Journal of Ethnopharmacology 140 (2012) 455–457

Journal of Ethnopharmacology

journal homepage: www.elsevier.com/locate/jethpharm

Editorial

Good Practices: The basis for evidence-based medicines

In the past years the journal has emphasized the importance of setting standards for studies of medicinal plants (e.g. Cos et al., 2006; Gertsch, 2009). Standards are required for studies to be considered as valid evidence for safe and effective use of traditional medicines, and thus may contribute to an official registration with governmental agencies, like FDA or EMA, as evidence based drugs. At present there is a window of opportunity for such studies, among others because of the changing global economic scene.

With 30,000–70,000 plant species being used somewhere in this world as a medicine there is an enormous potential for the development of novel products. But that requires making choices. Because with superficial studies, e.g. studying one plant species after another in a simple pharmacological model at a single dose, we end up with an enormous amount of information, but little data for evidence-based use of any plant. What is needed is a clear strategy about what should be considered as active in terms of the required dose and to address from the very beginning adverse effects and toxicity.

Development of evidence-based traditional medicines is the only valid argument to convince skeptic Western medical doctors of the application of such medicines. Experimental evidence is needed and not only historical evidence of safe use since ancient times. Therefore our major challenge in the coming years is to come to evidence-based traditional medicines. If we fail in this task, the present window of opportunity will be closed and the support for such research will diminish, and worse, the old knowledge will be lost including an important gateway to novel discoveries for drug development.

Traditional medical knowledge has two potential values, one as an easy accessible and low-cost source of medicines for primary health care, the other as the source for finding novel leads and/or targets for drug development. Based on the paradigm of “single compound single target”, pharmaceutical industry has developed good drugs for most targets. However, present day drug development using these known targets has more or less stalled. Novel approaches are needed that might lead to novel drugs. In the past 50–60 years Western medicines have to a great extend been developed on the basis of compounds that originate from Mediterranean-European traditional medicines. Poppy, belladonna and digitalis are examples of plants that stand at the basis of essential modern drugs. Traditional medicine might thus be the start for such novel approaches.

A novel approach is the use of multicomponent drugs. The successful treatment of HIV-patients with mixtures of compounds is a clear example. The cause of many diseases is multifactorial, the use of combinations of drugs rather than single compounds thus makes sense. The same applies to drugs for which resistance is built up, e.g. antibiotics and antitumor medicines. The problem of such an approach in rational drug design is the modeling of the effect of a combination of drugs, as at any moment there will be a different ratio of active compounds in the system. That is where traditional medicine comes into the picture.

In traditional medicine often mixtures are applied, in which the individual ingredients are said to play a different role. That means that mixtures of active compounds are used, which may have some sort of synergism, such as acting on different targets, affecting bioavailablity, suppressing adverse side effects, and altering drug metabolism and excretion. Such traditional formulations can be further explored, which may lead to novel insights in human diseases and pharmacology. The omics applied in a systems biology type of approach offer excellent novel tools for such studies (Verpoorte et al., 2005; Wang et al., 2005).

Traditional medicine is often based on personalized medicine. Personalized medicine is the dream of modern pharmacy with the ultimate goal of human genetics based tailor made pharmacotherapy. About 90% of the present western drugs is estimated not to work in about 60% of the patients using them (Editorial, 2012), therefore the concept of personalized medicine in traditional Chinese medicine might be worth some further study.

Many aspects of traditional medicine might thus be good sources of inspiration for research. The outcome could be novel single leads for drug discovery, combination preparations, new targets or modes of action. But in all cases it will lead to a safe and effective use of traditional medicines.

With all these great perspectives it is an absolute must to get our act together in the field of ethnopharmacology and related areas in order to be successful in obtaining applications. Obviously research should be of high quality. Statistics, proper controls and reproducibility are among the keywords for “Good Practices” in performing experiments. Of course there are generally accepted rules for experimental work in drug development. But studies of traditional medicine have some special problems, such as how to translate traditional diagnosis to western medicine (Lu and Chan, 2012), naming of the materials (Chan et al., 2012), how to deal with complex mixtures of variable quality and personalized medicine (Buriani et al., 2012; Chan et al., 2012; Pelkonen et al., 2012; Sheridan et al., 2012). For example the general set-up of clinical trials does not suit the idea of personalized medicine.

In this issue of the journal the conclusions and recommendations from three years of intensive discussions among experts from

0378-8741
doi:10.1016/j.jep.2012.02.033

the relevant disciplines united in the EU-project "Good Practices in Traditional Chinese Medicine in the Post-genomic Era" (GP-TCM) are summarized. The goal was to define "Good Practices" in the various types of studies that are needed to document the safety and efficacy of the traditional medicines, and thus may be part of registration files. That means in designing, performing and reporting studies on traditional medicines the goal is not a publication in itself but the contribution to evidence-based medicine. That requires in-depth studies on the pharmacology and toxicology, and a proper assessment of the findings.

The overall conclusions from the survey made by the GP-TCM network (Uzuner et al., 2012) are in line with this analysis. Interestingly, the clarification of standards from the side of the regulatory authorities comes out as an important item as well. Because of the complexity and the importance of the registration of evidence-based traditional medicine, an intensive collaboration and discussion between all stakeholders is of great importance and should help to develop a model for studies in traditional medicine. The inventory of the regulations concerning herbal medicine in different countries all over the world shows that there is still a long way to go to achieve some sort of global rules (Fan et al., 2012).

A major item will be the development and validation of novel approaches to deal with the complexity of the problem. As can be seen from the outcome from the survey (Uzuner et al., 2012), participants of the project recognized the importance of the omics. Whereas respondents outside the project did not mark omics as a high priority. Whether this is based on extensive experience in the use of omics or the opposite is not clear, at least the two groups differ in their professional background. But the positive attitude towards the omics that is reflected in earlier publications on this topic (e.g. Verpoorte et al., 2005; Wang et al., 2005) and in the present issue shows that the appreciation of these methods in a systems biology approach is growing exponentially.

Metabolomics in combination with multivariate data analysis is an excellent tool for quality control of botanicals and complex formulations (Buriani et al., 2012; Pelkonen et al., 2012; Sheridan et al., 2012). In combination with biological testing of different accessions, extracts or fractions from a plant one may be able to find the active compound(s), including prodrugs and synergy, by means of multivariate analysis of all data (Buriani et al., 2012; Pelkonen et al., 2012; Sheridan et al., 2012; Taketa et al., 2008; Yuliana et al., 2011). Such an approach using metabolomics on the animal/human side as well as on the plant side are now becoming common practice in pharmacology and in pharmacognosy (Barlow et al., 2012; Buriani et al., 2012; Pelkonen et al., 2012; Sheridan et al., 2012). This approach also holds promise for studying the effect of other TCM such as acupuncture (Jia et al., 2012).

Besides the omics, also other research tools are needed. Tools that cover the whole chain from the production of the plant (Booker et al., 2012; Zhao et al., 2012) to the formulation of the medicine (Luo et al., 2012), to the pharmacology and toxicology, including animal experiments (Garcia et al., 2012; Liu and Yung-Chi Cheng, 2012) and to clinical trials (Luo et al., 2012; Robinson et al., 2012). Once evidence-based traditional medicines are on the market pharmacovigilance studies are required, that means monitoring for possible adverse effects and toxicity (Shaw et al., 2012).

Now this issue is published I look back to a period of enjoyable and intense discussions in the GP-TCM European project, and I look forward to further discussions in this field with the authors, reviewers and editorial board members of the journal to implement the recommendations in our work.

This special issue is an important step towards defining rules for the "Good Practices" in our research, and setting standards for evidence-based traditional medicines. But these rules, these standards should all the time be subject of further discussion, to continue our efforts to improve our research to the benefit of all people's healthcare. It is amazing to see how few publications are recognized as valid in meta studies assessing efficacy of medicines. Our goal should be that any study done on traditional medicine counts for the assessment of safety and efficacy of traditional medicine, if not, it means that we have wasted our precious time and money. That also means that we must be honest in our conclusions, one should dare to write that there is no or only weak activity. Too many of the presently submitted papers give the impression that another wonder drug has been found, e.g. making a ubiquitous compound like sitosterol to a real panacea.

Here I should like to thank all the authors, reviewers and the guest editors for their great efforts to get this special issue published. Also I want to acknowledge the great vision of EU-commission that recognized the need for high quality studies in the field of traditional medicine, resulting in the grant for the GP-TCM project. This resulted, among others, in this special issue, which will be a very important landmark for the future research in the field of traditional medicine. A field asking for extensive global collaborations: east-west and north-south, all to the benefit of human health.

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16 February 2012
Available online 24 February 2012