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TEMI

Botanicals and the Regulatory Framework on Food Supplements in the European Union: a Tricky Relationship*

*Pamela Lattanzi***

Sommario: 1. Introduction – 2. The regulatory status of botanical-based foodstuffs – 3. Botanical food supplements – 4. Botanical borderline products: food supplements or medicinal products? – 5. The safety assessment of botanical food supplements – 6. The thorny question of the labelling of botanical food supplements – 7. Conclusion.

1. Introduction

In the EU and many other countries (China, Japan, Usa, Canada, etc.), there is a growing interest in producing and consuming *health food products*, e.g. foods which affect health and wellbeing due to components that are naturally present in the food or added (such as: food supplements, fortified or enriched foods, functional foods, also known as nutraceuticals, superfood, etc.). Despite global economic downturn, health foods markets around the world continue to have a positive growth (De Boer and Bast, 2015). This is driven by several factors but above all by current consumer perceptions. The search for "natural" products, the increasing cost of many pharmaceuticals and their negative effects, the increasing perception of the need for a healthy diet and its importance in health and homeostasic imbalance conditions feed consumer demand for *health food*s (Nicoletti, 2012). Moreover, governments of many countries are looking for effective ways of

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** Università degli Studi di Macerata.

minimizing healthcare costs and maximizing citizens' health. The rise in lifestyle and diet related diseases, the ageing population as well as the awareness that healthier diets today may lead to fewer diseases tomorrow exacerbate this trend (Malla *et al.*, 2014). Furthermore, firms are exploiting the burgeoning *health food* markets (*ibid.*, 2014).

At European level, there is no common legal framework for *health food*. Therefore, such a comprehensive category can be specified only through interpretation (Petrelli, 2016). However, *ad hoc* classifications have been defined and the production and marketing of some *health foods* have been regulated (Petrelli, 2016), such as: "Food Supplements" (Directive 2002/46/EC, Food Supplements Directive, hereinafter Fsd); "The addition of vitamins, mineral and other substances to foods" (fortified or enriched food) (Regulation (EC) No. 1925/2006); "Foods for specific groups" (Regulation (EU) No. 609/2013)[1]. The use of all nutrition and health claims voluntarily made on foods is also regulated (Nutrition and Health Claims Regulation, Regulation (EU) No. 1924/2006, hereinafter Nhcr)[2].

Botanicals (e.g. plants and preparations made from plants, algae, fungi or lichens) represent a large segment of the *health food* category and present additional problems relating to their complex nature and multifaceted usage (Lattanzi, 2016).

The first group of problems stems from the lack of *ad hoc* legislation at EU level regulating the use of botanicals both as foodstuffs and as food supplements, the latter being the category in which botanicals are generally found.

[1] On 20 July 2016 Regulation (EU) No. 609/2013 on "Food for Specific Groups" repealed the Directive 2009/39/EC, also called Parnuts Directive, which established rules for the marketing of food for particular nutritional uses. The new Regulation aims to provide a better environment for businesses, better application of rules, and better protection for consumers regarding the content and marketing of "special" food products: infant formulae and follow-on formulae; processed cereal-based foods and baby foods; food for special medical purposes and total diet replacement for weight control. See Meisterernst (2011).

[2] Regulation 1924/2006 defines a nutrition claim as «any claim which states, suggests or implies that a food has particular beneficial nutritional properties due to: (a) the energy it provides; or provides at a reduced or increased rate; or does not provide; and/or (b) the nutrients or other substances it contains; it contains in reduced or increased proportions; or does not contain», for example "low in sugar", "high in fibre". A health claim is defined as «any claim that states, suggests or implies that a relationship exists between a food category, a food or one of its constituents and health», for example, "Vitamin D is needed for the normal growth and development of bone in children". Health claims are divided into three types: function health claim (relating to the growth, development and functions of the body; referring to psychological and behavioural functions; on slimming or weight-control); risk reduction claim (on reducing a risk factor in the development of a disease) and health claims referring to children's development. For more see Petrelli (2016); Coppens and Petteman (2014); Gulati Ottaway and Coppens (2014).

Of course, this sector is not completely without regulation, yet it is covered by horizontal legislations applicable to foodstuffs in general and by specific legislation on health foods, as explained below. Nevertheless, the lack of harmonised legislation at EU level by means of specific legislation – especially related to botanical food supplements – leaves room for national legislations and consequently produces a heterogeneous framework. This leads to problems in the field of mutual recognition.

Another group of problems, which is also a consequence of the abovementioned lack, arises from the multifunctional nature of some plants that can be allocated to various markets (pharmaceuticals, food, cosmetics and medical devices markets) governed by different legal frameworks without clear and well-defined boundaries. Thus, it leads to several issues on the legal classification of botanical products (Peraltra, Botija and Martin, 2016). This is particularly evident in the case of plants and their preparations used in both food supplements and medicinal products.

A third group of problems derives from the deficit of implementation of the Nhcr in the field of botanicals.

All the aforementioned issues give rise to: «distortions on the market, inconsistencies and lack of clarity for food business operators and competent Authorities, as well as cause confusion and safety concerns for consumers» (Food Chain Evaluation Consortium, 2016, p. 6).

This article therefore gives an overview of the most important issues relating to the regulation of botanicals in the food supplements sector. After a brief description of the regulatory status of botanical-based foodstuffs, it outlines the legal framework of botanical food supplements, taking into consideration the interferences between the pharmaceutical domain and the food sector in the classification of borderline botanical products and the issue of the safety assessment of botanicals. In the final part, it deals with the thorny question of the health claims made on such products.

2. The regulatory status of botanical-based foodstuffs

The European Food law lacks a legal definition of botanicals and, more generally, of plants and their preparations[3]. However, herbal substances are

[3] The European Food law also lacks legal definitions of other names frequently used for marketing botanical foodstuffs such as functional foods and nutraceuticals. As for functional foods, the European Commission Concerted Action on Functional Food Science in Europe (Fufose), launched in 1995, proposed this working definition of functional food: «a food that beneficially affects one or more target functions in the body beyond adequate nutritional effects in a way that is relevant to either an improved state of health and well-being and/or reduction of

defined in some detail in the European Medicine legislation (Directive 2001/83/EC on the Community code relating to medicinal products for human use) as «all mainly whole, fragmented or cut plants, plants parts, algae, fungi, lichen in an unprocessed, usually dried form, but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author)»[4].

The definition of botanicals used by the European Food Safety Authority (hereinafter Efsa) is very close to that given by the law on medicinal products. According to Efsa the term botanicals includes all botanical materials (e.g. whole, fragmented or cut plants, plant parts, algae, fungi and lichens) and the term botanical preparations includes all preparations obtained from botanicals by various processes (e.g. pressing, squeezing, extraction, fractionation, distillation, concentration, drying up and fermentation) (Efsa, 2009).

There is no authorization procedure centralized at EU level for the use of botanicals and derived preparations in food[5]. Nonetheless, this use has to comply with the general requirements set out in Regulation (EC) No. 178/2002 (laying down the general principles and requirements of food law as well as the procedures in matters of food safety and establishing the European Food Safety Authority, known as the General Food Law) and all the relevant legislation covering hygiene, additives, residues and contaminants in food, labelling, irradiation, extraction solvents and so on. Moreover, if botanical-sourced food products (or botanical ingredients) are sold as (or contained in) food supplements, foods for specific groups or fortified food they must comply with the requirements set out in the specific legislation[6].

risk of disease. It is consumed as part of a normal food pattern. It is not a pill, a capsule or any form of dietary supplement». The term "nutraceutical" was originally used by Defelice (1995) with the definition: «Food or part of food that provides medical or health benefits, including the prevention and treatment of disease». See Koch *et al.* (2014); Gulati and Ottaway (2006).

[4] Directive 2001/83/EC also defines "traditional herbal medicinal product" («herbal medicinal product that fulfils the condition laid down in Article 16a»), "herbal medicinal product" («any medicinal product, exclusively containing as active ingredients one or more herbal substances or one or more herbal preparations, or one or more such herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations») and "herbal preparations" («preparations obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates»).

[5] Efsa, *Botanicals*, http://www.efsa.europa.eu/en/topics/topic/botanicals.htm.

[6] The discipline on fortified food is mainly focused on vitamins and minerals, however Regulation No. 1925/2006 includes also "other substances" defined as any «substance other

Furthermore, if the botanical food (or botanical ingredient) is derived from genetically modified plants, it needs to respect the applicable legislation on Genetically Modified Organisms (hereinafter Gmos) (Regulation (EC) No. 1829/2003). Moreover, if the botanical food (or botanical ingredient) has not been used for human consumption in the EU to a significant degree before May 15, 1997, it also has to comply with the requirements set out in Regulation (EU) No. 2015/2283[7]. «Botanical extracts are in particular affected by this Regulation, since a plant extract that was not on the internal EU market, or not being produced, before the date of entry into force of the Regulation could, if it falls under one of the novel food categories and is significantly different from existing counterparts, in principle, be considered a novel ingredient, even though the plant from which it is extracted would not be considered "novel"» (Gulati, Ottaway and Coppens, 2014, p. 235)[8].

3. Botanical food supplements

Although the use of botanicals in food supplements has been covered under food law since 2002 by the Fsd, specific requirements for the use of botanicals in food supplements only exist at national level[9]. In fact, the Fsd

than a vitamin or a mineral that has a nutritional or physiological effect», such as plants and herbal extracts. Article 8 of the Regulation permits the scrutiny of and, if necessary, restriction on the use of substances added to foods or used in the manufacture of foods under conditions that would result in the ingestion of amounts greatly exceeding those reasonably expected to be ingested under normal conditions of consumption of a balanced and varied diet and/or would otherwise represent a potential risk to consumers. These substances have to be listed in Annex III (while Annex I and Annex II concern the list of vitamins and minerals or sources of vitamins and minerals which may be added to foods). Annex III is currently still empty. However, Regulation (UE) No. 307/2012 of 11 April 2012 has established the implementation of rules for the application of Article 8 and the Commission has received a request from a Member State to initiate the procedure under Article 8 of the Regulation for the Ephedra species (Ephedra spp.) and for yohimbe (Pausinystalia yohimbe), see http://ec.europa.eu/food/food/labellingnutrition/vitamins/index_en.htm.

[7] To market a novel food or ingredient, companies must obtain an EU authorization, presenting a scientific information and safety assessment report. Regulation (EU) No. 2015/2283 repealed Regulation No. 258/97, which previously regulated the field, and introduced a centralized authorization system. See Rizzioli (2016).

[8] See also Hermann (2009).

[9] The Fsd establishes harmonised rules for the labelling of food supplements and introduces specific rules on vitamins and minerals in food supplements. The aim is to harmonise the legislation and to ensure that these products are safe and appropriately labelled so that consumers can make informed choices. Annex I lists the vitamins and minerals which may

has not yet harmonized two important areas: the maximum levels of vitamins and minerals used in food supplements; and the use of ingredients other than vitamins and minerals (including botanicals) for nutritional/physiological purposes[10].

Therefore, in many EU Member States the use of botanicals in food supplements is regulated by positive and/or negative lists[11] and needs to comply with national procedures for notification and assessment[12]. This means, for example, that the use of the same herbal substance in one State could be unrestricted while in another subject to authorization or prohibited on the basis of a non-harmonized national list of substances. Moreover, in some countries, product status for some botanicals is automatically linked to pharmacy-only status.

Obviously, this generates a heterogeneous situation that could give rise to several problems such as those relating to the effectiveness of controls on food supplements carried out by national competent Authorities and relating to trade barriers between Member States[13]. Such barriers are avoidable due to the application of the principle of free movement of goods. In fact, according to the principle of mutual recognition, products that are lawfully marketed in one Member State are in principle free to be sold in all other Member States. However, mutual recognition is not free from the risk that technical obstacles to the free movement of the products concerned can

be used in the manufacture of food supplements. Annex II of Fsd lists permitted vitamin or mineral substances that may be added for specific nutritional purposes in food supplements.

[10] In 2008, the European Commission adopted a *Report on the advisability of establishing specific rules for the use of substances with a nutritional or physiological effect other than vitamins and minerals in food supplements* (European Commission, 2008) where the issues concerning both the necessity and feasibility of the specific rules on those substances were evaluated. The Commission concluded that laying down specific rules was not justified.

[11] Italy, Belgium, and France, for example, have introduced legal positive lists and, in some cases negative lists, of botanicals that can or cannot be used in food supplements. Belgian, French and Italian Health Authorities have decided to develop a common approach for the evaluation of botanicals in the Belfrit project. As output of this initiative, a list of plants whose potential use in food supplements has been prepared. For more details on the Belfrit project, see Cousyn *et al.* (2013). For more insights on the Italian framework, see Klaus and Corinti (2015).

[12] According to article 10 Fsd, EU Member States have the choice as to whether or not to set up a mandatory notification procedure for the first marketing of food supplement products in their country. All EU Member States, with the exception of Austria, Lithuania, the Netherlands, Sweden and the UK, decided to introduce a mandatory notification procedure. The requirements of food supplement notification procedures vary from country to country. See Gulati, Ottaway and Coppens (2014, pp. 226-227).

[13] For an overview of the problems arising from such a heterogeneous situation, see Food and Veterinary Office (2015).

be maintained or created[14]. Nevertheless, these risks should be put into perspective, in that the Court of Justice, as part of its judicial supervision, has set precise limits within which the Member States may validly exempt themselves from mutual recognition by availing themselves of Article 36 of the Treaty on the Functioning of the European Union[15].

4. Botanical borderline products: food supplements or medicinal products?

A plant, such as garlic or ginger, can be used both as an active principle in a medicinal product for the treatment of a disease or medical condition and an ingredient in a food or food supplement depending on the intended use of the product, its modalities of use, its presentation and also its claimed effect (Coppens and Petteman, 2014, p. 215). In both cases, the end-product should be in conformity with the rules of the applicable framework, namely the medicinal products legislation or the food legislation, respectively (Coppens, 2008).

Consequently, if a herbal product – produced in the EU or abroad – does not match the legal requirements established for medicinal products, it

[14] See for more insights European Commission (2015a).

[15] «The Court frequently reiterates that, it is for the Member States, in the absence of harmonisation and to the extent that uncertainties continue to exist in the current state of scientific research, to decide on their intended level of protection of human health and life and on whether to require prior authorisation for the marketing of foodstuffs, always taking into account the requirements of the free movement of goods within the Community. However, in exercising their discretion relating to the protection of public health, the Member States must comply with the principle of proportionality. The means which they choose must therefore be confined to what is actually necessary to ensure the safeguarding of public health; they must be proportional to the objective thus pursued, which could not have been attained by measures which are less restrictive of intra-Community trade. Furthermore, since Article 30 EC (now Article 36 Treaty on the Functioning of the European Union) provides for an exception, to be interpreted strictly, to the rule of free movement of goods within the Community, it is for the national authorities which invoke it to show in each case, in the light of national nutritional habits and in the light of the results of international scientific research, that their rules are necessary to give effective protection to the interests referred to in that provision and, in particular, that the marketing of the products in question poses a real risk for public health (see, most recently, paragraphs 86 to 88 of the judgment in the [...] case C-319/05, Commission v Germany). In other words, the Member States are entitled to invoke the need to protect the interests referred to in Article 30 EC, including health protection, only when the conditions laid down by the Court and referred to above have been met, and to the extent that there is no harmonised Community legislation capable of protecting the same interests» (European Commission, 2008).

could be placed on the market as food supplement instead of medicine, respecting the applicable EU and national food legislation.

> It is the manufacturer who decides the intended use of its product and assures compliance with the respective rules of the applicable legal framework. It is the role of enforcement authorities to control such compliance and challenge the manufacturer's decision if he were to have chosen an inappropriate legal framework. The consequence is that the compliance with the applicable framework needs to be assessed on the level of the end-product, taking into consideration the product's composition, properties and presentation (Coppens and Petteman, 2014, p. 215).

It is well known that in order to be marketed in the EU, all medicinal products, including herbal medicines, need to obtain pre-market approval. This is established by Directive 2001/83/EC, which sets out the general requirements for the marketing authorization or registration of medicines.

In particular, with regard to herbal medicines, the Traditional Herbal Medicinal Products Directive – Directive 2004/24/EC), hereinafter Thmpd, amending Directive 2001/83/EC, introduced a simplified registration based on "traditional use" (the so-called "traditional use registration"). According to the Thmpd, «the long tradition of the medicinal product makes it possible to reduce the need for clinical trials, in so far as the efficacy of the medicinal product is plausible on the basis of long-standing use and experience». Thus, for registration as traditional herbal medicine the product is required to show a history of use of 30 years, including at least 15 years in the EU. Nevertheless, all registered herbal medicines must comply with general provisions applying to all medicinal products (such as pharmacovigilance, good manufacturing practices, manufacturing licence, etc.)[16].

The Thmpd created a seven-year transitional period for traditional herbal medicinal products already on the EU market (from 30 April 2004 to 30 April 2011). After the transitional period came to an end, Member States granted a limited "sell-through period" during which it was permitted to sell any stock of unlicensed herbal medicines as a "medicinal product". However, since the close of the transitional and national "sell-through periods", retailers have no longer been able to sell unlicensed herbal remedies as "medicinal products". All traditional herbal medicines industrially produced now need to be registered[17].

[16] The rules on labelling of traditional herbal medicinal products require that labels must claim their therapeutic effect in a specific way: «Traditional Herbal Medicinal Product used...»; moreover, they must state: «The product is a traditional herbal medicinal product for use in specified indications exclusively based upon long-standing use».

[17] Herbal medicines may also fall within the following two categories other than the "traditional use" category: "well-established use", which requires the provision of scientific literature establishing that the active substances of the medicinal products have been in well-established medicinal use within the Union for at least ten years, with recognised efficacy and an acceptable level of safety; and "stand alone application" or "mixed application", which require only safety and efficacy data from the company's own development or a combination of own studies and bibliographic data in the case of the mixed application. For more insights see European Medicines Agency, *Herbal medicinal products*, http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000208.jsp.

Despite the simplified registration introduced by the Thmpd, this «has had an inhibitory effect on the registrations, as a large number of products have not been able to demonstrate the requirement of 15 years on the market in the EU. Even for products that can meet this requirement, significant change may have taken place to the product composition. Consequently, relatively few Traditional Herbal registrations have been authorized. In parallel, a large number of botanical materials are being used as ingredients in food supplements» (Gulati, Ottaway and Coppens, 2014, pp. 228-229). This is the case with several imported Chinese herbal products which do not satisfy the European pharmaceutical legislation conditions. If very few Traditional Chinese herbal medicines have been authorized up until now, in parallel, a large number of Chinese herbal products are in common use as food and, especially, food supplements[18].

It is worth noting that there are substantial differences in terms of costs for entering the pharmaceutical or the food supplements market, the latter being considerably cheaper. This aspect, jointly with the difficulties arising from the strict pharmaceutical regulation, influences choices made by business operators, who prefer the food supplements market.

Obviously, this choice leads to several consequences such as those regarding product safety (pharmaceutical products have higher safety standards), labelling (food supplement labels cannot refer to preventing or curing diseases, as explained below), and inclusion in national health insurance schemes (food supplements are normally excluded) (Snyder, Yi and Yazdani, 2014).

[18] The first marketing registration for a Chinese herbal medicine product was only granted on 14 march 2012 by the Dutch Medicines Evaluation Board. As reported by the China Chamber of Commerce for Import & Export of Medicine and Health Products (Cccmhpie), in its "Analysis in the First Half and Outlook in the Second Half of 2011 of Import and Export of Pharmaceutical Products", the Traditional Chinese Medicine exports to the EU in June 2011, after the transitional period established by Thmpd, dropped by almost 50% compared with June 2010.

It is worth noting that herbs and granules of single herbs, used as raw materials for the production of individual Traditional Chinese Medicine formulations in pharmacies, are not affected by the Thmpd, which concerns industrially made pharmaceuticals sold without medical prescription (i.e. over-the-counter pharmaceuticals), see Koch *et al.* (2014).

However, as result of the EU pharmaceutical legislation and the lack of harmonized legislation on botanical food supplements at EU level, Member States have the power to decide on the classification of a borderline product as food or as a medicine.

The European Union Court of Justice had to recognize that, in such a situation, it is difficult to avoid the existence of differences in the classification of the products as medicinal products or foodstuffs between Member States. The fact that a product is classified as a foodstuff in another Member State cannot prevent it from being classified as a medicinal product in the Member State of importation if it displays the characteristics of such a product[19].

4.1 The distinction between a medicinal product and a botanical food supplement according to the Court of Justice of the European Union

The Court of Justice of the European Union has had several occasions to define the demarcation line between medicinal products and food, in particular food supplements consisting of vitamin and mineral preparations. More recently, the EU Court of Justice has also ruled on the classification of botanical borderline products[20].

First of all, it should be pointed out that article 2 of the General Food Law defines food (or foodstuff) as «any substance or product, whether processed, partially processed or unprocessed, intended to be, or reasonably expected to be ingested by humans». This provision explicitly excludes medicinal products from the category of foodstuffs (Germanò and Rook Basile, 2016). Medicinal products are defined by Directive 2001/83/EC. This definition consists of two parts, one relating to the presentation as a medicinal product and the other to the function[21]. A product falling into the scope of one or other or both of those parts is considered a medicinal product. Moreover, article 2.2 of Directive 2081/83/EC states that in cases of doubt, where, taking into account all its characteristics, a product may fall within the definition of a "medicinal product" and within the definition of a product covered by other Community legislation, the provisions of the Directive 2001/83/EC will prevail and apply (namely «the rule of doubt»).

As for the definition of food supplement, Directive 2002/46/EC defines "Food Supplements" as «foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drops, dispensing bottles and other similar forms of liquids and powders designed to be taken in measured small unit quantities».

In defining the demarcation line between medicinal product (especially medicinal by function) and food supplement, the EU Court of Justice has identified some classification criteria[22]. It stated that in order to determine whether a product can be defined as medicinal by function, it is necessary to perform a case-by-case analysis, taking into account all the characteristics of the product, in particular its pharmacological properties, to the extent to which they can be established in the present state of scientific knowledge, the manner in which it is used, the extent of its distribution, its familiarity to consumers and the risks which its use may entail[23].

The EU Court of Justice observed that products containing medicinal plants are not medicinal products *per se*: products, which irrespective of their composition, do not significantly affect the metabolism and do not strictly modify the way in which it functions should not be classified as medicinal products by function[24]. It is not sufficient that a product has properties beneficial to health in general, to qualify it as a medicinal product, but it is necessary that it has the specific function of treating or preventing disease[25]. The production of a physiological effect is not exclusive to the category of medicinal products, since this aspect is also part of the criteria used to define food supplements[26]. What should be taken into account is the content in active substances as a characteristic of the composition[27].

[19] See Judgement of 15 November 2007 in the Case C-319/05, Commission of the European Communities v. Federal Republic of Germany (Garlic Judgement). See Capelli (2009).

[20] See Melchor and Timmermans (2009).

[21] Any substance or combination of substances advertised as having properties for treating or preventing disease in human beings (medicinal by presentation); or any substance or combination of substances which may be used in or administered to human beings either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis (medicinal by function). «Contrary to the definition of medicinal product "by virtue of its presentation", the broad interpretation of which is designed to protect consumers from products which do not have the effectiveness which they are entitled to expect, the definition of a medicinal product "by virtue of its function" is intended to cover only those substances which have a genuine medical therapeutic effect», Melchor and Timmermans (2009, p. 185).

[22] See for more insights Korzycka-Iwanow and Zboralska (2010).

[23] Judgement of 9 June 2005 in joint cases C-211/03, C-299/03 and C-316/03 to C-318/03, Hlm Warenvertrieb and Ortica.

[24] Judgement of 15 November 2007 in the Case C-319/05, cit.

[25] Judgement of 15 November 2007 in the Case C-319/05, cit.

[26] Judgement of 15 January 2009, in the Case C-140/07, Hect-Pharma GmbH v Staatliches Gewerbeaufsichtsamt Lüneburg.

[27] Judgement of 5 March 2009, in the Case C-88/07, Commission of the European Communities v Spain. See Melchor and Timmermans (2009); Lachenmeier *et al.* (2012).

In contrast to the restrictive interpretation of the category of "medicinal product by function" and of the "rule of doubt"[28], there is a correspondingly broad interpretation of the notion of "medicinal product by presentation". A product is presented for treating or preventing disease when it is expressly "indicated" or "recommended" as such, possibly by means of labels, leaflets or oral representation, however the EU Court of Justice noted that the mere similarity between the packaging of a product and a medicinal product cannot be the determining factor in the classification[29].

5. The safety assessment of botanical food supplements

The safety of botanicals and botanical preparations in food supplements is regulated under the General Food Law. Although this regulation does not require prior marketing authorisation for each individual foodstuff, a whole set of rules has been established to protect consumers and assure the safety of the products. The primary legal responsibility for the safety of food products placed on the market is attributed to business operators.

Food supplements can be a real risk to food safety (Food and Veterinary Office, 2015). The differences in national legislations on botanicals amplifies this risk: «the lack of approved harmonised lists of botanicals means

[28] See Judgement of 15 January 2009, in the Case C-140/07, cit. The ECJ ruled that Article 2(2) must be interpreted as meaning that the Medicinal Products Directive «does not apply to a product in respect of which it has not been scientifically established that it is a medicinal product by function, even if that possibility cannot be ruled out». Thus, «in other words, botanical food supplements are presumed to fall out of the scope of the Medicinal Products Directive unless the national authorities, having regard to the entirety of the products' characteristics, prove the contrary. This principle closes the door to those Member States who rely on the application of the precautionary principle in order to justify the aprioristic classification of "suspicious" (i.e. borderline) products as medicinal products», Melchor and Timmermans (2009, p. 189).

[29] Judgement of 15 November 2007 in the Case C-319/05, cit.

In the Case C-140/07 (Hect-Pharma GmbH v Staatliches Gewerbeaufsichtsamt Lüneburg), the Advocate General underlined the disadvantages which result from an overly extensive interpretation and application of the definition of medicinal product: «first of all, the concept of "medicinal product" would cease to have any distinguishing force if it were to include products the properties and action of which did not justify such classification. This would harm, rather than serve, the interests of human health. Secondly, it could result in the specific Community rules governing certain categories of food – containing provisions relating to the particular risks of the products – losing their regulatory purpose; one thinks, in the present case, of Directive 2002/46 on food supplements. Thirdly, a "creeping" extension of the scope of Directive 2001/83 to include extraneous products would be detrimental to the free movement of goods». See Opinion of Advocate General Trstenjak delivered on 19 June 2008, in the Case C-140/07, p. 68.

that the safety criteria are not transparent to traders, inspectors and consumers» (Food and Veterinary Office, 2015).

Accordingly, because of widely raised concerns in Member States regarding the safety of botanical preparations used in food (such as risks of chemical or microbiological contamination, concentrations of bioactive agents over safe limits), guidelines for the evaluation of botanical food supplements have been published by many national and international organizations.

In 2009, Efsa developed and published a guidance document for the safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements (Efsa, 2009). In collaboration with Member States, Efsa also began to develop a Compendium of Botanicals (published in 2012) listing those plants reported to contain toxic substances or components that might otherwise be of concern (Efsa, 2012).

The Guidance developed by Efsa describes a two tier approach in which the first level (Level A) is a safety assessment based on available knowledge. At this level, it may be concluded that a botanical or botanical preparation for which an adequate body of knowledge exists could benefit from a "presumption of safety" without any need for further testing. If the available data are considered inadequate for reaching a sound conclusion on safety, Level B applies which foresees the generation of additional (toxicological) data.

Both the Guidance and the Compendium are tools intended to aid the assessment of botanicals and botanical preparations and are not intended to produce a list of botanicals and botanical preparations that might be presumed safe.

More recently, the Efsa Scientific Committee has been asked to consider the applicability of the Qualified Presumption of Safety (hereinafter Qps) approach for the safety assessment of botanicals/botanical preparations. Since 2007 Qps has been developed and applied by Efsa for the assessment of microorganisms introduced into the food chain. This process allowed Efsa to identify, characterize and evaluate the pathogenicity of these microorganisms, taking into account the intended use. The Scientific Committee concluded that the Qps approach is equally applicable to botanicals and botanical preparations and recommends that all panels dealing with botanicals to use the Qps process as an extension to the 2009 guidance on the safety of botanical (Efsa, 2014).

6. The thorny question of the labelling of botanical food supplements

The labelling of botanical food supplements has to comply with the general rules established by Regulation (EU) No. 1169/2011 on the provision of food information to consumers[30] as well as with the specific rules established by the Fsd[31]. It is also covered by the Nhcr[32].

According to the Fsd, presentation and advertising must not attribute to foodstuffs the property of preventing, treating or curing a human disease, or refer to such properties. However, labels may refer to properties having positive effects on health and wellbeing provided they respect the requirements laid down by the Nhcr. This Regulation requires that all nutrition and health claims made voluntarily on foods (including food supplements) can only be used when they have been approved by the European Commission following an assessment of the scientific data available by Efsa.

As for the health claims, the scientific assessment must demonstrate the cause-and-effect relationship between intake of a compound and a health benefit. By contrast to the evaluation of traditional herbal medicines, the "traditional use" is not considered as valid proof by Efsa's scientific assessment methodology, which is centred on evidence at the "highest possible standard". Human studies are considered a fundamental part for achieving such evidence. Therefore, evidence based solely on use and experience over time is not sufficient.

Consequently, when Efsa started its assessment of the scientific evidence, more than 500 claims for botanicals failed because their dossiers were only based on the notion of "traditional use". «This has resulted in a situation where the requirement for demonstrating simple health effects for food are more demanding than for therapeutic effects for medicinal products» (Coppens and Petteman, 2014, p. 216)[33].

[30] Except the rules on the nutrition declaration that do not apply to food supplements. For more insights on food labelling see: Albisinni (2011); Borghi (2015).

[31] According to the Fsd, the labelling of food supplements shall bear: (a) the names of the categories of nutrients or substances that characterise the product or an indication of the nature of those nutrients or substances; (b) the portion of the product recommended for daily consumption; (c) a warning not to exceed the stated recommended daily dose; (d) a statement to the effect that food supplements should not be used as a substitute for a varied diet; (e) a statement to the effect that the products should be stored out of the reach of young children. Morever, the labelling shall not include any mention stating or implying that a balanced and varied diet cannot provide appropriate quantities of nutrients in general.

[32] In the case of novel food, Gmo, the labelling also needs to respect the labelling rules established by the applicable legislation.

[33] See also: Anton, Serafini and Delmulle (2012, 2013).

However, the European Commission recognized the difference between pharmaceutical law and food law in their treatment of plants and in 2010 stopped the assessment of botanicals pending further reflection.

In May 2012, the European Commission adopted Regulation (EU) No. 432/2012 establishing a list of 222 permitted health claims ("function health claims"). Simultaneously, the Commission identified a list of more than 2,000 claims, also concerning the effects of botanical substances, not yet assessed by Efsa and the European Commission and not yet listed on its webpage in the "list of health claims on hold". According to the Commission, such health claims could continue to be used in accordance with transitional measures (Article 28, par. 5 and 6 of Regulation No. 1924/2006), provided they comply with the applicable EU and national legislation.

In August 2012, the European Commission published a discussion document addressed to the Member States. This document asked for inputs on one of two options: a) Option 1: to ask Efsa to continue the assessment of claims for botanicals as was originally foreseen; b) Option 2: to recognize the specificity of the botanicals case with respect to other categories of substances used in foods and explore the opportunity to change the existing legal framework in order to give recognition to evidence based on "traditional use" as sufficient for substantiating health claims[34].

Since then, health claims on botanicals have been on hold (in a transitional period with no defined endpoint) for several years and a recent judgment of the EU General Court has recognized the legality of this situation[35].

[34] As opportunely underlined «choosing the first opinion would legitimate the unequal treatment of food products as an appropriate risk management measure but not solve any of the problems, while the second option would offer the possibility of developing further harmonization in this area. The responses by the Member States have shown the deep divide that exists between the Member States, and a marked and vigorous opposition to option 2 has been expressed by many pharmaceutical stakeholders, largely defending the use of botanicals under medicinal legislation only. Until a decision is taken, both product categories, Thmps and food supplements, can continue to be marketed in parallel. It is clear, however, that both legislations have resulted in considerable overlap: on the one hand Thmp indications described in monographs elaborated by the European Medicines Agency are similar to health effects accepted for foods in opinions published by Efsa, and on the other hand, health claims are permitted to refer to the reduction of disease risk. The acceptance of health claims for a number of substances that are considered to be restricted to medicinal products by many Member States (e.g., melatonin, red rice yeast, lactulose) is a further element that is likely to shift the legal borderline between medicinal products and food. In the end, the risk management decision lies with the EC, an institution that is obliged to observe the basic principles as established by the CJEU in terms of necessity and proportionality» (Coppens and Petteman, 2014, pp. 216-217).

[35] Judgement of 12 June 2015, Case T-296/12, *The Health Food Manufacturers' Association and Others v European Commission.*

The main issue in this case concerned the procedural aspect of adopting the above-mentioned list of 222 function health claims. Although the Court avoided entering into the discussion on what science is needed to assess botanical health claims, the decision is highly relevant for the assessment of botanicals.

The judgement dismissed an attempt to annul Commission Regulation No. 432/2012 on several grounds relating to general principles of EU law. The applicants (several trade associations and health food companies) requested the annulment of Regulation No. 432/2012 alleging, on the one hand, the lack of a legal basis and an infringement of the principles of legal certainty, good administration and non-discrimination when adopting the decision to split the authorisation procedure for health claims into several stages; and, on the other hand, an infringement of the principle of good administration, the principle of legal certainty and the duty of collaboration with national food authorities, as well as the obligation to state reasons when not including a large number of health claims in the list of permitted claims.

The Court rejected all the arguments of the applicants, stating that, according to the Nhcr, the Commission had the discretionary power to establish the list on a gradual basis. In this way, although indirectly, the decision recognized the conformity with the EU legislation of "the list of health claims on hold".

A contribution towards overcoming the pending situation will derive from the evaluation of the Nhcr in the context of the Better Regulation approach (European Commission, 2015b). Within this context, the Commission launched (European Commission, 2015c), as part of its Refit programme[36], the evaluation of the Nhcr with regard to nutrient profiles and health claims made on plants and their preparations. This evaluation also takes into consideration the current general regulatory framework for the use of such substances in foods since it is considered closely related to the use of health claims[37].

Within the ambit of Refit, in October 2015 the Commission adopted a *roadmap* which represents the first of several evaluation steps (such as external study, consultations, on line surveys, etc.), that will end in June 2017.

It is worth noting that the Nhcr evaluation will «also look into whether adapting the rules foreseen in the Regulation concerning the use of health claims relating to plants and their preparations used in foods, to recognise "traditional use" for the scientific substantiation of such claims, would ensure the objectives of the Regulation in the spirit of the co-legislators» (European Commission, 2016).

[36] Regulatory Fitness and Performance programme (Refit). Refit is the Commission's programme for ensuring that EU legislation remains fit for purpose and delivers the results intended by EU lawmakers.

[37] For more information on the Refit process of Nhcr see http://ec.europa.eu/food/safety/labelling_nutrition/claims/refit_en.

7. Conclusion

Over the centuries, herbs have traditionally been used for maintaining or optimizing health or well-being as well as for the prevention and treatment of disease. They have been, and are still, used both in food and medicinal products. EU legislation, through its pharmaceutical and food laws, takes into account the dual-use character of botanicals, covering both the medicinal use of plants and that of plants in food and food supplements. However, this coexistence of both legal frameworks has caused issues in certain Member States and the EU Court of Justice has often ruled on borderline cases.

The legal uncertainty deriving from the lack of a clear demarcation between medicinal products and food supplements, the trade obstacles due to the differences in national legislations on botanicals, the growing interest in the standardization of the safety assessment of such foodstuffs as well as the criticism linked to the application of the nutrition and health claims legislation demonstrate the complexity of the issues relating to botanicals and the need for a better harmonized and *ad hoc* regulation at European level.

Abstract

Botanicals and the Regulatory Framework on Food Supplements in the European Union: a Tricky Relationship

In the EU and many other countries (China, Japan, Usa, Canada, etc.), there is a growing interest in producing and consuming *health food products*. Botanicals (e.g. plants and preparations made from plants, algae, fungi or lichens) represent a large segment of the health food category and their regulation presents several critical issues due to their complex nature and multifaceted usage.

This article therefore gives an overview of the most important issues related to the regulation of botanicals in the food supplements sector. After a brief description of the regulatory status of botanical based foodstuffs, it outlines the legal framework of botanical food supplements, taking into consideration the interferences between the medicinal domain and the food sector in the classification of borderline botanical products and the issue of the safety assessment of botanicals. In the final part, it deals with the thorny question of the health claims made on such products.

Sommario

Prodotti botanici e regolamentazione degli integratori alimentari nell'Unione Europea: una complessa relazione

In Europa e in molti altri Paesi (Cina, Giappone, Usa, Canada ecc.), vi è un crescente interesse per la produzione e il consumo di alimenti salutistici. I prodotti botanici (cioè piante e preparati ottenuti da piante, alghe, funghi o licheni) costituiscono un vasto settore di tale categoria di alimenti e presentano molteplici profili critici in conseguenza della loro complessa natura e del loro poliedrico impiego.

L'articolo intende offrire una ricostruzione dei più rilevanti aspetti della regolamentazione dei prodotti botanici nel settore degli integratori alimentari. Dopo una breve descrizione della disciplina concernente gli alimenti a base di sostanze vegetali, delinea il quadro giuridico dei prodotti botanici quali integratori alimentari, tenendo in considerazione le interferenze tra il settore farmaceutico e quello alimentare nella classificazione dei prodotti botanici di *frontiera* e gli aspetti attinenti alla loro sicurezza. Infine, si sofferma sulla spinosa questione delle dichiarazioni sulla salute apposte sulle etichette di tali prodotti.

Keywords: Botanical, Health Food, Food Supplement, Borderline Product, Safety, Labelling.

Parole chiave: prodotto botanico, alimento salutistico, integratore alimentare; prodotto borderline, sicurezza, etichettatura.

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