

Commentary

A role for physicians in ethnopharmacology and drug discovery

Mohsin Raza*

Department of Physiology, School of Medical Sciences, Tarbiat Modares University, P.O. Box 14115-111, Tehran, Iran

Received 27 October 2005; received in revised form 8 January 2006; accepted 10 January 2006

Available online 3 February 2006

Abstract

Ethnopharmacology investigations classically involved traditional healers, botanists, anthropologists, chemists and pharmacologists. The role of some groups of researchers but not of physician has been highlighted and well defined in ethnopharmacological investigations. Historical data shows that discovery of several important modern drugs of herbal origin owe to the medical knowledge and clinical expertise of physicians. Current trends indicate negligible role of physicians in ethnopharmacological studies. Rising cost of modern drug development is attributed to the lack of classical ethnopharmacological approach. Physicians can play multiple roles in the ethnopharmacological studies to facilitate drug discovery as well as to rescue authentic traditional knowledge of use of medicinal plants. These include: (1) Ethnopharmacological field work which involves interviewing healers, interpreting traditional terminologies into their modern counterparts, examining patients consuming herbal remedies and identifying the disease for which an herbal remedy is used. (2) Interpretation of signs and symptoms mentioned in ancient texts and suggesting proper use of old traditional remedies in the light of modern medicine. (3) Clinical studies on herbs and their interaction with modern medicines. (4) Advising pharmacologists to carryout laboratory studies on herbs observed during field studies. (5) Work in collaboration with local healers to strengthen traditional system of medicine in a community. In conclusion, physician's involvement in ethnopharmacological studies will lead to more reliable information on traditional use of medicinal plants both from field and ancient texts, more focused and cheaper natural product based drug discovery, as well as bridge the gap between traditional and modern medicine.

© 2006 Elsevier Ireland Ltd. All rights reserved.

Keywords: Physician; Ethnopharmacology; Traditional medicine; Drug discovery

1. Introduction

Ethnopharmacology provides an opportunity for both multidisciplinary and interdisciplinary scientific collaboration between the investigators of botany, pharmacology and toxicology, chemistry, anthropology and sociology (Schultes, 1962; Malone, 1983; Sandberg, 1987; Verpoorte, 1989; Etkin, 1993). Ethnopharmacologic exploration, involving both field visits, as well as experimental research has lead in past to highly valuable information about medicinal plants used in different cultures and many were developed into drugs (Bruhn and Holmstedt, 1981; Holmstedt, 1991; Fabricant and Farnsworth, 2001).

Physicians by their training are exposed to several disciplines of science relevant to ethnopharmacological investigations. Indeed, the need for physicians as an active member of ethnopharmacological team has been felt in the past and fail-

ures and limitations have been attributed due to the lack of their participation (Weniger, 1991; Anonymous, 1993; Farnsworth, 1994; Lozoya, 1994; Cordell and Colvard, 2005). However, no clear role or scope of activities is defined for physicians. This article discusses the role physicians could play in various aspects of ethnopharmacological research and discovery of drugs based on traditional knowledge.

2. Historical background

Enormous ethnopharmacological research was carried out by physicians with expertise or interest in chemistry, pharmacology, botany or anthropology during the early period of medicinal plant research 250 years ago. The classic example is of Dr. William Withering, who in 1775 discovered the use of foxglove in the treatment of 'dropsy' (i.e. edema) due to cardiac ailment (now known as congestive heart failure). The plant was used for the cure of 'dropsy' in the form of aqueous tea of 20 or more herbs by an old woman in Shropshire. Withering combined his medical expertise and knowledge of botany and discovered that

* Tel.: +98 21 88011001x3577; fax: +98 21 88013030.

E-mail address: mohsinrazahej@yahoo.com.

Table 1
Selected physicians and their contributions in ethnopharmacological investigations

Willem Pies (1611–1678)	Medicinal uses of <i>Pilocarpus jaborandi</i>
William Withering (1741–1799)	Use of Foxglove in “Dropsy” (congestive heart failure)
Robert Christison (1797–1882)	Toxicology of <i>Physostigma venenosum</i>
John Hutton Balfour (1808–1884)	Description of <i>Physostigma venenosum</i>
Claude Bernard (1813–1878)	Pharmacological investigation of curare
Paolo Mantegazza (1831–1910)	Medicinal uses of coca
John Kirk (1832–1922)	Effect of African arrow poison (<i>Strophanthus</i> sp.) on CVS
Symphonio Olympio Cezar Coutinho (1832–1887)	Investigation of medicinal uses and introduction of <i>Pilocarpus jaborandi</i> in medical practice
Douglas Argyll Robertson (1837–1909)	Introduction of <i>Physostigma venenosum</i> in ophthalmic medicine
Thomas Richard Fraser (1841–1920)	Pharmacology of <i>Physostigma venenosum</i>
Nagai Nagayoshi (1844–1929)	Chemistry and pharmacology of ephedrine
John Raleigh Briggs (1851–1907)	Investigation of peyote
Arthur Heffter (1860–1925)	Chemistry and pharmacology of peyote alkaloids
Thomas Moreno Y Maiz (1868) ^a	Pharmacological investigation of cocaine

For more details see: Aronson (1987), Holmstedt (1972, 1991), Holmstedt et al. (1979), Holmstedt and Fredga (1981) and Heinrich and Gibbons (2001).

^a Year of completion of thesis.

foxglove was the active ingredient, and that only dropsy related to heart ailment was curable (Aronson, 1987).

Several investigators (Table 1) who played leading role in the discovery and/or use of physostigmine, cocaine, ephedrine, emetine, pilocarpine, strychnine, etc. from traditional sources were physicians (Holmstedt, 1972, 1991; Holmstedt et al., 1979; Holmstedt and Fredga, 1981; Heinrich and Gibbons, 2001). These physicians while working with experts from other disciplines performed several roles, from field studies during explorations, to working both as botanists and anthropologists to conducting lab experiments as chemists and pharmacologists.

With the advancement of synthetic approaches in recent years, there has been a general lack of classical ethnopharmacological approaches in medicinal plant research both as a source of lead compounds for new drugs as well as in published research (Etkin, 2001; Cordell and Colvard, 2005). For several years there has also been reduced collaboration between different disciplines and clinicians that has contributed to a decline in the number of new drugs (Farnsworth et al., 1985; Tyler, 1986; Anonymous, 2002). Due to public reliance on traditional therapies and use of herbal products, the curricula in some countries have been recently modified (Giordano et al., 2002) and consequently physicians are becoming more familiar with concepts and practices of traditional medicine systems. In the future they may serve to integrate and ‘translate’ traditional knowledge into modern medicine.

3. Areas of ethnopharmacological studies where a physician could contribute

3.1. Ethnopharmacological field work

Field observations of traditional therapies are of pivotal importance for investigating their pharmacological effects in humans and isolating their active principles (Holmstedt and Bruhn, 1982). A physician can carry out field observation of pharmacological effects of traditional therapies in humans with precision (Holmstedt and Bruhn, 1982), which in turn could guide a pharmacologist working in a lab.

3.1.1. Interviewing traditional healers and interpretation of traditional concepts

Interviewing traditional healers for accurate information about herbal recipes, their component herbs, their medicinal and other uses constitutes an important activity in ethnopharmacological field investigation (Lipp, 1989). A major problem has been the translation of indigenous diseases or concepts of illness into their modern counterparts and vice versa (Cox, 1994). Description of a disease and its diagnostic criteria, signs, symptoms, treatment, dosage schedule and its progress (Table 2) are all to be noted by the field worker (Lipp, 1989). Commonly, confusion in data interpretation occurs when information about an illness is obtained in the field by a non-physician, such as an ethnobotanist, biologist, anthropologist or even a trained interviewer (Lewis and Elvin-Lewis, 1994; Lozoya, 1994). For example, a mere description of fever, pain at any site, tremor, skin lesion, fainting, or edema can be interpreted as various illnesses. (I have personally experienced how difficult it is to interpret heard or written information from a non-physician field worker due to crucial missing data which could point to a specific illness.) Up to 35% of diseases remain undiagnosed when a traditional healer is interviewed by a non-physician worker in the field (Cox, 1994) and essential information is lost only because physicians were not involved.

New medical discoveries and advancement of associated technology is further widening the gap between traditional concepts of diseases, their treatment by healers and the present day physicians. A physician interested in ethnopharmacology could fill this gap and offer modern explanation of old concepts of healing. However, all this requires a modest and collaborative attitude of physicians with healers, botanists and anthropologists which the key to successful acquisition of the information (Lozoya, 1994).

For various reasons, it may be difficult to get information on medicinal uses of plants from healers which could later be used in biomedical research (Malone, 1983). Direct observations by physician (vide Table 2 for summary) may reduce the need of cross-checking information obtained from one healer or using different interviewing techniques.

Table 2

Activities that a physician could perform in ethnopharmacological field work (adopted from Lipp (1989))

Physician's role in ethnopharmacology field work

1. General idea about diseases prevalent in a particular area by direct observation of geographical features of the area and landscape, people, living conditions, food, sanitation, etc. and informal interview of translator, local residents or contacts
2. Interviewing the healer and watching her/him treating an illness
3. Interpretation of information obtained from interview and visual observation
 - a. Traditional concepts of disease terms
 - b. Diagnostic criteria used by healer
 - c. Etiology of illness
 - d. Signs and symptoms of illness
 - e. Treatment prescribed, its route of administration, dosage, mode of effectiveness and total duration with different phases
 - f. Dietary, sexual or other restrictions
 - g. Side-effects or contraindications
 - h. Association with any rituals
 - i. Social restrictions related to age, sex, class, etc.
 - j. Whether treatment is prohibited in certain individuals and reason for it
 - k. Beliefs or myths or other views associated with disease or its specific treatment with the plant
4. Examination of patient and diagnosis of illness
 - a. History taking
 - b. Physical Examination and routine test
 - c. Diagnosis of illness
 - d. Follow up
 - e. Result/s of treatment whether effective or otherwise
5. Analysis and verification of 'heard' verses 'seen' information collected from healer, other team members and personal observation
6. Recording information (by means of photographs or video camera) regarding signs, symptoms of illness, administration of an herbal treatment and effects of treatment

A physician can comprehend the nature of illness and effectiveness of its treatment, even if the information is translated from another language. While opening the conversation with a healer, the physician could ask about common health problems in the area and have an idea as to the type of diseases or symptoms prevalent before actually talking about a specific condition. He can interpret physical signs and symptoms described by the healer that point either to a systemic illness or a functional one. A physician, by asking few relevant questions, can form an opinion about the nature of disease and effectiveness of the herb used to treat it.

3.1.2. Medical history, examination and diagnosis of patients treated by healers

If allowed to take a medical history and examine a patient being treated by the healer, a physician, by asking few key questions, and with the help of simple paraphernalia (such as stethoscope, blood pressure apparatus, otoscope, ophthalmoscope, thermometer and the like that can be easily carried in a brief case) can make a diagnosis. Unlike in the remote past, several 'dipstick' tests are now available to facilitate rapid diagnosis. This is particularly important as many traditional healers are not accustomed to diagnosing disorders where detection of sign and symptoms requires an apparatus or test. An example is 'frightening syndrome' popular in the South American Jivaro

community, which is characterized by shortness of breath. A physician by simple examination and few questions could easily determine if this is due to respiratory, cardiac or psychological causes (Lewis and Elvin-Lewis, 1994). He can also differentially diagnose the disease or pathological state if the accurate diagnosis is not possible, limiting it to few specific diseases. Improvement in the patient's condition allows her/him to give a reasonable explanation of the site of action of the herb and also the nature of illness. For example, if a definite viral illness is cured by a herb, this indicates possible presence of antiviral substances in it or, if a patient had disease symptoms due to hypertension, a reduction in blood pressure or diuresis point to a probable site of action or exclude others.

3.2. Systematic study and scrutiny of ancient traditional literature

Many signs and symptoms described in ancient texts apply very well to modern day's clinical medicine. Advancement of science and technology has added new terminologies and microscopic depth to human observation, particularly in relation to diagnosis of illness. However, visual observation by the naked eyes has not changed. Rather, ancient healers and traditional medicine systems relied more on direct observation of disease symptoms and signs. These were observed in more depth and detail, without any support from instruments or equipment at that time and relying only on interpretation of information obtained through five senses. In addition, as opposed to modern medicine which relies more on laboratory investigations, in past, there was emphasis on a patient's medical history. Thus, going through ancient texts, one finds more graphic description of diseases and conditions which makes the task of a researching physician much easier to predict diagnoses or at least broadly categorize a condition for which herb/s or recipes mentioned in ancient texts were used.

An enormous amount of ancient literature from Greek and Latin medical texts, pre-modern Western medicine, Chinese medicine, Ayurveda and Unani medicine needs to re-examined in the light of modern medical knowledge (Holland, 1994; Tunon and Bruhn, 1995; Buenz et al., 2004). It could be very cost effective if a few plants from ancient medical texts are chosen for targeted pharmacological study. Physicians by carefully scrutinizing ancient literature for the signs and symptoms for which a particular herb or herbs were used in the past in one or more systems of medicine, can actually diagnose or at least establish a probable diagnosis in many cases. Several disorders present as syndromes that have three or more signs and symptoms in a patient which could be easier to recognize if a physician can interpret the terms used in old texts in the light of modern medicine. A recent example is the description of clinical signs of a condition known as *Kampavata* (*Kampa* is tremor and *vata* is responsible for all movements and sensations including motor actions) in ancient Ayurveda text which resembles Parkinson's disease (Manyam and Sanchez-Ramos, 1999).

Information related to ethnomedical knowledge and scientific research on medicinal plants is now available in the form of databases. However, such databases have their own limi-

tations. For example, NAPALERT (Farnsworth, 1994) 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. There are 1299 records of uses for reducing ‘fever’, 1879 for ‘inflammation’ and 733 for ‘liver’ disorders. However, the database only provides a single word or phrase for the use of medicinal plants and no description or background information is available (Verpoorte, 1989; Farnsworth, 1994). Analyses of such database with accurate precision by a physician could lead to reasonable and specific prediction and link specific plants to certain disorders. For example, if a plant is reported to be used for fever, headache and also for nasal catarrh and skin disorders, the possibility of its use as anti-viral or anti allergic could be concluded.

Several medical disorders present with varied signs and symptoms due to cross-cultural variations in the expression of illness, but are still linked by a common pathology of biological system (Kleinman, 1987; de Haes and Olschewski, 1998). This is especially true for the disorders that have psychological symptoms specific to a culture (Janca and Isaac, 1997). For example, signs and symptoms resulting from addiction, depressive illness, or somatic anxiety have common elements in different cultures (Ulusahin et al., 1994; Piccinelli and Simon, 1997; Yardley et al., 1999). Thus, description of such disorders in ancient literatures may vary considerably. However, since all traditional systems approach the disease in a holistic manner (Vogel, 1991) and have many similarities, their description has some common signs which can be interpreted by an experienced physician.

Recent advances in technology to rapidly scan and digitize the ancient herbal texts can involve interested physicians more easily. In addition, development of software and electronic resources to better interpret old linguistic, botanical and medical terminologies can further assist physicians to overcome language barriers, saving a lot of time and manpower (Buenz et al., 2004).

3.3. *Clinical observations on herbs and herb-drug interactions*

A significant number of patients simultaneously use herbal and modern drugs in industrialized countries and underdeveloped world. In addition, several traditional communities have started incorporating modern medicine in their treatment regimen. One such example is of Hausa-Fulani community of Nigeria where this trend has been clearly documented (Etkin et al., 1990). These situations create an opportunity for physicians to clinically evaluate the benefits and side effects of herbal drugs in a particular illness, discover new indications for traditional herbs, as well as note herbal-drug interactions.

Introduction of new single compounds drugs adds to the therapeutic armamentarium of physician, leading to new herbal-drug interactions, and possible contraindications. Physicians practicing in well-equipped hospitals or clinics or a family physician in a community have access to patients consuming both herbals and modern drugs. Thus, a physician in this situation will be able to clinically observe the benefits or side effects of both herbals and drugs introduced recently and when used in combination.

Specialist physicians could perform more specific evaluation of patients consuming both herbals and modern drugs.

3.4. *Advice to pharmacologist/s for laboratory investigation of herb*

Information provided by a physician from a field visit or clinical observation on the effectiveness of a herb to a well-trained pharmacologist can lead to proper selection of in vivo or in vitro models of various diseases for laboratory research. A physician can properly guide a pharmacologist in this regard and suggest a primary action of an herbal recipe or of a particular plant in humans that he observed during his field work. For example, a plant that was found to be curative for a bacterial infection will help a researcher to select appropriate antimicrobial tests. A plant effective in seizure or epilepsy will guide one to explore its effects in relevant animal models. Thus, physicians can play a very important role in enhancing drug discovery. This could minimize time, save resources and speed up the process for discovery of compound/s responsible for a specific pharmacologic activity observed directly in humans.

3.5. *Strengthening the existing traditional medicine system in a community*

In communities where the tools and trades of traditional medicine and the use of medicinal plants are kept as secrets, traditional healers often have concerns about the violation of intellectual property rights, patenting and profiteering by local or foreign drug companies. Local physicians in cooperation with the elders of the community or traditional healers could work in collaboration and actually strengthen the prevalent culture of use of medicinal plants. In this setting, a physician can guide the healers on use of herbs or recipes in the light of modern research, apprise them of toxicity, precautions or new uses and ‘update’ their traditional or oral herbal pharmacopoeia. For example, a physician can advise a healer that certain medicinal plants that lower the platelet aggregation can make blood ‘thin’ and should not be given to the patients or their doses be reduced if they are already taking aspirin. However, for working closely with the traditional healer, a physician has to first build trust and treat her/him as his colleague and friend. The knowledge and experience of a traditional healer has to be considered valuable as it comes from thousands of years of trial and error and forms the basis of modern medicine and therapeutics.

4. Conclusion

Globalization and advancement in technology is expected to promote plant derived medicinal preparations and traditional medicine (Verpoorte, 2005). Physicians could ‘come back’ and like their predecessors, use their expertise of basic sciences and clinical knowledge to contribute in ethnopharmacological studies and drug discovery. Those associated with academia or industries should perform field studies with ethnobotanists and get authentic and specific information on the use of medici-

nal plants. Their involvement could lead to a highly targeted approach in discovery of drugs from industry and significantly reduce the cost of drug development. A systematic study of ancient texts by physicians could lead to better interpretation of the medicinal uses of plants in different cultures. Physicians practicing medicine in a community where the use of medicinal plants is common could contribute by closely working with the local healers. They could discuss new discoveries about medicinal plants, new drugs and herbal-drug interactions with the healers and publish their observations. However, this will require a change of approach on the part of physicians towards traditional medicine and adopting proper attitude towards the traditional healers. Several medical disorders are awaiting therapeutic cure and the pharmaceutical industry has yet to come up with effective drug treatments. Participation of physicians in ethnopharmacological studies will ultimately benefit patients with incurable diseases and also fulfill the main goal of the field of ethnopharmacology.

Acknowledgements

I thank Dr. Nina L. Etkin for her valuable comments on an earlier version of the manuscript and Dr. K.M. Hedayat for reviewing the English language.

References

- Anonymous, 1993. Research Guidelines for Evaluating the Safety and Efficacy of Herbal Medicines. WHO, Regional Office for the Western Pacific, Manila.
- Anonymous, 2002. Towards more effective drug discovery. *Nature* 415, 1.
- Aronson, J.K., 1987. The discovery of the foxglove as a therapeutic agent. *Chemistry in Britain* 23, 33–36.
- Bruhn, J.G., Holmstedt, B., 1981. Ethnopharmacology: objectives, principles and perspectives. In: Beal, J.L., Reinhard, E. (Eds.), *Natural Products as Medicinal Agents*. Hippocrates-Verlag, Stuttgart, pp. 405–430.
- Buenz, E.J., Schnepfle, D.J., Bauer, B.A., Elkin, P.L., Riddle, J.M., Motley, T.J., 2004. Techniques: bioprospecting historical herbal texts by hunting for new leads in old tomes. *Trends in Pharmacological Sciences* 25, 494–498.
- Cordell, G.A., Colvard, M.D., 2005. Some thoughts on the future of ethnopharmacology. *Journal of Ethnopharmacology* 100, 5–14.
- Cox, P.A., 1994. The ethnobotanical approach to drug discovery: strengths and limitations. *Ciba Foundation Symposium* 185, 25–36.
- de Haes, J.C., Olschewski, M., 1998. Quality of life assessment in a cross-cultural context: use of the Rotterdam Symptom Checklist in a multinational randomised trial comparing CMF and Zoladex (Goserlin) treatment in early breast cancer. *Annals of Oncology* 9, 745–750.
- Etkin, N.L., 1993. Anthropological methods in ethnopharmacology. *Journal of Ethnopharmacology* 38, 93–104.
- Etkin, N.L., 2001. Perspectives in ethnopharmacology: forging a closer link between bioscience and traditional empirical knowledge. *Journal of Ethnopharmacology* 76, 177–182.
- Etkin, N.L., Ross, P.J., Muazzamu, I., 1990. The indigenization of pharmaceuticals: therapeutic transitions in rural Hausaland. *Social Sciences and Medicine* 30, 919–928.
- Fabricant, D.S., Farnsworth, N.R., 2001. The value of plants used in traditional medicine for drug discovery. *Environment and Health Perspectives* 109 (Suppl. 1), 69–75.
- Farnsworth, N.R., 1994. Ethnopharmacology and drug development. *Ciba Foundation Symposium* 185, 42–51.
- Farnsworth, N.R., Akerele, O., Bingel, A.S., Soejarto, D.D., Guo, Z., 1985. Medicinal plants in therapy. *Bulletin of the World Health Organisation* 63, 965–981.
- Giordano, J., Boatwright, D., Stapleton, S., Huff, L., 2002. Blending the boundaries: steps toward an integration of complementary and alternative medicine into mainstream practice. *Journal of Alternative and Complementary Medicine* 8, 897–906.
- Heinrich, M., Gibbons, S., 2001. Ethnopharmacology in drug discovery: an analysis of its role and potential contribution. *Journal of Pharmacy and Pharmacology* 53, 425–432.
- Holland, B.K., 1994. Prospecting for drugs in ancient texts. *Nature* 369, 702.
- Holmstedt, B., 1972. The Ordeal bean of Calabar, The pageant of *Physostigma venenosum* in medicine. In: Swain, T. (Ed.), *Plants in the Development of Modern Medicine*. Harvard University Press, Cambridge, MA, pp. 303–360.
- Holmstedt, B., 1991. Historical perspective and future of ethnopharmacology. *Journal of Ethnopharmacology* 32, 7–24.
- Holmstedt, B., Bruhn, J., 1982. Is there a place for ethnopharmacology in our time? *Trends in Pharmacological Sciences* 3, 181–183.
- Holmstedt, B., Fredga, A., 1981. Sundry episodes in the history of coca and cocaine. *Journal of Ethnopharmacology* 3, 113–147.
- Holmstedt, B., Wassen, S.H., Schultes, R.E., 1979. Jaborandi: an interdisciplinary appraisal. *Journal of Ethnopharmacology* 1, 3–21.
- Janca, A., Isaac, M., 1997. ICD-10 and DSM-IV symptoms of somatoform disorders in different cultures. *The Keio Journal of Medicine* 46, 128–131.
- Kleinman, A., 1987. Anthropology and psychiatry. The role of culture in cross-cultural research on illness. *The British Journal of Psychiatry* 151, 447–454.
- Lewis, W.H., Elvin-Lewis, M.P., 1994. Basic, quantitative and experimental research phases of future ethnobotany with reference to the medicinal plants of South America. *Ciba Foundation Symposium* 185, 60–72.
- Lipp, F.J., 1989. Methods for ethnopharmacological field work. *Journal of Ethnopharmacology* 25, 139–150.
- Lozoya, X., 1994. Two decades of Mexican ethnobotany and research in plant drugs. *Ciba Foundation Symposium* 185, 130–140.
- Malone, M.H., 1983. The pharmacological evaluation of natural products—general and specific approaches to screening ethnopharmaceuticals. *Journal of Ethnopharmacology* 8, 127–147.
- Manyam, B.V., Sanchez-Ramos, J.R., 1999. Traditional and complementary therapies in Parkinson's disease. *Advances in Neurology* 80, 565–574.
- Piccinelli, M., Simon, G., 1997. Gender and cross-cultural differences in somatic symptoms associated with emotional distress. An international study in primary care. *Psychologic Medicine* 27, 433–444.
- Sandberg, F., 1987. The integrated natural products research in the development of plant derived pharmaceuticals. *Fitoterapia* 58, 309–313.
- Schultes, R.E., 1962. The role of the ethnobotanist in the search for new medicinal plants. *Lloydia* 25, 257–266.
- Tunon, H., Bruhn, J.G., 1995. Drugs in ancient texts. *Nature* 376, 546.
- Tyler, V.E., 1986. Plant drugs in the twenty-first century. *Economic Botany* 40, 279–288.
- Ulusahin, A., Basoglu, M., Paykel, E.S., 1994. A cross-cultural comparative study of depressive symptoms in British and Turkish clinical samples. *Social Psychiatry and Psychiatric Epidemiology* 29, 31–39.
- Verpoorte, R., 1989. Some phytochemical aspects of medicinal plant research. *Journal of Ethnopharmacology* 25, 43–59.
- Verpoorte, R., 2005. Perspectives of ethnopharmacology. *Journal of Ethnopharmacology* 100, 1–2.
- Vogel, H.G., 1991. Similarities between various systems of traditional medicine. Considerations for the future of ethnopharmacology. *Journal of Ethnopharmacology* 35, 179–190.
- Weniger, B., 1991. Interest and limitation of a global ethnopharmacological survey. *Journal of Ethnopharmacology* 32, 37–41.
- Yardley, L., Medina, S.M., Jurado, C.S., Morales, T.P., Martinez, R.A., Villegas, H.E., 1999. Relationship between physical and psychosocial dysfunction in Mexican patients with vertigo: a cross-cultural validation of the vertigo symptom scale. *Journal of Psychosomatic Research* 46, 63–74.