

# Ethnopharmacology- A Novel Approach for Drug Discovery

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## ABSTRACT

*The era of blockbuster drugs is now ending, the pharmaceutical industry is not as innovative due to shortage of new lead structures. Ethnopharmacology and natural product drug discovery remains a significant hope in the current scenario. Ethno pharmacology provides a divergent approach involving indigenous knowledge with current technology for drug development using new approaches. Natural products have been the source of active ingredients of many medicines from 1981 till date. Aspirin, artemisinin, colchicine, digoxin, ephedrine are few important drugs that were developed from medicinal plants in the past. Hurdles like lack of trials, safety and efficacy records, gap between old concepts and modern understanding, malpractice due to intense competition in drug research, carelessly carried out bioassays and biopiracy stop this knowledge from becoming mainstream. Physician can play an important role in overcoming some of these hurdles and strict guidelines are required for ethnoergogenics. A sincere effort needs to be made to prevent the loss of this rich traditional knowledge which can help drug discovery for many years to come.*

**Keywords:** Ethno pharmacology, Drug discovery, Biopiracy, Physician, Holistic

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## INTRODUCTION

Ethno pharmacology is a highly diversified approach for drug discovery which involves the observation, description and experimental investigation of indigenous drugs and their biologic activities that is based on botany, chemistry, biochemistry, pharmacology, and other disciplines (anthropology, archaeology, history, and linguistics) contributing to the discovery of natural products with biologic activity.<sup>(1)</sup> WHO defines -Traditional medicine is the sum total of the knowledge, skills, and practices based on the theories, beliefs, and experiences indigenous to different cultures, whether explicable or not, used in the maintenance of health as well as in the prevention, diagnosis, improvement or treatment of physical and mental illness. Traditional medicine covers a wide variety of therapies and practices which vary from country to country and region to region. In some countries, it is referred to as "alternative" or "complementary" medicine (CAM).<sup>(2)</sup> In developed countries, 70% and 80% population have used CAM because they believe that this type of treatment is more "natural" and therefore "risk-free", or as an adjunct to treatment for a chronic, debilitating or incurable disease.<sup>(3)</sup> India has a rich ancient heritage in traditional medicine. Indian Materia medica provides abundant

information on ethnic folklore practices and traditional aspects of therapeutically important natural products.<sup>(4)</sup>

## HISTORY

Ethno pharmacology was initiated by the missionaries in the colonies interested in the use of pharmacologically active plants, like the Jesuits in 16th century Latin America. Luis Lewin [1850–1929], Carl Hartwich [1851–1917], Alexander Tschirch [1856–1939] and Richard Evans Schultes [1915–2001] established Molecular ethno pharmacology. Robert Gordon Wasson [1898–1986] and Albert Hofmann [1906–2008], resulting in the isolation of psilocybin from psychoactive mushrooms. Discovery of the pharmacological principles in foxglove i.e. digitalis, curare, first antimalarial quinine from cinchona. Similarly, aspirin was developed based on ethno pharmacological studies with the bark of the willow tree which has been used traditionally in Europe to treat fever and inflammation. Recent example of model research in ethno pharmacology is the work on the Chinese antimalarial plant *Artemisia annua* L., resulting in the recent development of artemisinin into new clinical semisynthetic antimalarial agent artemether.<sup>(5)(6)(7)</sup>

## CONTRIBUTION TO MODERN MEDICINE

Natural products have been the source of active ingredients of many medicine from 1981 to 2007. Almost half of the drugs approved since 1994 are based on natural products. Thirteen natural product related drugs were approved from 2005 to 2007<sup>(8)</sup>. 60% of the anticancer drugs and 75% of the anti-infectious disease drugs approved from 1981-2002, could be traced to natural origins. In addition, 61% of all new chemical entities introduced worldwide as drugs during the same

period could be traced to or were inspired by natural products.<sup>(9)</sup>

Aspirin, atropine, artemisinin, colchicine, digoxin, ephedrine, morphine, physostigmine, pilocarpine, quinine, quinidine, reserpine, taxol, tubocurarine, vincristine and vinblastine are a few important examples of drugs developed from medicinal plants. Many plant-derived drugs are originally discovered through the study of traditional cures and folk knowledge, some of these are still not substituted despite the enormous advancement in synthetic chemistry.<sup>(10)</sup>

Numerous molecules have come out of Ayurvedic experiential base, including rauwolfia alkaloids for hypertension, psoralens for vitiligo, holarrhena alkaloids in amoebiasis, guggulsterons as hypolipidemic agents, picosides for hepatic protection, phyllanthins as antivirals, curcumines for inflammation, withanolides and many other steroidal lactones and their glycosides as immunomodulators.<sup>(11)</sup>

Currently more than 100 natural product derived compounds are under research and many in preclinical development.<sup>(12)</sup> World Health Organization, European Agency for the Evaluation of Medicinal Products and European Scientific Cooperation of Phytomedicine, US Agency for Health Care Policy and Research, European Pharmacopoeia Commission, Department of Indian System of Medicine have started creating new mechanisms to induce and regulate quality control and standardization of botanical medicine.<sup>(13)</sup>

### NEED FOR ETHNO PHARMACOLOGY

The drug discovery process has become very complex and capital-intensive and companies with lead discovery as a greater bottleneck.<sup>(14)</sup> The usual distinctions between breakthrough and me-too drugs may not be very meaningful and today the pharmaceutical industry is technology intensive, not as innovative due to shortage of new lead structures with the strict regulatory processes adding more years to the discovery cycle and increasing cost due to post-approval or post-marketing withdrawals.<sup>(15)</sup>

Random screening of plants used traditionally by pharmaceutical industries to discover new leads or drugs is expensive and time consuming but the ethno directed approach to traditional knowledge has been extremely useful in screening and identification of bioactive compounds with valuable application in drug development. This has significantly increased the chances of discovery of new biomolecules with potential therapeutic application while reduction in the cost and time involved in this process. There is also increased demand due to problems with drug resistant microorganisms, side effects of modern drugs, and emerging diseases with no available treatment knowledge of the indigenous people can give new sources.<sup>(16)(11)</sup>

The ethno pharmacology knowledge, its holistic approach supported by experiential base can serve as an innovative and powerful discovery engine for newer, safer and affordable medicines.<sup>(5)</sup>

### ETHNO PHARMACOLOGY AND NATURAL PRODUCT DRUG DISCOVERY

Ethno pharmacology and natural product drug discovery remains a significant hope in the current target-rich, lead-poor scenario.<sup>(15)</sup> Commonly, industrial drug discovery process makes use of medium and high-throughput bioassay screening platforms for discovering promising compounds for a particular target, ethno pharmacology goes the opposite way where anecdotal efficacy of medicinal plants is put to test in the laboratory trying to understand the pharmacological basis of culturally important plants.<sup>(5)</sup>

Approaches towards the value of natural products:

- 1) **Activity profiling of extracts:** This involves screening mixtures of compounds obtained from plant extracts or from microbial broths. But primary screens may not always contain novel compounds with the expected biological activity.
- 2) **Biology-oriented synthesis:** Here natural products act as a starting point for the search of active agents in new medicines. In order to match the natural material to its corresponding enzyme, scientists mimic nature by either introducing chemical residues into areas of biological relevance.<sup>(8)(17)</sup>

Now technology to measure gene expression, the proteome and the metabolome is available, which helps us better understand the mode of action of new compounds by comparing the changes in the transcriptome, proteome and metabolome patterns to those observed with known drugs. Such an approach is now known as a systems biology approach.<sup>(18)(19)</sup>

Metabolomics: Goal of metabolomics is to qualitatively and quantitatively analyze all metabolites in an organism. Currently the methods that are being used in metabolomics can basically be classified into three groups:

- I. chromatography based methods (GC, HPLC);
- II. molecular weight based methods (mass spectrometry);
- III. physical characteristics based methods (NMR spectrometry).<sup>(19)</sup>

### PROBLEMS WITH ETHNO PHARMACOLOGY

Many Traditional preparations have been used for years and claimed to be the most potent and effective dosage forms but very few scientific studies are carried out on these products due to lack of communication amongst traditional healers, physicians and scientists. this gap can be filled by translating the old concepts in modern understanding providing possible explanation and hypothesis.<sup>(20)</sup>

Another problem for ethno pharmacology is the intense

competition in drug research of medical field. There is requirement of stringent criteria to avoid development of false positive results.<sup>(7)</sup>

Malpractice in scientific method of ethno pharmacology is based on carelessly carried out bioassays using high concentrations of an extract or a natural product to demonstrate a pharmacological response.<sup>(5)</sup> The general requirement for new drugs worldwide is quality, safety and efficacy but traditional medicine does not have double-blind studies or even well described case records. Results of treatment of anecdotal observations in single patients cannot be submitted to Health Authorities anywhere in the world and in most cases sufficient quality control and drug standardization is lacking for traditional recipes.<sup>(21)</sup>

Pharmaceutical biopiracy is a term used generally to describe the legal practice by pharmaceutical companies exploiting the indigenous people's traditional knowledge of medicine. The protection of intellectual property on traditional medicines should also be based on the guidelines for the protection of intellectual property on traditional medicines to be developed by the World Intellectual Property Organization (WIPO) with treatment guidelines and evidence-based evaluation guidelines for ethnoergogenics.<sup>(22)(8)</sup>

A botanical drug or a preparation thereof is now regarded as one active substance in its entirety, whether or not the constituents with therapeutic activity are known. This is a major step in the development of new generation standardized botanical medicines. The WHO has published official documents on medicinal plants and WHO monographs on selected medicinal plants.<sup>(23)</sup>

### ROLE OF PHYSICIAN

Physicians can play many roles in the ethno pharmacological studies to facilitate drug discovery as well as to rescue authentic traditional knowledge of use of medicinal plants.

These include:

1. Ethno pharmacological field work like interviewing healers, interpreting traditional terminologies into their modern counterparts, examining patients taking herbal remedies and identifying the disease for which the herbal remedy is used to strengthen traditional system of medicine.
2. Clinical studies on herbs and their interaction with modern medicines and on herbs observed during field studies.
3. Suggesting proper use of old traditional remedies in the light of modern medicine. Physicians practicing in clinics or a family physician in a community have access to patients consuming both herbals and modern drugs will be able to clinically observe the benefits or side effects of both herbals and drugs introduced recently and when used in combination.<sup>(24)</sup>

### DATABASE

Information related to ethno medical knowledge and scientific research on medicinal plants is now available in the form of databases. For example, NAPALERT is the largest database of natural products, with entries of over 27,000 plants with a list of 300 or more associated symptoms or diseases.<sup>(25)(26)</sup>

### CONCLUSION

Ethno pharmacology is a holistic approach to drug development, using the latest technology for measuring as many different parameters as possible to discover possible leads to the mode of action with ethno botanists, ethno pharmacologists, physicians and phytochemists playing a key role. It has already contributed to the development of modern medicine and is likely to play more significant role in the years to come. The World Health Organization has been active in creating guidelines and standards of botanical medicines, this will have great impact on future drug development and will prevent the loss of knowledge of traditional medicines and the loss of natural resources used as traditional medicines particularly if some mechanism of royalty comes into practice.

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