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Anticancer Potential of Medicinal Plants of the Western Ghats of India: Phytochemistry, Molecular Mechanisms, Therapeutic Prospects and Conservation Challenges

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Abstract

Cancer has been a constant battle globally with a lot of development in cures and preventative therapies. The disease is characterised by cells in the human body continually multiplying with the inability to be controlled or stopped. Consequently, forming tumours of malignant cells with the potential to be metastatic. Current treatments include chemotherapy, radiotherapy and chemically derived drugs. Treatments such as chemotherapy can put patients under a lot of strain and further damage their health. Therefore, there is a focus on using alternative treatments and therapies against cancer. The Western Ghats of India constitute one of the world's major biodiversity hotspots and harbour a remarkable diversity of medicinal and endemic plant species traditionally used by indigenous communities for the management of numerous ailments. Increasing interest in plant-derived anticancer agents has highlighted the Western Ghats as a valuable reservoir of structurally diverse secondary metabolites with potential chemo preventive and therapeutic applications. Alkaloids, flavonoids, phenolics, terpenoids, tannins, xanthenes, lignans and other specialized metabolites derived from

medicinal plants have demonstrated antiproliferative, pro-apoptotic, anti-inflammatory, antioxidant, anti-invasive and anti-angiogenic activities in experimental models. Among Western Ghats-associated medicinal plants, *Nothapodytes nimmoniana* is particularly significant because it is a natural source of camptothecin, a potent topoisomerase-I inhibitor from which clinically important anticancer derivatives such as irinotecan and topotecan have been developed. Population-level investigations of *N. nimmoniana* from the Western Ghats have demonstrated substantial variation in camptothecin accumulation, highlighting both pharmaceutical potential and conservation concerns. Recent research has also demonstrated anticancer activity of *Tarenna alpestris* collected from the Megamalai Hills of the Western Ghats against HT-29 colon cancer cells, providing evidence for continued exploration of less-studied regional taxa. This review critically summarizes the ethnomedicinal importance, major phytochemical classes, experimental anticancer activities and possible molecular mechanisms associated with medicinal plants of the Western Ghats. Particular attention is given to apoptosis, cell-cycle arrest, oxidative stress modulation, inhibition of PI3K/Akt, MAPK and NF- κ B-associated pathways, suppression of angiogenesis and inhibition of DNA topoisomerases. The review also discusses limitations of current evidence, including extract variability, incomplete phytochemical characterization, inadequate pharmacokinetic studies, toxicity concerns and the predominance of *in vitro* investigations. Sustainable harvesting, plant tissue culture, metabolite production through biotechnology and conservation of threatened medicinal plants are considered essential for translating biodiversity into clinically relevant anticancer discoveries. The Western Ghats therefore represent an important natural resource for anticancer drug discovery, but systematic pharmacological validation and conservation-oriented research are required to bridge the gap between traditional knowledge and evidence-based oncology. This review also explains an overview of potential therapeutic plants, including a brief description of their pharmacological effect and mechanism of action.

Keywords: Western Ghats; medicinal plants; anticancer activity; phytochemicals; apoptosis; camptothecin; *Nothapodytes nimmoniana*; ethnomedicine; drug discovery; conservation.

Introduction

Globally cancer is a disease which harshly effects the human population. There is a continuous demand for new therapies to treat and prevent this life-threatening disease. Scientific and research interest is drawing its attention towards naturally-derived compounds as they are careful to have less toxic side effects compared to current treatments such as chemotherapy.

The Plant Kingdom produces naturally occurring secondary metabolites which are being examined for their anticancer activities leading to the development of new clinical drugs. With the attainment of these compounds that have been developed into main drugs for cancer treatment new technologies are developing to develop the area additional. The National Cancer Institute collected about 35,000 plant samples from 20 countries and has screened around 114,000 extracts for anti-cancer activity (Shoeb, 2006). Cancer represents a heterogeneous group of diseases characterized by uncontrolled cellular proliferation, resistance to programmed cell death, genomic instability, invasion and metastatic dissemination. Although substantial progress has been achieved in surgery, chemotherapy, radiotherapy, targeted therapy and immunotherapy, treatment-associated toxicity, multidrug resistance, tumour recurrence and limited therapeutic selectivity continue to stimulate the search for new anticancer molecules. Natural products have historically contributed substantially to pharmacotherapy and remain an important source of chemically diverse lead compounds. Medicinal plants are particularly attractive in drug discovery because their secondary metabolites can interact with multiple biological targets (Greenwell and Rahman, 2015). Alkaloids, flavonoids, phenolic acids, terpenoids, quinones, lignans and related compounds have been investigated for their ability to modulate cell proliferation, apoptosis, oxidative stress, inflammation, angiogenesis and metastatic processes. Importantly, plant-derived molecules have already demonstrated the capacity to progress from natural-product discovery to clinically useful anticancer drugs. Camptothecin derivatives and several other plant-derived compounds illustrate the importance of botanical resources in modern oncology. India possesses exceptionally rich plant diversity and an extensive traditional medicinal heritage represented by Ayurveda, Siddha, Unani and numerous community-based healing systems. The Western Ghats, extending along the western side of peninsular India, are especially important because of their high species richness, endemism and ethnobotanical significance. The region contains numerous medicinal plants used traditionally by local and indigenous communities. At the same time, many medicinal plants are threatened by habitat loss, overexploitation and unsustainable collection. A recent review specifically emphasized the conservation concerns surrounding medicinal plants of the Western Ghats. The pharmaceutical importance of Western Ghats plants is particularly well illustrated by *Nothapodytes nimmoniana* (Graham) Mabb. The species is a valuable natural source of camptothecin (CPT), a monoterpene indole alkaloid with potent antitumour activity. Investigations of populations distributed across the Western Ghats have demonstrated considerable variation in CPT concentration among populations and individual trees. Ramesha *et al.* reported individuals

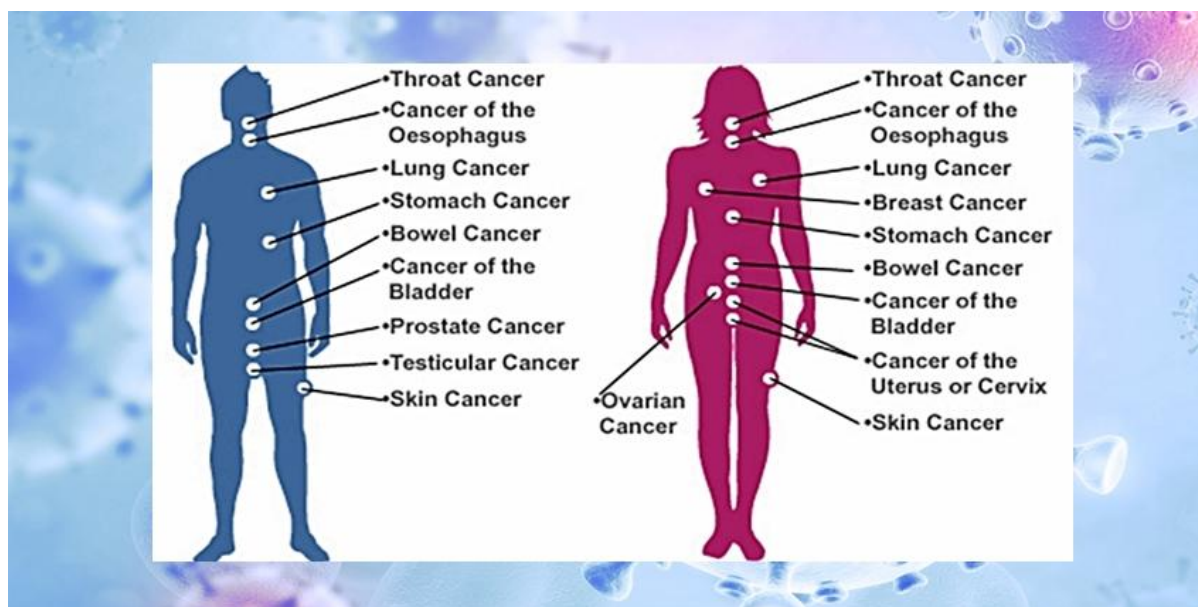
producing substantially higher levels of CPT than previously documented, indicating the potential for selection of high-yielding genotypes. The importance of this species extends beyond pharmacology to conservation biology. Increasing demand for CPT has placed pressure on natural populations of *N. nimmoniana*, and destructive harvesting of plant material has been recognized as a major concern (Ramesha *et al.* 2008). Studies have therefore proposed elite selection, clonal propagation, tissue culture and alternative production systems to reduce pressure on wild populations.

Recent research further demonstrates that the anticancer potential of Western Ghats flora extends beyond established drug-producing species. For example, *Tarennia alpestris*, a medicinal plant native to the Megamalai Hills of the Western Ghats, has recently been investigated for phytochemical composition, antioxidant properties and anticancer activity against human HT-29 colon cancer cells. The study combined phytochemical analysis with MTT, AO/EtBr, DAPI and flow-cytometric approaches, demonstrating the increasing integration of phytochemistry and cellular oncology in the evaluation of regional medicinal plants.

Despite this potential, the available literature remains fragmented. Many investigations are restricted to crude extracts and preliminary *in vitro* assays, whereas comparatively fewer studies establish the active molecules, molecular targets, pharmacokinetics, toxicity, bioavailability and *in vivo* efficacy. Therefore, a critical synthesis specifically addressing medicinal plants associated with the Western Ghats is warranted.

The present review evaluates the anticancer potential of Western Ghats medicinal plants from four interconnected perspectives: (i) ethnomedicinal and phytochemical significance, (ii) experimental anticancer evidence, (iii) molecular and cellular mechanisms, and (iv) conservation and translational challenges. The review also identifies research gaps that should be addressed to facilitate the development of scientifically validated plant-derived anticancer agents.

TYPES OF CANCER



The Western Ghats as a Reservoir of Medicinal Plant Diversity

The Western Ghats represent a biologically rich mountain system containing numerous endemic plant species and diverse vegetation types. Its ecological heterogeneity, ranging from evergreen forests and semi-evergreen forests to montane ecosystems, provides multiple habitats for medicinal plants.

Traditional communities inhabiting the Western Ghats possess extensive knowledge concerning the identification, collection and utilization of medicinal plants. Leaves, roots, bark, stems, fruits, seeds and rhizomes are traditionally prepared as decoctions, pastes, powders, juices and other formulations.

However, the pharmacological value of medicinal plants is accompanied by significant conservation challenges. Several medicinal species have experienced population decline due to habitat fragmentation, commercial exploitation and unsustainable collection. Consequently, anticancer drug discovery should not be separated from conservation biology.

The case of *Nothapodytes nimmoniana* provides an important example. Although the species represents a valuable source of CPT, destructive collection for its bark and wood has created pressure on natural populations.

Plant compounds Associated with Anticancer Properties

Medicinal plants of the Western Ghats contain diverse classes of secondary metabolites. Their potential anticancer activities can broadly be associated with the following groups. Plant derived agents are being used for the treatment of cancer. Several anticancer agents including taxol, vinblastine, vincristine, the camptothecin derivatives, topotecan and irinotecan, and etoposide derived from epipodophyllotoxin are in clinical use all over the world.

Major Anticancer Phytochemicals and Their Plant Sources

Below is a structured overview of the most prominent plant-derived compounds clinically utilized or heavily researched for cancer therapy:

Phytochemical Class	Common Example Compound	Source Plant Species	Primary Anticancer Mechanism
Taxanes	Paclitaxel (Taxol)	<i>Taxus brevifolia</i> (Pacific Yew)	Stabilizes microtubules to halt cell mitosis.
Vinca Alkaloids	Vincristine & Vinblastine	<i>Catharanthus roseus</i> (Madagascar Periwinkle)	Disrupts mitotic spindles to prevent cell division.
Polyphenols	Curcumin	<i>Curcuma longa</i> (Turmeric)	Modulates cell signaling and suppresses transcription factors like NF-κB.
Lignans	Podophyllotoxin	<i>Podophyllum peltatum</i> (Mayapple)	Inhibits tubulin polymerization (used to make Etoposide).
Quinoline Alkaloids	Camptothecin	<i>Camptotheca acuminata</i>	Inhibits Topoisomerase I to cause DNA damage.
Organosulfur	Allicin	<i>Allium sativum</i> (Garlic)	Triggers antioxidant mechanisms and epigenetic changes.

How Phytochemicals Target Cancer Cells

Medicinal plant compounds do not rely on a single path; they execute a multi-targeted attack on tumor development:

- **Induction of Apoptosis:** Compounds like **Silymarin** from Milk Thistle (*Silybum marianum*) and **Withaferin A** from Ashwagandha (*Withania somnifera*) reactivate the body's natural cellular suicide pathways in mutated cells.
- **Cell Cycle Arrest:** Phytochemicals can lock cancer cells into specific phases (such as the G2/M phase), stopping them from reproducing.

- **Blocking Metastasis and Angiogenesis:** Many flavonoids inhibit the signaling pathways (like PI3K/Akt and MAPK) that tumor cells use to migrate to other organs or recruit blood vessels for nutrient supply

Medicinal plants have been used for thousands of years in folk medicines in Asian and African populations and many plants are consumed for their health benefits in developed nations. According to the World Health Organisation (WHO) some nations still rely on plant-based treatment as their main source of medicine and developing nations are utilising the benefits of naturally sourced compounds for therapeutic purposes ¹³. Compounds which have been identified and extracted from terrestrial plants for their anticancer properties include polyphenols, brassinosteroids and taxols.

Alkaloids

Alkaloids constitute one of the most important classes of plant-derived anticancer compounds. Their biological activities include inhibition of DNA replication, interference with microtubules and modulation of cell-cycle progression.

Camptothecin from *Nothapodytes nimmoniana* represents one of the most significant examples associated with the Western Ghats. CPT acts primarily by stabilizing the DNA-topoisomerase-I cleavage complex, resulting in DNA damage and subsequent cancer-cell death.

Flavonoids

Flavonoids such as quercetin, kaempferol, luteolin and related compounds have attracted considerable attention because of their antioxidant, anti-inflammatory, antiproliferative and pro-apoptotic properties.

Their reported anticancer mechanisms include:

- modulation of reactive oxygen species;
- induction of apoptosis;
- inhibition of proliferation;
- cell-cycle arrest;
- modulation of PI3K/Akt and MAPK pathways;

- inhibition of inflammatory signalling;
- suppression of angiogenesis.

Phenolic compounds

Phenolic acids and polyphenols can interact with oxidative-stress and inflammatory pathways. Their potential chemopreventive activity is frequently attributed to their capacity to influence cellular redox balance and signalling pathways involved in tumour development.

Terpenoids

Terpenoids constitute another important group of plant metabolites with potential anticancer properties. Depending on their structures, they may influence mitochondrial function, apoptosis, inflammation, cell-cycle progression and metastatic behaviour.

Xanthones and related polyphenolic compounds

Plants belonging to the genus *Garcinia*, which occur in the Western Ghats, are notable sources of xanthone derivatives and related secondary metabolites. Such compounds have been investigated for cytotoxic, antioxidant and signalling-related activities. However, species-specific evidence should be distinguished carefully from generalized claims concerning the entire genus.

Herbal Treatment

Dietary modifications, cessation of tobacco use, efficient treatment of inflammatory diseases, and the use of nutritional supplements that boost immune functioning are all essential preventative approaches for the majority of malignancies. Chemotherapy, radiotherapy, and chemically generated medications are among the current cancer treatments (Mari-Anne *et al.* 2009). Anti-metabolites, platinum analogs, alkylating drugs, and anti-tumor antibiotics are among the most regularly utilized as cancer chemotherapeutic drugs. Chemotherapy and radiation, on the other hand, put patients under a lot of stress and harm their health. As a result, novel anti-cancer medicines derived from nature, particularly plants, are now being researched. Plants have always been the foundation of traditional medicinal systems, and they have given humans ongoing cures for thousands of years.

***Nothapodytes nimmoniana*: A Model Western Ghats Anticancer Plant**

Among the medicinal plants of the Western Ghats, *Nothapodytes nimmoniana* deserves particular attention because its significance is supported by both phytochemical research and pharmaceutical relevance.

CPT was initially identified from *Camptotheca acuminata*, but *N. nimmoniana* became an important Indian source. Population studies in the Western Ghats have demonstrated substantial differences in CPT concentration between geographical populations and individual plants.

Ramesha *et al.* identified high-yielding individuals and reported the occurrence of additional camptothecins, including 10-hydroxycamptothecin. Their findings suggested opportunities for selecting elite trees and developing sustainable production systems.

Importantly, the pharmacological importance of CPT is well established. It inhibits topoisomerase I, thereby interfering with DNA replication and producing lethal DNA lesions in susceptible cells. CPT derivatives such as irinotecan and topotecan subsequently became important anticancer drugs.

Thus, *N. nimmoniana* represents a successful example of how a plant metabolite can progress from biodiversity resource to clinically relevant anticancer pharmacology (Suhas *et al.* 2007).

Emerging Evidence from Other Western Ghats Medicinal Plants

The anticancer potential of Western Ghats flora is not limited to CPT-producing plants. Numerous medicinal species contain metabolites that warrant investigation through modern cancer biology approaches.

A particularly relevant recent example is *Tarennia alpestris* from the Megamalai Hills. A 2025 study evaluated its phytochemical composition and antioxidant properties and examined its activity against HT-29 human colon cancer cells. Multiple experimental approaches—including MTT-based cell viability assessment, AO/EtBr staining, DAPI analysis and flow cytometry—were used to investigate cytotoxicity, apoptosis and cell-cycle effects (Sagayaraj *et al.* 2025)

Such studies are important because they move beyond traditional ethnomedicinal claims and begin to establish measurable biological effects. Nevertheless, *in vitro* cytotoxicity should not be interpreted as proof of clinical anticancer efficacy. Further investigations involving purified compounds, mechanistic assays, animal models, pharmacokinetics and toxicological evaluation are required.

Major Molecular Mechanisms of Plant-Derived Anticancer Activity

The anticancer activity of medicinal plant constituents is generally multifactorial.

Induction of apoptosis

Apoptosis is an important mechanism through which damaged or abnormal cells are eliminated. Plant-derived metabolites may activate intrinsic mitochondrial pathways involving:

Bax/Bcl-2 imbalance → mitochondrial membrane permeabilization → cytochrome-c release → caspase activation → programmed cell death Cell-cycle arrest

Cancer cells frequently display uncontrolled progression through the cell cycle. Plant metabolites may interfere with cyclins, cyclin-dependent kinases and checkpoint proteins, resulting in arrest at the G0/G1, S or G2/M phases.

DNA damage and topoisomerase inhibition

CPT represents a particularly important example of this mechanism. Inhibition of topoisomerase I interferes with DNA replication and transcription, producing DNA damage and ultimately cell death.

PI3K/Akt signalling

The PI3K/Akt pathway regulates cell survival, proliferation and metabolism. Aberrant activation of this pathway occurs in several cancers. Plant-derived phytochemicals have been reported to modulate this signalling network.

MAPK signalling

MAPK pathways regulate proliferation, differentiation and stress responses. Modulation of ERK, JNK and p38 signalling can contribute to the antiproliferative effects of phytochemicals.

NF- κ B and inflammation

Chronic inflammation is closely associated with tumour development. Phytochemicals may inhibit NF- κ B-associated inflammatory signalling, thereby potentially influencing tumour-promoting inflammatory microenvironments.

Oxidative stress

Reactive oxygen species have a dual role in cancer biology. Moderate increases in oxidative stress can promote cancer-cell death, whereas antioxidant activity may protect normal cells from oxidative damage. Consequently, the biological effect of a phytochemical depends on concentration, cellular context and molecular target rather than simply its antioxidant capacity.

Conservation and Sustainable Utilization

The development of anticancer compounds from Western Ghats plants must be compatible with biodiversity conservation.

The *Nothapodytes nimmoniana* example demonstrates the potential conflict between pharmaceutical demand and conservation. High-value metabolites can create economic incentives for destructive harvesting.

Several strategies may help address this problem:

1. Selection of high-yielding elite plants
2. Seed-based propagation
3. Micropropagation and tissue culture
4. Hairy-root culture
5. Cell suspension culture
6. Endophyte-based metabolite production
7. Metabolic engineering
8. Cultivation outside natural forests
9. Community-based conservation
10. Development of sustainable harvesting protocols

Research on *N. nimmoniana* has specifically suggested tissue culture and biotechnology-based approaches for increasing CPT production while reducing destructive pressure on natural populations.

Research Gaps and Future Perspectives

Despite considerable promise, several limitations remain.

Major research gaps

1. Lack of standardized extracts:

Variation in geographical origin, season, plant part, extraction solvent and processing can produce markedly different phytochemical profiles (Namdeo *et al.* 2010).

2. Predominance of *in vitro* studies:

Many reports demonstrate cytotoxicity using cancer-cell lines without subsequent animal or clinical validation.

3. Limited molecular validation:

Changes in gene or protein expression do not necessarily establish direct molecular targets.

4. Poor pharmacokinetic information:

Bioavailability, metabolism and tissue distribution are often insufficiently studied.

5. Toxicity:

A plant extract may be cytotoxic to cancer cells but also harmful to normal cells. Selectivity indices therefore require systematic evaluation.

6. Conservation concerns:

The discovery of high-value anticancer compounds can increase pressure on wild populations (Malavika and Athira 2023).

7. Limited clinical translation:

Only a small proportion of promising plant-derived molecules progress to clinical development.

Future research should integrate ethnobotany, metabolomics, molecular biology, network pharmacology, computational chemistry, nanotechnology, tissue culture and conservation biology (Rajasekharan and Kareem 2011).

Particular attention should be given to identifying Western Ghats species that contain novel compounds rather than repeatedly evaluating already well-characterized plants.

Metabolomic-guided fractionation and bioassay-guided isolation may accelerate the discovery of chemically novel anticancer candidates.

Conclusion

The Western Ghats constitute a rich and largely underexplored reservoir of medicinal plants with significant potential for anticancer drug discovery. The success of camptothecin from *Nothapodytes nimmoniana* highlights the importance of this region as a source of pharmacologically valuable natural products. Investigations of species such as *Tarennia alpestris* further demonstrate promising opportunities for identifying novel anticancer compounds. Nevertheless, most available evidence is preclinical and requires rigorous validation through phytochemical, molecular, in vivo, pharmacokinetic, toxicological and clinical studies. Future research should integrate traditional knowledge, modern drug-discovery approaches and conservation strategies to ensure sustainable utilization and protection of the Western Ghats' valuable medicinal plant diversity.

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