Commentary

Ethnopharmacology, sustainable development and cooperation: The importance of gathering clinical data during field surveys

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A R T I C L E  I N F O

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This commentary aims to focus, among the “multiple roles of data generated in ethnopharmacological field studies” (Heinrich et al., 2009, p. 1), on the systematic collection of clinical data. Even if this issue may somewhat resemble what has long been said (Martin, 1996), recent experiences with clinical assessment of the effectiveness of medicinal plants may shed some new light. This commentary is also a call for better cooperation between ethnopharmacologists, physicians, traditional healers and the populations concerned: that is the condition for ethnopharmacological work to be useful at the level of local populations and, if included in a development project, for the design of sound health policies (Elisabetsky and Nunes, 1990).

A common research process is to go from field survey to phytochemistry, with the idea that the research can contribute to economic development if a new drug can eventually be found and marketed while appropriate and ethical relationships are maintained with the owners of the traditional knowledge (ten Kate and Laird, 2002). However, the road to development of a new drug is excessively long, even in the rare cases where it is successful (e.g. Hoodia gordonii: see van Heerden, 2008). In the example of a phytochemical and pharmacological review on Garcinia mangostana, the authors concluded that “a serious weakness in our knowledge is the lack of clinical data and it is not yet clear to what extent the findings about pharmacological activities are of potential clinical relevance” (Obolskiy et al., 2009, p. 1047).

In the meantime, local traditional treatments continue to be used. In our experience, local users are always interested in the results of ethnopharmacology research and insist on the systematic organisation of restitution sessions. They are interested in the analysis of clinical data collected during the surveys, because it provides indices of treatment quality and has implications for local sustainable development. At the village level, it may improve population health; at the district and national level, it can stimulate the local economy and create a corpus of knowledge that helps patients to make their choice among the very numerous traditional medicines. One example can be found in Mali, where a set of “Médicaments traditionnels améliorés” (improved traditional treatments) of guaranteed quality are produced by the “Département de Médecine Traditionnelle” and researchers from Bamako University (Sanogo, 2002). These products are grown, dried and sold in the country.

1. Where there are no modern drugs . . .

Access to good quality traditional medicine is always important, especially where and when it is the only easily accessible treatment. It is particularly so wherever logistical, political or economic problems make access to modern medicine scarce and difficult.

In many cases there are no modern drugs of guaranteed quality, but mountains of tablets are for sale on the market or by travelling sellers. An estimated one out of every four packets of medicine sold in street markets in developing countries may well be counterfeit (Burns, 2006). With traditional medicines, users and relatives are in principle protected against the risk of fake drugs when they correctly identify the plants and prepare their own treatments. There are reasons to believe that most traditional medicine is actually not a professional activity, but a local/self-medication process conducted by lay people, members of the family or neighbours (Diallo et al., 2006). However cases of forgery and fraud abound in the market of commercial herbal drugs. For example a cheap plant can be sold in place of a more expensive one or a natural product adulterated with industrial drugs (Bogusz et al., 2006). It is urgent to develop simple and affordable quality control methods adapted to herbal drugs. The World Health Organisation reference (WHO, 1998), freely available online, discusses a few specific herbal preparations but does not directly address the detection of adulteration.
An open access and peer-reviewed information source on this subject would be a significant step towards better quality control of commercially supplied traditional drugs.

Ethnopharmacology can contribute to the exploration of phytotherapeutic resources for use in local contexts and countries of origin (Etkin and Elisabetsky, 2005) and can provide data that will help (along with other research methods that will be discussed below) to answer questions such as: “Among all the different local treatments for a given ailment, which is the most effective?” This question, our experience in the field shows, interests traditional healers and indeed everyone concerned with healing others, i.e. virtually every adult in a community.

To provide locally useful scientific answers, many difficulties must be overcome. Some have been extensively discussed in ethnopharmacological textbooks: understanding local health concepts and disease classifications, identifying ingredients and preparations, addressing ethical matters and, in the case of market opportunities, benefit sharing (Chadwick and Marsh, 1990; Cunningham, 1993; Elisabetsky and Etkin, 2005; Etkin and Tan, 1994; ten Kate and Laird, 2002). Some difficulties are specific to clinical studies and can be overcome by collaboration between ethnopharmacologists, physicians and practitioners of traditional medicine.

Health specialists of different cultures can often find a common language and create a good working relationship as awareness of the similarities between them grows. With different diagnostic and therapeutic tools, they do the same job. Disease identification across two medical systems will be easier with the following favourable conditions: clearly defined symptoms, well-defined clinical assessment of the patient progress, and knowledge of the “natural history” (i.e. progress without treatment) of the disease.

2. . . . there could be a safe and effective local treatment

Is it conceivable that some traditional medicines might be as effective – or even more so – than our modern treatments? Interestingly enough, paradigm shifts in current pharmacodynamics now elicit new subsidies for the “phytotherapy rationale” (Elisabetsky, 2007). First is the current trend of moving away from the unlikely notion that a single molecular abnormality is the cause of complex diseases (Roth et al., 2004). In consequence, there is an interest in developing drugs with multiple mechanisms of action, formerly referred to as “dirty” drugs (Elisabetsky, 2001; Youndim and Buccafusco, 2005; Hopkins, 2008). Second is the idea introduced by Hyman and Nestler (1996) that repeated perturbations of receptors – instead of a acute drug–receptor interaction – lead, over time, to adaptive changes that are ultimately responsible for a new functioning status of these receptors (and eventually tissues and organs). This idea is perfectly attuned to the “small dosages for longer periods of time” often expected from plant-based treatments, especially when plants are locally prepared. Last but not least, there is the now commonly accepted concept of synergy between multiple active ingredients, probably a rule rather than an exception in traditional plant-based formulas. This concept is increasingly backed up by scientific findings (Ehrman et al., 2007; Wagner and Ulrich-Merzenich, 2009).

Before any “scientific evidence” of the effectiveness of a local traditional treatment can be provided, a common worry is the variation of dosages in traditional recipes. It is often argued that we cannot recommend the use of traditional medicines because we have no control of the biochemical content of the preparations. Two arguments plead for the possibility of a safe and effective treatment without a precise and stable dose of active constituents: first, the therapeutic range (range between minimal clinically significant effect and excessive toxicity) can be large enough to allow for wide dose variations; and second, one should remember that modern medicine deals with precise doses is a very partial view of the whole drug-to-organ process: in fact, after prescription of a precise dose (determined in accordance to weight, gender, age, etc.) the end-organ dose can vary extensively, due to specific and individual variations in absorption, enzymatic diversity and clearance capabilities. The situation in the real world is even further from the fictitious fixed-dose because patients often forget to take their prescribed medicines. Moreover prescribers may not always prescribe the recommended dose or treatment, lack time to explain the treatment to the patient, etc. The result may be that as few as 10% of patients absorb the correct dose (Nsungwa-Sabiiti et al., 2005).

3. Traditional medicines for public health: the contribution of ethnopharmacology

Ethnopharmacology could contribute decisively to development if it can lead to a dissemination of the knowledge of tested effectiveness among locally available traditional medicines. For public health professionals, such knowledge can help create the basis for a health system that is more respectful towards local practices and foster better collaborations across medical systems. Public health professionals use the classical designs of clinical studies as proof of effectiveness. Basic clinical data collected during field surveys can pave the way for adequate clinical studies. It is not necessary to be a clinician to collect such data, but a clinician should be involved at the stage of protocol preparation and pre-testing. In order to gather basic clinical data during field surveys, a small set of questions was developed and tested in the field (Diallo et al., 2006). The suggested questions refer to beneficial and adverse effects of local recipes, and precautions. However simple it may appear, such a “user’s perspective” in ethnopharmacology can provide the essential basic information for sound effectiveness and safety studies (see Table 1).

Thanks to sound clinical data collected in a field survey, a proper clinical study can then be designed and conducted, with two characteristics that will make its results of immediate interest not only for public health professionals and physicians, but also for local populations. First, it studies a traditional treatment as it is (not a special extract but the local preparation), and second it provides observations of treatment effect on humans (not animals or in vitro essays).

Most of the time, a classical clinical assessment design can be used; in some cases, original designs are necessary. Small but rigorous clinical studies on traditional medicines can be conducted at relatively low cost, if one works with local/regional research institutes and doctoral students, with a focus on meaningful clinical measures (Graz et al., 2007). Clinical trials of traditional medicines are made easier than the usual clinical trials because a good documentation of traditional use alleviates the constitution of the toxicology/safety file, so long as the clinical study is conducted with the traditional medicine being prepared and applied according to

<table>
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<tr>
<th>Questions to be asked during field work in order to provide basic information on effectiveness and safety of a traditional treatment.</th>
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<td>(Last time you used this treatment for that health problem…)</td>
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<td>. . . what was the patient progress? (cured/better/same/worse).</td>
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<td>After how many days?</td>
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<td>What are the side effects (or undesirable effects) of this treatment?</td>
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<td>Can this treatment be used with pregnant women?</td>
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<td>Can this treatment be used with small children?</td>
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<td>Is there anything that should not be eaten or done at the same time?</td>
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<td>Are there any other precautions to be taken with this treatment?</td>
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the selected local customary recipe (WHO, 2000). Once basic clinical data have been collected on indications, effects and precautions regarding a particular treatment (Table 1), a clinical study will be easier to design and better focused.

4. Clinical studies based on ethnopharmacological findings

Clinical studies conducted on the basis of clinical data collected during ethnopharmacological field survey can provide answers to questions such as the following:

4.1. What is the most effective among many traditional treatments used in one area for a given ailment?

A field survey with a few questions as shown in Table 1 allow for a statistical analysis (retrospective treatment-outcome study) that will show correlations between patient progress and all the different treatments used (Graz et al., 2005). For the selection of potentially medically active medicinal plants, several ethnopharmacological methods are used, e.g. the numbering of independent citations, but, discrepancies are often observed between frequency of users or strong ethnopharmacological reputation and laboratory results (Bourdy et al., 2008) – and then also between laboratory results and clinical outcome. It can happen that the plants quoted with the highest frequency are not the ones whose use is followed by the best patient progress (Diallo et al., 2006). Frequency of use or quotes may not be the best way of finding the most effective traditional treatments.

Rather than frequency of use or quotes, clinical data may be more relevant in selecting effective treatments because they directly relate to the outcome of interest in those concerned, the patients. Answers to questions shown in Table 1 can be obtained from traditional healers and, in our field experience at least, with acceptable quality from “lay persons” alike. In a study on malaria, Malian “lay people” gave details about the last episode in their family, the treatment used and the clinical outcome.

4.2. What is the effectiveness of a traditional treatment?

This question may arise from the previous one, once a given treatment has been selected through an analysis of treatment – outcome correlations. At this point, a prospective dose-escalating quasi-experimental clinical trial can be organised with a small group. This is possible when a traditional preparation is given in doses that vary widely and that reported uses and outcomes indicate that the therapeutic range is large and the probability of toxicity at the doses used is very low. If differences in outcome can be detected between dose groups, the interpretation can be that a dose–effect phenomenon is present, indicating a specific activity of the studied preparation (Willcox et al., 2007). In a next step, if all pre-requisites are met, a classical trial (prospective randomised controlled trial) might be conducted, with some adaptations.

An example is the Argemone mexicana decoction used in Mali against malaria. Patients with presumed uncomplicated malaria (median age 5 years) were randomly assigned to receive the decoction or the standard modern treatment. The comparison of the traditional treatment with the modern one showed that the two had very similar outcomes. This information could be used by both local population and policy makers to make informed choices on their health strategies (Graz et al., 2010). Once this clinical study has been carried out, determination of active compounds provides the basis for quality control methods. For example, Eritrean public health professionals sent samples of Argemone mexicana collected near Asmara in order to know if their plant had an active compounds profile comparable to Malian batches, and thus could be treated as a locally produced antimalarial. Phytochemical investigations on products selected through clinical studies can help in the selection of a given plant’s cultivars or ecotypes suitable for production projects. Phytochemical analysis can also detect known toxic constituents in order to ensure that their concentration remains well below the toxic level (e.g. sanguinarine in Argemone mexicana preparations).

Since the same medicinal plant can be found in very far-apart human cultures, transferring clinically proven usages of a plant from one place to another could be one of the most sustainable elements of “South–South” development in remote areas, mainly based on information rather than material aid.

The importance of correct identification must be addressed by intense and high quality information. This can be especially important when working with refugees: because of their displacement, they may well be unfamiliar with local flora. Meetings between displaced and local traditional healers can be organised, if possible with a botanical outing, for refugees to learn to recognise local plants and avoid dangerous ones.

5. Conclusion: traditional medicines for health and human development

Conclusions of this commentary are twofold: the importance of incorporating the suggested questions into field survey questionnaires; the necessity of better collaboration between ethnopharmacologists and physicians.

Incorporating the suggested questions in field survey questionnaires allows for the design of subsequent locally relevant clinical studies. Such studies are welcomed by communities because they help them make the best use of local resources, while retaining their identity, pride and specific knowledge. In short: improving the collection of sound clinical data on traditional medicines can be a contribution to locally meaningful and sustainable development.

Better collaboration between ethnopharmacologists and physicians can help the development process. Suitable physicians for this should have experience in clinical research, excellent communication skills and demonstrate an open-minded relativist perspective of their own academic medical knowledge, allowing for a positive and critical view on all medicines.

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