



BIOACTIVE COMPOUNDS OF CATHARANTHUS ROSEUS AND THEIR ROLE IN ANTICANCER ACTIVITY

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ABSTRACT

Cancer continues to be a leading cause of global mortality, and the search for effective, less toxic therapies has highlighted the importance of plant derived compounds in oncology. Catharanthus roseus (Madagascar periwinkle) is one of the most significant medicinal plants, renowned for producing the vinca alkaloids vincristine and vinblastine, which remain integral to modern chemotherapy. This review explores the botanical background, ethnopharmacological relevance, and phytochemistry of *C. roseus*, emphasizing its diverse alkaloid profile of more than 130 compounds. The mechanisms of anticancer action—ranging from microtubule inhibition and cell cycle arrest to apoptosis induction and anti-angiogenesis—are discussed in detail, alongside the clinical applications of vincristine, vinblastine, and their semi synthetic derivatives such as vindesine and vinorelbine. Analytical approaches including phytochemical screening, chromatographic

techniques, spectroscopic methods, and in vitro cytotoxicity assays are highlighted as essential tools for identifying and quantifying these bioactive compounds. Despite their therapeutic success, challenges such as low natural yield and dose limiting toxicities persist. Emerging strategies.

KEYWORDS

- Catharanthus roseus
- Madagascar periwinkle
- Vinca alkaloids

- Vincristine
- Vinblastine
- Vindesine
- Vinorelbine
- Anticancer activity
- Microtubule inhibition
- Apoptosis induction
- Phytochemistry
- Plant tissue culture
- Metabolic engineering
- Nanotechnology drug delivery
- CRISPR biosynthetic enhancement.

1. INTRODUCTION

Cancer is one of the most pressing global health challenges, accounting for nearly 10 million deaths annually. Despite advances in synthetic drug development, plant derived compounds remain indispensable in oncology. Natural products provide structural diversity and biological specificity that synthetic libraries often cannot match^[1,2] Among medicinal plants, *Catharanthus roseus* (Madagascar periwinkle) has emerged as a cornerstone in anticancer drug discovery. Initially used in traditional medicine for diabetes and infections, it later became the source of two of the most important chemotherapeutic agents: **vincristine** and **vinblastine**.^[3,4] These vinca alkaloids revolutionized cancer treatment and remain in clinical use today.

This review provides a comprehensive analysis of the bioactive compounds of *C. roseus*, their mechanisms of action, analytical methods for their study, and their clinical applications.

AIM:- The aim of this review is to critically evaluate the bioactive compounds of *Catharanthus roseus*, with a particular emphasis on vinca alkaloids such as vincristine and vinblastine, and to assess their mechanisms, analytical approaches, and clinical applications in anticancer therapy.^[3,7]

OBJECTIVES

- To explore the botanical and ethnopharmacological background of *C. roseus* and its traditional medicinal uses that led to the discovery of anticancer alkaloids.^[3]

- To review the phytochemical diversity of *C. roseus*, emphasizing the biosynthesis and classification of its major alkaloids.^[8]
- To examine the mechanisms of anticancer action of vinca alkaloids, including microtubule inhibition, cell cycle arrest, apoptosis induction, and anti-angiogenic effects.^[7]
- To highlight analytical approaches such as phytochemical screening, chromatographic profiling, and in vitro cytotoxicity assays used to identify and quantify these compounds.^[8,7]
- To assess clinical applications and limitations of vincristine, vinblastine, and their semi synthetic derivatives in cancer therapy.^[3,7]
- To discuss future prospects including plant tissue culture, metabolic engineering, nanotechnology, and CRISPR based strategies for sustainable production and improved efficacy.^[8,7]

2. Botanical Background and Ethnopharmacology

C. roseus is a perennial herb belonging to the family Apocynaceae. Native to Madagascar, it is now cultivated worldwide in tropical and subtropical regions.^[5] Traditionally, it has been used in Ayurveda and Chinese medicine for treating diabetes, malaria, and hypertension.^[6] The ethnopharmacological use of *C. roseus* provided the first clues to its therapeutic potential. In the 1950s, Canadian researchers investigating its antidiabetic properties unexpectedly discovered its strong cytotoxic effects on bone marrow and white blood cells, leading to the isolation of vincristine and vinblastine.^[7]

3. Phytochemistry of *Catharanthus roseus*

The plant produces more than 130 alkaloids, broadly classified into

- Indole alkaloids (vincristine, vinblastine, vindoline, catharanthine)
- Terpenoids
- Flavonoids
- Phenolic compounds.^[8,9]

The biosynthesis of vincristine and vinblastine is complex, involving the coupling of catharanthine and vindoline in specialized plant tissues.^[10] This low natural yield (0.0005% dry weight) makes large scale production challenging.^[11]

4. Major Anticancer Alkaloids

4.1 Vincristine

- Mechanism: Binds to tubulin, preventing microtubule polymerization.
- Clinical use: Acute lymphoblastic leukemia, Hodgkin's lymphoma, pediatric cancers.^[12]
- Side effects: Neurotoxicity, peripheral neuropathy.^[13]

4.2 Vinblastine

- Mechanism: Similar to vincristine but with different pharmacokinetics.
- Clinical use: Breast cancer, testicular cancer, Kaposi's sarcoma.^[14]
- Side effects: Myelosuppression.^[15]

4.3 Semi synthetic Derivatives

- **Vindesine:** Used in lung cancer and melanoma.^[16]
- **Vinorelbine:** Effective in breast and non small cell lung cancer.^[17]

5. Mechanisms of Anticancer Action

The anticancer activity of vinca alkaloids involves multiple pathways:

- Microtubule inhibition → prevents spindle formation during mitosis.^[18]
- Cell cycle arrest → halts cells at metaphase.^[19]
- Apoptosis induction → activates caspase dependent pathways.^[20]
- Anti angiogenesis → reduces tumor vascularization.^[21]
- Synergistic effects → enhanced efficacy when combined with other chemotherapeutics.^[22]

6. Analytical Approaches

6.1 Phytochemical Screening

Qualitative tests such as Mayer's and Dragendorff's for alkaloids, Shinoda for flavonoids, and ferric chloride for tannins provide preliminary insights.^[23]

6.2 Chromatographic Techniques

- TLC: Used for preliminary separation of alkaloids.^[24]
- HPLC: Gold standard for quantification of vincristine and vinblastine.^[25]

6.3 Spectroscopic Methods

- LC MS and NMR confirm structural identity.^[26]

6.4 In vitro Assays

- MTT assay for cytotoxicity.
- Flow cytometry for apoptosis and cell cycle analysis.^[27]

7. Clinical Applications

Vincristine and vinblastine are integral to chemotherapy regimens such as:

- CHOP (Cyclophosphamide, Doxorubicin, Vincristine, Prednisone) for lymphomas.^[28]
- MOPP (Mechlorethamine, Vincristine, Procarbazine, Prednisone) for Hodgkin's disease.^[29]

Their inclusion in combination therapies reduces resistance and enhances efficacy.

8. Challenges and Future Prospects

- **Low yield:** Natural production is insufficient for global demand.^[30]
- Biotechnological solutions: Plant tissue culture, metabolic engineering, and synthetic biology are being explored.^[31,32]
- Nanotechnology: Liposomal and nanoparticle formulations may reduce toxicity and improve delivery.^[33]
- CRISPR based metabolic engineering: Potential to enhance alkaloid biosynthesis.^[34]
- 9. Advantages and Disadvantages Advantages
- Proven Anticancer Efficacy: The vinca alkaloids vincristine and vinblastine, derived from *Catharanthus roseus*, are clinically validated and widely used in treating various cancers, including leukemia, lymphoma, and breast cancer.^[3]
- Multifaceted Mechanism of Action: These compounds exhibit multiple anticancer mechanisms such as microtubule inhibition, cell cycle arrest, and apoptosis induction, making them effective against rapidly dividing tumor cells.^[8]
- Natural Origin and Structural Diversity: As a plant-derived source, *C. roseus* offers a rich reservoir of over 130 alkaloids, providing opportunities for the development of novel derivatives and analogs with improved therapeutic profiles.^[3]
- Disadvantages

1. Low Natural Yield: The concentration of vincristine and vinblastine in the plant is extremely low (approximately 0.0005% of dry weight), making extraction inefficient and costly.^[8]

2. Toxicity and Side Effects: Despite their efficacy, vinca alkaloids are associated with dose-limiting toxicities such as neurotoxicity (vincristine) and myelosuppression (vinblastine), which can compromise patient quality of life and limit dosage.^[3]

3. Complex Biosynthesis and Limited Sustainability: The biosynthetic pathway of these alkaloids is highly complex, and large-scale production remains a challenge without advanced biotechnological interventions.^[8]

9. CONCLUSION

The exploration of *Catharanthus roseus* as a medicinal plant underscores the profound impact that natural products can have on modern oncology. From its humble beginnings in traditional medicine to its pivotal role in the discovery of vincristine and vinblastine, *C. roseus* has become a cornerstone of plant-based chemotherapy. The plant's phytochemical richness, with over 130 identified alkaloids, highlights its extraordinary biosynthetic capacity, yet also reveals the challenges of harnessing these compounds due to their extremely low natural yield.

The vinca alkaloids—vincristine, vinblastine, and their semi-synthetic derivatives—remain among the most effective microtubule-targeting agents in clinical oncology. Their mechanisms of action, including microtubule inhibition, cell cycle arrest, apoptosis induction, and anti-angiogenic effects, provide a multifaceted approach to halting tumor progression. Their integration into combination regimens such as CHOP and MOPP has further cemented their role in standard cancer care. However, dose-limiting toxicities such as neurotoxicity and myelosuppression continue to restrict their therapeutic window, underscoring the need for improved formulations and delivery systems.

Analytical advances—ranging from phytochemical screening and chromatographic profiling to spectroscopic characterization and in-vitro cytotoxicity assays—have been instrumental in identifying, quantifying, and validating these bioactive compounds. These tools not only ensure quality control but also provide the foundation for biotechnological innovations aimed at enhancing alkaloid production.

Looking forward, the greatest challenge lies in bridging the gap between the plant's therapeutic potential and its limited natural productivity. Biotechnological strategies such as plant tissue culture, metabolic engineering, and synthetic biology offer promising avenues for sustainable production. Emerging technologies, including nanotechnology-based drug delivery and CRISPR-mediated pathway optimization, hold the potential to overcome current limitations by improving yield, reducing toxicity, and enhancing therapeutic efficacy.

In essence, *Catharanthus roseus* exemplifies the enduring value of medicinal plants in the fight against cancer. Its journey from ethnomedicine to frontline chemotherapy demonstrates how traditional knowledge, combined with modern science, can yield life-saving therapies. Continued interdisciplinary research—integrating pharmacognosy, biotechnology, nanomedicine, and clinical oncology—will be essential to fully realize the therapeutic promise of this remarkable plant. By addressing the challenges of production and delivery, the next generation of vinca alkaloid-based therapies may not only sustain but also expand the legacy of *C. roseus* in global cancer care.

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