

Phytotherapy and Herbal Medicinal Products in the European Union

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Medicinal plants and their preparations belong to the oldest known health-care products that have been used by human beings all over the world. With respect to their legal status however, in some countries phytomedicines are well-established, whereas in other countries herbal preparations are regarded as food and therefore are not allowed to make any therapeutical indication claims. In Europe as well as over the world big differences in the regulatory situation depending on the ethnological, medical, and historical background of each country can be observed.

In Europe, herbal products are in general classified as medicinal products if they claim therapeutic or prophylactic indications. They are not considered as medicinal products if they do not have these claims. Products not classified as medicinal products belong in most cases to the food or the cosmetic area, however sometimes they contain plants which have pharmacological properties.

The European market

Although herbal medicinal products have a long tradition as medicinal products, recognition of their clinical, pharmaceutical and economic value and the interest of the public in them are still growing. According to a research performed by IMS in 1995, the European Market for herbal medicinal products was estimated to be worth US \$ 5,600 million at public price level. The leading countries are Germany (44 %) and France (28 %), followed by Italy, United Kingdom, Spain, Netherlands, Belgium and others.

The French market

According to further research performed by IMS, the total OTC market in France was US \$ 4 billion (ex manufacturer price) in 1998, herbal products formed 29 % of the total French OTC market. Among the herbal medicinal products, circulatory products retained a strong leadership, followed by digestives, cough/cold remedies, urogenital products, calming remedies, and others.

The German market

In Germany, most of the herbal medicinal products (82 %) were sold in pharmacies in 1998, whereas 18 % were sold in other outlets such as supermarkets and drugstores. Herbal medicinal products formed about 30 % of the total market of non-prescription bound medicinal products (DM 4.43 billion / DM 14.86 billion) in 1998. About half of this 30 % share were herbal medicinal products prescribed by doctors and reimbursed, half were herbal medicinal products bought by the patients themselves. Leading categories of herbal medicinal products in self-medication were cough/cold, stomach/digestion, circulatory medicines, calming medicines, tonics/geriatrics, analgesics/antirheumatics and others, as demonstrated by

sales through pharmacies. It can be shown that many of these categories are driven by self-medication sales at a different degree, e.g. 64 % self-medication in case of cough/cold medicines, and 30 % self-medication in case of circulatory products, as found by IMS in 1998.

Consumers' attitude

In Germany there is a positive trend towards the use of natural medicines (of which herbal medicinal products form a large part), as could be shown by a study performed by the Institute for Demoscopic Research Allensbach in 1997. According to this study, the group of users of natural medicines now comprises two thirds of the German population (65 %). In 1970, only 52 % of the population of West Germany was included in this group. A pronounced trend towards self-medication in connection with health problems and minor illnesses could be seen. In 1978 only 44 % of the West German population had agreed with the statement that when they feel ill and think that it is nothing serious, they get their own medication at the pharmacy and do not need to consult a doctor. By 1997, this attitude had become the majority opinion (59 %). The opposing statement that when people feel ill they go to the doctor, even if they do not think it is anything serious, is now supported by only 28 %.

According to the users of natural medicines, a high percentage of natural medicines used today are paid by the consumers themselves (56 %), only 22 % are obtained in the pharmacy on prescription basis. 21 % of the medicines were partly paid by the patients themselves and partly prescribed by a doctor.

The population estimates the risk attached to natural medicines much lower than to chemical pharmaceutical products. 80 % of the population believes that the risk of natural medicines is low, whereas 47 and 37 % respectively of the population estimate the risk of chemical medicines as middling and great respectively.

Natural medicines are particularly important in the area of prevention. A total of 84 % of persons who take preventive medicine take natural medicines. From 1989 to 1997 there was an increase from 79 %.

Only a minority of users of natural medicines exclusively relies on these medicines in case of illness or health problems. Most users of natural medicines take these medicines among other medicines, in case of illness (64 %) and for health problems (72 %). The trend is rising.

According to the Allensbach study natural medicines helped people to alleviate various disorders such as cold, flu, digestive troubles, headache, insomnia, stomach trouble, nervousness, circulatory disorders, bronchitis, skin disease and exhaustion.

In the Allensbach study, people have been asked whether from their point of view, the experience of doctors and patients or the scientific proof is more important for the assessment of efficacy of natural medicines. It could be demonstrated that 61 % rely on experience to assess the efficacy of a product, whereas 22 % are in favour of the scientific proof. These results demonstrate two options which are provided by the German Medicines Law since a long time: the assessment of efficacy either by documented experience or by a severe scientific proof e.g. by a clinical study.

A total of 75 % of users of natural medicines with mandatory state health insurance believes that it is "very important" (27 %) or "important" (48 %) that natural medicines continue to be covered by the health insurance system.

There is also a positive opinion on natural medicines with a view to the future: 41 % of the population expects that more natural remedies will be used in Germany after a period of 50 years, whereas 24 % estimate the amount the same and only 7 % expect that less than today will be used.

The regulatory situation of herbal medicinal products in the EU

The European Union has developed a comprehensive legislative network in order to facilitate the free movement of goods, capital, services and persons in the community, and the regulation of medicinal products is part of this legislation. According to the European Directives, pharmaceutical products require pre-marketing approval before gaining access to the market. Documentation of quality, safety, and efficacy as well as respective expert reports on these items are required. As herbal medicinal products have in most cases well-known active ingredients for which a lot of experience exists, performance of new clinical and pharmacological/toxicological studies does not seem necessary. For this reason, in principle data from literature can be used to answer the questions on safety and efficacy when a marketing authorisation is applied for.

Attempts to harmonize scientific assessment criteria

In 1989, ESCOP, the European Scientific Cooperative on Phytotherapy was founded as an umbrella organisation of six national scientific associations on phytotherapy, and during the past years a large number of further associations have joined ESCOP. From the regulatory point of view uniform criteria on a European level regarding the assessment of safety and efficacy of herbal medicinal products did not exist for a long time, only a guideline on the quality. For this reason, harmonization of scientific assessment was regarded to be an essential precondition for adjustment of different opinions of national authorities in the system of mutual recognition of marketing authorization decisions, particularly in case of products having different national traditions and assessment criteria. The main objectives of this organization have therefore been to establish harmonized criteria for the assessment of herbal medicinal products, to give support to scientific research and to contribute to the acceptance of phytotherapy on a European level.

In order to provide harmonized criteria for the assessment of herbal medicinal products, proposals for monographs on medicinal plants and their medicinal use have been prepared taking into account all the legislative criteria on the respective plant that exist in Europe and taking into consideration all the relevant scientific literature. In October 1990, the first five monographs were presented at the first ESCOP Symposium in Brussels and were officially handed over to representatives of the European Community. After a thorough assessment the Committee on Proprietary Medicinal Products (CPMP) adopted four monographs on anthraquinone laxatives in May 1994, whilst no decision was made in case of *Matricariae flos* and *Valerianae radix*. Nevertheless ESCOP continued preparing harmonized SPC proposals in order to fulfil an obligation to the European Union of 50 monographs by end of December 1996. ESCOP has published its finalized monographs as a loose-leaf binder which to date contains 50 monographs and which will be amended soon.

Activities of WHO in the field of traditional medicines

A WHO consultation had drafted "Guidelines for the Assessment of Herbal Medicines" in 1991. Their objective had been to assist national regulatory authorities, scientific organizations, and manufacturers to undertake an assessment of the documentation for herbal medicinal products. Within these guidelines, a general rule for the assessment was that traditional experience which means long-term use as well as the medical, historical, and ethnological background of these products should be taken into account. These guidelines contain basic criteria for the assessment of quality, safety, and efficacy of herbal medicines as well as important requirements for the labelling and the package insert which is useful for consumers' information. They are intended to facilitate the work of regulatory authorities, scientific bodies and industry in the development, assessment and registration of herbal medicines.

WHO's project on Model Monographs

Based on the "Guidelines for the Assessment of Herbal Medicines" which define basic criteria for the evaluation of quality, safety and efficacy of herbal medicines, WHO's Traditional Medicine Programme (TRM) has prepared a technical document entitled "Model Monographs of Widely used Medicinal Plants" for primary health care. These monographs include summaries of the botanical characteristics, quality control and major active chemical constituents as well as clinical applications, pharmacology, posology, contraindications and adverse reactions. 28 model monographs were adopted during a WHO consultation in Munich in July 1996 and have been published recently. Further 30 monographs have been developed, and publication is scheduled for the near future.

The health authorities' activities

In 1996, the Ad Hoc Working Group on Herbal Medicinal Products was founded by the European Agency for the Evaluation of Medicinal Products, EMEA. The group consists of representatives from national health authorities as well as from the EMEA, the European Commission, the European Pharmacopoeia Commission and the European Parliament. It has met 2-3 times each year for two days under the chairmanship of Dr. Konstantin Keller, German Federal Institute for Drugs and Medical Devices. Since 1999, the group has the status of a permanent working group.

During the past years the group has developed new guidance and common criteria for interpretation how to adequately prove quality, safety and efficacy of herbal medicinal products with particular reference to new scientific data as well as to the well-established use of herbal medicinal products as referred to bibliographic applications for marketing authorization. The group examined the application of existing legislation on well-established medicinal products to herbal medicinal products, discussed the existing provisions in the Good Manufacturing Practice (GMP) of herbal medicinal products and starting materials, and proposed common criteria for the evaluation of quality, safety and efficacy of herbal medicinal products. In particular, the group revised the existing guideline "Quality of Herbal Medicinal Products" and developed guidance on the non-clinical testing of herbal drug preparations with long-term marketing experience. Furthermore they started assessing the monographs published by WHO and ESCOP and drafted so-called "Core SPCs" based on these monographs.

The group has expressed its opinion that the monographs drafted by ESCOP and WHO offer a valuable and updated overview on published scientific literature, which together may be used in support of the demonstration of the safety and efficacy of a medicinal product. The group at present evaluates these monographs in order to develop official assessment criteria for herbal medicinal products that can be used as a scientific reference for marketing authorizations. From all interested parties these developments are highly appreciated, and it can be hoped that further steps towards a European-wide rational assessment of herbal medicinal products can be achieved in the near future.