Pharmaceuticals Policy and Law 2 (1999) 1–5
IOS Press

Editorial

Introduction

In the last years, the Committee on Environment, Public Health and Consumers' Protection of the European Parliament had to suffer long debates on the so-called *alternative medicines*. It is not possible to give a comprehensive definition of this term. It can only be indicated that it refers to all theories, beliefs and medical practices not accepted by science and scientific medicine.

In every civilisation, there has always existed a recognised, scientific and orthodox medicine. Contemporarily to this *scientific medicine*, other heterodox methods, based on popular beliefs, folklorism and superstition were developed. Scientific medicine has been practised by health professionals (doctors and pharmacists) holding an official authorisation and submitted to laws and strict responsibilities. On the other hand, *popular* medicine was the occupation of fast talkers, magicians, witches and tricksters. Its exercise was prohibited and punished.

Incredibly, our present society is largely characterised by what can be defined as a schizophrenic behaviour in which values are reversed. The surprise to-day is not the existence of *alternative medicines*, they were always there, but the attempt of some of their supporters to make them *official* and therefore practised by entitled health professionals.

The situation is getting serious. Governments are not aware of the fact that these *alternative medicines* are being practised by medical and pharmaceutical graduates, protected by their official degrees and recognised professional competencies, leaving the patient defenceless, and jeopardising not only the right to health but their economic interests.

The situation gets worse every day. Many health professionals threatened by increasing unemployment in the sector practice these *alternative medicines* with the greatest ease and no less profit. The responsibility for health authorities is enormous, but they do not dare to defend the patients' interests because these are not well organised and do not create enough pressure.

Furthermore, this is not a debate among technicians or scientists, among experts in the matter. It is an ideological debate with political and social implications. Some lobbies have presented it as *a social demand*, and even introduced the concept of *therapeutic freedom* that, I am afraid, will succeed because of the aggressiveness of its mentors and their ability for proselytism.

In the general debate on *alternative medicines*, medicinal plants have always been a key issue. This trend has been supported by unscrupulous industrial groups, that find in this *social movement* an excellent source for profit. The worst thing that

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can occur to regulation and use of medicinal plants is to be a part of this subversive political debate against the establishment that mean *alternative medicines*.

Herbal remedies are the result of 10,000 years and more of empirical experimentation (generally expressed in a pre-scientific manner, even in the Chinese tradition). The study and knowledge of medicinal plants has a long and brilliant trajectory in western civilisation. The outstanding starting point of this tradition can be found in Teofrasto and the Hipocratical School, that was later completed and improved by the Hellenistic world and culminated in the works of Dioscorides. The Arab doctors enriched this knowledge appreciably. Middle-Age books kept for centuries a knowledge that was purified and shaped by European Renaissance pharmacopoeia. This implies a long process, perfectly documented, that allows us to study in depth the change in the uses of medicinal plants in European therapeutics. We can find compared studies on medicinal plants from the origins of European Pharmacopoeia to the present day. Throughout the centuries, the number of works dedicated to medicinal plants has inexorably been reduced and, nowadays, European Pharmacopoeia contains just a handful of monographs. However this decrease in the amount of pharmacopoeia monographs should not mask the replacement of the use of many medicinal plants by their active principles.

But I would like to stress that the most important thing is to emphasise that medicinal plants and their preparations are essential elements of scientific pharmacology and official medicine. Its study, characterisation and property description are the object of thousands of scientists. Medicinal plants are not the heritage of charlatans, social activists, unscrupulous entrepreneurs or opportunistic health professionals.

Citizens have to know that research therapy and phytomedicines is the occupation of thousands of scientists. The Phytochemical Dictionary, edited by Harborne and Baxter, published in 1993, lists 2793 bioactive compounds from plants. The medicinal plant research journal on Phytomedicine and Phytopharmacology, namely, Planta Médica, included hundreds of reports on the biological activity of plant chemicals. The largest number of reports concerned effects on the antibacterial and antitumour effects, on the immune system, pharmacological action over key enzyme systems and the inflammatory cascades. The series *Methods in Plant Biochemistry* lists different major bioassay types encompassing in vitro, ex vivo and in vivo tests. Undoubtedly, much of the motivation for this work lies in the prospect of finding either new therapeutic molecules or leads to new therapeutic compounds based on the natural molecule. We have not only phytochemical and phytopharmacological data to support the medicines we use but we also need clinical evidence of the effectiveness of many of these medicines. For many phytomedicines detailed clinical evidence is available. We still need standard clinical trials and to deepen toxicity testing. Guidelines for toxicity tests give information on test procedures for the evaluation of acute toxicity and short-term toxicity. Additional risk assessments are needed in the field of teratology, studies on metabolism and pharmacokinetics, neurotoxicity studies and in immunotoxicity studies, notwithstanding mutagenic and carcinogenic

risk evaluation. Double blind modern randomised clinical studies would often require an excessively high number of patients to be statistically significant, given the mild effects attributed to many herbal remedies. This limitation of our current methodologies should therefore be underlined.

The number of reports on unwanted side effects of phytomedicines increased in the last years. In some instances, a lack of pharmaceutical quality was found. The unqualified recommendation of herbal remedies may represent a considerable risk for the user. The use of a herbal remedy with unproven efficacy can represent a risk for the user when a more effective and necessary treatment will therefore be stopped or omitted. This circumstance must be taken into account by the governments, the inspection services, the doctors and the judges themselves. The trivial approach to these *miracle products* and the fraud do not receive the necessary punishment because if the product does not have any therapeutic property it cannot entail any harm either. However, the legal principle of profit cessation must be considered. A clear responsibility and tangible damages can be determined after being treated with an *innocuous preparation* instead of an effective medicine. There exists a loss of opportunities to heal and even the added risk that, in the meantime, the illness gets worse.

The main problem in the use of medicinal plants is the *unscientific ideology*, promoted by the so-called nonconformist and progressive social sectors, that creates uncertainty and mistakes public opinion. This is the perfect culture medium for huge economic frauds and considerable health risks.

Citizens are being persuaded that this *alternative medicine* or *unconventional medicine* is based on its low or even absent toxicity. A good efficacy is assumed as self-evident, and therapeutic benefit without risks is expected. Many users prefer *natural medicines* instead of synthetic remedies. However, we cannot stop stressing, once again, that toxic effects of phytomedicines can also be observed when the efficacy of a drug is proven and the pharmaceutical quality satisfied.

The activities of the Committee for Medicinal Products (CPMP) of the EEC

The present discussion on herbal remedies has a long history within the EEC Commission and the Committee for Proprietary Medicinal Products (CPMP). Already in March 1978 a working group for *medicinal products of plant origin* was established. The result of a 10 year discussion was the note for guidance *Quality of Herbal Remedies* of November 1988.

Dr. Konstantin Keller (Germany) has been a main actor and an exceptional promoter throughout all these years. The meetings of the working group for medicinal products went on for years. In 1997, upon the initiative of the European Parliament, the European Commission and the EMEA Executive Director, an *ad hoc* working group on herbal medicinal products was established at the European Medicinal Products Evaluation Agency whose Chairman was again tireless Dr. Keller.

The main thrust of the working group since 1997 has been the protection of public health by preparing guidance intended for successful mutual recognition of marketing authorisation in the field of herbal medicinal products and hopefully restricting arbitration to a minimum. The *Report from the ad hoc working group on herbal medicinal products 1997/1998* was presented on 10 February 1999 (EMEA/HMPNG/25/99). This report gives an overview of the current status of the proposals from the EMEA working group. In the presentation of the report, Dr. Fernand Sauer, Executive Director of EMEA, indicates *that it is sometimes assumed that the European Agency for the Evaluation of Medicinal Products should only focus its activity on innovative and biotechnology/biological products and would not consider herbal medicinal products in the remit of this core responsibilities. However, in keeping with its mission statement to contribute to the protection and promotion of public health in Europe, the Agency has endeavoured to prevent possible conflicts in the Mutual recognition of national authorisation, which are referred to the Committee for Proprietary Medicinal Products* (*CPCP*) *for arbitration.* Dr. Keller, for his part, stressed that *over six meeting and in accordance with its original mandate, the group reviewed the criteria set out in European legislation and guidelines for the demonstration of pharmaceutical quality, pre-clinical, safety, and clinical efficacy in applications for marketing authorisation of herbal medicinal products.*

Additionally, the EMEA Management Board decided on 10 February 1999 to grant a permanent status to the working group on herbal medicinal products at the EMEA.

Legal status of herbal remedies

Herbal remedies are medicinal products as defined in Article 1 of Council Directive 65/65 EEC. Two decisions of the European Court of Justice support this interpretation. As a consequence of the legal status of herbal drugs as medicinal products, marketing authorisations according with Article 4 of Council Directive 65/65 EEC are obligatory. The applicant has to document quality, safety and efficacy of his product in compliance with Council Directive 75/318 EEC. To reach consensus on the Summary of Product Characteristics (SPC) in the case of generic application, will pose a major problem. What makes the situation even more complicated is that one SPC for a herbal remedy covers different active constituents. Notwithstanding the fact that the so-called minor secondary metabolites found in phytomedicines are the key to their activity.

In some Member Sates, herbal remedies are generally labelled as *traditionally used* products, whereas other Member States use a *regular* indication. For Dr. Keller, *it is clear that the label traditionally used will not be accepted at a EEC level*.[1] Considering that herbal remedies are often used by way of self-medication,

[1] The European Commission adopted a clarification of medicines with well-established use on 8 Septem-

all Member States agree that comprehensive patient information is crucial. This include unambiguous information on indications and adverse reactions, counter-indications, interactions as well as details of the route of administration and dosage. Apart from these aspects, a clear definition of the herbal drug preparation is the basis of any discussion on efficacy.

The future of the regulation on medicinal plants in Europe

In this issue of our review *Pharmaceuticals Policy and Law*, we want to contribute to the debate currently carried out at the European Commission, the European Parliament and the EMEA, in which scientists, industry representatives and several social associations are taking part.

We asked Dr. Hubertus Cranz to co-ordinate our monograph. His professional capabilities and his prominent position in the industry have given him the opportunity to study the problems of medicinal plants in-depth and to receive the impressions of experts coming from the five continents, throughout multiple meetings and symposiums. He asked some of the best experts in the field to collaborate in this survey. [2] Dr. Cranz has directed a report on *Herbal medicinal products in the European Union* made by the AESGP on behalf of the European Commission. This study, which was carried out in 1998, is available on the website of the European Commission. [3]

As Editor-in-Chief of *Pharmaceuticals Policy and Law*, I want to thank Dr. Cranz for his dedication and guidance in the elaboration of this work. I also would like to express my highest consideration to the authors involved in this survey: Dr. Konstantin Keller, Dr. Barbara Steinhoff, Prof. Xiaroui Zhang, Prof. Jos é María Suñé and Dr. Fabian Lutz, for their documented articles that will be very useful in order to facilitate the debate between health authorities and bodies in charge of the registration of pharmaceuticals, as well as among health professionals. We also hope that this work will be a useful tool to make public opinion aware of the relevance of this debate, which latest aim is to preserve citizens' right to health, as well as their economic interests.

Granada, 30 September 1999
Prof. José Luis Valverde
Editor-in-Chief

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ber 1999. Actually, the directive amends the annex to the directive 75/318/EEC and is regarded as an important clarification for products with well-established use, including many herbal medicinal products. If you wish to have a look at the text, it is available under the following address: http://europa.eu.int/eur-lex/en/oj/1999/l_24319990915en.html.

[2] THese articles were all subnitted in 1997.

[3] http://dg3.eudra.org/dgiiie3/news.htm (date: 15/03/99).