



Ethnopharmacology in the Genomics and Metabolomics Era: bridging traditional knowledge with modern drug discovery

Mayank Singh^{1*}, Deepak Kumar Saini¹, Jitendra Kumar Pandey¹, Shivali Rathore¹, R P Singh¹, Amita Arjariya²

¹ Department of Botany Government, KRG PG Autonomous College, Gwalior, India

² Maharaja Chhatrasal Bundelkhand University Chhatarpur, India

Abstract

Ethnopharmacology represents the scientific study of traditional knowledge related to medicinal plants and their healing properties. Many of today's pharmaceutical drugs, such as aspirin, quinine, and morphine, have their origins in ethnobotanical traditions. However, traditional studies often face challenges due to the absence of standardized methodologies, limited mechanistic insights, and variability in plant composition. Recent advances in genomics and metabolomics have transformed ethnopharmacological research by providing tools to explore plant diversity at molecular and biochemical levels. Genomic approaches help identify genes and biosynthetic pathways responsible for the production of secondary metabolites, which are often the key bioactive constituents. Metabolomics, on the other hand, generates detailed chemical fingerprints that allow the identification and quantification of metabolites, facilitating the discovery of novel compounds with therapeutic potential. The integration of computational biology, network pharmacology, and artificial intelligence (AI) further strengthens the bridge between traditional medicine and modern pharmacology. These tools can predict biological activities, model multi-target interactions, and accelerate the drug discovery pipeline. Despite these advancements, ethical concerns remain central—particularly regarding intellectual property rights, biopiracy, and equitable benefit-sharing with indigenous communities who have preserved this knowledge for generations. This review highlights how genomics and metabolomics are reshaping ethnopharmacology, offering a framework for validating traditional claims and uncovering new leads for plant-based drug discovery. Future research should focus on interdisciplinary collaboration, data integration, and ethical frameworks to ensure sustainable and respectful use of traditional medicinal knowledge.

Keywords: Ethnopharmacology, genomics, metabolomics, medicinal plants, drug discovery

Introduction

Ethnopharmacology is the study of how people use plants and other natural resources for healing. It links cultural traditions, medicinal knowledge, and scientific approaches. For centuries, traditional medicine systems such as Ayurveda, Traditional Chinese Medicine, and Indigenous healing practices have relied on medicinal plants as their primary resource. Many of today's most widely used drugs originated from ethnomedicinal knowledge. Well-known examples include aspirin from *Salix* species, morphine from *Papaver somniferum*, and artemisinin from *Artemisia annua* (Cragg & Newman, 2013; Heinrich *et al.*, 2012) [4, 7, 23, 37]. These discoveries highlight the lasting value of indigenous knowledge for modern pharmacology.

According to the World Health Organization (WHO, 2013) [14], nearly four out of five people worldwide depend on plant-based remedies for primary health care. This reliance is particularly strong in developing countries, where access to modern healthcare may be limited. However, even in developed nations, herbal medicines and plant-based supplements are gaining popularity due to consumer interest in natural therapies and holistic health approaches (Ekor, 2014) [5]. Despite this global relevance, ethnopharmacological research faces challenges. Much traditional knowledge is undocumented, at risk of being lost, or transmitted orally. In addition, scientific validation of traditional claims is often inconsistent, with problems in

standardization, reproducibility, and mechanistic explanation (Fabricant & Farnsworth, 2001) [6, 22, 39].

Recent scientific advances offer solutions to these limitations. Genomics and metabolomics have emerged as powerful tools for understanding medicinal plants at the molecular and biochemical levels. Genomics allows researchers to map the genetic information responsible for secondary metabolite production. This enables the discovery of biosynthetic pathways, metabolic genes, and enzymes involved in the synthesis of bioactive compounds (Rai & Saito, 2016) [10]. For instance, genomic studies on *Withania somnifera* have identified key genes in the withanolide biosynthesis pathway, which supports the medicinal use of this plant in traditional systems (Sinha *et al.*, 2021) [12].

Metabolomics complements genomics by analyzing the full spectrum of metabolites in a plant. Using high-resolution tools such as GC-MS, LC-MS, and NMR, metabolomics generates chemical fingerprints that reveal both known and novel bioactive molecules (Wolfender *et al.*, 2015) [13, 18, 56]. This approach has been used to validate ethnomedicinal plants such as *Curcuma longa* and *Ocimum sanctum*, confirming their phytochemical richness and linking metabolites to pharmacological activity (Shyur & Yang, 2020) [11]. By providing high-throughput, reproducible data, metabolomics enhances quality control of herbal medicines and supports drug discovery. Integration of genomics and metabolomics has transformed ethnopharmacology into a data-driven field. Together, these technologies support

systems-level understanding of medicinal plants, linking genetic potential with metabolic outcomes. This integrated approach helps identify bioactive compounds, verify traditional claims, and uncover novel therapeutics. Moreover, advances in computational biology and bioinformatics are expanding the field even further. Network pharmacology allows the study of plant compounds that act on multiple targets, a property common to herbal medicines (Hopkins, 2008; Li & Zhang, 2013)^[8, 9, 41]. Artificial intelligence and machine learning are now being applied to predict biological activities and design new phytochemical-based drugs (Zhou *et al.*, 2020)^[15].

Case studies demonstrate the value of these approaches. Artemisinin, once an ethnopharmacological discovery from Chinese medicine, has been studied using genomics to optimize its production in *Artemisia* species. Similarly, metabolomics has been applied to validate traditional African and Indian medicinal plants, providing evidence for their antimicrobial, antioxidant, and anti-inflammatory potential (Choudhury *et al.*, 2022)^[3]. These examples illustrate how omics technologies bridge the gap between ancient wisdom and modern science. Despite progress, challenges remain. Intellectual property rights and benefit-sharing with indigenous communities are pressing ethical concerns (Balick & Cox, 2020)^[1, 16, 20]. Sustainable harvesting of medicinal plants is another challenge, as demand continues to rise. Moreover, regulatory frameworks for herbal medicines vary widely, and lack of harmonization hinders global acceptance (Booker *et al.*, 2020)^[2]. Addressing these issues is crucial to ensure fair use of traditional knowledge and long-term conservation of medicinal plant resources.

The future of ethnopharmacology lies in integration. Combining traditional knowledge with genomics, metabolomics, and computational tools can reshape drug discovery. Personalized medicine may also benefit from ethnopharmacology, as pharmacogenomics helps explain

individual variation in responses to plant-derived drugs (Hasan *et al.*, 2022). Metagenomics is opening new avenues for studying microbial interactions in traditional fermented medicines, adding another layer to the field. Ultimately, ethnopharmacology in the genomics and metabolomics era represents a unique convergence of heritage and innovation. This review highlights how these modern approaches are reshaping the field. It examines advances in genomics and metabolomics, discusses their applications in validating traditional medicine, and explores challenges and future opportunities. By doing so, it seeks to demonstrate how ethnopharmacology continues to evolve as a bridge between traditional wisdom and evidence-based drug discovery.

Ethnopharmacology and Traditional Knowledge Systems

Traditional knowledge has played an important role in the discovery of new medicines. Communities across the world have preserved information on the healing properties of plants through oral traditions and cultural practices. Ethnopharmacology helps to record and evaluate this knowledge using scientific methods, creating a bridge between traditional healing systems and modern pharmacology (Heinrich *et al.*, 2012; Fabricant & Farnsworth, 2001)^[6, 7, 22, 23, 39]. Several well-known drugs were first identified from traditional medicine. The antimalarial drug artemisinin was discovered from *Artemisia annua*, a plant used in Chinese medicine for centuries (Tu, 2016)^[26].

Morphine, a widely used analgesic, was isolated from *Papaver somniferum*, long employed for its pain-relieving effects (Brownstein, 1993)^[21]. Aspirin was developed from salicin in willow bark (*Salix* spp.), which was used in European folk medicine to reduce pain and fever (Vane & Botting, 2003)^[27]. These examples show how indigenous practices have guided the development of modern drugs.

Table 1: Examples of Drugs Derived from Ethnomedicinal Knowledge

Plant (Botanical name)	Derived Drug	Traditional Use	Modern Application	Reference
<i>Artemisia annua</i>	Artemisinin	Used in Chinese medicine for fever and malaria	First-line antimalarial therapy	Tu (2016) ^[26]
<i>Papaver somniferum</i>	Morphine	Used in ancient medicine for pain relief	Strong analgesic for severe pain	Brownstein (1993) ^[21]
<i>Salix</i> spp. (Willow bark)	Aspirin (acetylsalicylic acid)	Folk remedy for pain and fever	Widely used analgesic, anti-inflammatory, cardioprotective	Vane & Botting (2003) ^[27]
<i>Catharanthus roseus</i>	Vincristine, Vinblastine	Used in folk medicine for diabetes	Anticancer agents in leukemia and lymphoma therapy	Cragg & Newman (2013) ^[4, 38]
<i>Digitalis purpurea</i>	Digoxin	Traditional remedy for dropsy (edema)	Treatment of heart failure and arrhythmia	Sneider (2005)

Despite these successes, several challenges exist. The loss of traditional knowledge is a major concern, as many oral traditions are disappearing with cultural change and urbanization (Balick & Cox, 2020)^[1, 16, 20]. Ethical issues also arise, including the recognition and fair compensation of communities whose knowledge contributes to scientific progress (Sharma *et al.*, 2021)^[25]. In addition, biopiracy—the use of biological resources and indigenous knowledge

without proper consent or benefit-sharing—remains a global issue (Robinson, 2010)^[24].

Protecting indigenous knowledge, ensuring benefit-sharing, and promoting ethical research practices are essential. Ethnopharmacology, when combined with modern science, can preserve cultural heritage while supporting the discovery of new and safe medicines.

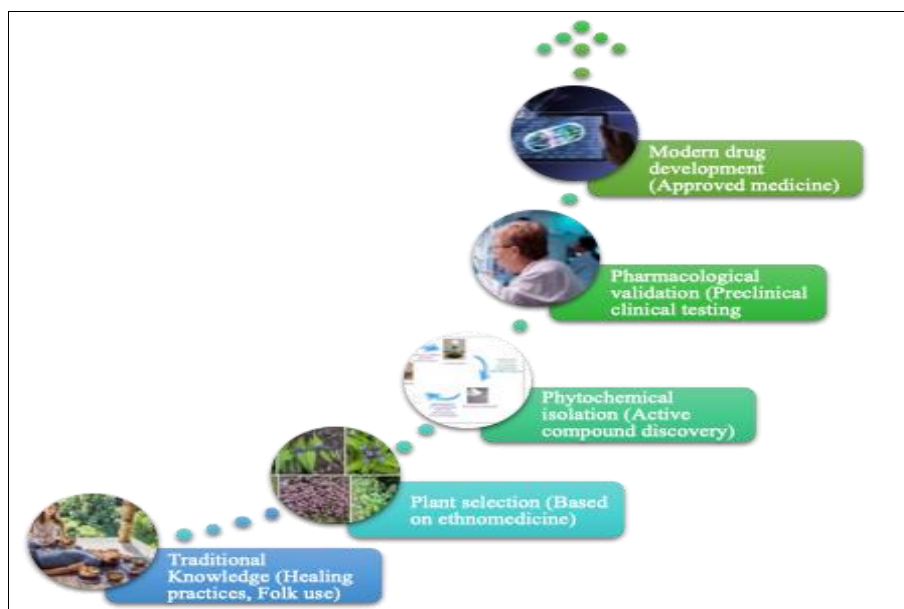


Fig 1. Pathway linking traditional knowledge with modern drug development.

Genomics in Ethnopharmacology

Genomics has transformed ethnopharmacology by providing molecular insights into drug discovery and plant-based therapeutics. Pharmacogenomics helps to explain the genetic basis of drug responses, highlighting why individuals and populations often exhibit variable efficacy and side effects when exposed to the same therapeutic compound (Ma & Lu, 2011) [45]. This knowledge is crucial for developing personalized medicine strategies rooted in traditional remedies. Plant genomics plays a vital role in identifying genes responsible for the biosynthesis of secondary metabolites, many of which possess pharmacological activity (Sangwan *et al.*, 2013) [47]. Advances in next-generation sequencing (NGS) have accelerated the discovery of biosynthetic pathways in medicinal plants, enabling metabolic engineering and synthetic biology approaches for enhanced production of bioactive compounds (Mochida & Shinozaki, 2011) [46]. Several case studies demonstrate how genomics-assisted research has uncovered pathways for bioactive metabolites. For instance, genomic studies in *Artemisia annua* identified key genes regulating artemisinin biosynthesis, improving yields of this vital antimalarial compound (Shen *et al.*, 2016) [48].

Similarly, transcriptomic analyses in *Papaver somniferum* have shed light on morphine alkaloid pathways (Desgagné-Penix & Facchini, 2012) [44]. Genomic databases further support ethnomedicine research. Resources such as the KNApSACk Core Database and the Medicinal Plant Genome Database provide comprehensive information on plant metabolites, gene functions, and pharmacological activities (Afendi *et al.*, 2012; Zhang *et al.*, 2021) [43, 49]. These platforms bridge traditional plant use with modern molecular approaches, facilitating drug discovery pipelines.

Metabolomics in Ethnopharmacology

Metabolomics has emerged as a powerful tool in ethnopharmacology, allowing comprehensive profiling of bioactive compounds in medicinal plants. Unlike classical phytochemical studies, which focus on individual compounds, metabolomics enables the simultaneous identification and quantification of a wide range of

metabolites, thereby generating chemical fingerprints that reflect plant biochemical diversity (Patti *et al.*, 2012) [53]. These fingerprints are essential for validating traditional medicines and linking them to specific therapeutic properties. Advanced analytical platforms such as gas chromatography–mass spectrometry (GC–MS), liquid chromatography–mass spectrometry (LC–MS), and nuclear magnetic resonance (NMR) spectroscopy are widely employed for metabolite profiling (Wolfender *et al.*, 2015) [13, 18, 56]. Hyphenated approaches like LC–MS/MS and GC–MS/MS enhance sensitivity and accuracy, making it possible to detect trace compounds that contribute to pharmacological activity. These methods have become indispensable for standardizing herbal formulations and uncovering novel bioactive molecules (Dunn *et al.*, 2011) [52]. Several case studies highlight the utility of metabolomics in ethnopharmacology. For example, metabolomic analysis of *Panax ginseng* has revealed correlations between metabolite composition and therapeutic efficacy, supporting its long-standing use in traditional medicine (Yuan *et al.*, 2016) [57]. Similarly, LC–MS-based metabolite profiling of *Withania somnifera* identified key withanolides responsible for adaptogenic and immunomodulatory effects (Chandrasekhar *et al.*, 2012) [50]. Such studies provide molecular evidence that strengthens the pharmacological relevance of traditional plant-based therapies. Integration of metabolomics with chemoinformatics and systems biology further enhances its application. Computational approaches allow the mapping of metabolite networks and prediction of bioactivity, providing insights into synergistic interactions among plant constituents (Wishart, 2016) [54]. By combining metabolomics with genomics and transcriptomics, researchers can also link metabolic pathways to genetic regulation, thereby accelerating drug discovery from ethnomedicine.

Bridging Traditional Knowledge and Modern Drug Discovery

Bridging ethnopharmacology with modern drug discovery relies on the integration of traditional knowledge with advanced molecular and computational approaches.

Bioprospecting, guided by ethnomedical use, continues to serve as a rational strategy for selecting plants with therapeutic potential. When combined with genomics, metabolomics, and transcriptomics, this approach allows researchers to validate bioactivity at a molecular level, reducing the randomness often associated with natural product screening (Fabricant & Farnsworth, 2001; Harvey *et al.*, 2015) [6, 22, 39, 40].

Network pharmacology: has emerged as a powerful framework for studying multi-target interactions of phytochemicals. Unlike single-compound strategies, this approach considers the synergistic effects of plant metabolites across multiple biological pathways, thereby reflecting the holistic principles of traditional medicine (Hopkins, 2008) [8, 41]. Such systems-level analyses help to explain the clinical effectiveness of polyherbal formulations and support their development into evidence-based therapies.

Recent advances in artificial intelligence (AI) and machine learning (ML) have further transformed ethnopharmacological research. AI tools can analyze large-scale phytochemical, genomic, and pharmacological datasets to predict bioactivity, toxicity, and drug-likeness of plant-derived compounds (Chen *et al.*, 2018) [37]. Machine learning algorithms also facilitate virtual screening and drug–target interaction modeling, significantly accelerating the drug discovery pipeline from traditional remedies.

Several **case studies** highlight the success of this integrative approach. The development of artemisinin, derived from *Artemisia annua* and informed by Chinese traditional medicine, remains a landmark example of ethnopharmacology guiding modern therapeutics (Tu, 2011) [42]. Similarly, salicylic acid (the precursor of aspirin) from *Salix alba* and morphine from *Papaver somniferum* illustrate how traditional remedies, when validated through modern science, yield globally significant drugs (Cragg & Newman, 2013) [4, 38]. These examples emphasize the value

of combining ethnomedical wisdom with modern omics technologies to advance pharmaceutical innovation.

Challenges and Ethical Considerations

While ethnopharmacology holds great promise for modern drug discovery, it is accompanied by several challenges and ethical concerns. One of the most pressing issues is related to intellectual property rights (IPR) and benefit-sharing. Indigenous knowledge has historically been exploited without fair recognition or compensation to local communities. Instances of biopiracy, such as unauthorized patenting of neem (*Azadirachta indica*) and turmeric (*Curcuma longa*), highlight the urgent need for ethical frameworks that ensure equitable benefit-sharing and proper acknowledgment of traditional custodians (Shiva, 2001; Patwardhan *et al.*, 2005) [34, 35]. International agreements such as the Convention on Biological Diversity (CBD) and the Nagoya Protocol provide guidelines for access and benefit-sharing, but their implementation remains inconsistent (Kamau *et al.*, 2010) [33].

Another challenge is the standardization and reproducibility of ethnopharmacological research. Variations in plant chemotypes, harvesting practices, and extraction methods can result in inconsistent pharmacological outcomes (Heinrich *et al.*, 2009) [32]. Without rigorous protocols and validated analytical techniques, translating traditional remedies into reproducible modern drugs becomes difficult. Advanced metabolomic and genomic tools can help address these issues, but harmonized global standards are still lacking.

Finally, there is a strong need for international collaboration and policy frameworks to regulate the use of ethnomedicine. Cross-disciplinary and cross-border partnerships are essential to ensure ethical research practices, scientific rigor, and equitable access to resources (Soejarto *et al.*, 2012) [36]. Building trust with indigenous communities and promoting transparent benefit-sharing mechanisms are critical for sustaining ethnopharmacological research in a socially responsible manner.

Challenge	Description	Possible Solutions
Intellectual Property Rights (IPR) & Benefit-Sharing	Indigenous knowledge often exploited without proper recognition or fair compensation (biopiracy cases: neem, turmeric).	Implement CBD and Nagoya Protocol; ensure community participation and equitable benefit-sharing.
Standardization Issues	Variation in plant chemotypes, harvesting methods, and extraction protocols leads to inconsistent results.	Develop global standards for phytochemical analysis; adopt validated metabolomics/genomics techniques.
Reproducibility in Research	Lack of rigorous protocols makes translation of ethnomedicine into reproducible drugs difficult.	Use multi-omics validation, establish harmonized guidelines, encourage peer-reviewed verification.
Ethical Concerns	Misappropriation of indigenous knowledge without consent undermines cultural heritage.	Establish prior informed consent (PIC); strengthen legal protection of traditional knowledge.
Need for International Collaboration	Fragmented efforts hinder large-scale validation of ethnomedicine.	Promote cross-disciplinary and cross-border partnerships; foster transparent policy frameworks.

Future Perspectives

The integration of ethnopharmacology with modern omics tools offers significant opportunities for future drug discovery and healthcare. One promising direction is the application of personalized medicine, where pharmacogenomics can guide the selection of plant-based therapies according to an individual's genetic background, optimizing efficacy and minimizing adverse effects (Schork, 2019) [31].

Another frontier is the integration of multi-omics data with ethnobotanical databases, which can provide holistic insights into phytochemical diversity, mechanisms of action, and cross-cultural therapeutic applications. Such integration can enhance the predictive power of computational approaches in drug discovery (Gonzalez *et al.*, 2021) [29].

The rise of metagenomics offers potential in the study of traditional fermented medicines, allowing the identification of microbial communities and their contribution to

therapeutic properties. This may expand our understanding of symbiotic relationships between plants, microbes, and human health (Marco & Abrams, 2021) [30]. Furthermore, advances in biotechnology, such as synthetic biology and metabolic engineering, hold promise for the sustainable production of ethnomedicinal compounds. By transferring biosynthetic pathways into microbial or plant hosts, it becomes possible to scale production without overharvesting wild resources, ensuring both conservation and accessibility (Chemler & Koffas, 2008) [28].

Conclusion

Ethnopharmacology continues to be a powerful framework for discovering novel therapeutics, as it leverages centuries of traditional wisdom rooted in cultural practices and indigenous knowledge. The incorporation of genomics and metabolomics has significantly advanced the field by strengthening scientific validation, enabling precise phytochemical characterization, and supporting reproducibility in ethnomedicinal research (Heinrich & Jäger, 2015; Wolfender *et al.*, 2015) [17, 13, 18, 56]. Moving forward, a holistic approach that integrates traditional knowledge with cutting-edge technologies—such as pharmacogenomics, metabolomics, and systems biology—holds promise for sustainable and ethical drug discovery. Such an approach not only enhances the credibility of ethnomedicine but also ensures that indigenous communities benefit from their contributions while addressing global health challenges (Balick & Cox, 2020; Zhang *et al.*, 2019) [1, 16, 19, 20]. In this convergence of heritage and innovation lies the future of medicine, where respect for cultural diversity combines with scientific rigor to deliver safer, effective, and sustainable therapies.

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