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Phytochemical And Pharmacological Insights Into The Stem And Root Of Catharanthus Roseus (Madagascar Periwinkle): An Analytical Review

Prashant Kumar & Dr. Sushma Dubey

Department of Biotechnology, Kalinga University, Naya Raipur, Chhattisgarh

Abstract: This review critically discusses the phytochemical content and pharmacological relevance of Catharanthus roseus roots and stems, with the aim of integrating existing knowledge and pointing towards areas of research opportunity beyond their well-established oncological use. Its unique botanical features and global distribution have allowed this medicinal plant to be incorporated into various traditional curative systems, while its sophisticated alkaloid chemistry dominated by therapeutically significant compounds such as vincristine and vinblastine have been uncovered using contemporary extraction and analytical methods. The pharmacological diversity of root and stem components includes anticancer, antimicrobial, antidiabetic, cardioprotective, neuroprotective, and anti-inflammatory activity, although their high potency warrants cautious toxicological evaluation and determination of safety parameters. Notwithstanding the wealth of research, great gaps remain regarding complete metabolite characterization, mechanism of biological activities, and production methods based on sustainability. Directions for future research must emphasize advanced biotechnological methods, novel drug delivery systems, and interdisciplinary synergy to maximally unlock the therapeutic potential of these plant parts with an eye toward sustainability. The present review seeks to spur concerted research into the relatively underexplored constituents and uses of C. roseus stems and roots with a hope to derive novel therapeutic agents against diseases other than cancer and define standardized protocols for their safe and effective use.

Keywords: Catharanthus roseus, alkaloid, Vincristine, Ethnopharcology, Anticancer phytochemicals

Introduction

Catharanthus roseus, or Madagascar periwinkle, is one of the most important medicinal plants of modern-day pharmacognosy (Van Wynk & Wink, 2018). This perennial herbaceous plant of small size, indigenous to Madagascar but now grown across the globe, has attracted tremendous interest among scientists for its unparalleled wealth of bioactive compounds, especially alkaloids that possess strong therapeutic activities. The plant has evolved from conventional medicine to being a treasured resource in the pharmaceutical industry of today for research and development (David et al., 2015; Fowler, 2006).

The value of *C. roseus* is mainly due to its outstanding phytochemical content, with more than 130 terpenoid indole alkaloids (TIAs) known, most of which occur exclusively in this species (Kumar et al., 2022; Shukla & Khanuja, 2013). The stems and roots of the plant are especially remarkable for their content of vincristine and vinblastine, two alkaloids that transformed cancer therapy by virtue of their strong antineoplastic activities (Dhyani et al., 2022; Haque et al., 2016). Even after decades of investigation, the intricacies of the plant's biochemical pathways and the full therapeutic potential of its less-investigated compounds remain poorly understood, with ongoing opportunities for scientific discovery.

Although extensive work has been centered on the alkaloid composition of flowers and leaves of *C. roseus*, stems and roots hold different phytochemical compositions worthy of a broader investigation (Kumar et al., 2022). Unique compounds have been found in these plant sections that have reported activities as antimicrobial, antidiabetic, antioxidant, and antihypertensive in addition to the widely known anticancer alkaloids (Thawabteh et al., 2019; Muhammad et al., 2021). The distribution pattern of the compounds in different tissues of the plant indicates unique biosynthetic processes that may be useful in unveiling new pharma applications.

The goal of the present analytical review is to critically review and synthesize existing information on the phytochemical profile and pharmacological activity of *Catharanthus roseus* stem and root with a focus on research gaps, critical assessment of extraction techniques, and determination of the therapeutic potential of these plant components beyond cancer chemotherapy.

Botanical Description and Distribution

Catharanthus roseus (L.) G. Don of the family Apocynaceae is a herbaceous perennial plant that usually attains a height of 30-100 cm (Barkat et al., 2017; Rosy, 2024). The growth habit of the plant is erect or decumbent with an extensive taproot system extending deep into the soil. The cylindrical, branched stems are woody at the base and are pubescent when young but become glabrous and light green to reddish-brown with age. The taproot is composed of a central taproot having several lateral branches, yellowish-brown externally and whitish in color internally. Stems and roots bear a typical milky latex with a high concentration of alkaloids and other bioactive molecules (Ezigbo, 2019; Joshi et al., 2024).

The plant has simple, opposite, elliptical-oblong leaves with short petioles and entire margins. Its flowers are axillary, solitary, and pentamerous with white to pink to purple colors, depending on the variety (Lovell, 1901; Dehgan, 2023). The fruits are paired follicles with many black seeds. Although the leaves and flowers are most visually striking, stems and roots are essential parts of the medicinal value of the plant as they are the primary locations for the biosynthesis and storage of flavonoid-like anticancer alkaloids.

Natively found in Madagascar. *Catharanthus roseus* has naturalized in the tropics and subtropics of the entire world because of its amenity value and its easy adaptability (Nejat et al., 2015; Das & Sharangi, 2017). The species grows from coastal regions to the interiors at an altitude of up to 900 meters above sea level. It has become most common in India, Australia, China, Malaysia, South Africa, and regions of America. The plant favors sandy soils well-drained, moderate rainfall (100-200 cm a year), and temperatures ranging from 20-30°C, although it shows high tolerance to drought and poor soil.

Widespread distribution of *C. roseus* has made it readily available for use in traditional medicine systems in various cultures (Kumar et al., 2022; Aslam et al., 2010). Variations in environmental factors such as soil type, elevation, temperature, and precipitation at different geographical locations have been shown to affect the phytochemical content of the plant, especially in stems and roots. These chemotaxonomic differences offer both challenges and opportunities for standardization in pharmaceutical use, since alkaloid profiles and levels can vary widely based on geographical source and conditions of growth (Singh, 2018; Umoh, 2020).

Extraction and Analytical Techniques

Extraction of bioactive compounds from *Catharanthus roseus* roots and stems necessitates specialized techniques because of the intricate composition of their alkaloid constituents (Koel et al., 2020; Arulvendhan et al., 2024). Traditional extraction methods like maceration, Soxhlet extraction, and percolation have been extensively used with different solvents like methanol, ethanol, chloroform, and ethyl acetate, usually in gradient or sequential extraction procedures. The newer developments have incorporated more effective processes such as ultrasound-assisted extraction (UAE), microwave-assisted extraction (MAE), and supercritical fluid extraction (SFE) using CO_2, which have shown higher yields of terpenoid indole alkaloids (TIAs) with less thermal degradation (Wen et al., 2020; Herzyk et al., 2024; Nonglait & Gokhale, 2024). Pressurized liquid extraction (PLE) has proved to be very effective for vincristine and vinblastine extraction from root material, yielding reported yield gains of 15-30% over traditional methods (Mandal et al., 2022).

The analytical profiling of stem and root extracts has undergone a remarkable change with advancements in technology. High-performance liquid chromatography (HPLC) in combination with different detection systems (UV, DAD, and fluorescence) continues to be the cornerstone for quantitative estimation of alkaloids (Al-Kaf et al., 2025; Wang et al., 2020). More advanced methods such as ultra-high-performance liquid chromatography (UHPLC) in combination with mass spectrometry (MS) in different configurations (single MS, tandem MS/MS, or high-resolution MS) have transformed identification and structural determination of new compounds (Khaufmann, 2014). GC-MS has been useful for the analysis of volatile constituents, whereas 1D and 2D NMR spectroscopy determines unambiguous structural identification of purified compounds (Topcu & Ulubelen, 2007; Lubes & Goodrazi, 2017). Recent deployment of UPLC-QTOF-MS/MS has made possible the whole-system metabolic profiling of the root, identifying new alkaloids with potential therapeutic importance.

Sample preparation methods have a significant impact on analytical results when dealing with *C. roseus* root and stem samples. Important steps involve suitable drying (usually below 50°C to avoid alkaloid breakdown), fine grinding for enhanced surface area, and selective pretreatment procedures like acid-base extraction for alkaloid concentration. Solid-phase extraction (SPE) with specially designed sorbents has proven valuable in the removal of interfering substances before chromatographic separation (Badawy et al., 2022; Hennion, 1999). Sophisticated methods such as molecular imprinted polymers (MIPs) tailored for vincristine/vinblastine have shown remarkable selectivity in sophisticated root extracts. Furthermore, the application of metabolomics methodologies with multivariate statistical analysis has allowed thorough comparison of chemotypes between diverse geographical origins, cultivation, and plant parts and consequently deeper understanding of the biosynthetic correlations between the different alkaloids in stem and root tissues.
These extraction and analytical methods together offer a sound framework for exhaustive phytochemical study of *C. roseus* stems and roots (Arulvendhan et al., 2024; Javaria et al., 2025). Still, standardization is difficult owing to inconsistencies in procedures between various research groups, which underscores the need for validated protocols for ensuring the reproducibility and comparability of results. The ongoing development of extraction techniques and analytical hardware holds the potential for new insights into finding and characterizing new compounds in these worthwhile plant materials, especially for minor components that possibly were overlooked by traditional methods.

Pharmacological Activities

The roots and stems of *Catharanthus roseus* have extraordinary pharmacological diversity, best illustrated by their anticancer activity (Kumar et al., 2022; Gajalakshmi et al., 2013). The bisindole alkaloids vincristine and vinblastine, found mainly in the root system, are milestone findings in oncology, as they are powerful microtubule-destabilizing agents that inhibit cell division by tubulin binding and interference with mitotic spindle assembly. These alkaloids have become irreplaceable in the management of several malignancies such as Hodgkin's lymphoma, non-Hodgkin's lymphoma, acute lymphoblastic leukemia, and some solid tumors (Pandrangi et al., 2022; Hunis & Hunis, 2022). Recent studies have shown that stem extracts have other alkaloids such as leurosine, lochnerine, and tetrahydroalstonine that exhibit cytotoxicity against various cancer cell lines through mechanisms involving apoptosis induction, cell cycle arrest, and anti-angiogenesis. The synergistic activity seen among these compounds indicates that whole extracts could provide therapeutic benefits over individual constituents.
Aside from their anticancer uses, *C. roseus* roots and stems exhibit impressive antimicrobial, antidiabetic, and cardioprotective activities. Extracts of roots have shown strong broad-spectrum antimicrobial activities against many pathogenic bacteria and fungi, particularly inhibiting *Staphylococcus aureus*, *Escherichia coli*, and *Candida albicans*. The antidiabetic activity of root and stem preparations has been established through various mechanisms like augmentation of insulin release, increased peripheral glucose uptake, inhibition of α-glucosidase activity, and pancreatic β-cell protection (Aba & Asuzu, 2018; Ardalani et al., 2021). These activities are mainly due to alkaloids vindoline, ajmalicine, and serpentine, along with phenolic compounds and tannins of these plant extracts. Cardiovascular effects reported in both in vitro and in vivo experiments involve antihypertensive actions via vasodilation, calcium channel modulation, and antiarrhythmic action, mostly with ajmalicine and serpentine alkaloids found in high concentration in the roots (Dey et al., 2017; Amssayef & Eddouks, 2023; Moyeenudin et al., 2024).
The anti-inflammatory and neuroprotective action of *C. roseus* roots and stems are new fields of pharmacological interest with therapeutic value (Grosso et al., 2023; Rahbardar & Hosseinzadeh, 2020; Khan et al., 2024). Root extracts have exhibited noteworthy antioxidant activity, able to scavenge free radicals successfully and decrease markers of oxidative stress in different experimental models. This antioxidant activity combined with some characteristic alkaloids like vindolinine and tabersonine has been found to possess neuroprotective action in Alzheimer's disease and Parkinson's disease models through inhibition of acetylcholinesterase, β-amyloid aggregation inhibition, and dopaminergic neuronal protection. Stem and root extracts' anti-inflammatory action is expressed through inhibition of inflammatory cytokines (TNF-α, IL-1β, IL-6), down-regulation of cyclooxygenase and lipoxygenase pathways, and NF-κB signaling modulation (Nworu & Akah, 2015; Tasneem et al., 2019). These pharmacologically varied activities, authenticated both by traditional uses and recent scientific research, highlight the therapeutic diversity of *C. roseus* roots and stems above and beyond their documented position in cancer therapy.

Toxicity and Safety Evaluation

The toxicological profile of *Catharanthus roseus* stem and root justifies close consideration because of the extremely potent nature of the alkaloids comprising them (Kabubii, 2015). Toxicity studies in rodent models have shown dose-dependent deleterious effects with LD50 values of stem and root extracts usually being between 375-1250 mg/kg body weight, varying according to the solvent and method of extraction (Debebe et al., 2017; Monika et al., 2023). The most frequently noted expressions of toxicity are myelosuppression, neurotoxicity, gastrointestinal upset, and hepatorenal impairment. Histopathological analysis has demonstrated dose-dependent damage to bone marrow, liver, and kidney tissues at elevated doses (Bhat et al., 2018; Kumari et al., 2012). The toxic mechanisms are mainly due to the vinca alkaloids' capacity to interfere with microtubule dynamics, impacting rapidly dividing cells all over the body, and not only cancer cells, thereby justifying their narrow therapeutic window in clinical use.

Genotoxicity and reproductive toxicity testing have produced mixed results that are best interpreted carefully. Experiments using Ames test, chromosomal aberration assays, and micronucleus tests have shown that extracts of stems and roots in high concentrations have the potential to cause DNA damage, especially in the presence of metabolic activation (Araújo et al., 2016). Yet these are normally seen at levels far higher than therapeutic usage. Reproductive toxicology studies have demonstrated embryotoxic and teratogenic activity, with pregnancy exposure leading to reduced implantation rates, augmented resorption, and skeletal malformations in the developing fetus (Gilbert-Barness, 2010; Jamkhande et al., 2014). These observations are consistent with the pregnancy contraindication of vinca alkaloids in clinical oncology. Safety assessment studies underscore that the dose-related toxicity profile demands careful compliance with dosing recommendations for therapy and close observation, especially with the use of concentrated preparations.

Risk reduction strategies and safe use parameters have been established on the basis of thorough toxicity evaluations (Chapman et al., 1998; Dekant et al., 2010). Conventional medicinal preparations, which generally utilize water extracts at moderate levels, exhibit much lower toxicity profiles than concentrated alkaloid fractions, indicating that naturally occurring chemical matrices can influence bioavailability and toxicity. Standardization efforts have created safety limits, with suggested daily intakes for stem and root preparations typically not more than 100-250 mg of dried material, based on the method of preparation (Schilter et al., 2003; Brickmann, 2011). Drug interaction studies have revealed possible contraindications with CYP3A4 inhibitors, P-glycoprotein modulators, and hepatic enzyme inducers, which can greatly modify the metabolism and disposition of the plant's alkaloids (Asokkumar & Ramachandran, 2019; Pal & Mitra, 2006). Recent phytopharmaceutical strategies with emphasis on targeted delivery systems, such as nanoparticles and liposomes, have shown promising outcomes in optimizing therapeutic effectiveness and reducing systemic toxicity, which may extend the therapeutic window of such precious but active plant compounds.

Applications and Therapeutic Potential

The clinical uses of *Catharanthus roseus* roots and stems reach far beyond their established position in oncology. In modern medicine, vincristine and vinblastine derived mainly from root material are still cornerstone drugs in many chemotherapy protocols, and semi-synthetic analogs like vinorelbine and vindesine have broadened the therapeutic armamentarium (Dhyani et al., 2022; Quispe et al., n.d.; Torrence, 2017). Aside from cancer, stem and root extracts have also been used to treat diabetes mellitus, as clinical trials showed notable decreases in fasting blood glucose and glycosylated hemoglobin levels in patients treated with standardized extracts. Ethnopharmacological uses of root decoctions for treating hypertension have received scientific support based on clinical trials with moderate antihypertensive activity due to ajmalicine and serpentine alkaloids that are α-adrenergic receptor modulators. These traditional uses are but a small proportion of the therapeutic value contained within these plant tissues, with continuing translational work broadening their application to autoimmune diseases, neurodegenerative diseases, and antimicrobial treatment (Rahman et al., 2021; Tyler & Tyler, 2023).

The advent of new extraction processes and drug delivery platforms has sparked innovation in therapeutic uses of *C. roseus* stem and root compounds (Das et al., 2020; Wang n.d.). Alkaloid fraction nanoencapsulation has proven superior bioavailability, targeted delivery, and lowered systemic toxicity in preclinical models. Phytosomes based on phospholipid complexes have demonstrated the ability to enhance oral uptake of poorly water-soluble alkaloids, whereas polymeric micelles have increased circulation time and passive targeting to tumors (Chaudhary & Rajora, 2025; Barani et al., 2021; Khan et al., 2013). These novel formulation strategies overcome several of the drawbacks that plague traditional preparations, such as poor solubility, high rate of metabolism, and toxicities limiting doses. At the same time, investigation of synergistic interactions with traditional drugs and other herbal compounds has indicated intriguing therapeutic options, including vincristine-curcumin combinations with greater efficacy against multidrug-resistant lines of cancer cells and root extract-metformin combinations with better glycemic control than either drug used separately.

Therapeutic prospects for the future of *C. roseus* roots and stems are highly promising, with multiple upcoming uses being studied. Recent findings of stem tissue's immunomodulatory alkaloids have energized research on their promise for the treatment of inflammatory diseases and autoimmune disorders (Khan et al., 2021; Porwal et al., 2021). The neuroprotective activity of certain root-derived compounds, in particular against oxidative stress and protein misfolding, makes them potential candidates for the management of neurodegenerative disorders such as Alzheimer's and Parkinson's diseases. Advancements in biotechnology, including plant cell culture systems and metabolic engineering, are overcoming traditional limitations in alkaloid production, enabling sustainable manufacturing of both established and novel therapeutic compounds (Gunaseelan et al., 2025; Pasquali et al., 2006; Verpoorte et al., 1993). Most notably, the confluence of artificial intelligence and machine learning methodologies in drug discovery has propelled the identification of new, previously uncharacterized stem and root constituents with novel pharmacological profiles to significantly expand the therapeutic horizon far beyond the historically appreciated uses of this incredible medicinal plant.

Research Gaps and Future Directions

Notwithstanding widespread research into *Catharanthus roseus*, a wide gap still exists in extensive phytochemical characterization of stems and roots in comparison to the better understood leaf tissues. Analytical methods presently employed have been able to characterize only about 40-50% of the overall alkaloid content in these plant organs, indicating that many compounds are still uncharacterized. The intricate biosynthetic pathways for the accumulation of alkaloids in a tissue-specific manner, especially the mechanisms of compartmentalization in root cells, are poorly understood. High-resolution mass spectrometry coupled with advanced bioinformatics resources are required to elucidate the entire metabolic network. Comparative transcriptomic and proteomic studies of various plant tissues may also help uncover regulatory processes that control the preferential production of certain alkaloids in stem and root tissues. Standardization of extraction protocols and analytical methods is still poor, preventing cross-study comparisons and impeding the development of quality control parameters required for therapeutic uses.

The pharmacological potential of many minor alkaloids and non-alkaloid constituents of the stem and root of *C. roseus* is still not fully examined. Although vincristine and vinblastine have been the subject of extensive studies, alkaloids like hörhammericine, lochnericine, and other serpentine derivatives of these tissues have been sparingly studied regarding their bioactivities. Structure-activity relationship investigations to determine the pharmacophores responsible for a particular therapeutic effect could be used to direct the design of semi-synthetic derivatives with increased efficacy and lowered toxicity. The mechanisms of apparently synergistic interactions between combinations of alkaloids in crude extracts need to be explored systematically using sophisticated pharmacological tools like network pharmacology and systems biology. Preclinical and clinical research on the effectiveness of standardized stem and root preparations for indications other than cancer—such as neurodegenerative disease, metabolic syndrome, and chronic inflammation—is surprisingly sparse, a significant knowledge gap between traditional use and evidence-based practice.

Future research directions are to emphasize sustainable production and biotechnological strategies that help overcome the inherent constraints of dependency on natural sources. Development of plant cell and tissue culture systems specifically designed for root alkaloid productivity could help alleviate concerns regarding sustainability while facilitating controlled biosynthesis of target chemicals. Metabolic engineering concepts, including CRISPR-Cas9 technology, provide promising directions for further increasing alkaloid yields and possibly producing novel compounds through manipulation of pathways. The development of plant-based bioreactors designed to mimic the physiological conditions of root tissues could revolutionize the production of these valuable therapeutic agents. Additionally, emerging drug delivery technologies including targeted nanocarriers, stimuli-responsive systems, and biomimetic platforms should be explored to overcome the pharmacokinetic limitations and toxicity concerns associated with *C. roseus* alkaloids. Interdisciplinary collaborative research combining ethnopharmacological wisdom with contemporary scientific methodologies would more feasibly speed the translation of folk usage into established therapeutic uses, especially for less investigated indications like neurodegenerative illnesses, metabolic diseases, and antimicrobial treatments in an era of growing resistance.

Conclusion

This review highlights the outstanding pharmacological value of *Catharanthus roseus* stem and root as reservoirs of bioactive molecules of varied therapeutic uses. From the groundbreaking anticancer alkaloids vincristine and vinblastine to molecules showing antimicrobial, antidiabetic, cardioprotective, neuroprotective, and anti-inflammatory activities, these plant tissues are precious treasures in traditional medicine as well as contemporary pharmacotherapy. In spite of remarkable progress in extraction methods, analytical strategies, and therapeutic applications, considerable research gaps exist with respect to holistic phytochemical characterization, pharmacological evaluation of minor metabolites, and optimization of sustainable production processes. The multifaceted toxicological profile demands cautious attention to safety parameters as novel drug delivery systems present exciting opportunities for ensuring efficacy with reduced side effects. Future research directions focusing on biotechnological strategies, innovative formulation strategies, and interdisciplinary research will be critical to maximize the therapeutic potential of these incredible plant parts, closing the gap between traditional knowledge and evidence-based practice while addressing sustainability issues in the production of these precious medicinal resources.

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