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REVIEW ARTICLE

Received: 12/08/2025

Revised: 15/10/2025

Accepted: 16/10/2025

Ethnopharmacology in the Digital Age: The Evolution of Indian Herbal Medicine

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ABSTRACT

The disease preventive and health-promoting approach based on herbal medicine takes into consideration the promotion of health and treating ailments is holistic way and finds increasing acceptability in many regions of the world, India and China being in the forefront. The practice of herbal medicine basically depends on folklore and the experiences of people over a long period of time. However, very little research, especially in the area of basic science, has been conducted systematically. Medicinal plants with a long history of safe and effective use are likely to have a pharmaceutical effect. The use of plants in traditional medicine can be explained by physiologically active phytochemical compounds of a species and also by its ascribed meaning in a culture. Plants produce a great diversity of substances that could be of therapeutic significance in many areas of medicine. However, the chemical nature of plant compounds present naturally as such and in the extract is puzzling. It is important to know the constituents of plant extracts and their relative importance in their therapeutic value. The alkaloids and other compounds are characterized and tested for their medicinal value from these plants, which include not only the unexplored tribal plants but also the spices, condiments, and vegetables that are already in use. In the last decade, there has been a renewed interest in the development of herbal drugs, underlined by the understanding of the mechanism of action rather than based on faith and folklore, as it happened in the past. Several aspects of integrated approaches of drug development from herbs have explored many potential lead phytochemicals. Nonetheless, even the limited number of mechanistic experiments reveals that numerous mechanisms are likely involved in the various actions of even a single herbal medicine. It will be the elucidation of such mechanisms that will provide the scientific basis for establishing the efficacy and safety of not only Chinese and Indian herbal medicines but all forms of medicinal botanicals.

Keywords: Herbal, India, Medicinal, Plants and Phytochemical.

INTRODUCTION

The ayurvedic system of medicine not only provides cure for many general and chronic diseases but it also strengthens the inner body strength.

Generally, wasteland plants are called as weeds and said to be unwanted and undesirable plant species. On the contrary, as suggested by 'Ayurveda, "No plant of this world is useless". In ayurvedic system of medicines a large number of plants are employed for the treatment of several diseases like Alzheimer's disease, AIDS, cancer, depression, nervous disorders, diabetes, rheumatism, leprosy, skin disease, urinary stone track diseases, hepatic diseases, diseases of the digestive system, malaria, and paralysis. The World Health Organization estimates that about 80% of the population of most developing countries relies on herbal medicines for their primary health care needs (Gupta et al., 2010).

About 610 species of medicinal plants have been used by 42 lakhs population of tribals of Rajasthan (Singh and Pandey, 1998). Rajasthan, where 80% of its people live in the rural areas and cannot afford costly medicine. They depend on vegetation surrounding them and make perfect uses of them for their medicinal needs. A floristic survey of ethnomedicinal plants occurring in the tribal area of Rajasthan was conducted to assess the potentiality of plant resources for modern treatments. A large number of medicinally important tree species are present on Aravalli hill range and other areas including less hospitable North–West Rajasthan. An attempt was made to characterize tree species of the region and detailed ethnobotanical studies on them are in progress. In a floristic survey, 61 ethnomedicinal plant species belonging to 38 families were recorded from Aravalli hills of Mewar region of Rajasthan (Katewa et al., 2004; Katewa, 2009).

Ethnomedicinal uses of biodiversity from Tadgarh-Raoli wildlife sanctuary of Rajasthan was reported by Jain et al. (2007). Ethnobotanical survey of Sariska and Siliserh regions from Alwar district was reported by Jain et al. (2009). A categorical list of plant species along with their plant part/s used and the mode of administration reported to be for effective control in different ailments is prepared (Table 3).

The tribals who depend on forest (mostly their surrounding vegetation) wealth are the real custodians that safeguard the medicinal plants till now. Rapid deforestation caused by over–harvesting and exploitative trade of medicinal plants has significantly reduced the availability of the medicinal plants in arid and semi–arid region of Rajasthan (Srivastva, 1977; Singh and Pandey, 1980). Some medicinally important trees of Rajasthan are listed in Table 4. Generally the folk people are well acquainted with the medicinal properties of their surrounding vegetation particularly for their well being (Mishra and Kuamr, 2001). Some folk-lore claims with their related data are presented in Table 5. Kheep (*Leptadenia pyrotechnica*) is a widely distributed shrub in western Rajasthan. It is traditionally used as food and medicine (Singh et al., 2007).

Nowadays, natural products and herbal medicines have been recommended for the treatment of diabetes (Gupta and Kumar, 2002). Over 50 plants are present in arid zone of Rajasthan having anti diabetic potentials (Menghani and Ojha, 2010). In Dang region of Rajasthan, 36 plants species are used as cooling agents during summers (Sharma and Khandelwal, 2010). An extensive survey of southern part of Rajasthan including Chittorgarh, Udaipur, Banswara and Dungarpur districts was made to document the traditional knowledge of medicinal plants used by tribal communities (Meena and Yadav, 2010).

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Table 1. Ethnomedicinal plants of Rajasthan, India.

Name	Family	Local name	Official organ	Medicinal	How administered	Ailment	Tribe
				Properties			
<i>A. indica</i>	Meliaceae	Neem	Leaves		Poultice locally	Snakebite and	Sahariya, Bhil,
						scorpion sting	Kalbelia, Meena
<i>C. procera</i>	Asclepiadaceae	Arka, Aak	Roots		Applied locally	Scorpion sting	Kalbelia, Garasia
<i>A. catechu</i>	Mimosaceae	Khair	Bark, flower tops	Antiinflammatory	Juice + asafoetida	Gonorrhoea	Sahariya
<i>T. undulata</i>	Bignoniaceae	Rohida	Bark, branch	Antiseptic	Chewed	Syphilis	Bhil, Garasia
<i>A. barbedensis</i>	Liliaceae	Gwarpatha	Leaves	-	Orally	Sexual vitality	Garasia, Bhil
<i>R. communis</i>	Euphorbiaceae	Erand	Seeds	Anti-fertility	Oil, locally	Birth control	Meena, Sahariya
<i>D. metel</i>	Solanaceae	Kannkak	Leaves	Sedative	Extract, orally	Cure insanity,	Sahariya, Bhil
				cerebral		cerebral	
				depressant	extract locally	complications	

Popularity because of their low or no residual toxicity. Initially the plants are the main part of folk medicines. Gradually the folk medicines led to the rise of traditional system of medicine like Ayurveda in India. In Rajasthan (India), tribals are using herbal medicine for long time. Plants are providing humankind with all needs including food, clothing, shelter, flavours and fragrances as not the least, medicines. Plants form the basis of traditional medicine, Ayurvedic, Unani, Chinese amongst others. Medicinal plants have been used throughout the world, however, their wide usage had been limited to China, India, Japan, Pakistan, Sri Lanka, Thailand and African countries. Developed countries are also turning to encourage the usage of plant-based natural medicinal product in their healthcare systems. World Health Organization estimates that 80% of the world's inhabitants rely mainly on traditional medicines for their health care (Farnsworth, 1994; Mukherjee and Wahil, 2006). Plant products also play an important role in health care systems of the remaining 20% of the population, mainly residing in developed countries. The Natural Health Product Regulations of Canada promulgated in January 2004 is an important step toward modernization of plant-based product usage in healthcare (Siow *et al.*, 2005). This regulation encourages usage of modern technology and evidence-based scientific support toward promoting medicinal plants and the associated products.

With the advancement of Ayurvedic tradition and its scientific exploration, several classes of plant species have been studied in order to evaluate their therapeutic potentials and to isolate the lead compounds. Folk medicine in India.

Folk medicine is the mother of the healing systems of India (Valiathan, 2006). It is universally accepted now that traditional health care systems have their unique strengths and are worth exploring for their potential preventive and curative properties. Herbal remedies are considered the oldest forms of healthcare known to mankind on this earth. Prior to the development of modern medicine, the traditional systems of medicine that have evolved over the centuries within various communities, are still maintained as a great traditional knowledge base. Traditionally, this treasure of knowledge has been passed on orally from generation to generation without any written document (Perumal Samy and Ignacimuthu, 1998, 2000), and is still retained by various indigenous groups around the world. In India, there are about 54 million indigenous people of different ethnic groups inhabiting various terrains. These indigenous groups possess their own distinct culture, religious rites, food habit and a rich knowledge of traditional medicine (John, 1984; Pushpangadan and Atal, 1984; Anuradha *et al.*, 1986; Harsha *et al.*, 2002; Parinitha *et al.*, 2005). Even today, indigenous and certain local communities practice herbal medicine to cure a variety of diseases. Traditional system of medi-care is still practised by the people of rural areas as they are safe, no adverse effects, inexpensive and ease availability. However, a gradual decline in practice of traditional herbal medicines has been reported in the recent past. Hence, there is an urgent need to investigate in detail the indigenous

Ethnobotanical knowledge held by each tribal people before such valuable knowledge disappears. Further, it is also necessary to conduct scientific investigations to understand the mechanism of action.

Herbal reservoir

There are more than 20,000 species of higher plant, used in traditional medicines and are reservoirs of potential new drugs. As the modern medicine and drug research advanced, chemically synthesized drugs replaced plants as the source of most medicinal agents in industrialized countries. Nevertheless plants are an important source of lead compounds. However, in developing countries, the majority of the world's population cannot afford pharmaceutical drugs and use their own plant based indigenous medicines. In recent times, focus on plant research has increased all over the world, and a large body of evidence has been collected to show the immense potential of medicinal plants used in traditional systems. Various medicinal plants have been identified and studied using modern scientific approaches. The results revealed the potential of medicinal plants in the field of pharmacology (Tapsell *et al.*, 2006).

The use of plants in traditional medicine can be explained by physiologically active phytochemical compounds of a species and also by its ascribed meaning in a culture. Medicinal plants with a long history of safe and effective use are likely to have a pharmaceutical effect (Tabuti, 2008). In addition, the likeliness of a medicinal use being based on pharmaceutical properties rather than on a cultural context increases when this use is repeatedly found in different cultures.

According to Gurib-Fakim (2006) there are four basic ways in which plants that are used by tribal peoples are valuable for modern medicine:

1. Plants used as sources of direct therapeutic agents 2. Plants are also used as sources of starting points for the elaboration of semi-synthetic compounds 3. Plants can serve as sources of substances that can be used as models for new synthetic compounds. 4. Plants can also be used as taxonomic markers for the discovery of new compounds.

Recently explored medicinal plants - examples

Many plants have a long use in traditional Ayurvedic medicine for several diseases and the scientific studies are reconfirming them with modern relevance. The scientific basis for the statement that plants and their active constituents play an important role in the prevention of chronic and degenerative diseases is continuously advancing. In fact, the origin of many therapeutic substances is due to secondary metabolism in the plants.

A wide range of secondary metabolites including triterpenoids, flavonol glycosides, anthocyanins and steroids has been isolated from *Clitoria ternatea* Linn. Its extracts possess a wide range of pharmacological activities including antimicrobial, antipyretic, anti-inflammatory, analgesic, diuretic, local anesthetic, antidiabetic, insecticidal, blood platelet aggregation-inhibiting and for use as a vascular smooth muscle relaxing properties (Mukherjee *et al.*, 2008).

Samy *et al.* (2008) in a survey among medicinal practitioners called 'Vaidyars' in Tamil Nadu identified 72 medicinal plants belonging to 53 families that are used for the treatment of snakebite in a traditional way. They also report the partially purified extracts of *Aristolochia indica*, *Hemidesmus indicus*, *Gloriosa superba*, *Strychnos nux-vomica*, *Eclipta prostrata*, and *Andrographis paniculata* showing potent neutralizing effect against the snake venom both *in vitro* and *in vivo*.

Recently, effect of several new plants of Arunachal Pradesh viz., *Bombax ceiba*, *Canarium strictum*, *Chloranthus erectus*, *Xanthium indicum*, *Lycopodium clavatum*, *Coleus blumei*, *Batrachospermum atrum*, *Chlorella vulgaris*, *Marchantia palmata*, *Marchantia polymorpha*, *Eria pannea*, *Sterculia villosa* and *Alpinia galanga* are reported for the first time for the treatment of inflammation-related diseases (Namsa *et al.*, 2009).

Cassia occidentalis is an annual or perennial Ayurvedic plant which is used in several traditional medicines to cure various diseases. This weed has been known to possess antibacterial, antifungal, antidiabetic, anti-inflammatory, anticancerous, antimutagenic and hepatoprotective activity. A wide range of chemical compounds including achrosin, aloemodin, emodin, anthraquinones, anthrones, apigenin, aurantiobtusin, campesterol, cassiollin, chryso-obtusin, chrysophanic acid, chrysoarobin, chrysophanol, chrysoeriol etc. have been isolated from this plant (Yadav *et al.*, 2010).

Psidium guajava, is an important food crop and medicinal plant in tropical and subtropical countries is widely used like food and in folk medicine around of the world. Different pharmacological experiments in a number of *in vitro* and *in vivo* models have been carried out. A number of metabolites phenolic, flavonoid, carotenoid, terpenoid and triterpene particularly those from leaves and fruits possess useful pharmacological activities. Many pharmacological studies have demonstrated the ability of this plant to exhibit antioxidant, hepatoprotection, anti-allergy, antimicrobial, antigenotoxic, antiplasmodial, cytotoxic, antispasmodic, cardioactive, anticough, antidiabetic, antiinflammatory and antinociceptive activities, supporting its traditional uses (Gutiérrez *et al.*, 2008).

Albizia lebbek is reported to possess considerable potency in anti-inflammatory action and has prominent effects on adjuvant arthritis by alleviating paw edema (Babu *et al.*, 2009).

The mechanism of the effect may be due to the presence of flavanoids and saponins, however, further detailed studies will provide new insight into the anti-inflammatory activity of *Albizia lebeck*, and eventually lead to development of a new class of anti-inflammatory agent.

Many pharmacological studies have been carried out to describe multiple biological properties of *Withania somnifera* (Mishra *et al.*, 2000). These studies have shown that the plant preparation has antiinflammatory (Bhattacharya *et al.*, 1997), anticancer (Mohan *et al.*, 2004), antistress and immunomodulatory (Archana and Namasivayam, 1999; Ziauddin *et al.*, 1996), adaptogenic (Bhattacharya and Muruganandam, 2003), central nervous system (Chaudhary *et al.*, 2003; Jain *et al.*, 2001), endocrine (Panda and Kar, 1998) and cardiovascular (Mishra *et al.*, 2000; Mohanty *et al.*, 2004) activities, respectively.

The major biochemical constituents of *W. somnifera* are steroidal alkaloids and lactones, a class of constituents together known as withanolides (steroidal lactones with ergostane skeleton) (Elsakka *et al.*, 1990). So far 12 alkaloids, 35 withanoloids and several sitoindosides have been isolated and their structures have been elucidated (Mishra *et al.*, 2000; Matsuda *et al.*, 2001). The various alkaloids include withanine, somniferine, somnine, somniferinine, withanine, psuedo-withanine, tropine, psuedotropine, 3- α -gloyloxytropene, choline, cuscohygrine, isopelletierine, anaferine and anahydrine.

The genus *Hibiscus* contains 220 species distributed around the world. It is an interesting source of potential bioactive molecules, as phenolic compounds, triterpene derivatives, phytosteroids, with antioxidant, cardioprotective, antihypertensive and antiproliferative activities (Maganha *et al.*, 2010). Pharmacological investigations of the genus *Hibiscus* indicated the presence of some species with useful biological activities as antihypertensive, anti-inflammatory, antipyretic, hepatoprotective, anti-diarrhoeic, anti-spermatogenic, anti-tumour, antidiabetic, anticonvulsant, antihelminthic immunomodulator, antioxidant and antimutagenic agents (Sachdewa and Khemani, 2003). Amongst these species, less than 15 have had their biological effects studied. The majority of these studies mainly concentrated on *Hibiscus sabdariffa*.

Euphorbia fusiformis a dwarf perennial herb, grows wild in western peninsular India and warmer parts of eastern India. The plant is of recent discovery from Tamil Nadu (John Britto *et al.*, 2002). The dried root powder and fresh rhizome have been found to increase secretion of mother's milk. Extract of dried rhizome is also administered orally for relief from joint pain and rheumatism and it is more effective against diarrhea. Fresh latex is externally applied to heal chronic wounds and cracks and to cure skin diseases. Crushed leaf poultice is applied on forehead to get relief from acute headache. The earlier pharmacological studies have reported that this species possess effective anti-inflammatory (Singh *et al.*, 1984) and antimicrobial (Natarajan *et al.*, 2005) properties. Recently, Anusuya *et al.* (2010) justified the traditional claims and assessed the hepatoprotective effect of *Euphorbia fusiformis* tubers employing rifampicin intoxicated rat model and also assessed its safety upon administration. The use of different parts of *Ricinus communis* for the treatment of various diseases in traditional or folk remedies throughout the world has been reported. In the Indian system of medicine, the leaf, root and seed oil of this plant have been used for the treatment of inflammation and liver disorders as they have been found to be hepatoprotective (Visen *et al.*, 1992), laxative (Capasso *et al.*, 1994) and diuretic (Abraham *et al.*, 1986).

The antifertility activity of 50% ethanolic extract of *R. communis* has also been reported (Sandhyakumary *et al.*, 2003). Shokeen *et al.* (2008) reported the antidiabetic activity of 50% ethanolic extracts and purified fractions of *R. cummunis*.

Since a long time, medicinal plants have been used for the treatment of many infectious diseases without any scientific evidence. At present there is more emphasis on determining the scientific evidence and rationalization of the use of these preparations. Research is in progress to identify plants and their active principles possessing activity against sexually transmitted pathogens including human immunodeficiency virus (HIV) with an objective of providing an effective approach for prevention of transmission and treatment of these diseases (Mukhtar *et al.*, 2008).

In VIT University, characterization and testing of herbal extracts and their purified form are under meticulous investigation. Anticancer properties of plants like *Oroxylum indicum*, *Acacia nilotica*, *Bacopa monneirei*, *Picrorhiza kurroa* was studied using cancer cell lines. Methanolic and aqueous extracts of *O. indicum* was found to exhibit cytotoxic effect to cancer cell lines. The aqueous extract with its antioxidant activity exhibited DNA protection against free radical damage. *Costus pictus* which is popularly called as 'insulin plant' was investigated for its antidiabetic and antioxidant properties. Experiments on liver and kidney cells of diabetic rats indicated that this plant extracts do not have any cytotoxic effect in normal and cancer cells. The inhibitory activity on carbohydrate hydrolyzing enzyme might be attributed to the mode of action of this plant extract. In yet another study, the extracts of triphala was found to have anti-arthritis, analgesic effect, anti-pyretic action and anti-ulcerogenic activity. *Acacia nilotica*, *Curcuma longa* and *Lawsonia inermis* showed antioxidant activity which validates their potential role in alleviating cancer. *Costus pictus*, the insulin plant, showed significant reduction in FPG level of STZ induced diabetic rat and significant reduction in serum and organ lipid level suggesting the hypolipidimic activity of this plant. Significant effect on TNF-alpha production, humoral antibodies, lymphocyte proliferation and delayed type hypersensitivity were observed in arthritis rats administered with extract from *Triphala*, indicating the immune- modulatory function of this plant. Administration of triphala extract in animal models proved to be efficacious, specific and non toxic and hence warrants further investigation, before development of drug formulations.

Formulations and Testing

Testing the biological activity of medicinal or potentially medicinal plant materials demands a special approach. Investigations may be focused on understanding the bioactivity or a compounded plant extract or simply directed at isolating a single bioactive chemical compound. In the latter case, results often lead to oversimplification or wrong explanations or the bioactivity or extract preparations. On the other hand, thorough studies on single bioactive constituents provide important information for plant drug research. However, the much more complex array of molecular interactions and bioactivity mechanisms that arises from plant extracts represents a much greater and more fascinating challenge to science. Reverse pharmacology and herbal drug formulation the traditional knowledge-inspired reverse pharmacology described here relates to reversing the routine 'laboratory-to-clinic' progress to 'clinics-to-laboratories'. Patwardhan and Meshelkar (2009) suggest that drug discovery need not be always confined to the discovery of a single molecule. Many analysts believe that the current 'one drug fits all' approach may be unsustainable in the future.

The growing interest in polypill concept is indicative of the need to collectively address multiple targets, risk factors or symptoms.

The FDA and a few other agencies have come up with practical guidelines for botanical 'drug' development. A botanical drug product often has unique features and may include complex mixtures with as yet unknown active ingredients. No botanical products are, however, currently approved or marketed as prescription drugs. The FDA recognizes that prior human experience with botanical products may be documented in many different forms and sources, some of which may not meet the quality standards of modern scientific testing. The FDA maintains, however, the same standards for safety and efficacy for marketing approval whether it is a botanical-sourced product or a purified chemical.

Traditional herbal formulations could follow such regulatory guidance to create scientific evidence base with robust chemistry, manufacturing and controls. Department of Ayurveda, Yoga, Unani, Siddha, Homeopathy (AYUSH) in India has recently established a Research Center at the University of Mississippi, Oxford, MS, USA to facilitate scientific investigations on Indian herbal drugs. Such efforts should help improve quality assurance, enhancing the chance of regulatory approvals and improving the acceptance of botanical drug products and formulations.

Thus, if safe and effective herbal formulations are developed in accordance with stringent regulatory guidelines on a par with any modern drug, we hope that the conventional disbelief against herbals may slowly wane. Issues related to the appropriateness of conventional biomedical and clinical models for evaluating efficacy of traditional medicine remain, however, very crucial. A holistic approach based on systems biology seems much more suited to study therapeutic efficacy and pharmacodynamics of traditional medicine-based drug development. It can also be argued that instead of randomized controlled trials, strategies of pragmatic clinical trials may be better suited for traditional medicine-inspired reverse pharmacology approaches.

Concluding remarks

The use of herbal drugs for the prevention and treatment of various health ailments has been in practice from time immemorial. Many plants belonging to varied geography are being studied in large to identify the compounds of medicinal value. However, the researchers are still finding difficulties in characterizing the compounds from the pool of plant metabolites for a specific activity. The crude extracts of many plants are reported to have multiple beneficial effects on diseases and disorders. The relative efficiency of each compound and the possibilities of purifying them to homogeneity and developing a drug formulation is still beyond reach. Moreover, generally it is believed that the risk associated with herbal drugs is very less, but reports on serious reactions are indicating to the need for development of effective marker systems for isolation and identification of the individual components. Standards for herbal drugs are being developed worldwide but as yet there is no common consensus as to how these should be adopted. Standardization, stability and quality control for herbal drugs are feasible, but difficult to accomplish. Further, the regulation of these drugs is not uniform across countries. There are variations in the methods used across medicine systems and countries in achieving stability and quality control. The search for new molecules, nowadays, has taken a slightly different route where the science of ethnobotany and

ethnopharmacology are being used as guide to lead the biotechnologist towards different sources and classes of compounds. With intense research on the herbal compounds from our huge natural wealth, the development of herbal medicine technology for every of our diseases and disorders is not far from now.

ACKNOWLEDGEMENTS

Support and help provided by friends and colleagues are gratefully acknowledged.

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