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Commentary

The new European legislation on traditional herbal medicines: main features and perspectives

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Abstract

Under the Italian Presidency of the Council of the European Union (July 2003–December 2003) an agreement has been reached by the European Parliament and the Council on the approval of the proposal of Directive of the European Parliament and the Council amending the Directive 2001/83/EC as regards traditional herbal medicinal products. Once implemented in the E.U. Member States, this new Directive will remove the constraints that have made it difficult granting marketing authorisations of herbal substances and preparations as traditional medicinal products under the pre-existing Community legislation. The main features (i.e. traditional herbal medicine definition, simplified registration procedure, provisions for Community herbal monographs and Community list of herbal substances and preparations and establishment of the Committee for Herbal Medicinal Products) of this new Community legislation are analysed and discussed in the present paper together with some expected positive public health impacts.

Keywords: Traditional herbal medicines; European Parliament; Community

1. Introduction

Industrially-prepared herbal products are available and largely used in all the Member States of the European Union. In Europe, herbs are being largely used in

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medicine, in particular (in order of importance) as anti-varicose and cough remedies, to help circulation, to fight muscular pain, to help digestion, as cold remedies, for calming and sleeping, as laxatives, for bladder and kidney and as liver remedies [1–3]. Germany and France dominate the European herbals market with 39 and 29% of market share, based on value of sales [1]. In most European countries, the herbals market is mainly reliant on self-prescriptions (the European average of self-medication share is equal to approx. 60% and, as an average, the European herbal share of over-the-counter medicines sales is approx. 24%) [1]. Moreover, considerable amounts of herbal substances and herbal preparations are being used as food supplements and related products (as an example see the preliminary list [4] of more than 200 plants, different parts of which are present in food supplements notified to the Ministry of Health of Italy) as well as natural sources of food flavourings [2,5]. Other important uses of herbal substances and preparations include the manufacturing of cosmetics and perfumes [6] and other products.

Herbal medicinal products fall within the scope of the European Directive 2001/83/CE that foresees that marketing of each medicinal product requires an ad hoc authorisation to be granted on the basis of results of tests and experimentations concerning quality, safety and efficacy. Although for medicinal products that are, according to adequate published data, of well established use in the meaning of art. 10, para 1, letter (a), point (ii) of the above-mentioned Directive and as specified in Part 3 of Annex 1 of the same Directive, there is no need to provide safety and efficacy data, for a large number of the herbal products already in use for a long time there are no adequate published data to show the well established medical use; therefore, they are not eligible for an authorisation. Although new tests and experimentations could be carried on such products to make it possible to authorise them under the above-mentioned regulations, apart from the considerable associated costs, it would be very difficult to justify animal tests and human clinical trials on products for which a longstanding tradition of use makes possible to evaluate safety and efficacy.

It is not surprising, therefore, that the legal status and the practise of use of traditional herbal medicines vary significantly from one country to another thus making it difficult for the free circulation of such products within the E.U. and an appropriate information of consumers, thus possibly causing, under some circumstances, negative impacts on public health including a blurring of the distinction between medicinal and non-medicinal use of some herbal products and preparations.

To overcome this unsatisfactory situation, the Council and European Parliament have adopted several Resolutions [7–9] and a study was carried out in 1998 by the European Proprietary Medicines Manufacturers' Association (AESGP) on behalf of the European Commission [10].

2. Main features of the new European Directive on traditional herbal medicines

The proposal for a Directive of the European Parliament and of the Council, which modifies Directive 2001/83/EC on traditional herbal medicines, was transmitted to the European Parliament on 17 January 2002, and received the opinion of

the European Economic and Social Committee on 18 September 2002 and of the European Parliament, at first reading, on 21 November 2002. The Directive was examined by the Council's Pharmaceutical Group at several meetings in 2003, approved at first reading by the Council and transmitted to the European Parliament for a second reading on the occasion of the Parliamentary mini-session of 3 and 4 November 2003. During the plenary session of 17 December 2003, the Parliament voted only two minor amendments to the Council's common position, which had already been informally agreed upon by the Council.

2.1. Definition of traditional herbal medicinal products

A traditional herbal medicinal product is any medicinal product, exclusively containing as active ingredients one or more herbal substances (i.e. all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually in dried form but sometimes fresh, and certain exudates that have not been subjected to a specific treatment) or one or more herbal preparations (preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration and fermentation, including comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates), or one or more such herbal substances in combination with one or more such herbal preparations, as long as all the following conditions are fulfilled:

a It has indications exclusively appropriate to traditional herbal medicinal products, which, by virtue of their composition and purpose, are intended and designed for use without the supervision of a medical practitioner for diagnostic purposes or for prescription or monitoring of treatment;
b It is exclusively for administration in accordance with a specified strength and posology;
c It is an oral, external and/or inhalation preparation;
d Bibliographical or expert evidence exists to the effect that the medicinal product in question or a corresponding product (i.e. any product characterised by having the same active ingredients, irrespective of the excipients used, the same or similar intended purpose, equivalent strength and posology and the same or similar route of administration as the medicinal product applied for) has been in medicinal use throughout a period of at least 30 years preceding the date of application, including at least 15 years within the Community (at the request of the Member State where the application for traditional use registration has been submitted, the Committee for Herbal Medicinal Products shall draw up an opinion on the adequacy of the evidence of the longstanding use of the product, or corresponding product). The requirement concerning medicinal use throughout the period of 30 years is satisfied even where the marketing of the product has not been based on a specific authorisation. It is likewise satisfied if the number or quantity of ingredients of the medicinal product has been reduced during that period. Where the product has been used in the Community for less than 15

years, but is otherwise eligible for simplified registration, the Member State where the application for traditional use registration has been submitted shall refer the product to the Committee for Herbal Medicinal Products. The Member State shall submit relevant documentation supporting the referral. The Committee shall consider whether the criteria for a simplified registration are fully complied with. If the Committee considers it possible, it shall establish a Community herbal monograph, which shall be taken into account by the Member State when taking its final decision; and

e The data on the traditional use of the medicinal product are sufficient, in particular the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of longstanding use and experience.

The presence in the herbal medicinal product of vitamins or minerals for which there is well-documented evidence for their safety does not prevent the product from being eligible for registration as a traditional herbal medicinal product, provided that the action of the vitamins or minerals is ancillary to that of the herbal active ingredients. This reflects the fact that most of the traditional combination products between a herbal and non-herbal ingredient are indeed combinations with vitamins and minerals.

2.2. Traditional use registration and authorisation

In order to obtain traditional use registration, the applicant shall submit to the competent authority of the Member State concerned an application accompanied by the particulars and documents:

- referred to in Article 8(3)(a) to (h), (j) and (k) of Directive2001/83/EC;
- the results of pharmaceutical tests referred to in the first indent of Article 8(3)(i) of Directive 20001/83/EC;
- the summary of product characteristics without the data specified in Article 11(4) of Directive 2001/83/EC;
- in case of combinations, the information data relating to the combination as such and showing that the product proves not to be harmful in the specified conditions of use and the pharmacological effects or efficacy of the medicinal product are plausible on the basis of longstanding use and experience; if the individual active ingredients are not sufficiently known, the data need also relate to the individual active ingredients;
- any authorisation or registration obtained by the applicant in another Member State, or in a third country, to place the medicinal product on the market, and details of any decision to refuse to grant an authorisation or registration, whether in the Community or a third country, and the reasons for such a decision;
- bibliographical or expert evidence to the effect that the medicinal does fulfil the requirements for being a traditional medicinal product; and
- a bibliographic review of safety data together with an expert report, and where

required by the competent authority, upon additional request, data necessary for assessing the safety of the medicinal product.

Annex I shall apply by analogy to the particulars and documents specified above.

Traditional use registration shall be refused if the application does not comply with the above-mentioned requirements or if at least one of the following conditions is fulfilled:

a the qualitative and/or quantitative composition is not as declared; the indications do not comply with the conditions described above under the definition;
b the product could be harmful in the normal conditions of use;
c data on traditional use are insufficient, especially if pharmacological effects or efficacy are not plausible on the basis of longstanding use and experience; and
d the pharmaceutical quality is not satisfactorily demonstrated.

Each Member State shall, when evaluating an application for traditional use registration, take due account of registrations granted by another Member State.

2.3. Labelling and advertisement

In addition to the provisions laid down in Articles 54–65 of Directive 2001/83/EC, any labelling and user package leaflet shall contain a statement to the effect that:

- the product is a traditional herbal medicinal product for use in specified indication(s) exclusively based upon longstanding use; and
- the user should consult a doctor or a qualified health care practitioner if the symptoms persist during the use of the medicinal product or should adverse effects not mentioned in the package leaflet occur.

In addition to the provisions laid down in Articles 86–99 of Directive 2001/83/EC, any advertisement for a medicinal product registered under this chapter shall contain the following statement: 'traditional herbal medicinal product for use in specified indication(s) exclusively based upon longstanding use'.

2.4. Committee for Herbal Medicinal Products

The Committee for Herbal Medicinal Products has been established as a part of the Agency for the Evaluation of Medicinal Products (EMEA) to carry out tasks concerning the simplified registration and authorisation of medicinal products and, in particular, to establish Community herbal monographs and to list herbal substances and preparations (see Section 2.6.).

Each Member State shall appoint, for a 3-year term, which may be renewed, one member and one alternate to the Committee. The members of the Committee may be accompanied by experts in specific scientific or technical fields.

The Committee may co-opt a maximum of five additional members chosen on the basis of their specific scientific competence. These members shall be appointed

for a term of 3 years, which may be renewed, and shall not have alternates. With a view to the co-opting of such members, the Committee shall identify the specific complementary scientific competence of the additional member(s). Co-opted members shall be chosen among experts nominated by Member States or the Agency.

2.5. Community herbal monographs and list of herbal substances and preparations

Community herbal monographs for herbal medicinal products are to be established by the Committee for Herbal Medicinal Products with regard to the application of Article [10a] [10(1)(a)(ii)] of Directive 2001/83/EC as well as traditional herbal medicinal products. The herbal monographs shall be published. These monographs shall be taken into account by the Member States when examining an application.

A list of herbal substances, preparations and combinations thereof is to be established by the Committee for Herbal Medicinal Products in accordance with the procedure referred to in Article 121[2] of Directive 2001/83/EC. The list shall contain with regard to each herbal substance the indication, the specified strength and the posology, the route of administration and any other information necessary for the safe use of the herbal substance. If an application for traditional use registration relates to a herbal substance, preparation or a combination thereof contained in the list, only the particulars and documents listed in the first four indents of the previous Section 4 need to be presented together with the application.

Member States should recognise (mutually) registrations of traditional herbal medicines granted by another Member State based on Community herbal monographs or consisting of substances, preparations or combinations thereof listed in the above-mentioned list. The Committee for Herbal Medicinal Products is charged with the duty of making the final judgement in an arbitration process in cases where a mutual recognition procedure between EU Member States could not be finalised successfully.

2.6. Other issues

Articles 3(1) and (2), 6(1), 4(4), 12, 17(1), 19, 20, 23, 24, 25, 40 to 52, 70 to 85, 101–108, 111(1) and (3), 112, 116 to 118, 122, 123, 125, 126 s subparagraph, 127 of the Directive 2001/83/EC as well as Commission Directive 91/356/EEC apply, by analogy, to traditional use registration.

For the traditional herbal medicinal products as referred to in Article 1 of this Directive, which are already on the market on the entry into force of this Directive, the competent authorities shall apply the provisions of the present Directive within 7 years after its entry into force.

3. Perspectives

This Directive, once implemented in the E.U. Member Countries will offer to European patients a high level of health protection, while allowing them access to medicines of their choice, provided that all the necessary safeguards are present. It

Table 1
Synopsis of ESCOP and WHO monographs on medicinal plants

Absinthii herba	1	Foenugraeci semen	1	Rhei rhizoma	2
Aetheroleoum anisi	2	Frangulae cortex	1+2	Ribis nigri folium	1
Aetheroleoum lavandula	2	Gentianae lutea, scabrae radix	1+2	Rosmarini folium cum fiore	1
Agni casti fructus	1	Ginkgo folium	1+2	Rusci aculeati rhizoma	1
Allii cepae bulbus	2	Ginseng radix	1+2	Salicis cortex	1
Allii sativi bulbus	1+2	Glycyrrhizae radix	2	Salviae folium	1
Aloe	2	Gugguli gummi	2	Sambuci flos	2
Aloe capensis	1	Hamamelidis aqua	1	Schisandrae fructus	2
Aloe vera gel	2	Hamamelidis cortex	1	Scutellariae radix	2
Althaeae radix	1+2	Hamamelidis folium	1	Senegae radix	2
Ammi majoris fructus	2	Hamamelidis folium et cortex	2	Sennae folium	1+2
Ammi visnagae fructus	2	Harpagophyti radix	1+2	Sennae fructus	2
Andrographitis herba	2	Hederae helicis folium	1	Sennae fructus acutifoliae	1
Anethi fructus	2	Hippocastani semen	1+2	Sennae fructus angustifoliae	1
Angelicae sinensis radix	2	Hydrastis rhizoma	2	Serenoae repentis fructus	1+2
Anisi fructus	1+2	Hyperici herba	1+2	Silybi mariae fructus	2
Armeniacae semen	2	Ipecacuanhae radix	2	Solidaginis virgaureae herba	1
Arnicae flos	1+2	Juniperi fructus	1	Tanaceti parthenii	1+2
Astragali radix	2	Lavandula flos	2	Taraxaci folium	1+2
Azadirachtae folium	2	Lichen islandicus	1	Taraxaci radix	1+2
Azadirachtii oleum	2	Lini semen	1	Thymi herba	1+2
Betulae folium	1	Liquiritiae radix	1	Trigonellae foenugraeci	2
Boldo folium	1	Lupuli flos	1	Uncariae cortex	2
Bruceae fructus	2	Matricariae flos	1	Urticae folium/herba	1
Bupleuri radix	2	Melaleucae alternifoliae aetheroleum	2	Urticae radix	1+2
Calendulae flos	1+2	Meliloti herba	1	Uvae ursi folium	1+2
Carvi fructus	1	Melissae folium	1+2	Valerianae radix	1+2
Caryophylli flos	2	Menthae piperitae aetheroleum	1+2	Zingiberis rhizoma	1+2
Castani flos	2	Menthae piperitae folium	1+2	Zizyphi fructus	2
Centaurii herba	1	Myrrha gummi	1+2		
Centellae herba	2	Myrtilli fructus siccus	1		
Chamomillae flos	1	Ocimi sancti folium	2		
Chelidonii herba	1	Oenotherae biennis oleum	2		

Cimicifugae racemosae rhizoma	1+2	Ononidis radix	1
Cinnamomi cortex	1+2	Orthosiphonis folium	1
Coptidis rhizoma	2	Paeoniae radix	2
Crataegi folium cum flore	1+2	Passiflorae herba	1+2
Crocisigma	2	Piperis methystici rhizoma	1+2
Curcumae longae rhizoma	1+2	Plantaginis lanceolatae folium	1
Cynarae folium	1	Plantaginis ovatae semen	1+2
Echinaceae pallidae radix	1	Plantaginis ovatae testa	1+2
Echinaceae purpurae herba	1+2	Platycodi radix	2
Echinaceae purpurae radix	1	Polygalae radix	1
Echinaceae radix	2	Primulae radix	1
Eleutherococci radix	1+2	Pruni africani cortex	2
Ephedrae herba	2	Psyllii semen	1
Eucalypti aetheroleum	1+2	Rauwolfiae radix	2
Eucalypti folium	2	Rehmanniae radix	2
Filipendulae ulmariae herba	1	Rhamni purshianae cortex	1+2
Foeniculi fructus	1+2	Rhei radix	1

(1) ESCOP Monographs, 2nd edition, 2003.
(2) WHO Monographs on selected medicinal plants, Vol. I (1999), Vol. II (2002), Vol. III (in press), (courtesy of the AEGSP, modified).

will also promote the single market for the drugs in question, introducing consistent standards and procedures and encouraging cross-border trade of these products. The quality requirements to be complied with are identical to those applicable to all medicines. However, superfluous testing and charges borne by the companies is avoided, as the regulation does not require new clinical or pre-clinical testing if sufficient information on a given product is already available.

Moreover, a further facilitation of the registration of certain traditional herbal medicinal products and an enhanced harmonisation will derive from the establishment of Community herbal monographs and the Community list of herbal substances and preparations that fulfil certain criteria, such as being in medicinal use for a sufficiently long time, and hence considered not to be harmful in the normal conditions of use. These instruments together with the other roles of the new Committee for Herbal Medicinal Products, established to carry out tasks concerning the simplified registration and authorisation of medicinal products and, in particular, to make the final judgement in case of arbitration, will largely increase the confidence of consumers and manufacturers as they can now expect the best available expertise in the sector to be involved in the evaluation of these products. This Committee will make possible the continuation in a more formal framework of the valuable work of the EMEA Working Party on Herbal Medicinal Products established since 1997 to facilitate Mutual Recognition of marketing authorisations in the field of herbal medicinal products (http://www.eudra.org/emea.html) by creating a forum for exchange of experience and providing guidance on the assessment of herbal medicinal products;

The Committee for Herbal Medicinal Products will also facilitate the exploitation of the many monographs on selected medicinal plants produced so far by the World Health Organisation and by the European Scientific Cooperative on Phytotherapy (ESCOP) (Table 1).

This Directive also allows non-medicinal herbal products, fulfilling the criteria of food legislation, to be regulated under food legislation in the Community. By July 2007, the European Commission is expected to present a report on the advisability to include additional categories of substances (e.g. herbals, aminoacids and fatty acids) into the existing legal provisions for food supplements; until that time national provisions continue to prevail. In conclusion, provided that the respective legal provisions are respected, this will allow the use of herbal substances and preparations in medicines as well as in food supplements.

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