JPP Journal of Pharmacy and Pharmacology

JPP 2001, 53: 425–432

Received October 17, 2000
Accepted January 1, 2001
ISSN 0022-3573

Review Article

Ethnopharmacology in drug discovery: an analysis of its role and potential contribution

Michael Heinrich and Simon Gibbons

Abstract

In this paper we discuss some examples of ethnopharmacological research as it has been conducted during the last two centuries and look at the current role of this discipline in drug discovery (especially with respect to the American and European markets) and the further development of these phytotherapeutical resources for local use in the countries of origin (ethnopharmacology). Examples from 19th century research on curare (Humboldt and Bernard), from the 20th century on hallucinogenic mushrooms (Wasson), on Mexican Indian indigenous plants (our own research) and of current industry based research are used to illustrate the development of this discipline and to highlight the challenges for the future.

Introduction

Ethnopharmacology as a specifically designated field of research has had a relatively short history. The term was first used in 1967 as the title of a book on hallucinogens '*Ethnopharmacologic Search for Psychoactive Drugs*' (Efron et al 1970 [orig. 1967]) and is nowadays much more broadly defined:

"The observation, identification, description and experimental investigation of the ingredients and the effects of the ingredients and the effects of such indigenous drugs is a truly interdisciplinary field of research which is very important in the study of traditional medicine. Ethnopharmacology is here defined as the interdisciplinary scientific exploration of biologically active agents traditionally employed or observed by man" Bruhn & Holmstedt (1981).

This definition draws attention to the evaluation of indigenous uses and does not explicitly address the issue of searching for new bioactive drugs (drug discovery), although the latter issue has been in the core of the public's attention. Shortly before the start of the 20th century, the American botanist William Harshberger coined another frequently used term, 'ethnobotany'. It did not only focus on medicinal plants, but also on other natural products derived from nature such as foods, colouring agents, fibre plants, poison, fertiliser, ornamentals and oil plants.

But medicinal plants have always been one of the main research interests of ethnobotany and the study of these resources has also made significant contributions to the theoretical development of the field (Berlin 1992). These more anthropologically oriented fields of research are beyond the scope of this review. Here we look at the historical development of this field and some of its contributions to drug discovery since the 19th century.

Centre for Pharmacognosy and Phytotherapy, The School of Pharmacy, University of London, 29–39 Brunswick Square, London, WC1N 1AX, UK

Michael Heinrich, Simon Gibbons

Correspondence: M. Heinrich, Centre for Pharmacognosy and Phytotherapy, The School of Pharmacy, University of London, 29–39 Brunswick Square, London, WC1N 1AX, UK.
E-mail: phyto@ulsop.ac.uk

Ethnopharmacology in the 19th century: some examples

Ethnopharmacology in a modern sense only became possible with the scientific ability to study the effects of substances and extracts on model systems. Consequently Claude Bernard (1813–1878), who conducted detailed studies on the pharmacological effects of curare, has to be considered as one of the first researchers of this tradition. According to Bernard it is an essential goal to analyse the information provided by researchers in the field with experimental methods:

"In our physiological studies we were able to identify the effect of the American arrow poison curare as one on the nervous motoric element and subsequently to determine a mechanism which results in death, which is an inert ability of this poisoned substance, but do we have to stop here and have we reached the border which our current [19th century] Science allows us to reach? I do not think so. One has to separate the active principle of curare from the foreign substances, with which it is mixed, and one also has to study which physical and chemical changes the toxic substance imprints onto the organic element [i.e. the body] in order to paralyse its activity" (Bernard 1966 [orig. 1864]).

As we will see later these goals are not significantly different from modern ethnopharmacological researchers.

Curare was used by "certain wild tribes in South America for poisoning their arrows…" (Bernard 1966). Many early explorers and travellers documented this usage. Particularly well known are the very detailed descriptions of the process used to prepare poisoned arrows in the community of Esmeralda on the Orinoco river made by the German natural scientist Alexander von Humboldt in 1800. There he met a group of natives who celebrated their return from a gathering collection in order to obtain the raw material for making the poison and the fruit of *Bertholletia excelsa*. A. von Humboldt continues to describe the "chemical laboratory" used:

"He [an old Indian] was the chemist of the community. With him we saw large boilers (Siedekessel) made out of clay to be used for boiling the plant sap; planer containers, which speed up the evaporation process because of their large surface; banana leaves, rolled to form a cone-shaped bag, [and] used to filter the liquid which may contain varying amounts of fibres. This hut transformed into a laboratory was very tidy and clean" (Humboldt 1997).

As early as 1800 A. von Humboldt had to face one of the classical problems of ethnopharmacology:

"We are unable to make a botanical identification because this tree [which produces the raw material for the production of curare] only grows at quite some distance from Esmeralda and because [it] did not have flowers and fruit. I had mentioned this type of misfortune previously, that the most noteworthy plants cannot be examined by the traveller, while others whose chemical activities are not known [i.e. which are not used ethnobotanically] are found covered with thousands of flowers and fruit."

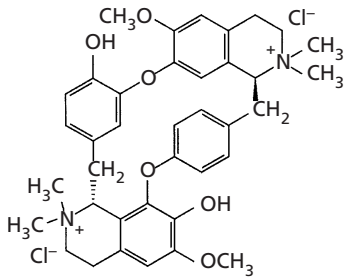
In later decades the botanical source of curare was identified as *Chondrodendron tomentosum* Ruiz et Pavon which produces the so-called tubocurarine (named because of the tube-shaped storage containers used). Other species of the Menispermaceae (*Chondrodendron* spp., *Curarea* spp. and *Abuta* spp.) and species of the Loganiaceae (*Strychnos* spp.) are used in the production of curares (Bisset 1991). The bio-scientific investigation of this poison is one of the most fascinating examples of transforming a drug used in an indigenous culture into a medication and research tool used in biomedicine (Bisset 1991).

One of the first systematic studies on the physiologic-pharmacological effects was conducted by the French physiologist Claude Bernard (1813–1878). It is worth looking at his description of the pharmacological effects of curare in some detail.

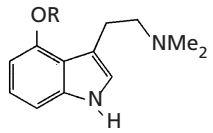
"If curare is applied into a living tissue via an arrow or a poisoned instrument, it results in death more rapidly if it gets into the blood vessels more rapidly. Therefore death occurs more rapidly if one uses dissolved curare instead of the dried toxin" (Bernard 1966). "One of the facts which was noted by all who reported on curare is the lack of toxicity of the poison in the gastrointestinal tract. The Indians indeed use curare as a poison and as a remedy for the stomach" (Bernard 1966).

Bernard also was able to demonstrate that the animals did not show any nervousness and no sign of pain. Instead the main sign of death induced by curare is muscular paralysis. If the blood flow in the hind leg of a frog is interrupted using a ligature without interrupting the innervations of this extremity, and if it is poisoned *via* an injury of the hind leg, it retains its mobility and the animal does not die of curare poisoning (Bernard 1966). These and subsequent studies allowed a detailed understanding of the pharmacological effects of curare in causing respiratory paralysis.

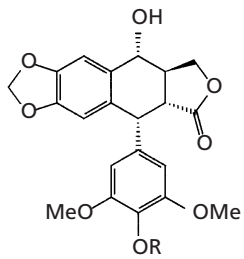
The most important natural product responsible for this activity was isolated for the first time from *Chondrodendron tomentosum* and in 1947 the structure of the bisbenzylisoquinoline alkaloid D-tubocurarine was finally established unequivocally. In many European countries the compound is nowadays used only sporadically, but for example in France it is still used frequently for muscular relaxation during operations (**1**, Figure 1). It was a template for one of the most important



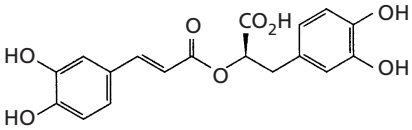
(**1**) Tubocurarine chloride



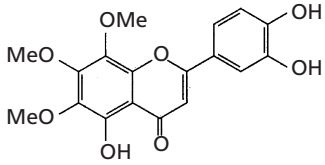
(**2**) R = H, psilocin
(**3**) R = phosphate, psilocybin



(**4**) R = Me, podophyllotoxin
(**5**) R = H, 4′-demethylpodophyllotoxin



(**6**) Rosmarinic acid



(**7**) Sideritiflavone

Figure 1. Examples of natural products from *Chondrodendron tomentosum* (**1**), *Psilocybe* spp. (**2**,**3**) and *Hyptis verticillata*.

synthetic muscle relaxants, atracurium, developed in the early 1970s.

There are many other examples of pharmaceutically relevant substances, which were developed based on detailed observations of indigenous uses during the last centuries (cf. Heinrich 2001). Some of the better-known examples include:

- *Cinchona succirubra* Pav [syn. *C. pubescens* Vahl] and C.spp. (Rubiaceae) – quinine
- *Colchicum autumnale* L. (Colchicaceae) – colchicine
- *Digitalis* spp. (Scrophulariaceae) – digitalis glycosides
- *Papaver somniferum* L. (Solanaceae) – morphine, codeine, papaverine
- *Physostigma venenosum* Balfour (Fabaceae s.str.) – physostigmine
- *Pilocarpus jaborandi* Holmes (Rutaceae) – pilocarpine

These examples not only demonstrate the enormous contribution of local knowledge to our pharmacopoeias, but also that this was only possible thanks to a multitude of meticulous studies by scholars from many disciplines (see also Schultes & Nemry 1998).

Ethnopharmacology in the 20th century

In the first half of the century the field remained a well-established and integral part of biological and pharmaceutical sciences. Only with the advent of antibiotics during the mid-20th century and the subsequent refocusing of pharmaceutical research did the field start to become less and less important. Consequently, it only survived in some hidden niches like the Botanical Museum at Harvard University, where R. E. Schultes built a school of botany oriented ethnobiological research. The field suddenly sprang back into the public attention with research by the journalist and bank manager R. Gordon Wasson (22.9.1898–23.12.1986), who was drawn into the field of ethnopharmacology by one of Schultes' earlier contributions. Wasson and his spouse Valentina Pavlovna Guercken became fascinated by hallucinogenic fungi and plants. They devoted much of their spare time to their study. R. G. Wasson and his team were the first 'aliens', who participated in a nightlong 'velada' (ritual) in the Mexican community of Huautla de Jimenez. In this velada, Maria Sabina, a healer, introduced the team to the use of 'Our Little Ones' or as they are now popularly known the Sacred Mushrooms (*Psilocybe* spp.) An article in *Life* (Wasson, 1957) showed the enormous popular interest in this field.

Phytochemical studies indicated that the pharmacological activity is due to relatively simple alkaloids, especially psilocybin and psilocin (**2**, **3**, Figure 1). The expectations for developing new drugs based on this ethnomycological information were ultimately not met. But for the regions of study, drastic socio-cultural changes were the result of these research projects, especially because of the popularisation of this sacred and

specialised information and the subsequent influx of non-natives.

Ethnopharmacology and the Convention of Biological Diversity (*Rio Convention*)

None of the studies discussed so far took the benefits for the providers (the states and their people) into account. This has changed in recent years. Ethnopharmacological research, and any other research involving the use of biological resources of a country, is today based on agreements and permits which in turn are based on international and bilateral treaties. The most important of these is the 'Convention of Rio' or the 'Convention on Biological Diversity' (see http://www.biodiv.org/chm/conv.htm), which in particular looks at the rights and tasks associated with biodiversity on an international level:

> The objectives of this Convention, to be pursued in accordance with its relevant provisions, are the conservation of biological diversity, the sustainable use of its components and the fair and equitable sharing of the benefits arising out of the utilization of genetic resources, including by appropriate access to genetic resources and by appropriate transfer of relevant technologies, taking into account all rights over those resources and to technologies, and by appropriate funding.

The basic principles of access are regulated in article 5:

> States have, in accordance with the Charter of the United Nations and the principles of international law, the sovereign right to exploit their own resources pursuant to their own environmental policies, and the responsibility to ensure that activities within their jurisdiction or control do not cause damage to the environment of other States or of areas beyond the limits of national jurisdiction.

This and the subsequent treaties significantly changed the basic conditions for ethnopharmacological research. Now the countries who provide the resources for natural product research and drug development have well defined rights and this specifically includes the sharing of the benefits which potentially may arise out of the research. The access to the resources is addressed in article 15 which is crucial for an understanding of the role of ethnopharmacology in drug development and for any other activity which may yield economically important products:

> 15.1. Recognizing the sovereign rights of States over their natural resources, the authority to determine access to genetic resources rests with the national governments and is subject to national legislation.
>
> 15.5. Access to genetic resources shall be subject to prior informed consent of the Contracting Party providing such resources, unless otherwise determined by that Party.
>
> 15.7. Each Contracting Party shall take legislative, administrative or policy measures ... with the aim of sharing in a fair and equitable way the results of research and development and the benefits arising from the commercial and other utilization of genetic resources with the Contracting Party providing such resources. Such sharing shall be upon mutually agreed terms.

Especially in the case of ethnopharmacological research, the needs and interests of the populations a researcher is collaborating with also become an essential part of the research. As pointed out many times "*there is an inextricable link between cultural and biological diversity*" (cf. http://users.ox.ac.uk/~wgtrr/index.html). This principle was first formulated at the 1st International Congress on Ethnobiology in Belem in the year 1988. No generally agreed upon standards have so far been accepted, but the importance of obtaining the informants' prior informed consent has been stressed by numerous authors (e.g. Cotton 1997, Martin 1996).

Ethnopharmacology and bioprospecting

Numerous studies dealing with medicinal and other useful plants as well as their bioactive compounds have used a multitude of concepts and methodologies. In many cases these were interdisciplinary or multidisciplinary studies combining such diverse fields as anthropology, pharmacology, pharmacognosy/pharmaceutical biology, natural product chemistry, toxicology, clinical research, plant physiology and others. In order to permit an analysis of their strengths and weaknesses and especially of the outcomes of the research, we distinguish two conceptually and methodologically different but closely related approaches: bioprospecting and ethnopharmacology (Table 1). 'Bioprospecting' focuses on the development of new drugs for the huge markets of the North. New potentially highly profitable pharmaceutical products are developed based on the biological and chemical diversity of the various ecosystems of the earth and the research requires an enormous financial input. The research goes from the collection of biogenic samples (plants, fungi, other microorganisms, animals), to the subsequent analysis of the biological-pharmacological activities and to the study of the organisms' natural products to the development of drug templates or new drugs. Essential in this search are high-throughput screening systems as they are established by the major international pharmaceutical companies. Huge libraries of compounds (and sometimes extracts) are screened for biological activity against specific targets. Biodiversity derived products are only one of the many sources of material for these test batteries. This serves as a starting point for drug

Table 1 Comparison between ethnopharmacology and bioprospecting.

	Ethnopharmacology	**Bioprospecting**
Goals	Drug development esp. for local uses Complex plant extracts (phytotherapy)	Drug discovery for international market Pure natural products as drug
Selected characteristics	Detailed information on a small segment of the local flora (and fauna)	Inventory (→ expanded herbaria)
	Database on pharmaceutical uses of plants	Database on many taxa (incl. ecology)
	Development of autochthonous resources (esp. local plant gardens, small scale production of herbal preparations	Economically sustainable alternative use to destructive exploitation (e.g. logging)
Key problems	Safety and efficacy of herbal preparations	Local agendas (rights) and compensation to access

development. Currently some companies envision the screening of 500000 samples a week against a single target. It thus becomes essential to have an enormous number of chemically diverse samples available (see below).

The other approach may best be termed an ethnopharmacological one. Ethnobotanical studies generally result in the documentation of a rather limited set of very well documented useful plants (mostly medicinal, but also those known to be toxic or used in nutrition). In ethnopharmacology an important goal is the development of improved preparations for the use by local people. Thus it is essential to get information on the bioactive compounds from these plants, their relative contribution to the effects of the extract (including, for example, synergistic or antagonistic effects), the toxicological profile of the extract and its constituents and on improved galenic preparations to be prepared under local conditions.

In restricting ethnopharmacology to the evaluation of indigenous uses we want to draw attention to the fact that even an interdisciplinary defined approach, as it is, for example, used by the editors of the *Journal of Ethnopharmacology*, does not take into account the need for developing research strategies for evaluating indigenous uses:

> Early man, confronted with illness and disease, discovered a wealth of useful therapeutic agents in the plant and animal kingdoms. The empirical knowledge of these medicinal substances and their toxic potential was passed on by oral tradition and eventually annotated in herbals and texts on *materia medica*. Many valuable drugs of today (e.g. atropine, ephedrine, tubocurarine, digoxin, reserpine) came into use through the study of folk remedies. Chemists continue to use plant-derived drugs (e.g. morphine, physostigmine, quinidine, theophylline, emetine) as prototypes in their attempts to develop more effective and less toxic medicinals. The search for pharmacologically unique principles from existing indigenous remedies continues and complements the achievements of modern medicine.

The importance of such nature derived products in the healthcare of the original keepers of such knowledge needs to become a main goal of truly interdisciplinary ethnopharmacological research. Along these lines ethnopharmacology may contribute to the development of new pharmaceutical products for the markets of the North, but this is only considered to be a sideline. Truly ethnologically (or anthropologically) oriented research on medicinal plants requires not only a detailed understanding of these medicines, but also the support in autochthonous developments to make better use of these products. Bruhn & Holmstedt, for example, indirectly imply this in their definition cited in the introduction.

It has been pointed out previously that the two approaches, ethnopharmacology and biodiversity prospecting, are not mutually exclusive and the two concepts 'ethnopharmacology' versus 'bioprospecting' as they are outlined here are hardly ever realised in such an extreme form. Instead, most projects generally contribute to a lesser or larger degree to both of them and thus are ethnopharmacology- and biodiversity-driven. The discussion in the previous paragraphs should specifically draw attention to the particular strengths and roles of both approaches. In bioprospecting programmes directed specifically towards infectious diseases, the use of ethnobotanical information surely is very useful and promising (Lewis 2000). This is not necessarily the case, for example, in the case of cancer chemotherapy.

Ethnopharmacological research in Mexico

An example of a project focusing on the evaluation of indigenous uses is the phytochemical and biological-pharmacological study of *Hyptis verticillata* (Lamiaceae), a medicinal plant used by the Lowland Mixe of Oaxaca, Mexico in the treatment of skin infections and

inflammation as well as gastrointestinal pain (Kuhnt et al 1994, 1995). In the case of skin problems, the plant is ground up with a little alcohol or the mashed leaves are applied directly and in both cases applied to the affected part. For gastrointestinal problems, a tea is prepared using 'a handful' of fresh leaves.

Phytochemical investigation, using an inflammatory model as well as antibacterial assay as a lead, led to the isolation of several lignans (**4**, **5**, Figure 1), rosmarinic acid and sideritoflavone (**6**, **7**, Figure 1). These compounds helped to explain the rationale behind the indigenous uses. The lignans are known to have strong antibacterial activity, which was also corroborated in our own studies. Both rosmarinic acid and sideritoflavone were shown to be active in some anti-inflammatory models.

Additionally we were able to show that the lignans are only extracted to a very limited degree if the plant material is prepared as a tea, while relatively large amounts were extracted in a process mimicking the indigenous extraction with 'aguardiente' (40–70% ethanol). The highly toxic lignans are thus present in much smaller quantities in the tea, reducing the health risk of this preparation (Kuhnt et al 1995).

In other cases the rationale for ethnopharmacologic uses may well be explained exclusively by making reference to published information. The following example is drawn from ongoing fieldwork in Eastern Guatemala with a Mayan-speaking people, the Chorti. They use fruit of *Ocimum micranthum* (Lamiaceae) in the treatment of infectious and inflammatory eye diseases (Kufer et al, unpublished). The fruits are approximately one millimetre in diameter and hard. Several of the entire hard fruits are applied directly into the eye. At first glance they seem to be an unlikely remedy for eye problems. The rationale behind this usage becomes evident when one considers the morphological and chemical makeup of the outer part of this fruit. The fruits of some members of the Lamiaceae are well known to be covered with a mucilaginous layer containing complex polysaccharides. If put into water they form a soft layer around the fruit (Heinrich 1992). This layer may well have a cleansing effect and polysaccharides are known to be useful in the treatment of inflammatory conditions and bacterial or viral infections. While there are no pharmacological data from experimental studies available, which corroborate this use, the information on the histochemical structure of the fruit makes it very likely that the treatment has some pharmacological basis.

These two examples demonstrate the relevance of ethnopharmacology specifically as it relates to the empirical evaluation of indigenous medical products. Ethnopharmacology as a science, which bridges the gap between natural sciences and anthropology/ethnology, should also look at symbolic and cognitive aspects. People select plants sometimes because of their specific pharmacological properties, but also because of the symbolic powers they may see in a plant. The understanding of these aspects of a plant's use requires cognitive and symbolic analyses of the field data. Again an example from our field studies with the Mixe. At the end of a treatment, the patient is sometimes given a petal of *Argemone mexicana* (Mixe: San Pedro Agats, Papaveraceae). The plant is well known to contain a large number of flavonoids and biologically active isoquinoline alkaloids. The yellow petals are presumably not used because they exert a pharmacological effect (at this dose), but because they symbolise the bread of the Last Supper according to Christian mythology and thus are a powerful symbol for the end of the healing process (for other examples of symbolic and empirical forms of plant use see Heinrich 1994).

All three examples point to an important role of ethnopharmacology, which goes beyond the one as it was defined previously. Ethnopharmacology thus does not only look at empirical aspects of indigenous and popular plant use, but also at the cognitive foundations of this use. Only if these issues are to be included will it be a truly interdisciplinary field of research (Bruhn & Holmstedt 1981). Key tasks of pharmaceutical researchers in this interdisciplinary process will be the evaluation of the pharmacological effects of the most widely used species (for selection criteria for the ethnopharmacologically most important taxa see Heinrich et al 1998a,b) of these ethnopharmacopoeias, the characterisation of the relevant natural products and the formulation of improved but relatively simple galenic preparations.

In another recent paper, an overview of some of our research in the last years is given (Heinrich 2000a). An important goal of this research is the evaluation of indigenous uses in order to contribute to the further development of the respective ethnopharmacopoeias. It clearly demonstrates the value of integrating ethnobotanical with phytochemical and pharmacological–phytochemical studies. While, for example, our group did not develop new therapeutic agents for use in biomedicine, we were able to demonstrate the value of some of the plants. Other plants were shown to have too many side effects or are highly toxic (Heinrich 2000a, 2001). In an example from the Highlands of Mexico, Bah et al (1994) showed that a species popularly used contains hepatotoxic pyrrolizidine alkaloids. Such plants are thus potential health risks. While this in-

formation is often available to the scientific community, the general public mostly is not aware of these risks. Such data have to be summarized in an appropriate way and have to be made available to the people of the respective regions where the plants are used. It will now be essential to develop partnerships with institutions, which can translate these results into an effective strategy.

Industry based research

Whilst ethnopharmacology as a discipline is very adept at identifying exceptionally potent pharmacologically active agents, surprisingly there has been little pursuance of this approach by the pharmaceutical industry. Why this is the case is unclear but may stem from several key factors:

(1) This approach requires highly trained botanists with expertise in the medicinal uses of plants who are required to live with an indigenous culture, learn its language and gain the trust of the community. Not only are such skilled individuals rare, but also pharmaceutical companies are unwilling to wait for the fruition of such projects, which may only yield small numbers of leads.
(2) Discovery programmes have concentrated on high-throughput screening of rapidly prepared extracts sourced usually in a random fashion. Unfortunately, due to the development of competing approaches such as combinatorial chemistry, the development of new comparable technologies such as natural product libraries has taken preference over exciting (and arguably more productive) ways of lead discovery such as ethnopharmacology.
(3) Natural products have suffered from fashionable trends, and investment in natural product discovery programmes has been cyclic according to which new technology was 'flavour of the month'. The fact that natural products are a tried and tested source of therapeutic agents is rarely considered when the opportunity to invest in the emergence of a new technology arises.

All of these factors have mitigated against using natural products and, implicitly, using the approach of ethnopharmacology as a source of chemical diversity for biological screening programmes.

Shaman Pharmaceuticals were a company dedicated to the discovery of leads from ethnobotanical sources and had an active screening process searching for antihyperglycaemic and antifungal agents (Lu et al 1999; Fort et al 2000). This company is now trading as Shaman Botanicals and discovers, develops and markets proprietary and novel botanical dietary supplements derived from tropical plant sources. One particular product, a normal stool formula (NSF), consists of a standardised extract from the sap of *Croton lechleri* (Euphorbiaceae). This extract contains SP-303, a polyflavan, which has recently been assessed in a phase II clinical study for the symptomatic treatment of diarrhoea in patients with AIDS (Holodniy et al 1999).

It is highly likely that in the future, ethnopharmacological leads may be developed into standardised herbal preparations rather than single chemical entities and this may be highly attractive to companies interested in exploiting the huge public interest in herbal medicines. Many of these preparations are marketed as dietary or nutritional supplements to avoid scrutiny by medical control agencies and whilst these products will be increasingly popular, thorough quality control and standardisation of active constituents is imperative.

Conclusions

In this review we restricted the use of the term 'ethnopharmacology' to the evaluation of indigenous uses and to the expansion of our knowledge base about medicinal plants in order to further develop the use of this local knowledge. Ethnopharmacology thus is complementary to bioprospecting, which uses an approach less focused on indigenous plant use. The examples given in this paper are intended to show the breadth of ethnopharmacolgy's contribution to drug development and to illustrate that pharmacy, by including ethnopharmacological approaches, may profit in many fields. But there are other tasks which are faced by ethnopharmacology. An important one is the study of the use of botanical resources in developed countries. Ethnopharmacology in this context will give important information on the role of plants in our societies. This approach, to be developed in close collaboration with researchers in pharmacy practice, may lead to a better understanding of the use of phytopharmaceutical and other OTC preparations by the general public, its expectation and the use of less well known pharmaceutical preparations by certain groups of people (e.g. users of TCM and Ayurvedic medicine).

References

Bah, M., Bye, R., Pereda-Miranda, R. (1994) Hepatotoxic pyrrolizidine alkaloids in the Mexican medicinal plant *Packera candidissima* (Asteraceae: Senecioneae). *J. Ethnopharmacol.* **43**: 19–30

Berlin, B. (1992) *Ethnobiological Classification. Principles of Categorization of Plants and Animals in Traditional Societies*. Princeton University Pr., Princeton, NJ.

Bernard, C. (1966) Physiologische Untersuchungen über einige amerikanische Gifte. Das Curare. Bernard, C. und N. Mani (Übs.) Ausgewählte physiologische Schriften. Huber Verlag. Bern. [frz. orig. 1864]. pp 84–133

Bisset, N. G. (1991) One Man's poison, another man's medicine. *J. Ethnopharmacol.* **32**: 71–81

Bruhn, J. G., Holmstedt, B. (1981) Ethnopharmacology: objectives, principles and perspectives. In: *Natural Products as Medicinal Agents*. Beal, J. L., Reinhard, E. (eds.). Hippokrates Verl., Stuttgart, pp 405–430

Cotton, C. M. (1997) *Ethnobotany*. Wiley and Sons, Chichester

Efron, D., Farber, S. M. , Holmstedt, B., Kline, N. L., Wilson, R. H. L. (1970) *Ethnopharmacologic Search for Psychoactive Drugs*. Government Printing Office. Public Health Service Publications No. 1645. (orig. 1967) Reprint, Washington, D.C.

Fort, D. M., Rao, K., Jolad, S. D., Luo, J., Carlson, T. J., King, S. R. (2000) Antihyperglycemic activity of *Teramnus labialis* (Fabaceae). *Phytomedicine* **6**: 465–467

Heinrich, M. (1992) Economic botany of American Labiatae. In: Harley, R. M., Reynolds, T. (eds) *Advances in Labiatae Science*. Kew Botanical Gardens, Richmond, pp 475–488

Heinrich, M. (1994) Herbal and symbolic medicines of the lowland Mixe (Oaxaca, Mexico): disease concepts, healers' roles, and plant use. *Anthropos* **89**: 73–83

Heinrich, M (2001) *Ethnobotanik und Ethnopharmakologie. Eine Einführung*. Wissenschaftliche Verlagsgesellschaft, Stuttgart (D)

Heinrich, M. (2000a) Ethnobotany and its role in drug development. *Phytother. Res.* **14**: 479–488

Heinrich, M. (2000b) Ethnobotany, phytochemistry and biological/pharmacological activities of *Artemisia ludoviciana* ssp. *mexicana* (Estafiate). In: Wright, C. (ed.) *Medicinal and Aromatic Plants: Artemisia*. Harwood Academic Publ., Chur (CH). In press

Heinrich, M., Ankli, A., Frei, B., Weimann, C., Sticher, O. (1998a) Medicinal plants in Mexico: healers' consensus and cultural importance. *Soc. Sci. Med.* **47**: 1863–1875

Heinrich, M., Robles, M., West, J. E., Ortiz de Montellano, B. R., Rodriguez, E. (1998b) Ethnopharmacology of Mexican Asteraceae (Compositae). *Annu. Rev. Pharmacol. Toxicol.* **38**: 539–565

Holodniy, M., Koch, J., Mistal, M., Schmidt, J. M., Khandwala, A., Pennington, J. E., Porter, S. B. (1999) A double blind, randomized, placebo-controlled phase II study to assess the safety and efficacy of orally administered SP-303 for the symptomatic treatment of diarrhea in patients with AIDS. *Am. J. Gastroenterol.* **94**: 3267–3273

Humboldt, A. von. (Hrsg. H. Beck) (1997) *Die Forschungsreise in den Tropen Amerikas*. Wissenschaftliche Verlagsgesellschaft, Studienausgabe Bd. 2, Teilband 3, Darmstadt.

Kuhnt, M., Rimpler, H., Heinrich, M. (1994) Lignans and other compounds from the Mixe Indian medicinal plant *Hyptis verticillata*. *Phytochemistry* **36**: 485–489

Kuhnt, M., Proebstle, A., Rimpler, H., Bauer, R., Heinrich, M. (1995) Biological and pharmacological activities and further constituents of *Hyptis verticillata*. *Planta Med.* **61**: 227–232

Lewis, W. (2000) Ethnopharmacology and the search for new therapeutics. In: Minnis, P. E., Elisens, W. J. (eds) *Biodiversity and Native America*. University of Oklahoma Pr., Norman.

Lu, Q., Ubillas, R. P., Zhou, Y., Dubenko, L. G., Dener, J. M., Litvak, J., Phuan, P. W., Flores, M., Ye, Z., Gerber, R. E., Truong, T., Bierer, D. E. (1999) Synthetic analogues of irlbacholine: a novel antifungal plant metabolite isolated from *Irlbachia alata*. *J. Nat. Prod.* **62**: 824–828

Martin, G. M. (1995) *Ethnobotany*. Chapman and Hall, London

Schultes, R. E., Nemry von Thenen de Jaramillo-Arango, M. J. (1998) *The Journals of Hipólito Ruiz: Spanish Botanist in Peru and Chile 1777–1788*. Timber Press, Portland (OR)

Wasson, G. R. (1957) Seeking the sacred mushrooms. *Life Magazine* **42**: 100–120