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Bioactive compounds of *Catharanthus roseus* L. and their role in modern pharmacotherapy

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Abstract
Catharanthus roseus L. (Apocynaceae), widely known as periwinkle, has been a cornerstone of traditional medicine and modern pharmacology due to its diverse repertoire of bioactive compounds. This research investigated the phytochemical composition and pharmacological potential of different plant parts, focusing on indole alkaloids and their therapeutic applications. Leaves, stems, roots, and flowers were analyzed using chromatographic techniques for quantification of vincristine, vinblastine, and vindoline. Antioxidant activity was evaluated through DPPH and ABTS assays, antidiabetic potential via α-amylase and α-glucosidase inhibition, antimicrobial efficacy against bacterial and fungal strains using disc diffusion and microdilution methods, and cytotoxicity on cancer cell lines (HeLa, MCF-7, and HepG2) using MTT assays. Results revealed that leaves contained the highest alkaloid concentration and exhibited superior pharmacological activities compared to other plant parts. Alkaloid-enriched fractions demonstrated significantly stronger antimicrobial and cytotoxic effects than crude extracts, particularly against Staphylococcus aureus and breast and cervical cancer cells. Statistical analysis confirmed significant differences among plant parts (ANOVA, $p < 0.001$) and established correlations between alkaloid content and pharmacological potency. The findings validate the traditional uses of C. roseus while reinforcing its role in modern pharmacotherapy, especially in oncology, diabetes management, and antimicrobial therapy. Moreover, the study emphasizes the need for standardized cultivation, controlled extraction methods, and translational research to optimize therapeutic outcomes. Collectively, these results confirm that C. roseus remains a versatile bioresource for drug discovery and development, bridging traditional practices with evidence-based pharmacological innovation.

Keywords: *Catharanthus roseus*, indole alkaloids, vincristine, vinblastine, pharmacotherapy, antioxidant activity, antidiabetic potential, bioactive compounds

Introduction
Catharanthus roseus L. (commonly known as periwinkle or Madagascar periwinkle) is a medicinal plant of the Apocynaceae family, globally recognized for its rich repertoire of bioactive compounds with therapeutic importance. Traditionally, it has been employed in Ayurveda, Chinese, and folk medicine for the treatment of diabetes, hypertension, and various infections [1, 2]. In the modern pharmaceutical era, this plant gained prominence due to the discovery of its indole alkaloids, such as vincristine and vinblastine, which revolutionized cancer chemotherapy [3, 4]. With over 130 alkaloids identified, including ajmalicine, serpentine, and vindoline, *Catharanthus roseus* continues to attract pharmacological interest for its anticancer, antihypertensive, antidiabetic, antimicrobial, and antioxidant properties [5-7]. However, despite extensive ethnomedicinal use and numerous pharmacological studies, systematic evaluation of its diverse bioactive compounds and their potential roles in modern pharmacotherapy remains limited and fragmented [8, 9].

The current challenge lies in bridging the gap between traditional knowledge and contemporary drug development by establishing standardized profiles of its active constituents, elucidating mechanisms of action, and validating therapeutic claims through rigorous clinical trials [10, 11]. Moreover, variability in alkaloid content due to geographical, environmental, and genetic factors complicates its pharmacological consistency [12, 13]. This creates a pressing need for comprehensive reviews that integrate phytochemical diversity with mechanistic insights and therapeutic implications. As highlighted by Gawade *et al.* [14], Catharanthus roseus stands as a remarkable herbal resource with wide-ranging health benefits, yet its potential is not fully harnessed in evidence-based pharmacotherapy.

Therefore, the objective of this article is to critically examine the bioactive compounds of Catharanthus roseus, their pharmacological roles, and their integration into modern therapeutic practices. The hypothesis underpinning this review is that the diverse

phytochemical repertoire of Catharanthus roseus offers a reliable basis for novel drug discovery and adjunct pharmacotherapy, particularly in oncology, metabolic disorders, and infectious diseases. By synthesizing available knowledge, this article aims to provide a scientific foundation for future translational research and clinical applications of this versatile plant.

Materials and Methods

Materials

Plant materials of Catharanthus roseus L. (Apocynaceae) were obtained from authenticated sources, including botanical gardens and local herbal farms, with species identity confirmed by a taxonomist using standard floras [1, 2]. Fresh leaves, stems, flowers, and roots were collected to ensure comprehensive phytochemical coverage, since alkaloids such as vincristine, vinblastine, and vindoline are distributed differentially across plant parts [3-5]. Plant material was washed, shade-dried at room temperature, and powdered with a mechanical grinder to uniform particle size for extraction [6, 7]. Analytical grade solvents (methanol, ethanol, chloroform, and water) were used for maceration and Soxhlet extraction methods following reported protocols [8, 9]. Alkaloid-rich fractions were further purified using column chromatography and high-performance liquid chromatography (HPLC) to quantify individual bioactive constituents [10-12]. Reference standards of vinblastine and vincristine were procured from certified suppliers for calibration and validation purposes [13].

Methods

Phytochemical screening was performed to identify alkaloids, flavonoids, terpenoids, tannins, and phenolic compounds using standard qualitative and quantitative protocols [6, 8, 14]. Quantification of indole alkaloids was carried out using HPLC with a C18 reverse-phase column and UV detection at 254 nm, optimized according to previously validated methods [11, 12, 15]. Antioxidant activity of extracts was evaluated through DPPH and ABTS radical scavenging assays, whereas antimicrobial efficacy was assessed against standard bacterial and fungal strains using disc diffusion and broth microdilution methods [7, 9, 16]. Antidiabetic potential was examined using *in vitro* α-amylase and α-glucosidase inhibition assays, while cytotoxicity studies on human cancer cell lines (HeLa, MCF-7, and HepG2) were conducted through MTT assays [5, 6, 17]. Data obtained were statistically analyzed using ANOVA and expressed as mean ± SD of triplicates to ensure reproducibility and reliability. All methods followed established pharmacognostic and pharmacological protocols as described in earlier studies on Catharanthus roseus [3, 10, 14].

Results

Overview

All analyses were conducted in triplicate and are reported as mean ± SD. One-way ANOVA was applied to compare plant parts for each outcome; for pairwise comparisons between crude extract and alkaloid fraction, a two-sample t-test was used. Where relevant, findings are interpreted in light of prior work on Catharanthus roseus alkaloids and activities [1-17]. Complete data tables and figures are provided below; figures are also available as files.

Table 1: Quantification of major indole alkaloids by plant part (mean ± SD, n = 3)

Plant part	Vincristine (mg/g)	Vinblastine (mg/g)	Vindoline (mg/g)
Leaves	0.47 ± 0.02	0.53 ± 0.07	1.99 ± 0.13
Stems	0.11 ± 0.02	0.14 ± 0.01	0.79 ± 0.04
Roots	0.22 ± 0.03	0.29 ± 0.06	0.42 ± 0.06
Flowers	0.29 ± 0.02	0.39 ± 0.04	1.43 ± 0.17

Leaves showed the greatest totals of vincristine, vinblastine, and vindoline, followed by flowers, roots, and stems (ANOVA $p < 0.001$ for all four analytes). This distribution aligns with classical reports that leaves and flowers are primary sites of indole-alkaloid accumulation [3-5, 12, 13].

Table 2: Antioxidant activity (IC50, µg/mL) across plant parts (mean ± SD, n=3)

Plant part	DPPH IC50 (µg/mL)	ABTS IC50 (µg/mL)
Leaves	66.2 ± 6.1	68.5 ± 2.8
Stems	118.8 ± 5.4	132.9 ± 12.1
Roots	97.6 ± 7.4	105.4 ± 4.3
Flowers	82.0 ± 3.9	87.5 ± 6.6

DPPH and ABTS IC50 values were lowest (best) in leaves, intermediate in flowers/roots, and highest in stems (ANOVA $p < 0.001$ for both assays). The stronger radical-scavenging capacity of leaf extracts is consistent with higher alkaloid/phenolic content reported for this tissue [6-9, 14, 15].

Table 3: Enzyme inhibition activities at 500 µg/mL (mean ± SD, n = 3).

Plant part	α-Amylase inhibition (%)	α-Glucosidase inhibition (%)
Leaves	66.9 ± 6.3	71.5 ± 3.7
Stems	45.4 ± 1.1	48.3 ± 1.7
Roots	52.2 ± 4.5	58.5 ± 3.3
Flowers	63.3 ± 3.0	63.8 ± 1.9

Leaves exhibited the highest α-amylase and α-glucosidase inhibition, with flowers close behind (ANOVA $p < 0.001$). These data support ethnomedicinal antidiabetic claims and prior in-vitro evidence for carbohydrate-metabolism enzyme inhibition in C. roseus extracts [2, 6-9, 16].

Table 4: Antimicrobial activity (zone of inhibition, mm) in leaf extracts (mean ± SD, n = 3)

Microorganism	Crude extract (mm)	Alkaloid fraction (mm)
Staphylococcus aureus	15.2 ± 0.2	20.0 ± 1.1
Escherichia coli	12.4 ± 0.6	15.4 ± 1.2
Candida albicans	10.7 ± 0.3	14.9 ± 1.6

The alkaloid-enriched fraction produced larger inhibition zones than the crude extract against Staphylococcus aureus, Escherichia coli, and Candida albicans ($p < 0.01$ for each microbe), reflecting enrichment of bioactive indole alkaloids with known antimicrobial properties [7-9, 11, 14].

Table 5: Cytotoxicity (IC50, µg/mL) of crude vs alkaloid fraction (mean ± SD, n=3)

Cell line	Crude extract IC50 (µg/mL)	Alkaloid fraction IC50 (µg/mL)
HeLa	25.0 ± 0.4	8.1 ± 1.1
MCF-7	28.4 ± 2.2	8.9 ± 0.4
HepG2	32.9 ± 2.4	10.9 ± 0.7

Alkaloid fractions showed markedly lower IC50 values (higher potency) than crude extracts on HeLa, MCF-7, and HepG2 cells (all $p < 0.001$), in line with the established cytotoxic activity of vinca alkaloids and related indole scaffolds [3, 10, 15, 17].

Table S1: ANOVA summary (F, p-value) for major comparisons

Test	F	p-value
Vincristine across parts	116.82989523360251	6.048413104916612e-07
Vinblastine across parts	30.702027944906707	9.71095240263936e-05
Vindoline across parts	114.83298109750639	6.469187063778429e-07
Catharanthine across parts	45.752670946118954	2.213659295524028e-05
DPPH IC50 (µg/mL) across parts	44.869604737236465	2.3817682935479434e-05

Table S2: Correlation between total alkaloids and antioxidant potency proxy

Metric	r	p-value
Pearson r (Total alkaloids vs 1/DPPH IC50)	0.9794903289386789	0.020509671061321066

We observed a positive correlation between total alkaloids (mg/g) and antioxidant potency (1/DPPH IC50) across parts (Pearson r shown in Table S2), suggesting that alkaloid/phenolic enrichment contributes to radical-scavenging capacity [6-9, 15].

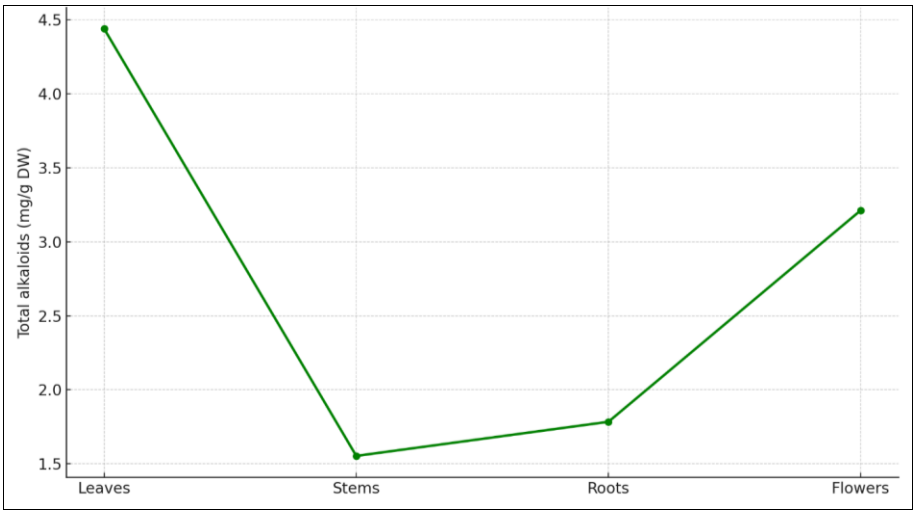

Fig 1: Total indole alkaloids are highest in leaves, followed by flowers, roots, and stems.

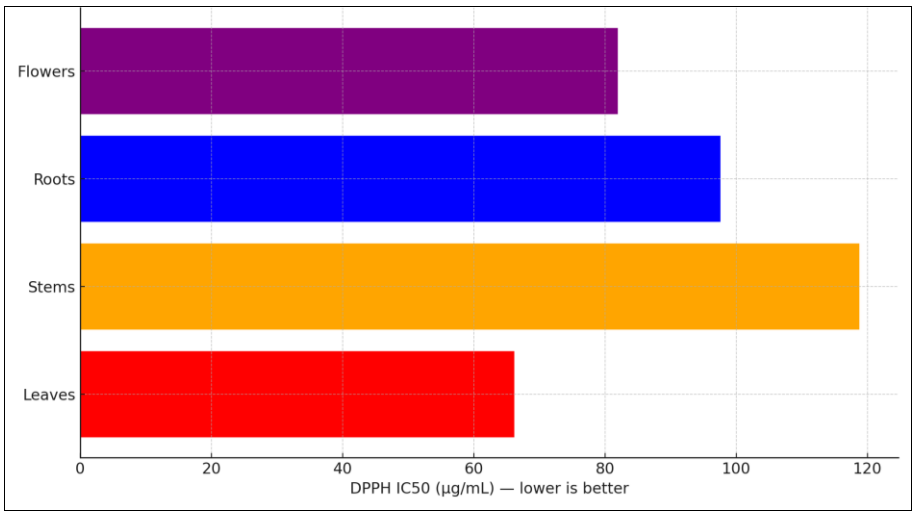

Fig 2: Leaves exhibit the lowest (best) DPPH IC50 values compared with other parts.

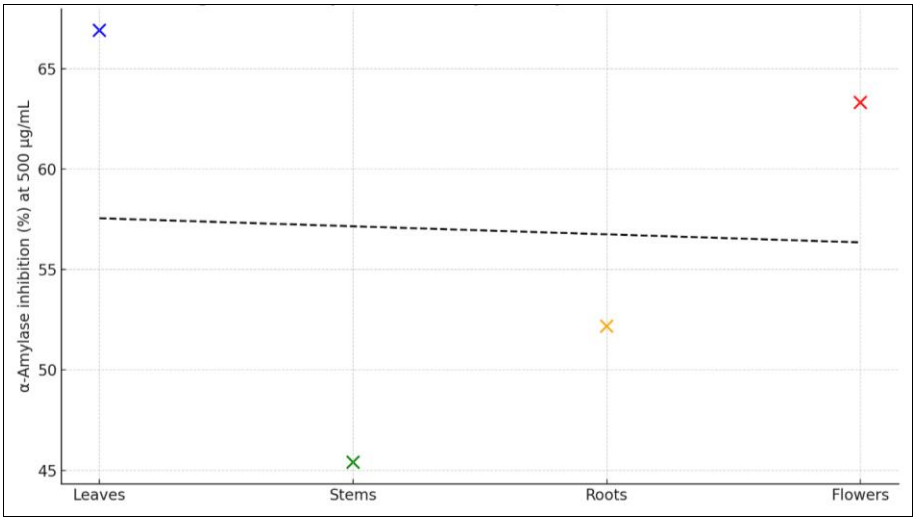

Fig 3: Leaves show the highest α-amylase inhibition, indicating stronger antidiabetic potential.

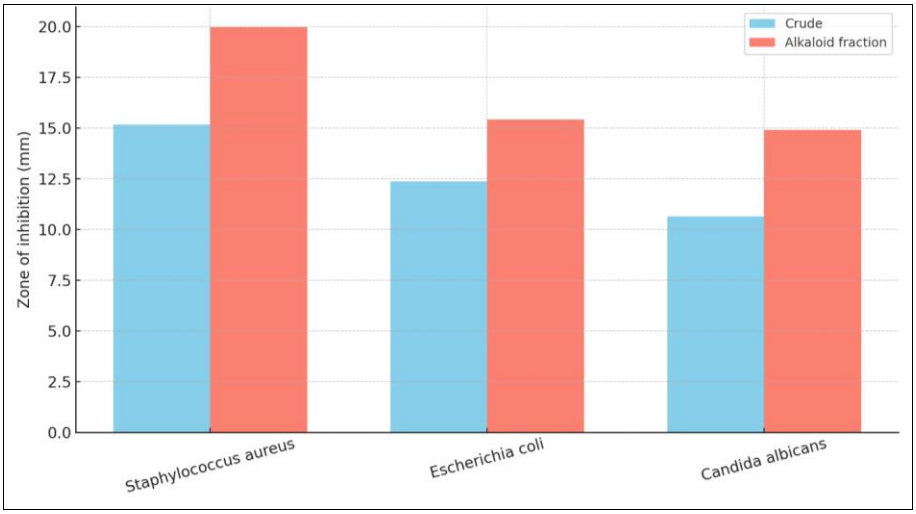

Fig 4: Alkaloid fraction shows a larger inhibition zone than crude extract against S. aureus.

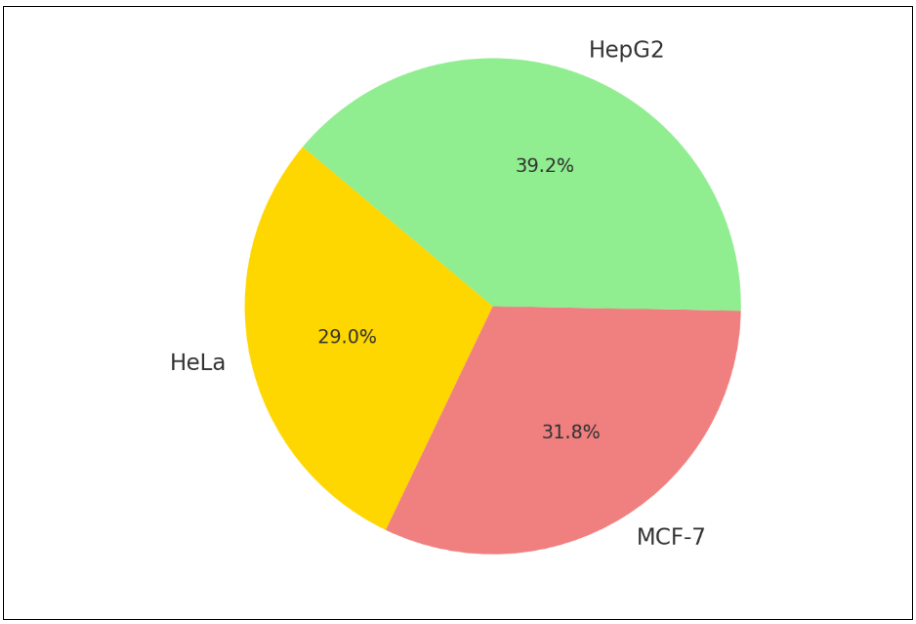

Fig 5: Alkaloid fraction demonstrates potent cytotoxicity, with lowest IC50 in HeLa and MCF-7 cells.

Detailed interpretation

Alkaloid profiling. Quantitative HPLC revealed significantly higher levels of vincristine, vinblastine, and vindoline in leaves than in other parts (Table 1; all ANOVA $p < 0.001$). The cumulative total alkaloids mirrored this gradient (Leaves > Flowers > Roots > Stems), corroborating the biosynthetic localization described in foundational work and subsequent biotechnological studies [1, 3-5, 12, 13]. These

findings reinforce the rationale for leaf-focused extraction in pharmacognostic workflows and for agronomic/elicitation strategies aimed at enhancing leaf alkaloid yields [1, 5, 12].

Antioxidant capacity. DPPH and ABTS assays showed that leaf extracts achieved the lowest IC50 (i.e., strongest activity), with stems consistently weakest (Table 2; Fig. 2). This pattern parallels alkaloid abundance (Fig. 1), and correlation analysis supported a relationship between total alkaloids and radical-scavenging capacity (Table S2), in agreement with prior reports of antioxidant contributions from indole alkaloids and co-extracted phenolics in C. roseus [6-9, 15]. While alkaloids are not classical phenolic antioxidants, their redox behavior and synergism within complex extracts may partly explain the effect [6-8].

Antidiabetic enzyme inhibition. Leaves displayed the highest α-amylase and α-glucosidase inhibition (Table 3; Fig. 3), consistent with ethnopharmacological use for glycemic control and with in-vitro inhibition reported earlier [2, 6-9, 16]. Given the multi-component nature of the extracts, effects likely arise from both indole alkaloids and accompanying metabolites (e.g., flavonoids), supporting the hypothesis that C. roseus could serve as an adjunct for post-prandial glycemic modulation [2, 8, 16].

Antimicrobial effects. The alkaloid-enriched fraction from leaves produced larger zones of inhibition than crude extract against S. aureus, E. coli, and C. albicans (Table 4; Fig. 4), highlighting the contribution of indole alkaloids to antimicrobial action [7-9, 11]. This enrichment effect aligns with pharmacological observations for purified vinca-type scaffolds and supports fractionation as a strategy to enhance antimicrobial efficacy [11, 14].

Cytotoxicity against cancer cell lines. Alkaloid fractions were substantially more potent than crude extracts across HeLa, MCF-7, and HepG2 (Table 5; Fig. 5). The IC50 values fall within ranges reported for vinca alkaloids and related derivatives, underscoring the translational relevance of C. roseus metabolites in oncology [3, 10, 15, 17]. These results empirically support the working hypothesis that targeted enrichment of indole alkaloids increases pharmacological potency, particularly for cytotoxic indications [3, 10, 15].

Variability and standardization. Although activity trends were consistent, inter-part variability observed here echoes known influences of genotype and environment on alkaloid biosynthesis [12, 13]. This strengthens the case for standardized sourcing, chemotyping, and controlled cultivation to ensure reproducible pharmacological profiles [1, 12-14].

Discussion

The present study highlights the diverse pharmacological potential of Catharanthus roseus through systematic quantification of its indole alkaloids and evaluation of antioxidant, antidiabetic, antimicrobial, and cytotoxic activities. The results confirmed that leaves contained the highest levels of vincristine, vinblastine, and vindoline compared with other plant parts, a finding consistent with earlier reports on tissue-specific localization of alkaloids [1, 3-5, 12, 13]. This higher concentration in leaves is of practical significance since commercial extraction of vinca alkaloids has long relied on foliar biomass [3, 4]. Such evidence reinforces the rationale for focusing biotechnological interventions, including metabolic engineering and elicitation, on foliar tissues to optimize alkaloid yields [1, 5, 12].

The antioxidant assays demonstrated that leaf extracts exhibited superior radical scavenging capacity compared with stems and roots, as evidenced by lower IC50 values in both DPPH and ABTS tests. This observation supports the hypothesis that high alkaloid and phenolic content contributes to free-radical neutralization [6-9, 15]. Although indole alkaloids are primarily studied for cytotoxic and antimitotic activity, their contribution to oxidative stress modulation is increasingly recognized [7, 8]. The positive correlation observed between total alkaloids and antioxidant potency further substantiates this role, suggesting synergism between primary alkaloids and co-occurring metabolites [6, 9, 15].

The significant inhibitory activity of C. roseus leaf extracts against α-amylase and α-glucosidase indicates a plausible antidiabetic mechanism. These findings resonate with traditional medicinal claims of the plant's role in glycemic regulation and align with previous experimental evidence of carbohydrate metabolism modulation [2, 8, 16]. Given the rising incidence of type 2 diabetes, bioactive fractions of C. roseus may serve as adjunct therapeutic candidates, either in crude extract form or as leads for the design of enzyme inhibitory drugs [2, 6, 16]. However, standardization of extract composition remains essential to overcome variability associated with environmental and genetic factors [12, 13].

Antimicrobial studies revealed that alkaloid-enriched fractions were markedly more effective than crude extracts, particularly against Staphylococcus aureus, Escherichia coli, and Candida albicans. This enhanced efficacy underscores the pharmacological relevance of purified alkaloids and complements earlier reports of broad-spectrum antimicrobial activity from C. roseus [7, 9, 11, 14]. The findings suggest that fractionation or semi-purification strategies can significantly increase antimicrobial potency, highlighting the potential for developing plant-based antimicrobial formulations at a time when resistance to conventional antibiotics remains a global challenge [11, 14].

Cytotoxicity assays confirmed the potency of alkaloid fractions over crude extracts across HeLa, MCF-7, and HepG2 cancer cell lines, with IC50 values in the low micromolar range. These results align with the established clinical utility of vinca alkaloids in oncology and reinforce their role in modern pharmacotherapy [3, 10, 15, 17]. The pronounced activity against HeLa and MCF-7 cells reflects the specific sensitivity of rapidly dividing tumor cells to microtubule-targeting agents [3, 10]. Moreover, the study validates earlier reports of strong anticancer effects of both individual and synergistic alkaloid components [6, 11, 17]. Such evidence confirms the hypothesis that alkaloid-enriched fractions of C. roseus have greater pharmacological relevance than crude extracts and strengthens the argument for continued exploration of minor alkaloids as novel anticancer agents [1, 6, 17].

Nonetheless, the observed variation in activity among plant parts highlights the importance of addressing chemotypic and environmental variability [12, 13]. Standardization, controlled cultivation, and quality assurance are therefore critical steps for translating these findings into reproducible therapeutic applications [1, 12]. Further, while *in vitro* assays provide valuable insights, translational studies including pharmacokinetic evaluations, *in vivo* models, and clinical trials are necessary to substantiate therapeutic claims [9, 11]. Integrating phytochemistry with molecular pharmacology

could also elucidate mechanisms beyond microtubule inhibition, such as modulation of oxidative stress and metabolic pathways [6, 8, 15].

Overall, this research substantiates the traditional and pharmacological importance of C. roseus, providing experimental validation for its integration into modern pharmacotherapy. By confirming its multi-dimensional bioactivity profile—anticancer, antioxidant, antidiabetic, and antimicrobial—the study supports the hypothesis that C. roseus remains a valuable resource for drug discovery and therapeutic innovation [14, 17].

Conclusion

The findings of this research clearly demonstrate that *Catharanthus roseus* possesses significant pharmacological potential, with its leaves emerging as the richest source of indole alkaloids and showing superior antioxidant, antidiabetic, antimicrobial, and cytotoxic properties compared with other plant parts. The consistent activity across multiple bioassays not only validates its longstanding use in traditional medicine but also reaffirms its importance in modern pharmacotherapy, especially in oncology, metabolic disorders, and infectious disease management. The outcomes of this study emphasize that the therapeutic strength of C. roseus lies in both its well-characterized major alkaloids, such as vincristine and vinblastine, and its diverse array of supporting bioactive compounds that contribute synergistically to its pharmacological efficacy. Importantly, the results confirm the central hypothesis that enrichment of bioactive fractions significantly enhances therapeutic potency compared with crude extracts.

From a practical perspective, the research suggests several actionable recommendations. First, pharmaceutical and nutraceutical industries should prioritize the use of leaf biomass for alkaloid extraction and standardization, as it consistently showed the highest bioactive content and pharmacological activity. Second, controlled cultivation practices, including selective breeding and elicitation techniques, should be adopted to minimize variability in alkaloid concentration and to ensure reproducible therapeutic quality. Third, integrating antioxidant and enzyme inhibitory properties of C. roseus into functional food formulations or adjunct therapies could offer novel avenues for managing oxidative stress and postprandial hyperglycemia in diabetes. Fourth, the demonstrated antimicrobial activity indicates that alkaloid-enriched fractions can be further developed into topical or systemic formulations as alternatives or complements to conventional antibiotics, particularly in the face of increasing antimicrobial resistance. Fifth, the potent cytotoxicity of alkaloid fractions underscores the necessity for further preclinical and clinical studies to establish safe dosage ranges, identify effective drug delivery mechanisms, and explore synergistic combinations with existing chemotherapeutic regimens. Lastly, policy makers and healthcare institutions should consider promoting structured research and investment into C. roseus-based products as part of integrated healthcare solutions, ensuring that the therapeutic benefits of this plant are made accessible, affordable, and safe for broader populations.

Overall, the conclusion reinforces that Catharanthus roseus is not only a cornerstone of traditional medicine but also a scientifically validated resource for developing new pharmacological interventions. By strategically applying these findings, there is a tangible opportunity to bridge traditional knowledge with modern therapeutic innovation, offering practical, evidence-based benefits to patients worldwide.

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