Voyager: Vol. XV, 2024 ISSN: (P) 0976-7436 (e) 2455-054X Impact Factor 8.419 (SJIF)
https://doi.org/10.31995/voyager.2024.v15.009

Identification and Utilization of Pharmaceutically Novel Chemicals from Plants for the Treatment of Cancer- A Critical Appraisal

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Reference to this paper should be made as follows:
Received: 09.12.2024
Approved: 15.12.2024

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Voyager: Vol. XV, 2024
Article No. 09 pp. 073-078

Online available at:
https://anubooks.com/journal-volume/voyager-vol-xv-2024

DOI: *https://doi.org/10.31995 voyager.2024.v15.009*

Abstract

Plant-derived natural products remain a critical source of novel anti-cancer agents. Emerging phytochemicals—such as taccalonolides, honokiol, betulinic acid, withaferin A + garcinol combinations, luteolin, palmatine, and synergistic blends from plants like Moringa oleifera—exhibit promising anticancer mechanisms including microtubule stabilization, apoptosis induction, and signal-pathway disruption. This critical appraisal surveys the source identification, isolation methods, mechanistic action, preclinical evidence, and movement toward clinical application. It also explores the role of computational docking, combination strategies, and bioengineering platforms enhancing yield and activity. While many compounds are preclinical, recent computational and synergistic studies show significant BCL 2, AKT 1, and KRAS targeting potential. The challenges of bioavailability, toxicity, resistance, and scale-up are evaluated. Ultimately, the review highlights select promising compounds and provides a roadmap for translating plant-derived molecules into cancer therapeutics.

Keywords*:*

Phytochemicals, anticancer agents, taccalonolides, honokiol, betulinic acid, computational docking, BCL 2 inhibition, novel plant compounds, synergy, pharmacokinetics

Introduction:

Cancer remains a significant global health challenge, with increasing incidence and mortality rates despite advances in therapeutic strategies. Chemotherapy, radiation, and surgery are the mainstays of cancer treatment, but they are often accompanied by severe side effects, limited efficacy, and drug resistance. In this context, plant-derived natural products offer a promising alternative due to their structural diversity, multi-targeted mechanisms, and relative safety.

Historically, plants have been a rich source of anticancer compounds, with examples such as paclitaxel, vinblastine, and camptothecin demonstrating the immense potential of phytochemicals in oncology. However, the exploration of new plant-based chemicals continues to yield exciting prospects. The recent focus has been on identifying novel phytochemicals with unique mechanisms, enhancing bioavailability, and overcoming chemoresistance. Computational tools, such as molecular docking and network pharmacology, have further accelerated this discovery process.

This article aims to provide a critical appraisal of pharmaceutically novel chemicals derived from plants for the treatment of cancer. It examines the identification and isolation of these compounds, elucidates their mechanisms of action, evaluates preclinical and clinical studies, and discusses the challenges and future directions in translating these natural products into effective cancer therapies.

1. Traditional and Novel Plant-derived Anticancer Agents

1.1 Classical Phytochemicals Classical phytochemicals have laid the foundation for modern cancer therapeutics. Paclitaxel, isolated from the bark of the Pacific yew tree (Taxus brevifolia), stabilizes microtubules and prevents cell division. Vincristine and vinblastine, derived from Catharanthus roseus, inhibit microtubule formation. Camptothecin, from Camptotheca acuminata, targets topoisomerase I, leading to DNA damage.

These compounds, while effective, are limited by issues such as toxicity, poor solubility, and resistance. Moreover, the complexity of their extraction and synthesis poses additional challenges. Nonetheless, their success has spurred the search for new phytochemicals with improved profiles.

1.2 Taccalonolides Taccalonolides, a class of steroidal compounds from Tacca species, have garnered attention for their microtubule-stabilizing activity. Unlike taxanes, taccalonolides bind covalently to tubulin, offering advantages in overcoming resistance mechanisms. Taccalonolides AF and AJ have shown potent activity against drug-resistant cancer cell lines. However, their complex structure and low natural abundance necessitate alternative production methods, such as semi-synthesis and microbial engineering.

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1.3 Honokiol Honokiol, a biphenolic compound from Magnolia officinalis, exhibits broad-spectrum anticancer activity. It induces apoptosis, inhibits angiogenesis, and suppresses metastasis through multiple pathways, including NF-êB, STAT3, and PI3K/Akt. Honokiol has shown efficacy in glioblastoma, leukemia, and breast cancer models. Its lipophilic nature facilitates blood-brain barrier penetration, making it suitable for brain tumors. Nanoformulations are being developed to improve its bioavailability and therapeutic index.

1.4 Betulinic Acid Betulinic acid, a pentacyclic triterpenoid from the bark of Betula species, selectively induces apoptosis in melanoma and neuroblastoma cells. It targets the mitochondrial pathway, leading to cytochrome c release and caspase activation. Betulinic acid also exhibits anti-inflammatory and antioxidant properties. Its poor water solubility and low oral bioavailability are being addressed through prodrug strategies and nanocarrier systems.

2. Synergistic Phytochemical Combinations and Computational Discovery

2.1 Withaferin A and Garcinol Withaferin A, from Withania somnifera, and garcinol, from Garcinia indica, have shown synergistic effects in inhibiting cancer cell proliferation. Molecular docking studies reveal high binding affinities to BCL 2 and AKT 1, suggesting their potential as combination therapies. These compounds modulate apoptosis, inhibit cell cycle progression, and suppress metastasis. Their combined use enhances therapeutic efficacy and reduces toxicity.

2.2 Moringa oleifera Compounds Moringa oleifera contains a variety of bioactive compounds, including flavonoids, phenolic acids, and isothiocyanates. Recent studies have identified synergistic interactions among these phytochemicals, leading to potent anticancer effects. Molecular docking indicates strong inhibition of BCL 2, with binding energies surpassing standard chemotherapeutic agents. The multi-targeted nature of Moringa compounds makes them suitable for combination therapies.

2.3 Luteolin and Palmatine Luteolin, a flavonoid found in celery and green peppers, inhibits cancer cell growth by modulating key signaling pathways, such as NF-êB and MAPK. It also enhances the efficacy of conventional chemotherapeutics. Palmatine, an isoquinoline alkaloid from Berberis species, induces apoptosis and cell cycle arrest in various cancer cell lines. These compounds exhibit favorable pharmacokinetics and low toxicity, making them attractive candidates for further development.

3. Newly Discovered Compounds and Preclinical Evidence

3.1 Phyllanthus and Glycosmis Lignans Phyllanthus species are rich in lignans and flavonoids with anticancer activity. (+)-Acutissimalignan A, isolated from Phyllanthus songboiensis, shows nanomolar cytotoxicity against colon cancer cells. Glycosmis ovoidea produces coumarins with synergistic effects against breast cancer. These findings highlight the potential of lesser-known plants as sources of novel anticancer agents.

3.2 Curcuma longa Extracts Curcumin, the principal curcuminoid of turmeric, has been extensively studied for its anticancer properties. It modulates multiple molecular targets, including p53, NF-êB, and STAT3. Despite its low bioavailability, curcumin has shown promise in preclinical models of colorectal, breast, and pancreatic cancers. Various formulations, such as liposomes, nanoparticles, and phospholipid complexes, are being explored to enhance its therapeutic potential.

3.3 Sweet Potato Leaf Polyphenols Polyphenols from sweet potato leaves exhibit antioxidant and anticancer activities. Studies demonstrate significant inhibition of lung and breast cancer cell proliferation. These effects are attributed to the modulation of oxidative stress, apoptosis induction, and inhibition of angiogenesis. Sweet potato leaves represent a dietary source of chemopreventive agents.

4. Modern Advances, Challenges, and Clinical Translation

4.1 Computational Screening and Docking Computational approaches, such as molecular docking, virtual screening, and network pharmacology, facilitate the identification of bioactive compounds and their targets. These tools reduce the cost and time associated with drug discovery. They also enable the prediction of synergistic interactions and toxicity profiles, guiding experimental validation.

4.2 Biosynthesis and Production The sustainable production of plant-derived compounds is a major challenge. Biotechnological methods, including plant cell cultures, microbial fermentation, and metabolic engineering, offer viable alternatives. For example, the biosynthesis of paclitaxel and artemisinin has been successfully scaled up using engineered microbes. These approaches can be applied to other promising phytochemicals.

4.3 Bioavailability and Delivery Methods Many phytochemicals suffer from poor solubility, rapid metabolism, and low bioavailability. Advanced drug delivery systems, such as nanoparticles, liposomes, solid lipid nanoparticles, and micelles, are being developed to overcome these limitations. These systems enhance drug stability, target specificity, and therapeutic efficacy.

4.4 Toxicity, Resistance, and Standardization Natural products are often perceived as safe, but comprehensive toxicity studies are essential. Some phytochemicals may exhibit off-target effects or interact with conventional drugs. Standardization of plant extracts is crucial for reproducibility and regulatory approval. Quality control measures, including chromatographic fingerprinting and bioassays, are necessary.

4.5 Steps Toward Clinical Trials Translating preclinical findings into clinical applications involves rigorous testing. Betulinic acid, honokiol, and curcumin have entered early-phase clinical trials. These studies assess safety, pharmacokinetics, and preliminary efficacy. Regulatory frameworks must be navigated, and collaboration among academia, industry, and government is vital for success.

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Future Perspectives and Recommendations The future of plant-derived anticancer agents lies in a multidisciplinary approach that integrates ethnobotany, phytochemistry, molecular biology, and computational sciences. Ethnobotanical knowledge can guide the selection of promising plants. Phytochemical analysis and bioassays identify active compounds. Molecular studies elucidate mechanisms, while computational tools optimize drug design.

Collaborative efforts are needed to build comprehensive phytochemical libraries and databases. High-throughput screening and artificial intelligence can accelerate discovery. Sustainable harvesting and conservation of medicinal plants are imperative. Policies that support traditional knowledge and equitable benefit-sharing are also important. Public awareness and acceptance of plant-based therapies can be enhanced through education and transparent communication. Integrating these therapies into conventional oncology requires evidence-based practices and clinical validation. Personalized medicine approaches, considering genetic and metabolic profiles, can optimize treatment outcomes.

Conclusion

Plant-derived natural products continue to be a valuable source of anticancer agents. Novel phytochemicals, such as taccalonolides, honokiol, betulinic acid, withaferin A, garcinol, luteolin, and palmatine, demonstrate diverse mechanisms of action and potential for clinical application. Advances in computational biology, drug delivery, and biotechnology are addressing traditional limitations.

Despite challenges, the integration of natural products into cancer therapy holds promise. Continued research, investment, and collaboration are essential to harness the full potential of phytochemicals. With strategic development, plant-based compounds can contribute to safer, more effective, and accessible cancer treatments.

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