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REVIEW ARTICLE

A Comprehensive Review of *Callistemon citrinus*: Unveiling its Medicinal Potency and Pharmacological Diversity

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ABSTRACT
This article explores the diverse pharmacological properties of Callistemon citrinus, shedding light on its rich potential as a natural medicinal resource. Originating from the Myrtaceae family, this plant boasts a range of bioactive compounds, including flavonoids, terpenoids, and essential oils. Through extensive investigation, it has been revealed that Callistemon citrinus exhibits a spectrum of medicinal activities, making it a significant contender in the realm of herbal medicine. The documented pharmacological attributes cover a broad spectrum of health-related functions. Notably, Callistemon citrinus demonstrates potent antimicrobial and antibacterial effects, portraying efficacy against various pathogens. Additionally, its antioxidant properties indicate promise in combating oxidative stress-related ailments. The "plants" anticonvulsant, antinociceptive, and potential antidepressant characteristics open avenues for neurological and mental health applications. Of particular significance is its antiplasmodial activity against malaria parasites, suggesting a potential role in combating this life-threatening disease. Findings regarding the reduction of malaria parasite vitality by extracts derived from the plant's leaves and flowers underscore its potential as a future candidate in antimalarial treatments. In summary, Callistemon citrinus emerges as a multifaceted botanical entity with a significant promise for the development of novel therapeutic interventions. While these findings are compelling, further extensive research and clinical trials are required to fully harness and understand its medicinal potential.
Keywords: *Callistemon citrinus, medicinal uses, pharmacological activity,*

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INTRODUCTION

Plant-based medicine has a long tradition in India. Many different botanicals, plant extracts, decoctions, and pastes are used by Indian tribes and folklore traditions to treat burns, wounds, cuts and many ailment[1]. Many modern medications have their roots in traditional medicine, which has traditionally relied on medicinal plants as the primary treatment for a wide range of illnesses[2] For many years, medicinal plants have been a rich source of biologically active substances that are employed either as pure compounds or as crude materials to treat a wide range of medical ailments[3] Additionally, it has been shown that industrialized civilizations are becoming more and more dependent on the usage of medical plants due to the extraction and production of various medications, including chemotherapeutics, from these plants as well as from traditionally utilized rural herbal treatments. [4] Consequently, there is a need for safer, more cost-effective, and plant-based bioactive chemical-based medicines.[5] The Latin term citrinus, which describes the lemony scent of the leaves, is derived from the Greek words "kalos," which means "beautiful," "stamen," and "*citrinus*". This tree belongs to the Myrtaceae family and is a gorgeous evergreen. India is home to gardens growing this native of Queensland and New South Wales. On rare occasions, it is utilized in place of Melaleuca. The plant is sometimes called bottle brush because of the close resemblance of the cylindrical, brush-like flowers to traditional bottle brushes. Indian farmers use different parts of plants for different uses.[6] Originally from the wet tropics, mainly Australia, South America, and tropical Asia, these woody, aromatic trees, or shrubs range in height from 0.5 to 7 meters.

Today, they may be found all over the world. Some varieties of *Callistemon* have lovely, thin leaves and a white, papery bark. The aromatic, lanceolate leaves of *Callistemon* species are 40–70 mm long and 3-6 mm wide. The flowers have prominent red stamens and are produced in 40–150 mm long spikes. Petals are tiny, inconspicuous, light-colored, and sometimes deciduous.[7] Australian native *Callistemon citrinus* is a fragrant, medicinal member of the Myrtaceae family of shrubs. It is a potentially useful medicinal herb that may be used topically to cure infections brought on by bacteria, fungi, viruses, and parasites as well as pain and gastrointestinal discomfort. Its leaves are used as a herbicide in addition to being a delightful revitalizing tea substitute. Extracts from this plant are also used to treat respiratory conditions including bronchitis and cough. Its essential oil is used as a pesticide as well as an antimicrobial and antifungal. [5]. Various portions of this herb have been employed in traditional medicines to treat rheumatism, dysentery, and diarrhea. In folk medicine, it is also used as a pesticide, anticough, water accent, and antibronchtits. *C. citrinus* is a valuable medicinal plant, as evidenced by its numerous medicinal characteristics, therapeutic applications, and phytochemical research.[8] *Callistemon* may improve the functioning of food or feed, control blood sugar levels, and prevent the formation of aggressive cancer in humans or foodborne diseases.[9] Because of its cylindrical brush-like blossoms that resemble traditional bottle brushes, *Callistemon* is also known as "bottle brush." *Callistemon citrinus* produces spikes of vibrant red blooms that are very rich in nectar, which draws a lot of insects and birds.[10]. It is an evergreen plant with aromatic, alternating, lanceolate leaves that have an entire margin and anomocytic stomata. The stem had a grey color. [6]. Of the 34 species of *Callistemon* genus, *Callistemon citrinus* (Curtis) Skeels is a flowering plant that is the most widely grown. This shrub, which reaches a height of almost 7.5 meters, features stunning crimson blooms with dark red anthers.[10] Its leaves have yielded many isolated flavonoids, saponins, quines, steroids, terpenoids, tannins, and phenolic chemicals. [11] Chemical investigations reveal that the plant's leaves and blooms contain high concentrations of essential oils, such as geraniol, α- and β-pinenes, α-terpineol, α-phellandrene, limonene, α-terpinene, linalool, trans-pinocarveol, and linalool. Among these, 1,8-cineole is the most widely utilized and is known for its flavoring and medicinal properties. [12] A provisional list of 29 chemicals was compiled. Essential oils were mostly composed of oxygenated monoterpenes, with eucalyptol being the main component. [13] The main ingredient in many products in the food and taste and medicinal sectors is eucalyptol.[14] Nowadays Because of its hardiness and versatility, it is now widely utilized as a decorative garden plant around the world. Furthermore, it is distinguished by brilliant red flower spikes with a lemony aroma (hence the popular name), which are present on the plant for practically all of the months of the year, but especially in November and December [15].

Figure 1. Plant Images (*Callistemon citrinus*)

MEDICINAL USES

The Australian Aborigines utilized the blossoms of the *Callistemon* plant as food. The nectar from the blooms was collected and used to produce delicious beverages. Additionally, Australian Aborigines used varieties of *Callistemon* as traditional bush remedies. The leaves were used to treat illnesses of the respiratory system. Regretfully, the majority of our knowledge on the antimicrobial properties of bacteria and fungi is limited to determining the extracts' toxicity and, consequently, their potential as therapeutic

drugs. The overuse of this plant for its volatile oils and secondary metabolites has made it necessary to create alternative methods for both conservation and industrial production of the plant's medicinal chemicals.[8] *C. citrinus* leaf infusion infused with hot water is used ethnomedically to treat TB, rheumatism, bronchitis, and cough. It is also used as an insecticide, to treat genitourinary tract cleaning, and to treat urinary incontinence. [16,17] Various portions of this herb have been employed in traditional medicines to treat rheumatism, diarrhoea, and dysentery. In folk medicine, it serves as an insecticide, anti-bronchitis, anti-cough, and water accent.[18]

PHARMACOLOGICAL ACTIVITY

Anti-microbial activity

C. citrinus leaves have broad-spectrum antimicrobial activity against a wide range of bacteria and fungi. The methanolic extract of *C. citrinus* leaves inhibited the capacity of bacteria to grow. Furthermore, flower extracts inhibited the growth of 64% of the bacteria tested. The leaf extracts of C. citrinus showed 27% suppression against gram-positive bacteria, while the flower extracts exhibited 55% inhibition against gram-negative bacteria, indicating their higher efficiency against gram-positive bacteria than gram-negative bacteria. *C. citrinus* alkaloids displayed antibacterial activity as well as the ability to prevent ATP-dependent compounds from flowing through cell membranes. As a result, alkaloids are probable plant components having antibacterial effects [19]. Lyophilized extracts of *C. citrinus* flowers and leaves have also been shown to have antimicrobial action against Listeria monocytogenes in beef burger.[15]

Anti-bacterial activity:

The chemical composition and antibacterial activity of essential oils extracted via hydro distillation from *Callistemon citrinus* and *Callistemon viminalis* leaves were investigated using GC and GC/MS. Twenty-four and twelve components were discovered to account for 92.0% and 98.3% of the total oils in *C. citrinus* and C. *viminalis*, respectively. *C. citrinus* and C. *viminalis* were largely made up of -pinene (13.4% and 6.4%, respectively) and 1,8-cineole (61.2% and 83.2%). The “essential oils” in vitro antibacterial efficacy against 12 distinct bacterial strains was studied using broth microdilution and disc diffusion. The antibacterial actions of the oils from the (leaves and flowers) were also investigated, and it was discovered that they have a wide spectrum of activity against bacterial strains. [10]

Antioxidant activity

The assay for antioxidants was conducted using the DPPH free radical scavenging assay using a spectrophotometric method (Genesis 10 UV spectrophotometer) [13]. The absorbance was measured at 517 nm using the standard protocol recommended by [20]. *C. citrinus* aerial part essential oil was prepared in methanol with varying concentrations ranging from 5 to 30 µg/mL to which 0.2 mM DPPH solution (1 mL) was added. The reaction mixture was then incubated in the dark for 30 minutes and the absorbance at 517 nm was measured using UV/Vis spectrophotometer. The percentage scavenging effect was computed using the following formula: A control = absorbance of DPPH and A sample = absorbance of DPPH + essential oil sample/standard of different concentrations.[14]

Anti-convulsant activity

The anticonvulsant techniques of pentylenetetrazol, strychnine, and maximal electroshock (MES) were applied. The volatile oil was dosed at 200, 400, and 800 mg/kg to distinct groups of albino mice. As a positive control, medication solutions containing 2 mg/kg diazepam for strychnine and 30 mg/kg phenobarbitone for MES and pentylenetetrazol models were given. Length, percentage mortality, and the onset of tonic leg extension were noted. The mice with 40% score in the MES model were considerably ($P<0.05$) less likely to have seizures when given doses of 200 and 400 mg/kg. In the pentylenetetrazol model, there was a dose-dependent decrease in the length of seizures, with reductions of 68.47, 70.27, and 81.08%. The strychnine model provided no substantial coverage. *C. citrinus* oil may help treat epilepsy medically as it shielded the mice from maximum electroshock-induced convulsion and pentylenetetrazol. [17]

Antinociceptive activity

The purpose of this study was to evaluate the antinociceptive (pain-relieving) properties of *Callistemon citrinus* (*C. citrinus*) extracts and ascertain compound 1's function in these properties. The writhing test with acetic acid is employed. The main objective of this test is to evaluate a substance's peripheral antinociceptive effects. Compound 1 administered at a dosage of 200 mg/kg in animals showed antinociceptive effects comparable to aspirin (ASA) at the same dose. Compound 1's high peripheral action became much more apparent when the findings were reported as a percentage of writhing inhibition.[21].

Anti-depressant activity

The antidepressant effect of *C. citrinus* chloroform fraction was equivalent to that of imipramine (10 mg/kg), a common medication. As was previously said, *C. citrinus* is rich in bioactive chemicals, the bulk of which are flavonoids and terpenoids, which are what provide the plant its health advantages. As a result, the application of *C. citrinus* in the management of depression is investigated in this work. To determine the active ingredients and assess the mechanism behind *C. citrinus* antidepressant action, more research may be conducted.[22]

Anti plasmodial activity

The parasite lactate dehydrogenase (pLDH) activity was used to determine the vitality of parasites. Positive controls included either artemisinin (Sigma Aldrich) or chloroquine (Sigma Aldrich). The samples were screened for malaria parasites at a concentration of 50 ug/mL before being introduced to the parasite cultures in 96-well plates and cultured for 48 hours in a 37 ̊C CO2 incubator. The plate was taken out of the incubator after 48 hours had passed. A fresh 96-well plate was filled with 125 µL of a combination of Malstat and NBT/PES solutions after twenty microliters of the culture were extracted from each well. When pLDH was present, a purple product was generated, and the absorbance of this product at 620 nm (Abs620) could be measured in a 96-well plate reader. The Abs620 reading showed the amount of parasites and pLDH activity in each well. Plasmodium falciparum's vitality was significantly reduced by the manufactured leaf nanoparticles derived from *Callistemon citrinus* at a dose of 50 µg/mL, and Plasmodium falciparum was also significantly reduced by the synthesized flower at the same quantity to (0.423 ± 1.125). [23]

DISCUSSION

The important component of the leaf oil α-pinene, is said to have broad-spectrum anticonvulsant and antioxidant properties [24] antimicrobial [25] antibacterial [26] antidepressant [27] antinociceptive activity [28] biological action.

CONCLUSION

This comprehensive exploration of *Callistemon citrinus* underscores its diverse pharmacological potential. It's evident that this plant, rich in bioactive compounds such as flavonoids, terpenoids, and essential oils, possesses a wide array of medicinal properties, making it a valuable resource for various health-related applications. The documented pharmacological activities include antimicrobial and antibacterial effects against a broad spectrum of pathogens, antioxidant properties, anticonvulsant, antinociceptive (pain relief), antidepressant, and antiplasmodial activities against malaria parasites. The antimicrobial properties against bacteria and fungi, along with the demonstrated ability to inhibit the growth of various pathogens, highlight its potential as an effective natural remedy. Additionally, the antioxidant activity signifies its potential in combating oxidative stress-related conditions. The plant's anticonvulsant properties, antinociceptive effects, and potential antidepressant capabilities offer promising leads for neurological and mental health-related research. Moreover, the antiplasmodial activity against malaria parasites suggests a potential role in combating this life-threatening disease. The study's findings, indicating the reduction of malaria parasite vitality through the use of leaf nanoparticles and flowers from the plant, suggest a promising direction for further exploration in the field of antimalarial treatments. The multifaceted pharmacological activities displayed by *Callistemon citrinus* emphasize its potential as a valuable natural resource for the development of new therapeutic agents. However, further research and clinical trials are warranted to fully understand and harness its medicinal potential.

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