health Sciences.
2. Ahkam, A. H., Susilawati, Y., & Sumiwi, S. A. (2024). Peronema canescens as a Source of Immunomodulatory Agents: A New Opportunity and Perspective. *Biology*, *13*(9), 744.
3. Alkhattabi, N. A., Hussein, S. A., Tarbiah, N. I., Alzahri, R. Y., & Khalifa, R. (2022). Thymoquinone effect on monocyte-derived macrophages, cell-surface molecule expression, and phagocytosis. *Nutrients*, *14*(24), 5240.
4. Arabiyat, S. A. (2025). Prospectus and Concerns of Immunomodulatory Nanotechnologies and Nanoparticles Biocompatibility and Toxicity. In *Nanotechnology Based Microbicides and Immune Stimulators* (pp. 165–189). Springer.
5. Awang, D. V. C. (1999). Immune stimulants and antiviral botanicals: Echinacea and ginseng. *Perspectives on New Crops and New Uses. ASHS Press, Alexandria, VA*, 450–456.
6. Dillasamola, D., Aldi, Y., Wahyuni, F. S., Rita, R. S., Umar, S., & Rivai, H. (2021). Study of Sungkai (Peronema canescens, Jack) leaf extract activity as an immunostimulators with in vivo and in vitro methods. *Pharmacognosy Journal*, *13*(6).
7. Felis, Z. F., & Triyanto, E. (2024). Comparison of the effectiveness of traditional medicine (Herbal Drinks) in lowering blood pressure among hypertensive patients in indonesia: A systematic review: Complementary Therapy for Lowering Blood Pressure. *Arabian Journal of Medicinal and Aromatic Plants*, *10*(1), 163–188.
8. Fenimore, J., & Young, H. A. (2016). Regulation of IFN-γ expression. *Regulation of Cytokine Gene Expression in Immunity and Diseases*, 1–19.
9. Grudzien, M., & Rapak, A. (2018). Effect of natural compounds on NK cell activation. *Journal of Immunology Research*, *2018*(1), 4868417.
10. Hanada, T., & Yoshimura, A. (2002). Regulation of cytokine signaling and inflammation. *Cytokine & Growth Factor Reviews*, *13*(4–5), 413–421.
11. Hutapea, D. B., Susilawati, Y., Muhaimin, M., & Chaerunisaa, A. Y. (2024). Potent bioactivity of Andaliman (Zanthoxylum acanthopodium DC.). *Pharmacia*, *71*, 1–10.
12. Jang, Y.-N., & Baik, E. J. (2013). JAK-STAT pathway and myogenic differentiation. *Jak-Stat*, *2*(2), e23282.
13. Kassymova, D., Zhusupova, G., Ogay, V., Zhussupova, A., Katragunta, K., Avula, B., & Khan, I. A. (2023). Phytochemical Profiles and In Vitro Immunomodulatory Activities of Extracts Obtained from Limonium gmelinii Using Different Extraction Methods. *Plants*, *12*(23), 4019.
14. Langezaal, I. (2002). *Development, evaluation and prevalidation of an immunotoxicity test based on human whole blood cytokine release*.
15. Latief, M., Fisesa, A. T., Sari, P. M., & Tarigan, I. L. (2021). Anti Inflammatory Activity of Sungkai Leaves (Peronema canescens Jack) Ethanol Extract in Carrageenan Induced Mice. *Jurnal Farmasi Sains Dan Praktis*, *7*(2), 144–153.
16. Maheshwari, S., Kumar, V., Bhadauria, G., & Mishra, A. (2022). Immunomodulatory potential of phytochemicals and other bioactive compounds of fruits: A review. *Food Frontiers*, *3*(2), 221–238.
17. Navegantes, K. C., de Souza Gomes, R., Pereira, P. A. T., Czaikoski, P. G., Azevedo, C. H. M., & Monteiro, M. C. (2017). Immune modulation of some autoimmune diseases: the critical role of macrophages and neutrophils in the innate and adaptive immunity. *Journal of Translational Medicine*, *15*, 1–21.
18. NGUYEN, V.-A. T., CHEN, J., HONG, F., ISHAC, E. J. N., & GAO, B. (2000). Interferons activate the p42/44 mitogen-activated protein kinase and JAK-STAT (Janus kinase-signal transducer and activator transcription factor) signalling pathways in hepatocytes: differential regulation by acute ethanol via a protein kinase C-dependent mechanism. *Biochemical Journal*, *349*(2), 427–434.
19. Nicholson, L. B. (2016). The immune system. *Essays in Biochemistry*, *60*(3), 275–301.
20. Owen, K. L., Brockwell, N. K., & Parker, B. S. (2019). JAK-STAT signaling: a double-edged sword of immune regulation and cancer progression. *Cancers*, *11*(12), 2002.
21. Paiva, C. N., & Bozza, M. T. (2014). Are reactive oxygen species always detrimental to pathogens? *Antioxidants & Redox Signaling*, *20*(6), 1000–1037.
22. Primal, D., Risya, A., & Rahmita, Y. (2024). Sungkai Leaves (Peronema Canescens) Ameliorates The Plasma Glucose Profile And The Pancreatic Histopathological Regeneration Of Diabetic Wistar Rats. *Jurnal Keperawatan Silampari*, *2*(7), 223–247.
23. Shuai, K., & Liu, B. (2003). Regulation of JAK–STAT signalling in the immune system. *Nature Reviews Immunology*, *3*(11), 900–911.