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Phytomedicine 4.0: Incorporating Omics Technology, Nanotechnology and Sustainable Chemistry to create next-generation plant-derived therapeutics

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ABSTRACT

The discipline of phytomedicine is entering a transformative period—what we might term "Phytomedicine 4.0"—where high throughput omics technologies, nano-enabled delivery systems, and frameworks for green and sustainable chemistry converge together to change the ways in which plant-derived therapeutics are discovered, developed and translated into practice. In this commentary, we outline the current state of the art, highlight major translational and regulatory challenges and propose a research agenda that will further advance the discipline through the mid-2020s and beyond.

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Dear Researchers and Specialists

In the past few years, the growth in capability for large-scale molecular profiling, paired with advances in nanotechnology and an increasing emphasis on sustainability, has resulted in the evolution of an age of plant-derived drug discovery from random excursions to planned and systematic approaches. Multi-omics approaches (genomics, transcriptomics, proteomics, metabolomics) are providing unprecedented insights into biosynthesis pathways and biological networks of medicinal plants which can assist researchers in determining species, genes and metabolites that have the potential to lead to the development of safe and effective therapies (Singh et al., 2022). At the same time,

nanoformulations of phytochemicals are facing novel methods to address often inherent issues of poor solubility, imperfect bioavailability and rapid metabolism. Moreover, green chemistry principles have begun replacing the traditional extraction and synthesis methods of phytopharmaceuticals that require hazardous solvents, energy, and resources in their determination (Kumari.et al., 2022). Overall, these trends signify the emergence of Phytomedicine 4.0; however, to actualize the expected return, an integrated framework is needed.

Current State of Affairs and Recent Developments

Omics-based Discovery High-throughput sequencing and mass-spectrometry methods have permitted the optimal characterization of medicinal plant genomes, transcriptomes and metabolomes. As an example, multi-omics in medicinal plants have characterized specific biosynthetic gene clusters and accompanying regulatory networks, leading to directed metabolic engineering of bioactive compounds (Singh et al., 2025). In summary, authors have recently reviewed the role of multi-omics in unlocking plant phytochemical diversity and accelerating the phytochemical drug-lead discovery from plants (Zhang. Et al., 2023) with the capabilities to prioritize plant species and pathways with greater translatable utility.

Nanotechnology and Nano-formulations

Plant-derived nanoparticles (PDNPs) and plant-derived nanovesicles like exosomes, nanoparticles and vesicles are becoming a versatile drug carrier for a spectrum of phytochemicals with an improved delivery, targeting, and therapeutic index. In one example, plant-derived nanovesicles can deliver small RNAs, proteins and secondary metabolites into mammalian cells, regulate the immune response, and improved bioavailability with little to no immunogenicity. A further comprehensive review of plant-derived nanotechnology in the healthcare setting has reported applications with respect to, but not limited to, targeted drug delivery, anticancer therapy and antimicrobial therapies, with both promise and safety issues addressed. Despite the above advances, clinical translation appears limited (Karnwal et al., 2024).

Sustainable and Green Chemistry in Phytomedicine

The utilization of green and sustainable chemistry principles in the assembly of phytopharmaceuticals is essential to ensure the environmental compliance, supply-chain resilience and regulatory acceptance. Review articles advocate for the inclusion of LCA (life cycle assessment), benign solvents, low-energy extraction, and recyclable catalysts in plant-based drug approaches (Barathi et al., 2024). As regulatory boards continue to require environmental justification, we anticipate that sustainable pipelines in phytomedicine will become superior compared to those that are not sustainable.

Consideration of Challenges

Standardisation and reproducibility: Variability in source plants, extraction methodologies, and processing of omics-data, all limit reproducibility. Standardisation of sampling, data management and reporting procedures is central to the credibility of phytomedicine research.

Translation from bench to bedside: Many nano-phytomedicine systems remain at proof-of-concept stage, and scalability, pharmacokinetics, long-term toxicology, and regulatory frameworks remain in development (Parvin et al., 2025).

Mechanistic Clarity & Network pharmacology: Plant-based therapeutic agents usually act on a variety of targets and pathways and therefore it is important to explain mechanisms using a network pharmacology and systems toxicology approach to prioritise leads and fulfil the expectations of regulatory agencies.

Sustainability and Ethical sourcing: The ecological sourcing of plant materials, including avoidance of biodiversity loss and ensuring traceable supply chains are pressing global issues for the next-generation phytomedicine (Alum. Et al., 2025).

Regulatory and safety frameworks: Nano-carrier systems and complex mixtures of phytochemicals present regulatory challenges that require a concise set of harmonised guidelines for phytomedicine nano-therapeutics (Nath et al., 2021).

Future Directions & Research Agenda

In order to move Phytomedicine 4.0 to a translatable therapeutic impact, we recommend the following themes and research priorities:

1. Integrated multi-omic pipelines publications - Encourage research to embed genomics/transcriptomics, metabolomics and bioactivity assays into an integrated framework of publications and share data openly.
2. Nano-phytomedicine translation platforms - Seed consortia to advance the establishment of 'nano-carrier + plant-derived cargo' systems into early-phase clinical translation, that include important ADME/Tox studies.
3. Green chemistry certification frameworks - Engage regulatory and industry partners to develop "green phytopharma" certification schemes that include life-cycle assessment and circular economy principles.
4. Integration of network pharmacology and systems toxicology: Broaden the utilization of computational models to predict interactions, toxicology profiles and synergistic combinations of phytocompounds, thereby decreasing attrition and increasing mechanistic rationales.
5. Integration of sustainable sourcing and ethnobotany-omics: Combine traditional ethnobotanical wisdom about sustainably sourced medicinal plants with omics-based study and sustainability assessment of ecological systems, thereby discovering new leads and protecting biodiversity.

Concluding remarks

Phytomedicine 4.0 represents a unique chance to accelerate the discovery and translation of plant derived therapeutics synthesising omics-supported discovery, nanotechnology and sustainable chemistry. If this is to be realised, the research, publishing and regulatory communities need to move from siloed approaches to an integrated framework, standardisation and translational pathways. With such synergy, plant derived therapeutics can make a significant contribution to the future of global human health.

Conflict of interest
The authors declare no potential conflicts of interest.

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