Exploring the Therapeutic Potential of *Canarium resiniferum* Leaves: Anxiolytic, Antidepressant, and Antioxidant Properties of Methanol Extracts

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ABSTRACT

Medicinal plants have served as a cornerstone of traditional medicine, providing a vast array of bioactive compounds for therapeutic development. Among these, Canarium resiniferum, a lesser-known species of the Burseraceae family, has recently gained attention for its diverse pharmacological properties. This review focuses on the anxiolytic, antidepressant, and antioxidant activities of methanol extracts from Canarium resiniferum leaves. The phytochemical constituents underlying these bioactivities, including flavonoids, phenolics, and alkaloids, are explored in detail. Experimental findings demonstrate the plant's significant potential in modulating key central nervous system pathways and combating oxidative stress. Challenges such as standardization, isolation of active compounds, and clinical validation are discussed alongside future research directions. This review highlights Canarium resiniferum as a promising source of natural therapeutics for addressing mental health disorders and oxidative stress-related conditions.

Keywords: Canarium resiniferum, bioactive compounds, anxiolytic, antidepressant, antioxidant, methanol extract, phytochemistry

Introduction

Mental health disorders, such as anxiety and depression, along with oxidative stress-related diseases, represent significant global health challenges. These conditions not only affect the quality of life but also impose substantial socio-economic burdens [1]. Conventional treatments for anxiety and depression, including pharmacological interventions such as benzodiazepines and antidepressants, are often associated with undesirable side effects and limited efficacy. Similarly, addressing oxidative stress, a critical factor in the development of chronic diseases, necessitates effective antioxidant strategies. In this context, there is a growing interest in exploring plant-based therapeutics that are both effective and safe. Medicinal plants have historically played a crucial role in traditional medicine systems across cultures, offering a plethora of bioactive compounds with diverse pharmacological activities [2]. *Canarium resiniferum*, a relatively understudied species within the Burseraceae family, has emerged as a potential candidate for therapeutic applications. Native to South and Southeast Asia, this plant has been traditionally used for its anti-inflammatory and healing properties. Recent scientific investigations have revealed its significant anxiolytic, antidepressant, and antioxidant potential, particularly in methanol extracts derived from its leaves [3]. This review aims to provide a comprehensive analysis of the bioactivities of *Canarium resiniferum* leaves, with a focus on their phytochemical composition and pharmacological properties. The anxiolytic and antidepressant activities of the plant are particularly promising, as they may address the limitations of current therapeutic options for mental health disorders [4]. Additionally, the plant's robust antioxidant properties, attributed to its high phenolic and flavonoid content, underscore its potential in mitigating oxidative stress and its associated pathologies.

Importance of Plant-Based Therapeutics

The increasing reliance on synthetic drugs has highlighted the need for alternative approaches that are safer, cost-effective, and environmentally sustainable. Plant-based therapeutics offer a holistic solution, leveraging the synergistic effects of multiple bioactive compounds. *Canarium resiniferum* exemplifies this potential, with its diverse phytochemical profile contributing to its multifaceted pharmacological activities [5].

Phytochemical Composition

Preliminary phytochemical analysis of *Canarium resiniferum* has uncovered a rich array of bioactive compounds, each contributing to the plant's potential therapeutic properties. Among these, flavonoids stand out for their well-documented antioxidant effects, which help combat oxidative stress and protect cellular structures from damage. Additionally, these compounds have neuroprotective properties, contributing to their ability to enhance brain health and function [6]. The plant also contains significant amounts of phenolic compounds, which are known for their powerful free radical-scavenging abilities, further aiding in the reduction of oxidative stress and potentially protecting against chronic diseases linked to oxidative damage. Tannins, another class of compounds identified in *Canarium resiniferum*, are recognized for their astringent properties, which can promote tissue healing and reduce inflammation [7]. These compounds also exhibit notable anti-inflammatory effects, which could be beneficial in treating inflammatory conditions. Furthermore, the plant is rich in terpenoids and alkaloids, which demonstrate a wide range of pharmacological actions, including anxiolytic and antidepressant effects. This diverse array of bioactive compounds underpins the plant's therapeutic potential, suggesting that *Canarium resiniferum* may be a valuable source of natural remedies for a variety of health concerns.

Preliminary phytochemical analysis of *Canarium resiniferum* has revealed a diverse and promising range of bioactive compounds, each contributing to the plant's therapeutic potential. Among the most significant are flavonoids, which are widely recognized for their powerful antioxidant properties. These compounds play a vital role in neutralizing free radicals, reducing oxidative stress, and preventing cellular damage, thus contributing to the plant's protective effects against aging and various chronic diseases [8]. Additionally, flavonoids have been shown to possess neuroprotective effects, enhancing cognitive function and offering potential benefits in the treatment of neurodegenerative diseases such as Alzheimer's and Parkinson's.

Phenolic compounds, another key component of *Canarium resiniferum*, are highly effective in scavenging free radicals, further mitigating oxidative stress and reducing the risk of conditions such as heart disease, diabetes, and cancer [9]. These compounds also contribute to the plant's anti-inflammatory properties, which are essential in reducing inflammation associated with numerous health conditions, including arthritis and inflammatory bowel disease. The presence of tannins in the plant adds to its medicinal value, as these compounds exhibit astringent properties that help tighten tissues, promote wound healing, and reduce inflammation in various parts of the body. In addition to their topical benefits, tannins also offer antioxidant activity, contributing to the overall health benefits of *Canarium resiniferum*, the plant contains terpenoids and alkaloids, both of which exhibit a broad spectrum of pharmacological effects. Terpenoids are known for their antimicrobial, anti-inflammatory, and anticancer activities, making them useful in the treatment of infections, chronic inflammation, and even cancer. Alkaloids, on the other hand, have been shown to possess anxiolytic and antidepressant effects, offering potential therapeutic benefits for mental health conditions such as anxiety and depression [10]. The presence of these compounds highlights the multifaceted bioactivity of *Canarium resiniferum*, suggesting that it may be an effective natural remedy for a variety of ailments ranging from physical inflammation to mental health disorders. Together, these diverse phytochemicals form the foundation of the plant's therapeutic potential, offering promise for its use in the development of new, plant-based treatments for a wide array of health conditions.

Anxiolytic Activity

The anxiolytic properties of *Canarium resiniferum* are thought to be primarily mediated through the modulation of the GABAergic system, a key inhibitory neurotransmitter pathway in the central nervous system (CNS). Flavonoids and alkaloids, which are present in the methanol extract of the plant, are believed to act as positive modulators of GABA-A receptors. This action likely mimics the effects of traditional anxiolytics, such as benzodiazepines, by enhancing the inhibitory neurotransmission that plays a crucial role in reducing anxiety and promoting relaxation [11]. The modulation of this system helps explain the calming effects associated with *Canarium resiniferum*.

Experimental evidence from recent studies involving animal models has provided robust support for the anxiolytic activity of *Canarium resiniferum*. In the Elevated Plus-Maze (EPM) test, animals treated with the methanol extract demonstrated a significant increase in the time spent in the open arms of the maze, a behavior associated with reduced anxiety. This is considered a clear indicator of anxiolytic effects, as animals generally avoid open, exposed spaces when they are anxious. Additionally, in the Open Field Test, subjects that received the extract exhibited enhanced exploratory behavior, further suggesting a reduction in anxiety levels [12]. These findings were comparable to the effects of diazepam, a well-known anxiolytic, underscoring the potential of *Canarium resiniferum* as a natural alternative for anxiety management. Together, these studies highlight the promising role of *Canarium resiniferum* in the development of plant-based anxiolytic therapies.

The antidepressant effects of *Canarium resiniferum* are believed to arise from the modulation of both serotonergic and noradrenergic pathways in the brain. Phytochemicals such as flavonoids are thought to enhance the levels of neurotransmitters like serotonin and norepinephrine by inhibiting the activity of monoamine oxidase (MAO), an enzyme responsible for the degradation of these neurotransmitters [12]. By reducing the breakdown of serotonin and norepinephrine, flavonoids increase their synaptic availability, which in turn can elevate mood and alleviate symptoms of depression.

Experimental evidence supporting the antidepressant activity of *Canarium resiniferum* has been obtained through studies employing well-established animal models, such as the Forced Swim Test (FST) and the Tail Suspension Test (TST). In both tests, animals treated with the methanol extract of the plant demonstrated a significant reduction in immobility time, a key indicator of antidepressant activity. This behavior suggests that the extract effectively alleviates the depressive-like states typically induced in these models. Furthermore, at higher doses, the antidepressant effects of the extract were found to be comparable to those of standard antidepressant drugs, such as imipramine, highlighting the potential of *Canarium resiniferum* as a viable alternative for managing depression. These findings underscore the promise of *Canarium resiniferum* as a natural antidepressant, offering a potentially safer and effective alternative to conventional pharmaceutical treatments.

Antioxidant Activity

The antioxidant activity of *Canarium resiniferum* is primarily attributed to its ability to scavenge free radicals and prevent oxidative damage to cellular components. Oxidative stress, caused by an imbalance between free radicals and the body's antioxidant defenses, is a key contributor to the development of various chronic and neurodegenerative diseases. The high levels of phenolic compounds and flavonoids present in the leaves of *Canarium resiniferum* play a central role in its potent antioxidant properties. These bioactive compounds work by neutralizing free radicals, thereby reducing cellular damage and helping to maintain overall health. The antioxidant capacity of *Canarium resiniferum* has been thoroughly validated through a series of in vitro assays [7]. The DPPH Radical Scavenging Assay demonstrated that the methanol extracts of the plant effectively neutralize free radicals, with low IC50 values indicating high potency in scavenging these harmful molecules. The ABTS Assay further supported these findings, showing significant antioxidant activity comparable to the well-known antioxidant ascorbic acid. Additionally, the FRAP (Ferric Reducing Antioxidant Power) assay highlighted the extract's ability to reduce ferric ions, which is a marker of its robust antioxidant potential [5]. Collectively, these assays underscore the capacity of *Canarium resiniferum* to mitigate oxidative stress, offering promising therapeutic benefits for managing conditions linked to oxidative damage, such as neurodegenerative disorders,

cardiovascular diseases, and other chronic health conditions. The methanol extract of *Canarium resiniferum* leaves exhibits significant anxiolytic, antidepressant, and antioxidant activities, which can be attributed to its rich phytochemical profile [13-14]. The presence of flavonoids and phenolics appears to play a central role in these bioactivities by modulating key CNS pathways and reducing oxidative damage. While these findings are promising, challenges such as standardization of extracts, identification of specific active compounds, and clinical validation need to be addressed. Additionally, ethical considerations regarding sustainable harvesting and conservation of *Canarium resiniferum* should be prioritized.

Conclusion

The diverse bioactivities of *Canarium resiniferum* underscore its significant potential as a natural source of therapeutics for managing mental health disorders and conditions related to oxidative stress. To fully harness its medicinal value, future research should focus on several critical areas. Firstly, isolating and characterizing the active compounds is essential to identify the specific bioactive molecules responsible for its pharmacological effects. This step will provide a deeper understanding of how these compounds interact with biological systems and their potential applications in therapy. Secondly, mechanistic studies are crucial for elucidating the molecular pathways involved in the observed effects, particularly how the plant's phytochemicals modulate neurotransmitter systems and combat oxidative stress at the cellular level. Such studies will provide a clearer picture of the plant's mode of action and pave the way for more targeted therapeutic applications. Thirdly, clinical trials are necessary to confirm the safety and efficacy of *Canarium resiniferum* in humans. While preclinical animal studies offer promising results, human trials are essential for determining appropriate dosages, long-term safety, and therapeutic outcomes. Lastly, sustainable utilization of *Canarium resiniferum* should be prioritized to ensure the plant's ecological viability. Responsible sourcing and cultivation practices will help protect the species and its habitats, allowing for sustainable harvesting without threatening its long-term availability. *Canarium resiniferum* has the potential to be established as a leading natural product in the field of therapeutic medicine, offering a valuable and sustainable alternative to conventional treatments.

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