Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 15 March 2026
Revised 24 April 2026
Accepted 18 May 2026

Natural Resources for Human Health 2026, Vol. 6 (3): 619–627

KEYWORDS:
plant-derived anticancer agents; traditional medicine; vinca alkaloids; taxanes; apoptosis; oncogenic signalling; phytochemicals; drug discovery

From Traditional Medicine to Modern Oncology: Mechanistic Insights into Plant-Derived Anticancer Agents

Praney Madan[1], K. Janakiraman[2], Shraddha Patel[3], Shivam Chandra[4], Ibrokhim Sapaev[5], Shanmuga Priyan[6], Bhavani Ganapathy[7]

[1]Centre for Research Impact & Outcome, Chitkara University Institute of Engineering and Technology, Chitkara University, Rajpura, 140401, Punjab, India. praney.madan.orp@chitkara.edu.in

[2]Department of Pathology, Vinayaka Missions Medical College, Karaikal, Vinayaka Mission's Research Foundation (DU), Tamil Nadu, India. janakiramankrishnakumar@gmail.com

[3]Department of Pharmacology, Parul Institute of Pharmacy, Parul University, Vadodara, Gujarat, India. Shraddhapatel692@gmail.com

[4]School of Pharmacy and Research, Dev Bhoomi Uttarakhand University. shivamchandra303@gmail.com

[5]Department of Physics and Chemistry, Tashkent Institute of Irrigation and Agricultural Mechanization Engineers National Research University, Tashkent, Uzbekistan; University of Tashkent for Applied Science; School of Engineering, Central Asian University, Tashkent, Uzbekistan. sapaevibrokhim@gmail.com

[6]Pharmacology, Meenakshi Medical College Hospital & Research Institute, Meenakshi Academy of Higher Education and Research, Enathur, Kanchipuram, Tamil Nadu 631552, India. priyan@maher.ac.in

[7]Department of Pharmacology, Meenakshi Ammal Dental College and Hospital, Meenakshi Academy of Higher Education and Research, India.ganapathy@maher.ac.in

ABSTRACT: The plant kingdom has been the single most productive source of clinically useful anticancer drugs, contributing an estimated 50–60% of the modern chemotherapeutic arsenal. What began as ethnomedical practice—the empirical use of medicinal plants across Ayurvedic, Chinese, and other traditional systems—was transformed, through mid-twentieth-century screening programmes, into four cornerstone drug classes: the vinca alkaloids (from Catharanthus roseus), the taxanes (from Taxus spp.), the camptothecin derivatives (from Camptotheca acuminata), and the epipodophyllotoxins (from Podophyllum spp.). This review traces that translational arc and dissects the molecular mechanisms that underpin it. The established agents act through precisely defined targets—vinca alkaloids destabilise and taxanes stabilise microtubules to arrest mitosis, while camptothecins and epipodophyllotoxins inhibit topoisomerases I and II, respectively, to trigger lethal DNA damage. A second, expanding wave of investigational phytochemicals—curcumin, resveratrol, EGCG, genistein, sulforaphane, withaferin A and others—acts pleiotropically across the hallmarks of cancer, inducing apoptosis (frequently p53-dependent), arresting the cell cycle, and simultaneously modulating the PI3K/AKT/mTOR, NF-κB, JAK/STAT3, Wnt/β-

Natural Resources for Human Health
eISSN: 2583-1194

catenin and MAPK pathways, suppressing angiogenesis, metastasis and cancer-stem-cell survival.

These compounds show micromolar in-vitro potency (representative IC_{50} values of ~2–50 μM) and multitarget action with comparatively low toxicity, but their clinical translation is constrained by poor bioavailability and rapid metabolism. Modern strategies—nanoformulation (exemplified by nab-paclitaxel), semisynthesis, network pharmacology and rational combinations—are being deployed to close this gap. The review concludes that plant-derived agents remain central to oncology, and that integrating traditional knowledge with modern mechanistic and delivery science is the most promising route to the next generation of anticancer drugs.

1. INTRODUCTION

For most of human history, the treatment of disease—including the tumours and "growths" recognised by ancient physicians—depended on plants. Traditional medical systems, from Ayurveda and traditional Chinese medicine to Unani, Kampo and countless folk traditions, accumulated vast empirical knowledge of botanical remedies, and this ethnopharmacological reservoir has proved extraordinarily valuable to modern drug discovery. [1,2] The plant kingdom remains an indispensable source for oncology: natural products and their derivatives account for roughly 50–60% of the anticancer agents in clinical use, and of the small-molecule anticancer drugs approved between 1940 and 2014, about half originated from natural sources. [2,3] Few areas of medicine owe more to nature.

The transformation of traditional plant knowledge into modern chemotherapy is one of the great translational narratives of pharmacology (Figure 1). Systematic screening of plant extracts, begun in earnest in the 1950s and expanded by dedicated collection programmes, yielded four foundational classes of anticancer drug—the vinca alkaloids and epipodophyllotoxins first, then the taxanes and camptothecins—whose development from isolation to clinical use spanned some three decades, from the early 1960s to the 1990s. [3,4] These agents remain backbones of curative and palliative regimens across haematological and solid malignancies.

Modern mechanistic biology has since revealed precisely *how* these molecules work, and has motivated a second wave of interest in dietary and medicinal phytochemicals—polyphenols, flavonoids, terpenoids, isothiocyanates and alkaloids—that act not on a single target but pleiotropically across the interlinked "hallmarks of cancer." [2,5] This review is organised around that dual story. We first trace the translational arc from tradition to clinic; we then dissect the mechanisms of the established agents and of the investigational phytochemicals, mapping them onto the cellular hallmarks and oncogenic signalling networks they engage; and we close with the pharmacokinetic and delivery challenges—and the modern nanotechnological and computational solutions—that will determine which of the next generation of plant-derived candidates reaches the clinic.

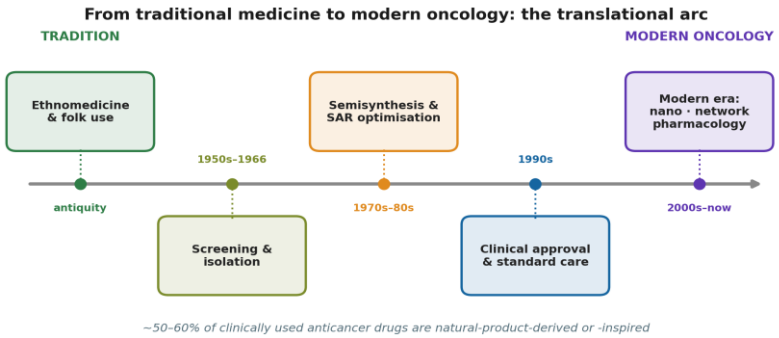

Figure 1. The translational arc from traditional medicine to modern oncology. Empirical ethnomedical use gave way to systematic screening and isolation (1950s–1966), semisynthesis and structure–activity optimisation (1970s–80s), clinical approval and integration into standard care (1990s), and today's era of nanoformulation and network pharmacology. Natural products account for roughly 50–60% of the clinical anticancer arsenal.

Natural Resources for Human Health
eISSN: 2583-1194

2. ESTABLISHED PLANT-DERIVED ANTICANCER DRUGS

Four classes of plant-derived compound form the historical and clinical core of the field (Table 1). Their success rests on the fact that each strikes a precise, essential target in dividing cells—either the mitotic spindle or the topoisomerase enzymes that manage DNA topology (Figure 2). [1,4,6]

Drug (class)	Plant source	Molecular target	Mechanism / cell-cycle effect
Vinblastine, vincristine (vinca alkaloids)	*Catharanthus roseus*	β-tubulin	Inhibit microtubule assembly → M-phase (mitotic) arrest
Paclitaxel, docetaxel (taxanes)	*Taxus brevifolia / baccata*	β-tubulin	Stabilise microtubules, prevent disassembly → mitotic arrest
Topotecan, irinotecan (camptothecins)	*Camptotheca acuminata*	Topoisomerase I	Trap cleavage complex → S-phase arrest, DNA damage
Etoposide, teniposide (epipodophyllotoxins)	*Podophyllum* spp.	Topoisomerase II	Stabilise cleavable complex → G2/M arrest, DNA breaks
Omacetaxine (homoharringtonine)	*Cephalotaxus* spp.	Ribosome (60S)	Inhibit protein-synthesis elongation → apoptosis

Table 1. Established plant-derived anticancer drugs, their botanical origins, molecular targets and mechanisms. Each class exploits an essential process of dividing cells—spindle dynamics, DNA topology or protein synthesis.

2.1 Microtubule-targeting agents

The mitotic spindle, built from dynamic microtubules, is exquisitely vulnerable during cell division, and the two great classes of spindle poison attack it from opposite directions. Vinca alkaloids—vinblastine, vincristine and their semisynthetic relatives from the Madagascar periwinkle—bind β-tubulin and *inhibit* its polymerisation, preventing spindle assembly; taxanes—paclitaxel from the Pacific yew and docetaxel—bind a distinct site and instead *stabilise* microtubules, preventing the disassembly that mitosis requires (Figure 2a). [1,4,6] Both outcomes converge on the same result: arrest at metaphase and, ultimately, apoptotic death of the dividing cell. The clinical impact has been immense, taxanes and vinca alkaloids remaining first-line agents across breast, lung, ovarian and haematological cancers.

2.2 Topoisomerase-targeting agents

Topoisomerases relieve the torsional strain generated when DNA is unwound for replication and transcription by transiently cleaving and re-ligating the strands. Two plant-derived classes convert this housekeeping function into a lethal liability by trapping the enzyme–DNA "cleavable complex." Camptothecin, isolated from *Camptotheca acuminata* in 1966, and its clinical derivatives topotecan and irinotecan inhibit topoisomerase I, producing S-phase arrest and replication-associated DNA damage; the epipodophyllotoxins etoposide and teniposide, semisynthetic derivatives of *Podophyllum* podophyllotoxin, inhibit topoisomerase II, generating double-strand breaks and G2/M arrest (Figure 2b). [3,4,6] Notably, while podophyllotoxin itself is a tubulin poison, its clinically used derivatives were re-engineered to act on topoisomerase II—an early and instructive example of how semisynthesis can redirect a natural scaffold toward a new, more useful mechanism.

Natural Resources for Human Health
eISSN: 2583-1194

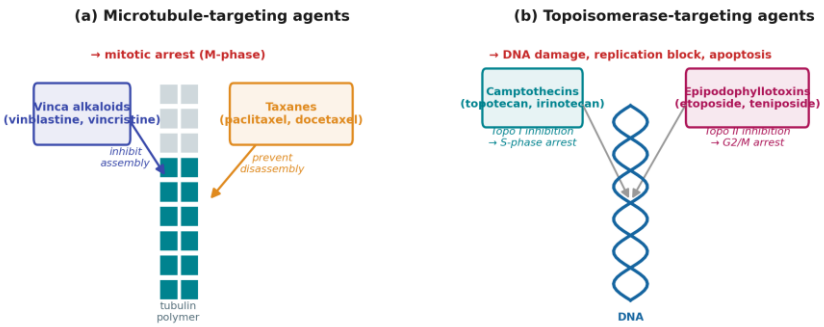

Figure 2. Mechanisms of the established plant-derived drugs. (a) Microtubule-targeting agents: vinca alkaloids inhibit tubulin assembly while taxanes prevent microtubule disassembly; both cause mitotic arrest. (b) Topoisomerase-targeting agents: camptothecins inhibit topoisomerase I (S-phase arrest) and epipodophyllotoxins inhibit topoisomerase II (G2/M arrest), both producing lethal DNA damage.

3. TARGETING THE HALLMARKS OF CANCER

Whereas the established cytotoxics act chiefly on the machinery of cell division, the broader universe of plant-derived agents engages the full range of cancer's defining capabilities. Figure 3 maps the principal targets. Beyond microtubule dynamics and topoisomerase inhibition, plant compounds induce apoptosis, arrest the cell cycle, suppress the oncogenic signalling that sustains proliferation and survival, inhibit tumour angiogenesis, block invasion and the epithelial–mesenchymal transition (EMT) that underlies metastasis, and reprogramme the epigenome and the cancer-stem-cell (CSC) pathways responsible for recurrence. [2,5,7] Table 2 summarises representative agents for each hallmark. It is this breadth—particularly the multitarget action of the investigational phytochemicals—that distinguishes plant-derived agents from most single-target synthetic drugs.

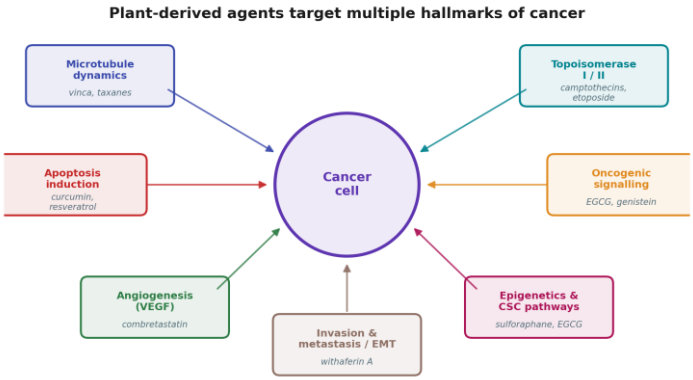

Figure 3. Plant-derived agents target multiple hallmarks of cancer. Established drugs act on microtubule dynamics and topoisomerases; investigational phytochemicals additionally induce apoptosis, modulate oncogenic signalling, and suppress angiogenesis, invasion/metastasis and cancer-stem-cell and epigenetic programmes—often several of these simultaneously.

Hallmark / target	Representative plant-derived agents
Microtubule dynamics	Vinca alkaloids, taxanes, combretastatin
Topoisomerase I / II	Camptothecins; etoposide, teniposide
Apoptosis induction (p53, caspases, Bcl-2)	Curcumin, resveratrol, withaferin A, thymoquinone
Cell-cycle arrest	EGCG, genistein, apigenin, sulforaphane

Hallmark / target	Representative plant-derived agents
Oncogenic signalling (PI3K/AKT, NF-κB, STAT3, Wnt, MAPK)	Curcumin, EGCG, resveratrol, genistein
Angiogenesis (VEGF)	Combretastatin, EGCG, curcumin
Invasion / metastasis / EMT	Withaferin A, resveratrol, curcumin
Epigenetics & cancer stem cells	Sulforaphane, EGCG, curcumin, genistein

Table 2. Hallmarks of cancer and representative plant-derived agents that target them. Many phytochemicals appear under several hallmarks, reflecting their characteristic multitarget, pleiotropic action.

4. INVESTIGATIONAL PHYTOCHEMICALS AND THEIR MECHANISMS

A large and growing group of dietary and medicinal phytochemicals is under preclinical and clinical investigation (Table 3). Their unifying mechanistic feature is the pleiotropic, simultaneous modulation of multiple oncogenic signalling pathways (Figure 4). Curcumin, from turmeric, activates p53-dependent apoptosis while inhibiting NF-κB, Wnt/β-catenin and ERK signalling; resveratrol, from grapes, triggers intrinsic (mitochondrial) apoptosis, frequently through p53, and modulates sirtuins and the PI3K/AKT axis; EGCG, the principal green-tea catechin, counters aberrant PI3K/AKT/mTOR and NF-κB activation; and sulforaphane, an isothiocyanate from cruciferous vegetables, activates the cytoprotective Nrf2 pathway and inhibits histone deacetylases and DNA methylation. [5,8,9,10] Together with genistein, withaferin A, thymoquinone, quercetin and apigenin, these compounds have been termed multitarget agents precisely because a single molecule perturbs several nodes of the network that cancer cells depend upon—an attractive property given the redundancy and adaptability of oncogenic signalling.

Phytochemical	Source	Chemical class	Key molecular targets
Curcumin	*Curcuma longa*	Diarylheptanoid polyphenol	p53↑; NF-κB, Wnt, ERK↓; apoptosis
Resveratrol	Grapes, berries	Stilbene polyphenol	Intrinsic apoptosis (p53); SIRT1; PI3K/AKT
EGCG	Green tea	Flavan-3-ol catechin	PI3K/AKT/mTOR↓; NF-κB↓; angiogenesis↓
Genistein	Soy	Isoflavone	Wnt, STAT3; phytoestrogen; CSC targeting
Sulforaphane	Broccoli / crucifers	Isothiocyanate	Nrf2↑; HDAC & DNA-methylation inhibition
Withaferin A	*Withania somnifera*	Steroidal lactone (withanolide)	NF-κB, HSP90; EMT/metastasis↓
Thymoquinone	*Nigella sativa*	Monoterpene quinone	p53; apoptosis; PI3K/AKT↓

Table 3. Leading investigational anticancer phytochemicals, their sources, chemical classes and principal molecular targets. Multitarget action is the defining characteristic of this group.

Natural Resources for Human Health
eISSN: 2583-1194

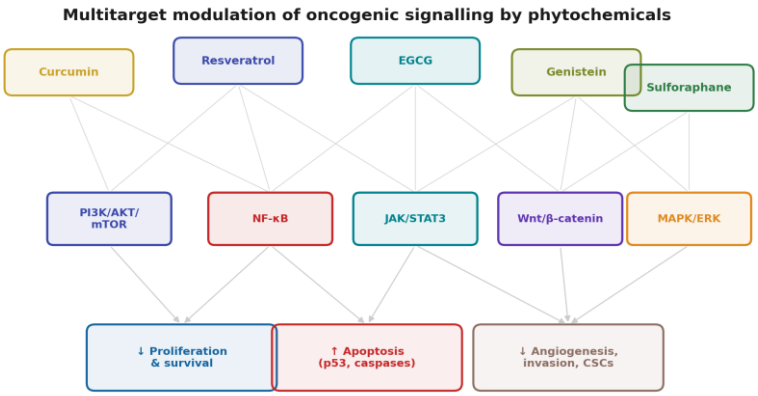

Figure 4. Multitarget modulation of oncogenic signalling by phytochemicals. Curcumin, resveratrol, EGCG, genistein and sulforaphane converge on the PI3K/AKT/mTOR, NF-ϰB, JAK/STAT3, Wnt/β-catenin and MAPK/ERK pathways, collectively suppressing proliferation and survival, inducing apoptosis, and inhibiting angiogenesis, invasion and cancer-stem-cell programmes.

4.1 Potency and the potency–toxicity trade-off

A candid assessment must acknowledge that investigational phytochemicals are far less potent than the established cytotoxics. Their in-vitro IC_{50} values typically lie in the micromolar range (Figure 5)—for example sulforaphane at ~15 μM against LNCaP prostate cells, curcumin at ~18 μM against BxPC-3 pancreatic cells, and resveratrol at ~50 μM against MCF-7 breast cells—whereas paclitaxel and the other established drugs act at nanomolar concentrations. [8] The steroidal lactone withaferin A is a notable exception, active in the low-micromolar range. This lower potency is partly offset by two advantages: multitarget action, which raises the barrier to resistance, and a generally favourable toxicity profile that makes these compounds attractive for chemoprevention and combination use rather than as stand-alone cytotoxics. [2,5]

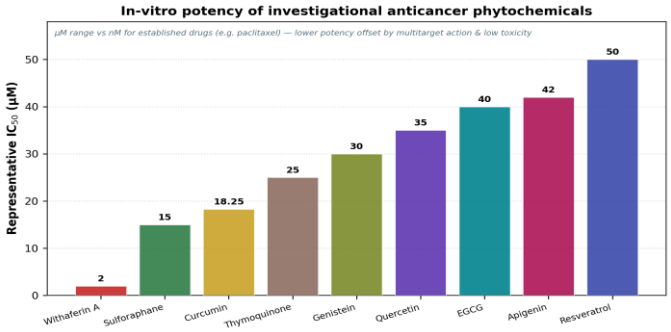

Figure 5. Representative in-vitro potency (IC_{50}) of investigational anticancer phytochemicals. Most act in the micromolar range—orders of magnitude weaker than the nanomolar established drugs—with withaferin A among the most potent. Lower intrinsic potency is offset by multitarget action and comparatively low toxicity. Values are representative figures compiled from the cited literature.

5. CLINICAL TRANSLATION: CHALLENGES AND MODERN SOLUTIONS

The central obstacle to translating investigational phytochemicals is pharmacokinetic. Most are poorly water-soluble, chemically unstable and rapidly metabolised, so that the micromolar concentrations required for activity in vitro are rarely sustained in plasma after oral dosing—a limitation that has repeatedly blunted otherwise promising candidates such as curcumin, resveratrol and quercetin. [9,11] Despite this, several have advanced into clinical trials (Figure 6b): curcumin and EGCG have reached phase III evaluation (curcumin in combination with gemcitabine for pancreatic and colorectal cancer, EGCG in prostate cancer and cervical dysplasia), while resveratrol, sulforaphane, genistein and quercetin are in phase I/II studies. [9,12]

Modern pharmaceutical science is addressing the bioavailability problem directly. Nanoformulation is the most advanced strategy and has a landmark precedent: albumin-bound (nab-)paclitaxel demonstrated that reformulating a plant-derived drug can improve delivery, tolerability and efficacy, and now polymeric, liposomal and PLGA nanoparticles are being used to stabilise and deliver curcumin, resveratrol, EGCG and sulforaphane, improving their pharmacokinetics and enabling tumour targeting (Table 4). [11,12] Complementary approaches include semisynthetic derivatisation to improve drug-likeness, rational combination with conventional chemotherapeutics to exploit synergy and lower toxic doses, and computational network-pharmacology and molecular-docking methods to prioritise the most promising multitarget candidates and combinations before experimental testing. [2,5,12] Figure 6a places these efforts in context: natural products remain the dominant contributor to the anticancer arsenal, and the pipeline of plant-derived candidates continues to grow.

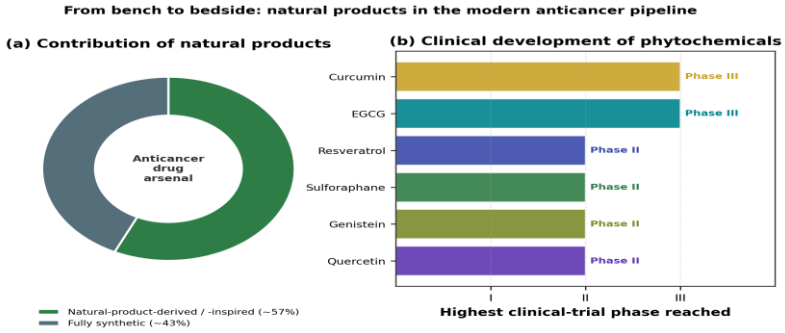

Figure 6. From bench to bedside. (a) Natural products and their derivatives account for roughly 50–60% of clinically used anticancer drugs. (b) Highest clinical-trial phase reached by leading investigational phytochemicals; curcumin and EGCG have advanced to phase III. Values are indicative figures compiled from the cited literature and trial registries.

Agent	Nanoformulation / strategy	Status / benefit
Paclitaxel	Albumin-bound nanoparticle (nab-paclitaxel)	Approved; improved delivery & tolerability
Paclitaxel	Polymeric micelle (e.g. Genexol-PM)	Clinical; solvent-free delivery
Curcumin	Polymeric / liposomal nanoparticles	Improved bioavailability; trials ongoing
Resveratrol	PLGA nanoparticles	Early-phase; ↑ apoptosis, ↓ systemic toxicity
EGCG	Liposomal formulation	Phase I; improved stability & uptake
Sulforaphane / genistein	Polymeric nanoparticles	Early-phase; enhanced pharmacokinetics

Table 4. Nanoformulation and delivery strategies for plant-derived anticancer agents. The clinical success of nab-paclitaxel provides the template for improving the bioavailability and tumour targeting of less-soluble phytochemicals.

6. CHALLENGES AND FUTURE PERSPECTIVES

Several issues will shape the field's trajectory. Bioavailability and delivery remain the primary barrier for investigational phytochemicals, and continued innovation in nanocarriers, prodrugs and structural optimisation is essential. Standardisation is a persistent concern: plant-derived preparations vary in composition and purity, and reproducible pharmacology demands well-characterised, standardised material and, where possible, single defined molecules. Selectivity and toxicity: even the established agents suffer from narrow therapeutic indices and dose-limiting toxicities, motivating targeted delivery and antibody–drug-conjugate approaches that couple potent natural-product warheads to tumour-selective antibodies. Clinical evidence: much of the data on investigational phytochemicals is preclinical or from small trials, and rigorously designed studies with pharmacodynamic biomarkers are needed to establish genuine clinical benefit. Discovery renewal: notably, no wholly new plant-

derived class has reached general clinical use in recent decades, underscoring the value of re-examining ethnomedical leads with modern high-throughput, computational and multi-omics tools. [2,3,4] The most promising path forward integrates three elements—traditional knowledge as a source of leads, modern mechanistic biology to define targets, and advanced delivery and computational science to enable translation.

7. CONCLUSION

Plant-derived agents are not a historical curiosity of oncology but its living foundation: they supply roughly half of the anticancer drugs in clinical use and continue to inspire new candidates. The established classes—vinca alkaloids, taxanes, camptothecins and epipodophyllotoxins—demonstrate how empirical ethnomedical knowledge, refined by screening, isolation and semisynthesis, can yield agents with precise and powerful mechanisms against the machinery of cell division. The investigational phytochemicals extend this legacy in a different register, acting pleiotropically across the hallmarks of cancer and the oncogenic signalling networks that sustain it, with multitarget action and low toxicity that suit them to chemoprevention and combination therapy. Their promise is real but conditional: it depends on solving the bioavailability problem through nanoformulation and structural optimisation, on standardising preparations, and on generating rigorous clinical evidence. The enduring lesson of this translational arc is that the most fruitful oncology draws on both traditions at once—the accumulated wisdom of medicinal-plant use and the mechanistic precision of modern science—and that their integration remains a rich and largely untapped source of future anticancer therapeutics.

Declarations

Funding: No external funding was received for this work.

Conflicts of interest: The authors declare no conflict of interest.

Author contributions: Conceptualisation, A.O.; investigation and writing—original draft, A.O. and A.T.; visualisation, A.T.; writing—review and editing, A.T.; supervision, A.O. All authors approved the final manuscript.

Data availability: No new primary data were generated; all data discussed are available in the cited references.

REFERENCES

[1] Belete TM, Beyna AT. Review on the ethnopharmacological use of medicinal plants and their anticancer activity from preclinical to clinical trial. Natural Product Communications. 2025;20(3).
[2] Anticancer agents derived from plant and dietary sources: a review. International Journal of Pharmacognosy. 2026.
[3] Newman DJ, Cragg GM. Natural products as sources of new drugs over the nearly four decades from 1981 to 2019. Journal of Natural Products. 2020;83(3):770–803.
[4] Botanical breakthroughs: the growing impact of plant-derived anticancer drugs. Ayush Journal of Integrative Oncology. 2025;2(2):62–67.
[5] Plant-derived bioactive compounds and their therapeutic potential in cancer. International Journal of Molecular Sciences. 2026;27(10):4275.
[6] Safe S, et al. Natural products as anticancer agents and enhancing their efficacy by a mechanism-based precision approach. Exploration of Drug Science. 2024.
[7] Nobili S, et al. Natural compounds for cancer treatment and prevention. Pharmacological Research. 2009;59(6):365–378.
[8] Nanotechnology-enhanced natural products for cancer chemoprevention: molecular mechanisms and clinical translation. The AAPS Journal. 2026;28:12.
[9] Scott EN, et al. The anticancer potential of plant-derived nutraceuticals via modulation of gene expression. Plants. 2022;11(19):2524.
[10] Kotecha R, et al. The "Big Five" phytochemicals targeting cancer stem cells: curcumin, EGCG, sulforaphane, resveratrol and genistein. Current Medicinal Chemistry. 2020;27(39):6222–6249.
[11] Therapeutic applications of nanoformulated resveratrol and quercetin phytochemicals in colorectal cancer—an updated review. Pharmaceutics. 2024;16(6):761.
[12] Curcumin, EGCG and apigenin in cervical cancer: mechanistic insights and therapeutic potential. Frontiers in Pharmacology. 2025.

[13] Cragg GM, Newman DJ. Plants as a source of anticancer agents. Journal of Ethnopharmacology. 2005;100(1–2):72–79.