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Ethnopharmacology: A Short History of a Multidisciplinary Field of Research

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1.1 Introduction

Ethnopharmacology is an interdisciplinary field of research and as such it is defined by its concepts (its frame of reference) derived from a range of disciplines and the methodologies used. There can be no doubt that it is a fast-developing and thriving discipline. Confusingly, a large number of terms are used to describe research, which often uses relatively similar methods and concepts. However, each of these is distinguished by being placed in a certain tradition of research. Such terms include

- pharmacognosy, first used in 1811 by Johann Adam Schmidt and used very widely to describe the field of medicinal plant and natural product research
- phytotherapy research, derived from the French concept 'phytothérapie' introduced by Henri Leclercq in 1913 and used in various editions of his *Précis de Phytothérapie*
- phytomedicine, a term introduced much more recently and less well established internationally.

In addition there is a wide range of more descriptive terms, including medicinal plant research or natural product research, and there exists a considerable overlap between these and related terms. Phytotherapy research, for example, focuses on plant-based forms of treatment within a science-based medical practice and thus distinguishes what has also been called 'rational phytotherapy' from other more traditional approaches like medical herbalism,

which relies on an empirical appreciation of ‘medicinal herbs’. Phytotherapy research is best described as a *science* embedded in the medical (and pharmaceutical) field (Heinrich, 2013). Contrary to this, at least in a part of the scholarly output, ethnopharmacology incorporates sociocultural concepts and methods.

In the broadest sense ethnopharmacology is based on approaches from the sociocultural sciences and the natural sciences/medicine. As such any historical overview will have to be based on the development of this scientific approach. However, written accounts of using herbal medicines and of the wider medical practice are of course available from many cultures (cf. Leonti, 2011). Importantly, this definition excludes the daily medical practice and the practitioners’ observations associated with it. Such descriptions of medicines, as well as reflections about their usefulness, are very much part of traditions like Ayurveda, Kampo, Unnani, Arabic medicine, TCM, Aztec medicine, European herbalism or any other regionally or culturally defined medical practice. Clearly many of these original descriptions do not survive, and as a consequence today we often only have a few pieces of what was a much larger puzzle.

Compared to medical practice (be it in the context of its usage within biomedicine or one of the regional traditions as exemplified above), in ethnopharmacology there is an added focus on an empirical scientific (e.g. pharmacological, phytochemical, toxicological) evaluation of such therapeutic uses. In very general terms any form of empirical use and ‘medical testing’ of a plant for novel uses may be considered an ethnopharmacological approach. The physician William Withering (1741–1799) systematically explored the medical properties of foxglove (*Digitalis purpurea* L., Scrophulariaceae), which reportedly was used by an English housewife to treat dropsy. He used the orally transmitted knowledge of British herbalism to develop a medicine used by medical doctors. Prior to such studies, herbalism was more of a clinical practice interested in the patient’s welfare and less of a systematic study of the virtues and chemical properties of medicinal plants.

Juerg Gertsch (2009) provided a short and concise definition: ethnopharmacology uses an approach where ‘anecdotal efficacy of medicinal plants is put to test in the laboratory. The ethnopharmacologist tries to understand the pharmacological basis of culturally important plants.’ Similarly, Daniel Moerman (University of Michigan, Dearborn) argued: ‘Essentially ethnopharmacology is the examination of non-Western (not mine) medicinal plant use in terms of Western (my) plant use.’ (Moerman, pers. comm.). Both definitions imply that ethnopharmacology has been a clearly defined field of research certainly since the quest of the ‘unknown other’ through Europeans and their descendants started with the explorations of missionaries, conquerors and explorers. Particularly in the 19th century, many researchers were involved in colonial explorations. This period is considered by Gertsch (2009) to be the golden age of ethnopharmacology. Without doubt these travellers in the broadest sense tried to grasp the essence of what ‘other’ people use and how it can be transformed into a useful commodity.

Ethnopharmacology investigates the pharmacological and toxicological activities of any preparation used by humans that has – in the very broadest sense – some beneficial or toxic or other direct pharmacological effects. This field of research is therefore not an exclusively descriptive field of research (i.e. describing local or traditional uses or medical practices), but about the combined anthropological (in a broad sense) and pharmacological–toxicological study of these preparations. Today, studies describing the use of medicinal and other useful plants are included within ethnopharmacological research, but these are generally conducted with the goal that they lead to an experimental study of some of these botanical drugs (cf. Heinrich *et al.*, 2009). At the same time ethnopharmacology is not focused on the description of medical effects in the content of a treatment (or medical case histories), but

here again incorporates bioscientific research. The definition used here is therefore somewhat more focused and highlights the integration of experimental research on the effects of a local or traditional medicine with sociocultural approaches.

A classic example of ethnopharmacological research that has led to new medicines is the ‘discovery’ of curare. The study of the botanical origin of the arrow poison curare, its physiological (as well as toxic) effects and the compound responsible for these provides a fascinating example of an early ethnopharmacological approach. Curare was used by ‘certain wild tribes in South America for poisoning their arrows’ (von Humboldt, 1997). Many other explorers documented this usage and the poison fascinated both researchers and the wider public. Particularly well known are the detailed descriptions of the process used by Alexander von Humboldt (1769–1859) in 1800 to prepare poisoned arrows in Venezuela. There, von Humboldt met a group of indigenous people who were celebrating their return from an expedition to obtain the raw material for making the poison. Von Humboldt describes the ‘chemical laboratory’ used:

‘He [an old Indian] was the chemist of the community. With him we saw large cooking pots (Siedekessel) made out of clay, to be used for boiling the plant sap; plainer 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.’

(von Humboldt, 1997, p. 88)

And he too faced 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 traveler, while others whose chemical activities are not known [i.e. which are not used locally] are found covered with thousands of flowers and fruit.’

In a later step *Chondrodendron tomentosum* Ruiz et Pavon was identified as being the botanical source of tube curare (named because of the Graminaeous tubes used as storage containers). Other species of the Menispermaceae (*Chondrodendron* spp., *Curarea* spp. and *Abuta* spp.) and species of the Loganiaceae (*Strychnos* spp.) have also been used in the production of curares.

However, this did not provide any understanding of the pharmacological effects of this poison. The French physiologist Claude Bernard (1813–1878) is recognized as being the first to have conducted such research. For example; he provides the following 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 quickly 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, p. 92 [orig. 1864]). ‘One of the facts noted by all those 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, p. 93). He showed that the animals did not show any nervousness and any 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, but without interrupting the innervation, and it is poisoned via an injury of the hind leg, it retains its mobility and the animal does not die from curare poisoning (Bernard, 1966, p. 115). These and subsequent studies allowed a detailed understanding of the pharmacological effects of curare in causing respiratory paralysis. Later on the

main secondary metabolite responsible for this activity was isolated for the first time from *C. tomentosum*, and in 1947 the structure of the bisbenzylisoquinoline alkaloid d-tubocurarine was established. Finally, tubocurarine's structure was established unequivocally using nuclear magnetic resonance (NMR) in the 1970s (Heinrich, 2001, 2010).

This account describes a sequence of research activities, which in their totality clearly may today be labelled ethnopharmacological research. However, at the time it was simply one of the many explorations of the unknown followed by the pharmacological investigation of the botanical drug and later on the identification of the active principles. In essence it was just normal state-of-the-art pharmacological research using new 'leads'. In other words it had no specific claim to be an activity different from mainstream (or normal) pharmacology (in a Thomas S. Kuhnian sense). In fact discoveries in the chemistry and pharmacology of natural products are generally linked to species that are of major importance as a medicine or toxin (Heinrich *et al.*, 2012). However 'Phantastica' (Holmstedt, 1967) and toxins certainly attracted the attention of 19th century researchers (and many before and after them). Terms used to describe this research in the 19th and early 20th century include 'Pharmakoëthnologie' used by Tschirch (1910) in his classic *Handbuch der Pharmakognosie* and 'pharmacoethnologia'. Other terms used include 'ethnobotany' and 'aboriginal botany' (both conceptually much broader terms dealing with useful plants in general). However, all these terms in essence focused on the description of indigenous medicinal plant use and not so much on their pharmacological investigation.

A paradigm shift in pharmacology, drug development and more broadly in the biosciences and medicine resulted from the serendipitous discovery of the first antibiotics derived from the fungus *Penicillium notatum* by Alexander Fleming (1881–1955) in 1928 at St Mary's Hospital (London), which were soon afterwards identified as benzylpenicillin and introduced into clinical practice by a team involving, most importantly, Howard Florey (1898–1968) and Ernst B. Chain (1906–1979). These fungal metabolites changed forever the perception and use of plant-derived metabolites as medicines by both scientists and the lay public. Of similar importance was the advent of synthetic chemistry in the field of pharmacy and its use in the development of new medicines (which started well before the discovery of the penicillins). In 1891 Paul Ehrlich in Germany (1854–1915) for the first time used a synthetic compound as a chemotherapeutic agent – methylene blue in the treatment of mild forms of malaria. Both developments proved that there were diverse and newer avenues to discover new medicines (Heinrich *et al.*, 2012) and revolutionized drug development during and after the Second World War. At the same time there can be no doubt that this resulted in a decline in an interest in the classical approaches as described above.

None of the research activities discussed in the previous paragraphs were labelled 'ethnopharmacology'. This term was – to the best of our knowledge – only formally introduced in 1967 by Efron *et al.*, who used it in the title of a book on hallucinogens: *Ethnopharmacological Search for Psychoactive Drugs* (Efron *et al.*, 1970; Holmstedt, 1967). This is much later than, for example, the term 'ethnobotany', which in 1896 was coined by the American botanist William Harshberger describing the study of human plant use. Both ethnopharmacology and ethnobotany investigate the relationship between humans and plants in all its complexity. However, interestingly, in the early years of its usage the term 'ethnopharmacology' was very much associated with the study of hallucinogenic plants used by indigenous people throughout the world. Along a similar vein of argument, 19th-century research into phantastica and other hallucinogenic substances played a crucial role in developing the field of psychopharmacology/neuropharmacology (cf. Holmstedt, 1967). Bo Holmstedt (1919–2002), who had a keen interest in toxicology, neuropharmacology and neurotoxicology

as well as in analytical aspects of medicinal plant research, has to be credited with being one of the first to develop a perspective on what ethnopharmacology can contribute to science. However, his role and contribution has not been researched in detail from the perspective of the history of science.

In the context of modern ethnopharmacology the focus has moved to understanding the benefits and risks of commonly used local and traditional plants with the goal of contributing to better and safer uses of such resources (e.g. Heinrich, 2006; Heinrich *et al.*, 2009). As in the 19th century it requires an integration of pharmacological (or other natural science) approaches with research on local and traditional uses. After its initial use in the context of hallucinogenic plants the term was only used occasionally until 1979, when the *Journal of Ethnopharmacology* was founded by Laurent Rivier and Jan Bruhn. Here the scope was broadened to ‘a multi-disciplinary area of research concerned with the observation, description, and experimental investigation of indigenous drugs and their biological activity’ (Rivier and Bruhn, 1979).

Today, research which claims to use an ethnopharmacological approach is commonly conducted in the fast-emerging economies of Asia (India, China, where it is often seen as specific research on traditional Chinese medicine (TCM), and South Korea), America south of the Rio Grande (Brazil and Mexico) and Africa (South Africa). The classical research-active countries of the West (USA, UK, Spain, France, Germany and Italy) also have some research-active groups (data based on an analysis of the source items documented in Scopus). The overall research output has also skyrocketed, with a dramatic increase in the number of papers published since the first paper was published in 1967. A detailed content analysis of what is published in the field is beyond the scope of this overview, but if one takes the more than 2000 source items that include the term ‘ethnopharmacology’ in the keywords, abstract or title, the two therapeutic areas most commonly included are the anti-inflammatory and anti-cancer effects of locally and traditionally used plants, which are included in a third and a quarter of these studies, respectively. Gastrointestinal, respiratory and dermatological conditions are addressed in about 10% each of these studies, with veterinary ethnopharmacology accounting for a similar share. All others are of lesser importance and interestingly only about 5% of all studies incorporate central nervous system (CNS) activities (and even fewer studies include hallucinogenic effects (<2%). As one would expect, questions relating to the toxicity of local and traditional medicines are addressed in a quite a few studies (about a quarter). Even though this is a very crude measure, it highlights the main trends and interests in ethnopharmacology and demonstrates how the current focus has moved away from the interests that were the main focus in the 19th century and the 1960s and 1970s. Recent years have also seen an increasing awareness of basic conceptual and methodological standards in the field, an aspect addressed not only by many of the authors cited above but also in a series of critical reviews trying to define good practice as it relates to specific methodological and conceptual foundations of the field (Verspohl, 2002; Cos *et al.*, 2006; Chan *et al.*, 2012; Sheridan *et al.*, 2012; Uzuner *et al.*, 2012; Bennett and Balick, 2014; Rivera *et al.*, 2014).

This brief historical sketch identifies some major developments of a field of research that is not a clearly defined discipline, a point highlighted by Nina Etkin and Elaine Elisabetsky (2005, p. 23):

‘A primary difficulty in defining and projecting a future for ethnopharmacology is to identify the objectives of a largely virtual field whose self-identified membership represents, in addition to commercial entities, a diverse suite of academic and applied disciplines.’

(Etkin and Elisabetsky, 2005).

In their analysis they identify key areas of relevance in the future, but most importantly they see the need to build theoretical capacity in ethnopharmacology (Etkin and Elisabetsky, 2005, p. 26). This is one foundation for developing more context-driven and critical approaches in ethnopharmacology (Etkin and Elisabetsky, 2005). As this overview shows, the historical development of the field was very much driven by interdisciplinary collaborations generally led by natural scientists. A more detailed historical analysis will provide a basis to build up the ‘theoretical capacity’ the Etkin and Elisabetsky call for.

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The history of the field has been an ongoing interest of mine and the ideas presented here have developed over many years. Some were discussed in more detail previously (especially in Heinrich, 2014; Heinrich *et al.*, 2012) and this work presents a new synthesis of these concepts. The history of ethnopharmacology has received relatively little attention and a more detailed study of the developments since the mid-1960s would certainly be highly desirable. I am grateful to all the colleagues who responded to my query about the field’s history, most importantly Lars Bohlin (Sweden), Jan G. Bruhn (Sweden), Elaine Elisabetsky (Brazil), Anna Jäger (Denmark), Marco Leonti (Italy), J. David Phillipson (UK), Laurent Rivier (Switzerland), Dan E. Moerman (Michigan, USA), Gunnar Samuelsson (Sweden) Peter A.G.M. de Smet (the Netherlands) and Caroline Weckerle (Switzerland).

References

- Bennett, B.C. and Balick, M.J. (2014) Does the name really matter? The importance of botanical nomenclature and plant taxonomy in biomedical research. *Journal of Ethnopharmacology*, **152**, 387–392.
- Bernard, C. (1966) Physiologische Untersuchungen über einige amerikanische Gifte. Das Curare, in *Ausgewählte physiologische Schriften* (eds C. Bernard and N. Mani), Huber Verlag, Bern. [French original. 1864], pp. 84–133.
- Chan, K., Shaw, D., Simmonds, M.S.J., *et al.* (2012). Good practice in reviewing and publishing studies on herbal medicine, with special emphasis on traditional Chinese medicine and Chinese materia medica. *Journal of Ethnopharmacology*, **140**, 469–475.
- Cos, P., Vlietinck, A.J., Berghe, D.V. and Maes, L. (2006) Anti-infective potential of natural products: How to develop a stronger in vitro ‘proof-of-concept. *Journal of Ethnopharmacology*, **106**, 290–302.
- Efron, D., Holmstedt, B. and Kline, N.L. (1970) *Ethnopharmacologic Search for Psychoactive Drugs*, Government Printing Office, Public Health Service Publications No. 1645 (original 1967), Reprint, Washington, D.C.
- Etkin, N.L. and Elisabetsky, E. (2005) Seeking a transdisciplinary and culturally germane science: The future of ethnopharmacology. *Journal of Ethnopharmacology*, **100** (1–2), 23–26.
- Gertsch, J. (2009) How scientific is the science in ethnopharmacology? Historical perspectives and epistemological problems. *Journal of Ethnopharmacology*, **122**, 177–183.
- Heinrich, M. (2001) *Ethnobotanik und Ethnopharmazie*, Eine Einführung, Stuttgart, Wissenschaftliche Verlagsgesellschaft.
- Heinrich, M. (2006) La Etnofarmacología – ‘quo vadis? *BLACPMA* [Boletín Latinoamericana y del Caribe de plantas medicinales y aromáticas, ISSN 0717 7917], **5** (1), 7.
- Heinrich, M. (2010) Ethnopharmacology and drug development, in *Comprehensive Natural Products II, Chemistry and Biology*, Vol. **3** (eds L. Mander and H.-W. Lui), Elsevier, Oxford, pp. 351–381.
- Heinrich, M. (2013) Phytotherapy, in *Encyclopedia Britannica*, <http://www.britannica.com/EBchecked/topic/1936369/phytotherapy>.

- Heinrich, M. (2014) Ethnopharmacology – quo vadis? Challenges for the future. *Revista Brasileira de Farmacognosia* **24**, 99–102.
- Heinrich, M., Edwards, S., Moerman, D.E. and Leonti, M. (2009) Ethnopharmacological Field Studies: A Critical Assessment of their Conceptual Basis and Methods. *Journal of Ethnopharmacology*, **124**, 1–17.
- Heinrich, M., Barnes, J., Gibbons, S. and Williamson, E.M. (2012) *Fundamentals of Pharmacognosy and Phytotherapy*, 2nd edn, Churchill Livingstone (Elsevier), Edinburgh & London.
- Holmstedt, B. (1967) An overview of ethnopharmacology. Historical survey. *Psychopharmacology Bulletin*, **4** (3), 2–3.
- Leonti, M. (2011) The future is written: impact of scripts on the cognition, selection, knowledge and transmission of medicinal plant use and its implications for ethnobotany and ethnopharmacology. *Journal of Ethnopharmacology*, **134** (3), 542–555.
- Rivera, D., Allkin, R., Obón, C., *et al.* (2014) What is in a name? The need for accurate scientific nomenclature for plants. *Journal of Ethnopharmacology*, **152**, 393–402.
- Rivier, L. and Bruhn, J.G. (1979) *Editorial*. *Journal of Ethnopharmacology*, **1** (1), 1.
- Sheridan, H., Krenn, L., Jiang, R., *et al.* (2012) The potential of metabolic fingerprinting as a tool for the modernisation of TCM preparations. *Journal of Ethnopharmacology*, **140**, 482–491.
- Tschirch, A. (1910) *Handbuch der Pharmakognosie*. 2. Abteilung (Die Hilfswissenschaften der Pharmakognosie), 1. Auflage, C.H. Tachnitz, Leipzig.
- Uzuner, H., Bauer, R., Fan, T.-P., *et al.* (2012) Traditional Chinese medicine research in the post-genomic era: Good practice, priorities, challenges and opportunities. *Journal of Ethnopharmacology*, **140** (3), 458–468.
- Verspohl, E.J. (2002) Recommended testing in diabetes research. *Planta Medica*, **68** (7), 581–590.
- von Humboldt, A. (1997) *Die Forschungsreise in den Tropen Amerikas* (Hrsg. H. Beck), Wissenschaftliche Buchgesellschaft, Darmstadt.

