Prospects of Functional Foods/ Nutraceuticals and Markets

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Abstract

Functional foods and nutraceuticals are reported as one of the top trends of the food industry, but because of the different definitions of the terms, it is uneasy to calculate their global market size. With a broad definition, this value is well over

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$40 billion, and is showing steady annual increases both in sales and new products launched. However, there are differences according to the ingredients and the claims used.

Several factors are considered crucial for the future market evolution: the degree of acceptance and awareness of functional foods by consumers, the association between manufacturers and academic researchers, and the effects of new regulations for nutrition and health claims. Concretely, the Regulation 1924/2006 will have a great impact on the number of products bearing a claim. We have analyzed European Authority of Food Safety (EFSA) opinions on plant extracts and phytochemicals, including phenolic compounds, since they can provide lessons for the development of functional foods all over the world.

Scientific research is indispensable for the substantiation of the evidence for functional foods. Advances in the characterization of plants ingredients by hyphenated MS and NMR technologies, standardization of human clinical trials, and emerging methodologies like bioinformatics or nutrigenomics can be crucial for the development of new functional products.

Keywords
Claims. EFSA • consumers • functional foods • Market

Abbreviations

EFSA	European Food and Safety Authority
FDA	Food and Drug Administration
ILSI	International Life Science Institute

1 Introduction

1.1 Definition of Functional Foods, Nutraceuticals, and Related Terms

The advent of functional foods and nutraceuticals on the market has blurred the distinction between pharma and nutrition [1]. Obviously, the concept of foods promoting health is not new. In 400 b.c., Hippocrates already sentenced "Let food be thy medicine and medicine be thy food" [2], and in the countries of the far East, influenced by Chinese culture, foods such as glutinous rice, wheat, sesame, jujube, gingiber, or leek were included in Chinese medicine books for their traditional use for chronic diseases [3]. Nowadays, the development of functional foods is one of the most intensive areas of food product development worldwide, opening multiple challenges for countries with a vast biodiversity and historical use of plant extracts [4].

However, estimating the market size values for functional foods can be difficult, because of the ambiguity of the term "functional food," the lack of an official or univocally accepted term (in many countries there is no regulatory

Table 80.1 Concepts related to functional foods and nutraceuticals

Functional foods	A food can be regarded as 'functional' if it is satisfactorily demonstrated to affect beneficially 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 risk of disease. Functional foods must remain foods and they must demonstrate their effects in amounts that can normally be expected to be consumed in the diet. They are not pills or capsules, but part of a normal food pattern	[6]
Nutraceuticals	A nutraceutical is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with food. A nutraceutical is demonstrated to have a physiological benefit or provide protection against chronic disease	[7]
Dietary supplements	A product that contains one or more of the following dietary ingredients: vitamin, mineral, herb, or other botanical, and amino acid (protein). Includes any possible component of the diet as well as concentrates, constituents of extracts or metabolistes of these compounds"	[8]
Food supplements	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, drop dispensing bottles, and other similar forms of liquids and powders designed to be taken in measured small unit quantities	[9]
Parnuts	Foodstuffs for particular nutritional uses are foodstuffs suitable for their claimed nutritional purposes and which are marketed in such a way as to indicate such suitability. They can include: – Infant and follow-on formulae – Processed cereal-based foods and baby foods for infants and young children – Food intended for use in energy-restricted diets for weight reduction – Dietary foods for special medical purposes – Foods intended to meet the expenditure of intense muscular effort, especially for sportsmen. – Foods for persons suffering from carbohydrate metabolism disorders (diabetes).	[10]
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 substances in combination with one or more such herbal preparations	[11]

definition) [5], and the diffused borders between concepts for commercial products also related to health-promoting functions such as "functional foods," "nutraceuticals," "superfoods," "dietary supplements," or "cosmeceutics," many of which respond to marketing criteria. Table 80.1 compiles some of the terminologies currently associated to functional foods and nutraceuticals.

Despite the ancestral knowledge of the link between diet and health, the appearance of specific terms related to foods promoting a health benefit is more recent.

In 1984, the concept of functional food was first promoted in Japan by scientists who were studying the relationships between nutrition, sensory satisfaction, fortification, and modulation of physiological systems [12]. The Japanese Ministry of Health and Welfare then introduced "Foods for Other Specific Health Use" (FOSHU) in 1991, promoting its use as a strategic action to reduce healthcare costs. The success of the initiative (in 2000, the total number of approvals under the FOSHU label reached 174, with an estimated market value of around $2 billion [13], while more than 500 products were labeled as FOSHU in 2005 [5]), united to the success of products with health claims in the USA, paved the way for the development of the functional foods market. However, consensus on a definition or categorization of these foods was established by heterogeneous criteria by manufacturers or scientists, not by regulatory agencies.

In Europe, the International Life Science Institute (ILSI) established an operational definition of functional foods: "a food product can only be considered functional if, together with its basic nutritional impact, it has beneficial effects on one or more functions of the human organism, either improving the general and physical conditions and/or decreasing the risk of evolution of diseases. The amount of intake and form of the functional food should be as it is normally expected for dietary purposes. Therefore, it could not be in the form of pill or capsule but only as a normal food form." This definition would establish a clear separation from nutraceuticals, which can be considered as diet supplements that deliver a concentrated form of a presumed bioactive from a food, presented in a nonfood matrix, and used with the purpose of enhancing health in dosages that exceed those that could be obtained from normal foods [14]. Nutraceuticals are sold in presentations similar to drugs: pills, extracts, tablets, etc. [15]. However, in many cases, the functional food market is referred as the "nutraceutics" market [16], and then, it is difficult to separate the exact values for each. A reason for this interconvertibility of terms is that much of the early development of the nutraceutical concept and products was driven from the USA, where the Dietary Supplement and Health Education Act (DSHEA) allowed considerable flexibility and blurred the boundaries between foods and medicines that can be found in other parts of the world [17]. Anyway, there is no definition for nutraceuticals in neither the UE nor the USA, although both have a definition for supplements, which could be considered equivalent to nutraceuticals.

In opposition, the federal Department of Canada has proposed, via Health Canada, differentiated definitions for nutraceuticals and functional foods. A nutraceutical is a product isolated or purified from foods that is generally sold in medicinal forms not usually associated with food. It is demonstrated to have a physiological benefit or provide protection against chronic disease. A functional food is similar in appearance to, or may be, a conventional food, is consumed as part of a usual diet, and is demonstrated to have physiological benefits and/or reduce the risk of chronic disease beyond basic nutritional functions. In this case, the difference of formulation between both kinds of products is well established [7].

Most functional foods definitions do not intend to exclude natural foods in the functional foods category. However, many manufacturers and the perception of the

general public would disagree, since for many of them, the functional food should imply an inherent fortification of the food with a bioactive ingredient. And from the pragmatic point of view of manufacturers concerned about regulation accomplishments, functional foods would be those that bear or intend to bear a nutritional or a health claim.

Another conflictive concept is the one for cosmeceuticals. Neither the FDA nor the EFSA recognizes this term, which is widely used by the cosmetic industry to refer to cosmetic products that have medicinal or drug-like benefits. Like cosmetics, cosmeceuticals are applied topically but differ in that they contain potent ingredients that can influence the biological function of the skin and deliver nutrients to promote healthy skin [18]. Nearly universally around the world, this has become the catchword for the millennium change in cosmetics to retard aging [19].

Other marketing concepts have arisen like "superfoods," which are referred to natural products that have a low glycemic index and provide key nutrients that are lacking in the typical western diets, like beans, dark green leafy vegetables, citrus, sweet potatoes, berries, tomatoes, fish high in omega-3 acids, whole grains, nuts, fat-free milk, and yogurt [20]. A derivative concept, "superfruits," has emerged to design natural fruits (including blueberries, blackberries, cranberries, pomegranate and exotic ones such as açai or goji) that have a high antioxidant capacity. However, neither of those terms has been recognized by the Food and Drug Administration or the European Food Safety Authority.

Finally, other terminologies that used to be popular such as vitafoods, alicaments, or pharmafoods have become obsolete and fallen out of use.

1.2 Socioeconomic Context of Functional Foods and Nutraceuticals

To understand the success in the functional foods and nutraceuticals sector and the reasons behind their expansion in the market as well as the menaces that can compromise their growing, it is necessary to describe the socioeconomic context, which includes many interactions between consumers, scientists, food manufacturers, and legislative bodies.

1.2.1 Functional Foods as a Vector for Health

In the last decades, the social economic development has induced profound changes in consumer behavior, involving, in particular, food consumption dynamics. The elements that have most influenced and still influence consumer eating habits are the lengthening of life expectancy, the progressive ageing of population, the health economic and social costs rising, the widespread desire for a better quality of life, and media and advertising [21].

Major current problem areas for population health include obesity, cardiovascular health, age-related cognitive decline, metabolic syndrome, insulin resistance, and diabetes [22]. All these concerns are expected to grow because of the change of the age pyramid to older societies. People are living longer, and so incidence

of specific diseases or conditions of elder people, such as cardiovascular diseases, diabetes type 2, osteoporosis, or neurodegenerative diseases, will increase. The biggest health concern nowadays is obesity and overweight, especially because of the highest increase in developing countries [23]. The WHO estimated in 2003 that over one billion people are obese and over 400 million people are clinically obese [22]. Cardiovascular diseases are also a big concern: They represent 30–50 % of cause of mortality in developed countries. High blood pressure and cholesterol levels have reached pandemic dimensions, and it is predicted that the worldwide incidence of diabetes will exceed 450 million people by 2025 [22]. The prevalence of arthritis and osteoporosis in the aging populations of developed nations is also growing: In 2010, more than 5.5 million people in the seven major markets were forecast to be suffering from rheumatoid arthritis (RA) [24].

Many of the major chronic diseases are caused substantially by poor diets. The consumption of whole grains and better lifestyle choices could represent a reduction of over 100,000 deaths per year in the UK [25]. Since a major issue for public research is targeting prevention of diet-related diseases [26], there is a growing interest about the links between food and health by public health officials [27]. Functional foods have the potential to improve population health in line with the objectives identified by national public health strategies [28], promoting the prevention and risk reduction of disease, and thus reducing mortality rates and medicinal costs associated to therapeutic treatments. For example, it was estimated that in the USA, total direct and indirect costs associated to diabetes and related disorders reached $98 billions in 1997 [22]. In 2005, $466 m were spent on pharmaceutical medication to treat obesity in the seven major markets, and these sales were set to triple to $1.5 billion by 2010. In 2005, $84 billion were spent in the USA and the 5 major European markets on the pharmaceutical treatment of CVD conditions. By 2010, sales were expected to rise to $105 billion. In 2005, it was estimated that around $22.5 billion were spent worldwide on the sale of drugs used to treat rheumatoid arthritis (antirheumatics), osteoporosis (osteoporosis agents), and inflammatory conditions, with $14 billion of this generated from sale of medicines in the top seven countries [24].

In this context, public health organizations and governments share a mutual interest in promoting health through nutrition and adequate lifestyles, thus reducing medical costs. For example, the consumption of whole grains and better lifestyle choices could represent a reduction of over 100,000 deaths per year in the UK [25]. In fact, this was the key reason why the Japanese government introduced the FOSHU system: to keep the aging population healthy through functional foods and to keep the health care costs down. Similar policies are spread all over the world. For example, agriculture, food, and health are significant themes in the European Union's current Seventh Framework Research Programme (FP7) [26].

1.2.2 The Perspective of the Consumer

Consumer acceptance of the concept functional foods, together with a better awareness of its determinants, is widely recognized as key success factor for market orientation, consumer-led product development, and successfully negotiating

market opportunities [29]. However, little research has been conducted to analyze the perspective of the consumers [30].

In fact, one of the main reasons of the success of functional foods has been the role of consumers undertaking new trends to a healthier lifestyle. Many objective data show this tendency. For example, between 2006 and 2007, vegetables and fruits were the top 2 products whose use increased in North America, Western Europe, and Nordic Europe, while processed foods, salty snacks, and sugars were some of the products with the biggest decrease in use. In the last 25 years, butter has decreased from around 70 % of the yellow fat market to 25 %, while low fat spreads have captured half this market. In the cooking fat sector, vegetable oils have taken over the animal fats. Skimmed and semi-skimmed milks have copped 2/3 of milk sales, while low calorie soft drinks have increased to 20 % of the soft drink market [31].

Apart from these examples of healthier choices taken from objective market data, several surveys are periodically conducted in developed countries to follow the public attitude toward health. In 2011, according to the International Food Information Council Foundation Food & Health Survey, 59 % of Americans declared that they were attempting to make changes to improve the healthfulness of their diets, in order to ameliorate their overall well-being (65 %), lose weight (56 %), improve their physical health (56 %), because of a specific health condition (32 %), and/or maintain weight (20 %) [32]. Similar tendencies can be found in European countries.

However, these pronouncements have to be considered carefully, because some data have reported lower frequencies of healthy food consumption in American consumers, despite their intention of eating healthily more often [33]. This distance between the consumers' aspirations and the real consumption is a clear menace to the success of the functional foods niche and should be overcome by providing functional products that are attractive to the potential buyer, both in price, and taste and efficacy.

Acceptance of Functional Foods and Willingness to Buy New Products

In the process of developing new functional ingredients or foods, there must be a consumer need or a problem that requires solution, and there must be self-awareness of the problem from the consumer. But it is also crucial that consumers must be willing to spend money to solve the problem or satisfy the need they have identified [23].

The Functional Foods/Foods for Health Consumer's trending survey is being conducted every 2–3 years since 1998 and provides ongoing American consumers insights into their interest and perceptions about food and beverages and the roles they have in promoting health and wellness [34]. This study summarizes some of the points that can explain the reasons for the success of functional foods. A first aspect to be considered is the acceptance by consumers that functional foods can have added health and wellness benefits. Most data from other surveys in other countries show conformity with this topic. According to the 2009 IFIC Functional Foods/Foods for Health Consumer Trending survey,

between 68 % and 85 % of Americans agree that foods or beverages can provide specific health benefits such as improving heart health, contributing to healthy grown and development in children, or improving bone health [34]. In Europe, even when consumers had not heard the term "functional foods," more than 50 % agreed to fortify functional ingredients in specific food products [35]. Japanese consumers have traditionally been aware of the importance of certain foods for the promotion of health.

Obviously, general health orientation varies systematically as a function of age and gender. According to the results obtained from different questionnaires, rational food consumers are the primary potential target of functional food producers. Women tend to be substantially more health-oriented than men, which explains the females' stronger purchase interest toward functional foods, an observation that has met consensus in different studies. In general, women have shown to be more reflective about food and health issue. Another relevant socio-demographic factor is the presence of children in the family. On the other hand, middle-aged and elderly consumers tend to be substantially more health-oriented than young consumers. In truth, middle-aged and elderly are the largest group who uses functional foods to target a specific health concern. In this case, it is hypothesized that this group is more likely to have confronted relatives' loss of good health, and this experience with illnesses and associated economic and social consequences increase probability of functional food acceptance [29]. In overall, the hypothesized effects of socio-demographic determinants are that acceptance of functional foods increases with higher age, being female, having young children, and having an ill family member.

At the same time, there are discrepancies about the role of education in the acceptance of functional foods. In Europe, it is biased toward the higher socioeconomic groups, reflecting a higher willingness or ability to pay a premium price; while in the USA, there is a higher acceptation among the lower educated. Another difference between American and European consumers is the far more critical attitude toward new product and technologies, and therefore, it can be hypothesized that European's acceptance of functional foods is less unconditional [5].

In conclusion, it seems to be a global acceptance of functional foods, but this must not be taken for granted and cannot reflect the perception of concrete functional foods. In this sense, another of the aspects addressed in consumers' research is the awareness of functional foods.

Concerning the awareness of the terminology of functional foods, different surveys show that consumers are not greatly informed about this concept, although there is a steady tendency to increase these levels of awareness in all the countries. For example, in an Italian quantitative survey conducted in 400 consumers, 24 % were unable to give a definition for functional foods, 20 % confused them with light and dietary products, and 16 % incorrectly associated them with food for those who have specific health problems [36]. In Belgium, 49 % of consumers were familiar with the term "functional food," but only 30 % in Hungary and 4 % in Poland [37].

Given the positive acceptance showed for functional foods in general, it should come to no surprise that most studies have shown a significant willingness to pay

for this kind of products. For example, Mintel Oxygen 2010 reported that more than half of consumers had bought a functional food or beverage in the 3 months previous to the study. More than half of the Americans reported in 2009 the consumption of foods or beverages for overall health and wellness (56 %), heart health benefit (55 %), or to contribute to a healthy body weight [34]. In a recent survey in Europe, 15 % of consumers reported a daily consumption of functional foods, 24 % reported a high-frequency consumption, and 28 % considered themselves occasional buyers. Only 21 % of respondents stated that they had never consumed these products [36].

Again, regardless of the global willingness to pay for healthy products, the acceptance of a specific functional ingredient is linked to the consumers' knowledge of the health effects. Functional ingredients which are in the mind of the consumers for a relatively long period of time (e.g., vitamins, minerals, fiber, low sugars, etc.) achieve considerably higher rates of acceptance than ingredients that are used for a short period of time. This can have a great impact in the context of the economic recession. Although it can be demonstrated that consumers are willing to spend for relevant functional benefits even in times of financial crisis, consumers are less likely to experiment with new functional foods and beverages: In this sense, the credibility of the health effect and the perceived effectiveness of the product, as well as a correct knowledge of the ingredient and a correct association between the ingredient and the health benefit, is crucial. For example, fiber, calcium, iron, and vitamin D are well-known ingredients and consumers are correctly aware of the kind of health benefit they can expect from them. Omega-3, probiotics, and phytosterols were less known, but thanks to the advertising policies communicating their health effects, consumers have a good knowledge of their benefits. In opposite, products like oligosaccharides, lutein, or peptides are less popular. It is of great importance to have well-informed consumers, conscious of the effects of the ingredients, in order to avoid incorrect expectancies that can further lead to deception and lack of trust in future products.

In sum, for those products with limited consumers' knowledge, there are strong needs for specific information and communication activities. Doctors, nutritional advisers, and public entities are the sources in which the consumers have most confidence (42–45 % of trust), while a lesser degree of confidence is given to producers and product labels [13, 36]. The implementation of specific regulations restricting the use of nutrition and health claims to products with a solid scientific evidence will also offer a reinforcement of the trust of consumers in the long term. But in the short term, the withdrawal of many health claims for top products, some of them very popular among consumers, because of insufficient scientific evidence, can have the contrary effect. So, it is advisable to reinforce the transparency on the information to consumers to avoid a bad global perception of the functional foods products.

1.2.3 Association of the Industry and the Scientific Community

It must not be forgotten that because of its innovative component, functional foods have been possible, thanks to the arousal of new knowledge about the relationship

between ingredients and health, which has mainly been provided by the advances in the scientific research on the subject.

Innovative concepts in the area may thus emerge from academic researchers, although they often are not aware of how to translate these ideas into final marketable food products [38]. In consequence, most frequently it is the industry that initiates the cycle of development, but working closely with academics (for example, through the formation of scientific advisory boards) to provide a solid ground to design a new functionality/ingredient, as well as to conduct the series of safety, efficacy, and bioavailability tests to prove the applicability of the new designs. This cycle of innovation can lead to breakthrough products, which can be defined as products, which provide a company with greater profits and longer-lasting competitive advantage in the marketplace in comparison to minor product development or line extensions [39], that can be as well a good and easier way to include a health claim in food products. But while the first case would in general be early-movers, in the second case, normally, it would be companies deciding to approach the functional food market in response to its astonishing growth [40]. This difference in the degree of innovation is well recognized in the UE Regulation 1924/2006, which distinguishes innovative products (Article 13.5), while at the same time provides a list (Article 13.1) that already states more usual ingredients-activities relationships.

2 Market Prospect of Functional Foods

2.1 Global Sales: A Steady Progression

Many market studies of global sales of functional foods differ in the data, depending on the criteria used for the inclusion of products in the analysis. For example, under a strict definition, according to Leatherheadfood, the functional food and drinks market had a combined value of $19.4 billion in 2007, whereas with a broader definition, the market raised to $41.9 billion [41]. In 2011, the global market for a strict definition of functional products as those offering specific health claims was estimated at $24.2 billion [42]. BCC research established a Nutraceuticals Global Market for nutraceutical foods, nutraceutical beverages, and nutraceutical supplements of $40 billion each.

Another source of confusion for the precise definition of the market size is that many functional ingredients were initially included in foods for reasons other than their health-promoting values. For example, the use of antioxidants for food preservation purposes was prior to their commercialization as health-enhancing functional additives, and bioactive compounds such as anthocyanins from red berries or lycopene from tomato were more appreciated because of their application as natural colorants rather than because of their biological activity against free radicals. Obviously, the higher added-value obtained because of their healthy properties has meant a faster growing development of these products. In 2007, global sales of antioxidants used in the manufacture of foods amounted to $788

million, representing a constant yearly increase of 3 %. Functional antioxidants in 2007 already accounted for the majority of sales, holding a value share of almost 56 %, with antioxidants used for food preservation purposes making up the remainder [43].

Despite this lack of precision concerning the data, functional foods have undeniably been reported as one of the top trends facing the food industry. They have been especially active since the last decade, when the annual growth rate of the functional foods market ranged from 15 % to 20 % at the end of the 1990s [29]. The global functional food market in 2002 was roughly estimated to be between $10 billion and $40 billion with an annual increase of about 8 % [39]. In 2008, when using a definition of functional foods that comprised all "products bearing a health claim," this group of products had arisen as the fastest-growing sector of the food market, with estimates forecasting an expected annual growth rate of 10 % for functional foods as compared to an average 2–3 % for the food industry as a whole [44]. Although growth rates estimates have decreased over time, the numbers remain impressive compared to growth rates for the food industry as a whole.

Even in the actual situation of economic recession, which should compromise the willingness of consumers to buy more expensive foods, recent estimates remain optimistic. Consumer interest in functional foods remains strong, and the rising costs of healthcare and the needs of an aging population should still encourage the consumers' commitment to health and wellness pursued through the diet. Recent data from 2007 by Pricewaterhouse Coopers [45] predicted that functional foods in the USA could grow by up to 20 % or five times that of the food industry as a whole [46], which is consistent with other reports by Leatherhead [47] that products making specific health claims –not including neither energy and mood drinks, nor food supplements – are predicted to grow at 4–5 % for the next few years [48]. According to market analyst Freedonia, demand for nutraceutical ingredients like botanicals, vitamins, minerals, and omega-3 s will grow 7.2 % annually until at least 2015 to be worth €18.5 billion with newer markets like Mexico and South Korea helping drive growth in the sector [49]. And a report by Global Industrial Analysts projected the global nutraceuticals market projected to exceed US$243 billion by 2015 [50].

Figure 80.1 shows this evolution in the functional foods and beverages market size.

Concerning differences between countries, according to Datamonitor, some of 90 % of total sales occurs in Europe, the USA, and Japan [51]. In Japan, according to a Leatherhead report utilizing tight functional food definitions, global sales in 2010 reached $24.22 billion, which would represent the 38.4 % of the global functional market, followed by the USA with 31.1 % and Europe (28.9 %) [48].

In the USA, with between $20 billion and $30 billion in sales a year, functional foods comprise about 5 % of the entire US food market [52].

In Europe, Germany, France, United Kingdom, and the Netherlands represent the most important countries within the functional foods market, but many other European markets are experiencing high growth rates, such as the Netherlands and Spain.

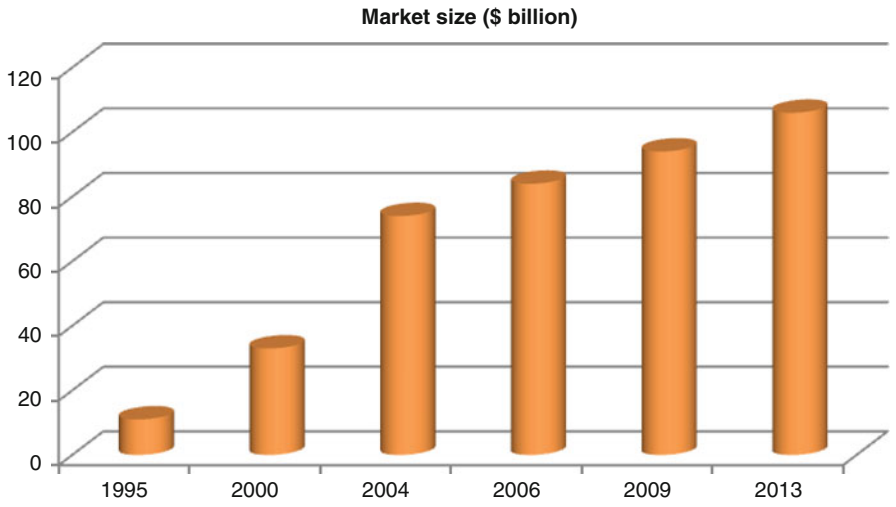

Fig. 80.1 Global market size of functional foods (Sources: New Nutrition Business (1995, 2000) [53]; Euromonitor International (2004, 2006, 2009) [54]; BCC Research (2013) (http://www.bccresearch.com/report/nutraceuticals-processing-markets-fod013c.html))

In addition, newly emerging markets like Hungary, Poland, and Russia are also well positionated [36].

2.2 Situation of Specific Product Launches, Ingredients, and Claims

The growth of the functional food market has been correlated with a steadying increase of the number of functional food products launches. According to Mintel analysts, the global launches of functional products between 2005 and 2009 were more than doubled, from 904 to 1859. Between 2008 and the first half of 2009, USA was the leader in healthy product launches (881 products), followed by Japan (314), Italy (325), UK (237), Germany (235), and France (150) [46].

The main functional foods category correspond to dairy products, that account for the 38 % of the market, followed by bakery and cereals (22.7 %), beverages (12.5 %), meat, fats and oils (8.1 %), fish and eggs (7.4 %), and soy products (5.8 %). In most cases, there has been a significant growth in the market. For example, according to Euromonitor the global market for pre- and probiotic spoonable yogurt had a growth of 128 % between 2004 and 2009, from $3.3 billion to $7.6 billion, while for drinking yogurt, it grew a 44 % to $11.2 billion [55]. Sales of functional spreadable oils and fats grew 54 %.

Classified according to health claims made on the product, digestive health has been the most used claim for new products (Fig. 80.2) [56].

It is relevant to state that food traditions and cultural heritage influence the interest of consumers in functional foods. For example, despite dairy is the biggest

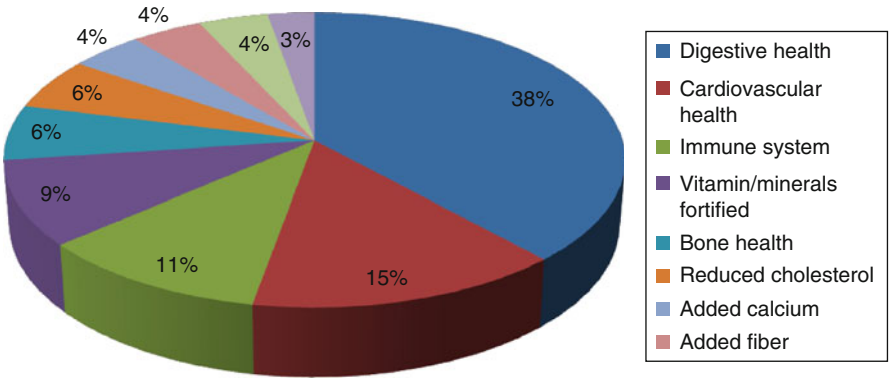

Fig. 80.2 Global distribution of health claims in functional products launches between 2005 and 2009 (Source: Mintel's Global New Products Database)

segment in the global market, in the USA, this predominance is for functional beverages, including energy and mood beverages. According to Leatherhead Food International, functional drinks account for 50 % of the US functional food market, followed by cereal products [48]. Another characteristic of the USA is that consumer expenditures on nutraceuticals are especially active, having reached a reported $20.50 billion in 2004, more than double the amount spent in 2004. Supplementation is also quite popular in Japan, whereas European consumers are less driven to these kinds of products. Another example of regional particularities is the fact that Japan is the world's largest market for green tea sold in leaf, which accounts for nearly 65 % of total leaf tea sales in the domestic market [43].

Concerning claims, digestive health is not the top claim in the USA, this honor belonging to cardiovascular health. On the opposite side, cardiovascular health claims are quite reduced in Japan (less than 10 % of the new functional foods launches). In the UK, cardiovascular health claims have represented a 20 % of the 530 new products between 2005 and 2009 [58].

2.3 New Perspectives

Despite the continuous introduction of new functional food or beverage products to the market, in the last few years, a certain reduction in the number of launches for some of the functional ingredients has been observed. Mintel reported in 2010 a slowdown in the market for energy drinks and fortified waters in the USA [57]. Figure 80.3 shows the reduction on the number of new products with claims related to the polyphenols family, according to Datamonitor. This reduction that can be attributed to different factors such as the development of new legislations such as the recent implementation of the UE 1924/2006 Regulation, that is limiting the use of nutrition and health claims by establishing the need of a strong substantiation of the evidence of the claimed effect. This has led to the dismissal of several health

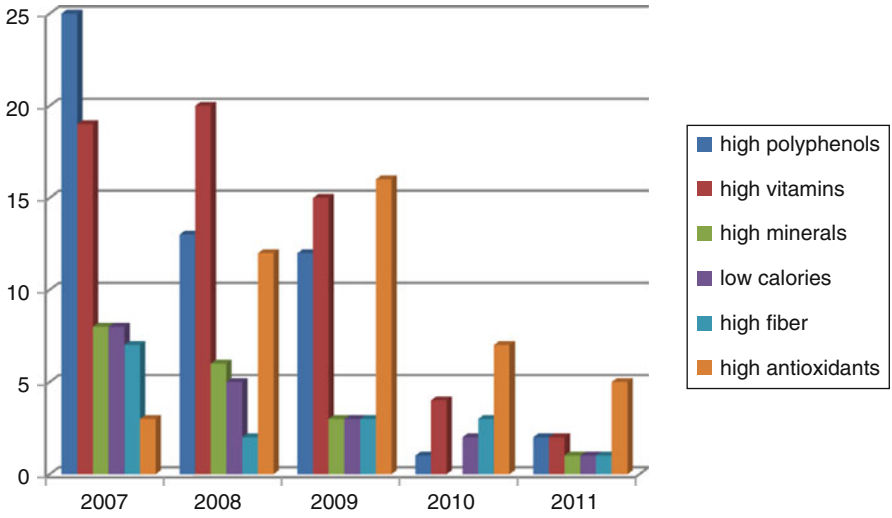

Fig. 80.3 Number of global launches of ingredients with polyphenols associated to different claims (Source: Datamonitor)

claims for many products, especially in areas like natural plant extracts or probiotics. This will mean a reduction on both the number of functional foods as well as their market value, at least according to the definition of functional foods as those wearing a nutrition or health claim. For example, there was an 11 % drop in the number of health claim-bearing launches between 2009 and 2010, even if the transition period for many products was still applied in the UE.

Additionally, in a global economic situation of recession, food companies can find difficulties to assume the costs associated to the development and scientific substantiation of evidence for new products, especially for cases that could imply expensive research.

The difference of the economic impact between products with health claims compared to those without them is uncertain. For example, in the USA in 2000, the market for functional foods with specific health claims achieved a turnover of around $0.5 billion, while functional foods without claims had an annual turnover of at least $15 billion [13].

3 Functional Foods Under Scrutiny: Situation of Natural Products Relating to the Substantiation of Evidence

3.1 Regulation of Functional Foods and Nutraceuticals Market

To ensure that the products are not misleading consumers, governments from various countries have developed regulation systems. Normally there exist

associated organizations that take care of the accuracy of the claims used for functional foods and nutraceuticals. Some of these organizations are the European Authority of Food Safety (EFSA) in Europe, the Food and Drug Administration (FDA) in the United States, or the Ministry of Health, Labour and Welfare (MHLW) in Japan. We will discuss the current situation of the USA and Europe in relation to the approval of claims.

3.1.1 USA

In the USA, claims on foods and dietary supplements can belong to three different categories: nutrient content claims, structure/function claims and health claims.

Structure/function claims can be used for dietary supplements, and describe the effect on the structure or function of the body [8, 58].

Nutrient content claims can be considered as "expressed nutrient content claims," which is any direct statement about the level (or range) of a nutrient in the food, or as "implied nutrient content claims," which denotes any claim describing the food or an ingredient therein in a manner that suggests that a nutrient is absent or present in a certain amount or suggests that the food, because of its nutrient content, may be useful in maintaining healthy dietary practices. Annex Table 80.3 shows the nutrient content claims of the USA.

Health claim means any claim (including statements, symbols, vignettes, etc.), made on the label or in labeling of a food or dietary supplement, that characterizes the relationship of any substance to a disease or health-related condition.

In their origin (1990), health claims had to be based on a very high standard of scientific evidence, evaluated by the FDA. However, after the result from a 1999 Court of Appeals Decision, Pearson v. Shalala, the *Qualified Health Claims* were introduced for substance/diseases relationships with lower standards of evidence, that is considered credible but without reaching a significant scientific agreement standard. In the case of Qualified Health Claims, the proposed claim has to include qualifying language that identifies limits to the level of scientific evidence to support the relationship [59].

Table 80.2 compiles the Health Claims and Qualified Health Claims approved by the FDA.

3.1.2 European Union

The EU Regulation 1924/2006 [60] distinguishes two types of claims:

Nutrition claims are claims that state, suggest, or imply that a food has particular beneficial nutritional properties due to the energy it provides or the nutrients it contains [61]. Annex Table 80.4 compiles these claims.

Health claims are any claim that state, suggest, or imply that a relationship exists between a food category, a food, or one of its constituents and health. *Reduction disease risk claims* are health claims that state, suggest, or imply that the consumption of a food category, a food, or one of its constituents significantly reduces a risk factor in the development of a human disease.

The regulation classifies health claims into three main types. Article 13.1 claims pertain to "general function" claims relating to growth, development, and functions

Table 80.2 Health claims and qualified health claims approved by the FDA

Health claims	
Calcium, Vitamin D	Osteoporosis
Dietary lipids (fat)	Cancer
Dietary saturated fat and cholesterol	Risk of coronary heart disease
Dietary non-cariogenic carbohydrate sweeteners	Dental caries
Fiber-containing grain products, fruits and vegetables	Cancer
Folic acid	Neural tube defects
Fruits and vegetables	Cancer
Fruits, vegetables and grain products that contain fiber, particularly soluble fiber,	Risk of coronary heart disease
Sodium	Hypertension
Soluble fiber from certain foods (whole oat, barley, psyllium seed husk)	Risk of coronary heart disease
Soy protein	Risk of coronary heart disease
Oatrim	Risk of coronary heart disease
Stanols/Sterols	Risk of coronary heart disease
Qualified health claims	
Tomatoes and/or tomato sauce	Prostate, ovarian, gastric, and pancreatic cancer risk
Calcium	Colon/Rectal cancer & calcium and recurrent colon/Rectal polyps risk
Green tea	Cancer risk
Selenium	Cancer risk
Antioxidant vitamins	Cancer risk
Nuts	Heart disease
Walnuts	Heart disease
Omega-3 fatty acids	Coronary heart disease
B vitamins	Vascular disease
Monounsaturated fatty acids from olive oil	Coronary heart disease
Unsaturated fatty acids from canola oil	Coronary heart disease
Corn Oil	Heart disease
Phosphatidylserine	Cognitive dysfunction and dementia
Chromium picolinate	Diabetes
Calcium	Hypertension, pregnancy-induced hypertension, and preeclampsia
0.8 mg folic acid	Neural tube birth defects

of the body. They should be based on generally accepted evidence and could be used by any manufacturers as long as the conditions of use are kept. Article 13.5 claims pertain to general function claims based on new and/or proprietary data. This type of claim is particularly relevant for manufacturers who have invested in innovation and wish to protect their claim and/or underpinning scientific data [62].

Article 14 claims refer to risk reduction claims or claims related to children's health and development.

According to the Regulation, the European Food and Safety Authority (EFSA) is the consulting organization for the analysis of the scientific substantiation of evidence of Health Claims. Its evaluating process, which started after the implementation of the Regulation, will imply a change in the allowed health claims for functional foods in Europe. The Fig. 80.4 compares, for some of the most popular ingredients, the successes and failures on obtaining a positive opinion about the scientific substantiation of evidence for the ingredient's intake and health relationship.

As it can be inferred from EFSA opinions, while there are some ingredients with well-established relationships of cause and effect between their intake and the claimed effects, for many other compounds, this association is much less proven.

On the positive side, with a high percentage of success, the cholesterol-lowering effect of phytosterols, the role of carbohydrate-electrolyte solutions for the enhancement of water absorption during physical exercise, or the importance of vitamins and minerals toward different processes is well accepted.

In opposition, the cause-effect relationship of probiotics, prebiotic fiber, and phytochemicals (including plant extracts), among other ingredients, has commonly been considered as insufficiently substantiated. For probiotics, an inadequate identification of the probiotic strains, as well as the difficulty to correlate the changes in microflora with a beneficial physiological outcome, can be stated as the main reasons for most of the negative opinions emitted. In the case of phytochemicals, the characterization is also a main reason of rejection, together with the quality of the studies presented and the relevance of biomarkers used to sustain the effect.

Other ingredients show a more equilibrated balance between positive and negative opinions. With reference to fatty acids, positive opinions, for example, in the case of some omega-3 fatty acids like docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), or linolenic acid and their role in maintenance of triglycerides levels, and for long-chain omega-3 fatty acids maintenance and development of vision and brain function have been published. In contrast, the evidence for conjugated linolenic acids or gamma-linolenic acids has been considered unsatisfactory. Concerning fibers, the importance of distinguishing the effects depending on the concrete fiber has been established. For example, the maintenance of normal blood cholesterol levels is well accepted for beta-glucans, glucomannans, or guar gum, but not for acacia gum or isomalto-oligosaccharides. The role of soluble and insoluble fibers is well known to be different, and in consequence, concrete claims related to non-well characterized fibers usually lack enough scientific evidence. For example, reduction on many claims for various foods related to glycaemic index control has been dismissed because of an inadequate definition of the type or carbohydrates.

It is out of the scope of this chapter to make an exhaustive analysis of the scientific gaps that have been found by the EFSA panel. However, they provide

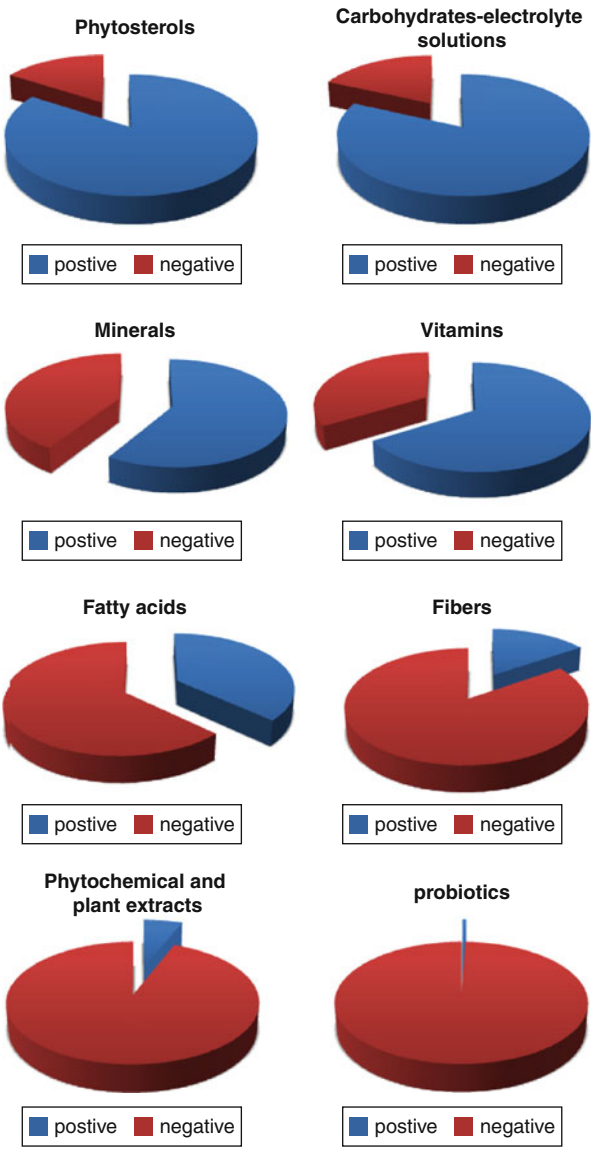

Fig. 80.4 Percentage of positive and negative opinion for different families of ingredients published by EFSA (Source: EFSA Journal, 2008–July 2012)

valuable lessons for the future development of future functional foods, and will undeniably have an impact on the market as well as on the approach to scientific evidence substantiation studies. In consequence, we will analyze some of the key aspects, focused on the families of plant extracts and phytochemicals, that scientists must take into account in order to assist in these developments.

3.2 EFSA Opinions on Phytochemicals and Plant Extracts

In the case of plant extracts and bioactive compounds deriving from them, the levels of success throughout the process of evaluation of health claims by EFSA have been modest at the best. Concerning phytochemicals, between 2008 and July 2012, very few compounds have obtained a positive opinion:

- Caffeine (from guarana, tea, chocolate, coffee, or as a pure form) and increased attention/alertness, reduction in the perceived effort, and increase in endurance capacity and physical performance during short-term high-intensity exercise.
- Polyphenols in olive and protection of LDL particles from oxidative damage.
- Monacolin K from red yeast rice and maintenance of normal LDL-cholesterol concentrations.
- Beta-carotene and maintenance of the normal function of the immune system.
- Cocoa flavanols and maintenance of normal endothelium-dependent vasodilation.

Other popular compounds such as lycopene, lutein, resveratrol, quercetin, catechins from tea, grapes, or cranberries, or soy isoflavones have not obtained a favorable opinion, except in cases where they were actually associated with other compounds that had already proven to have an effect like vitamin E or C.

Concerning plant extracts, many of them have been kept on hold by the European legislation. Prior to this reschedule, all those evaluated by the provisions of Article 13.1 obtained a negative opinion. But at the same time, stories of success have also arisen. It is an illustrative example the case of the tomato WSC extract, whose effect over platelets aggregation was well established by pertinent and company-proprietary clinical studies and was worth of being the first accepted ingredient via the Article 13.5.

This example illustrates how, although there have been more deceptions than triumphs in the evaluation of scientific evidence provided by plant extracts and phytochemicals, these results, rather than being seen as a disappointment, can be considered an excellent opportunity for manufacturers to invest in scientific research in order to complete standardized quality studies that clearly establish a cause-relation effect between the ingredient intake and the claimed effect, and thus obtaining specific claims according to the article 13.5 of the 1924/2006 Regulation.

3.3 Lessons Learned: Key Scientific Aspects to be Controlled for Obtaining a Health Claim

Following the lessons learned by the EFSA evaluation of health claims, 3 different aspects have to be assessed for obtaining a health claim:

1. Characterization of the ingredients
2. Relevance of the sustained claimed effect
3. Scientific evidence provided by efficacy studies

3.3.1 Characterization

Although many of the functional ingredients (vitamins, minerals, omega-3 fatty acids, etc.) possess reliable methodologies of quantification, this aspect is sometimes incomplete for plant extracts. In some cases, there was no reference to the content of bioactive compounds, the part of the plant used for the preparation, no indication of diary doses, or the extracts were used as multibotanical combinations without specification of the other components.

One of the main reasons for this lack of concretion is the complexity of plant matrices, whose diversified secondary metabolism includes a vast number of different compounds with close structures that can be hard to identify. Some of these families with a well-documented bibliography related to health effects comprise alkaloids, phenolic compounds (including phenolic acids, stilbenes like resveratrol, or flavonoids such as anthocyanins, procyanidins, or isoflavones), terpenoids, carotenoids, sulfur compounds (such as glucosinolates and isothiocyanates), etc. Their presence and amount in the plant source depend on multiple factors including variety, organ of the plant, soil, sun exposure, climate, or even ways of cultivation.

There are several fast tests that estimate the content of these compounds as a whole by spectrophotometric methodologies. However, it is well stated that many of these compounds interact with the metabolic pathways and exert their effect on a structure-dependent manner. So, for understanding the mechanism of action of an extract, and more important, to obtain standardized extracts on the bioactive principles, the development of validated methodologies of identification, analysis, and quantification of individual components should be mandatory.

3.3.2 Relevance of the Claimed Effect

Another aspect that must not be overlooked is the nature of the intended claim. The use of clinical claims should be avoided (these could fall under the scope of the Directive 2004/24/EC for traditional herbal medicinal products, but not for health claims on foods). Claims too vague and unspecific also fall out of the consideration of the Regulation. It would be the case of "energy and vitality," "tonic," or "detoxification," often used in plant extracts submissions.

Finally, it has to be assessed that the claimed effect has significance to human health. In this aspect, it is worthy to make a detailed analysis of the claims related to antioxidants.

"Antioxidant" Claims

More than half of the claimed effects for phytochemicals and plant extracts are related to their protective effect as antioxidants, and many products include this term on their presentations for marketing purposes.

In fact, a first discussion should contemplate the adequateness of the use of the term "antioxidants" as a nutrition claim. There are main differences between UE and US legislations.

In the USA, it has been finally included in the US Food Labeling Part of the Code of Regulations, § 101.54 (f), which states that "a nutrient content claim that characterizes the level of antioxidant nutrients present in a food may be used on the label or in the labeling of that food when: An RDI has been established for each of the nutrients; The nutrients that are the subject of the claim have recognized antioxidant activity; that is, when there exists scientific evidence that, following absorption from the gastrointestinal tract, the substance participates in physiological, biochemical, or cellular processes that inactivate free radicals or prevent free radical-initiated chemical reactions; The level of each nutrient that is the subject of the claim is sufficient to qualify for the claim The names of the nutrients that are the subject of the claim are included as part of the claim (e.g., – high in antioxidant vitamins C and E‖)."

In contraposition, the term "antioxidants" as a nutrition claim has not been included in the corresponding Annex for Nutrition Claims of the UE 1924/2006 Regulation or its amendments. In consequence, for submitting an antioxidant claim, it should be submitted as a health claim, and thus, the significance of the effect for human health has to be considered. And, in this case, the terminology used is of importance.

– "Antioxidant activity, antioxidant capacity, antioxidant properties": These claims would refer to the capacity of food/constituents to scavenge free radicals and/or to their reducing capacity, normally in in vitro models. Since there is no evidence that having antioxidant activity/content and/or antioxidant properties is a beneficial physiological effect on human health (factors such as bioavailability would affect the effects in human), it cannot be considered an acceptable claim [63].
– "Protection of DNA, proteins, and lipids from oxidative damage." This wording reflects correctly and effect that is significant for human health, and so it is acceptable.

3.3.3 Providing the Evidence from Science

The important objective for the development of health claims is to ensure that claims for food components and nutraceuticals are properly justified and they are scientifically substantiated [64]. The evidence provided has to be sufficient to establish a cause and effect relationship between the consumption of the ingredient and the claimed effect. For phytochemicals and plant extracts, it is often not the case. One of the main problems is that in many cases, only in vitro or animal studies have been conducted to sustain the evidence of the claim, or the human data consist of epidemiological studies. Information related to the pharmacopeia alone, often used for the plant extracts submissions, is also insufficient.

Substantiation of a claim should be based on human data, primarily from well-designed intervention studies considering target population, appropriate controls, adequate duration of exposure, and follow-up to demonstrate the intended effect [17]. Randomized clinical trials are the standard trials for providing evidence.

The design and quality of the human studies conducted is a key point to obtain a positive opinion about the scientific substantiation of the effect. Common mistakes include an inadequate choice of outcomes measured to assess the effect or the use of nonvalidated biomarkers, recruiting individuals not representative of the target population, or conducting studies with products that differ from the ingredient object of the claim.

The major factors involved in the design, conduct, and reporting of human studies can be adapted from the Consolidated Standards of Reporting Trials (CONSORT) checklist for medical trials [65]. Recently, the ILSI has published their own guidelines for the design, conduct, and reporting of human intervention studies to evaluate the health benefits of foods [66].

4 The Impact of New Methodologies for the Assessment of Functional Foods

4.1 Hyphenated Methods for the Characterization of Ingredients

The role of advances in chromatographic techniques has been a step point in the development of phytochemistry [67]. Because of the complexity of crude herbal extracts, various online hyphenated techniques have been developed for the analysis of the complex mixtures. These techniques include liquid chromatography (LC), mass spectrometry (MS), LC nuclear magnetic resonance (NMR), and LC-NMR-MS [68]. They facilitate the structure determination of unknown constituents in crude extracts. For example, they are of great applicability in the analysis of flavonoids and other phenolic compounds [69, 70].

Regarding MS instruments, time-of-flight detectors provide elevated mass resolution and accuracy over a broad mass of range, and thus help structural elucidation of nontargeted compounds based on accurate mass measurements and isotopic patterns. Triple quadrupole instruments are particularly well suited for targeted analysis and provide excellent sensitive and selectivity by performing tandem MS/MS analysis [71].

Despite the prominence attributed in scientific research to these hyphenated methodologies, other techniques are worth to be considered in the identification of bioactive vegetal compounds. High-performance thin-layer chromatography (HPTLC) is an evolution of thin layer chromatography (TLC) that remains the sole technique in which all the components of the sample are included in the chromatogram and presents the results as an image [67]. In HPLC, irreversible adsorption of some compounds can occur in the stationary phase, which in consequence cannot be eluted or detected, while TLC and HPTLC avoid this problem. Another technique avoiding this irreversible adsorption is countercurrent chromatography, which is an all-liquid separation technique which relies on the partition of a sample between two immiscible solvents [67],

and can be used for the fractionation of crude plant extracts (in multigram quantities) or for final purification steps.

4.2 Bioinformatics

In several aspects, the approach toward finding a new functional ingredient is quite similar to the development of new pharmaceuticals. Bioinformatics tools have been largely employed as the first steps for drug design and recently, they are beginning to be used in connection with food or food-related components in several areas of food chemistry [72]. It is widely reported that natural compounds in the diet can improve health conditions and prevent disease by direct interaction with key proteins in metabolic pathways. For example, pure monacolin K (lovastatin) has been shown to be effective in reducing total cholesterol and LDL-cholesterol concentrations in individuals with hypercholesterolemia and is a well-known inhibitor of HMG-CoA reductase.

Studies of molecular similarity, pharmacophore modeling, molecular docking, and quantitative structure-analysis relationships (QSAR), based on in silico calculations, can be good screening methodologies for selecting those ingredients with the best predicted probability to interact with those targets and to predict their activity. At the same time, they can assist in formulating theoretical plausible mechanisms of action for the ingredients.

Molecular similarity searches are based on the hypothesis that similar molecules will have similar properties. In pharmacophore modeling, the chemical features and conformation of the modulating ligands in relation to the target proteins is extracted from 3D structures, and in consequence the response of multiple ingredients can be screened depending on their fitting with this model. Molecular docking actually calculates the best conformation of a molecule to fit into the target-binding pocket. In the case of QSAR models, a prediction of the activity of molecules according to 2D or 3D descriptors is obtained after establishing a model with experimentally measured outcomes.

4.3 Omics Data

One of the biggest challenges in nutrition is the establishment of adequate biomarkers that are able to predict health benefits, as well as early indicators for disease risk [73]. Nowadays, new -omics technologies are used in nutrition research, giving access to holistic discovery of efficacy biomarkers by transcriptomics, proteomics, and metabolomics data. They are considered by the ILSI as emerging technologies for efficacy demonstration [74].

Transcriptomic studies, which analyze gene expression, have improved the understanding of the complex interaction between genetic and environmental factors, such as lifestyle and nutrition. Transcriptomic technologies have arguably

achieved the highest level of technical maturity of any of the functional genomics. Production of very high-quality, genome-wide expression profiling data by DNA microarrays is now a routine matter.

Proteomics is a central platform in elucidating the molecular events in nutrition: It can identify and quantify bioactive proteins and peptides and address questions of nutritional bioefficacy. The advances in methods of separation of peptides by microflow and nanoflows or chip detections, as well as mass spectrometry–rooted proteomic techniques like MALDI-TOF for protein identification and quantification have been pivotal in the application of these methodologies to understand nutritional effects of ingredients [75].

Metabolomics is the comprehensive analysis of metabolites and has gained a strong impact on nutritional research [76]. The great asset of these methodologies is the quantitative, noninvasive analysis of easily accessible human body fluids like urine, blood, saliva, and tears. The metabolome is complex, and thus requires multiple highly sophisticated techniques of separation and identification, such as NMR and MS. Additionally, the use of chemometrics for analyzing the complex data obtained is mandatory [73].

5 Conclusions

The functional foods and nutraceuticals market is one of the healthiest sectors in food industry, and is experiencing a continuous growth even in the context of an economic recession. However, to keep being successful, it is mandatory to assure the acceptance and awareness of consumers. The presence of many ingredients whose efficacy can be doubted can first mislead consumers and later compromise the credibility of the whole functional foods concept.

In consequence, manufacturers have to collaborate actively with academic researchers in order to provide the scientific evidence to substantiate health claims. This substantiation has to address three main points: the characterization of the ingredient, the relevance of the claimed effect, and the establishment of a cause and effect relationship between the ingredient's intake and the claimed effect by efficacy studies on human intervention trials. These trials have to follow strict criteria of quality and design in order to be successful, especially by choosing adequate participants, outcomes, and biomarkers.

At the same time, scientific research is very important for the development of new functional foods. Discoveries provided by holistic techniques like -omics methodologies are allowing a better comprehension of the effects of nutrition and the interaction with the human metabolism. This will allow to define new biomarkers, especially early indicators of disease risk, that will contribute to designing new functional products.

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Annexes

Table 80.3 Nutrient content claims approved In the USA

Nutrient content claims for protein, vitamins, minerals, dietary fiber, antioxidants in relation to the reference intake value or daily reference value	
"High," "Rich in," "Excellent source of"	20 % or more of the Reference Daily Intake (RDI) or the Daily Reference Value (DRV) per reference amount customarily consumed
"Good source," "Contains," "Provides"	10–19 % of the RDI or the DRV per reference amount customarily consumed
"High in fiber," "Good source of fiber," "more fiber"	If the food is not "low" in total fat, then the label shall disclose the level of total fat per labeled serving.
"More," "Fortified," "Enriched," "added," "Extra," "Plus" for Protein, Vitamin, Minerals, Dietary Fiber, Potassium" (Realtive claims)	10 % more of the RDI (Vitamins, minerals) of the RDI or the DRV per reference amount customarily consumed/per 100 g of food than an appropriate food
	10 % more of the DRV (Protein, Dietary fiber, potassium) of the RDI or the DRV per reference amount customarily consumed/per 100 g of food than an appropriate food
"High potency"	Individual vitamins or minerals at 100 % or more of the RDI per reference amount customarily consumed
High/Good source/More "Antioxidant"	An RDI has to be established for antioxidant nutrients
Nutrient content claims for "light" or "lite"	
"Light," "Lite" when the food derives 50 % or more of its calories from fat	Fat content reduced by 50 % or more per reference amount customarily consumed compared to an appropriate reference food
"Light," "Lite" when the food derives less than 50 % of its calories from fat	The number of calories is reduced by at least 33.33 %
	The fat content is reduced by 50 % or more per reference amount customarily consumed compared to an appropriate reference food
"Light," "Lite" for a product whose reference food contains 40 cal or less and 3 g fat or less per reference amount customarily consumed	Sodium content reduced by 50 % or more
"Light in sodium," "Lite in sodium" for a product whose reference food that contains more than 40 cal or more than 3 g fat or less per reference amount customarily consumed	Sodium content reduced by 50 % or more
"lightly salted"	50 % less sodium than which is normally added to the reference food, indicating when the product is "not low in sodium"
Nutrient content claims for the calorie content of foods	
"Calorie free," "Free of calories," "No calories," "Zero calories," "Without calories," "Trivial source of calories," "Negligible source of calories," "Dietarily insignificant source of calories"	The food contains less than 5 cal per reference amount customarily consumed and per labeled serving.

(*continued*)

Table 80.3 (continued)

"Low calorie," "Few calories," "Contains a small amount of calories," "Low source of calories," "Low in calories"	(a) The food has a reference amount customarily consumed greater than 30 gram (g) or greater than 2 tablespoons and does not provide more than 40 cal per reference amount customarily consumed (b) The food has a reference amount customarily consumed of 30 g or less or 2 tablespoons or less and does not provide more than 40 cal per reference amount customarily consumed and per 50 g (except for sugar substitutes) (c) For mails, if the product contains 120 cal or less per 100 g
"Reduced calorie," "Reduced in calories," "Calorie reduced," "Fewer calories," "Lower calorie," "Lower in calories"	The food contains at least 25 % fewer calories per reference amount customarily consumed than appropriate reference food
Sugar content claims	
"Sugar free," "free of sugar," "No sugar," "Zero sugar," "Without sugar," "Sugarless," "Trivial source of sugar," "Negligible source of sugar," "Dietarily insignificant source of sugar"	The food contains less than 0.5 of sugars per reference amount customarily consumed and per labeled serving
"No added sugar"; "Without added sugar"; "No sugar added"	No amounts of sugars, or any other ingredient that contains sugars that functionally substitute for added sugars is added during processing or packaging[. . .] The food that it resembles and for which it substitutes normally contents added sugars[. . .]
"Reduced sugar," "Reduced in sugar," "less sugar," "lower sugar," "Lower in sugar"	The food contains at least 25 % less sugar per reference amount customarily consumed than an appropriate reference food
Nutrient content claims for the sodium content of foods	
"Sodium free"; "Free of sodium," "Zero sodium," "Without sodium," "Trivial source of sodium," "Negligible source of sodium," "Dietary insignificant source of sodium"	The food contains less than 5 mg of sodium per reference amount customarily consumed and per labeled serving
"Very low sodium," "Very low in sodium"	The food has a reference amount customarily consumed greater than 30 g and contains 35 mg or less sodium per reference amount customarily consumed
"Low sodium," "Low in sodium," "little sodium," "contains a small amount of sodium," "low source of sodium"	The food has a reference amount customarily consumed greater than 30 g and contains 140 mg or less sodium per reference amount customarily consumed
"Reduced sodium," "Reduced in sodium," "Sodium reduced," "Less sodium," "Lower sodium," "Lower in sodium"	The food contains at least 25 % less sodium per reference amount customarily consumed than an appropriate reference food
"Salt free"	Only if the food is "sodium free"

(*continued*)

Table 80.3 (continued)

"Without added salt," "Unsalted," "No salt," "No salt added"	No salt is added during processing; the food that it resembles and for which it substitutes is normally processed with salt; and if the food is not sodium free, it includes a statement "not a sodium free food" or "not for control of sodium in the diet"
Nutrient claims for fat, fatty acid, and cholesterol content of foods	
"Fat free," "Free of fat," "No fat," "Zero fat," "Without fat," "negligible source of fat," "Dietarily insignificant source of fat"	The food contains less than 0.5 g of fat per reference amount customarily consumed and per labeled serving or, in the case of a meal product or main dish product, less than 0.5 g of fat per labeled serving; and
	The food contains no added ingredient that is a fat or is generally understood by consumers to contain fat unless the listing of the ingredient in the ingredient statement is followed by an asterisk that refers to the statement below the list of ingredients, which states "adds a trivial amount of fat," "adds a negligible amount of fat," or "adds a dietarily insignificant amount of fat;" and
	If the food meets these conditions without the benefit of special processing, alteration, formulation, or reformulation to lower fat content, it is labeled to disclose that fat is not usually present in the food (e.g., "broccoli, a fat-free food")
"Low fat"; "Low in fat," "Contains a small amount of fat"; "Low source of fat"; "Little fat"	The food has a reference amount customarily consumed greater than 30 g or greater than 2 tablespoons and contains 3 g or less of fat per reference amount customarily consumed; or
	The food has a reference amount of 30 g or less or 2 tablespoons or less customarily consumed and contains 3 g or less of fat per reference amount customarily consumed and per 50 g of food (for dehydrated foods that must be reconstituted before typical consumption with water or a diluent containing an insignificant amount of all nutrients per reference amount customarily consumed, the per 50-g criterion refers to the "as prepared" form); and
	If the food meets these conditions without the benefit of special processing, alteration, formulation, or reformulation to lower fat content, it is labeled to clearly refer to all foods of its type and not merely to the particular brand to which the label attaches (e.g., "frozen perch, a low fat food").
"Reduced fat"; "Reduced in fat"; "Fat reduced"; "Less fat"; "Lower fat"; "Lower in fat"	The food contains at least 25 % less fat per reference amount customarily consumed than an appropriate reference
"X % fat free"	The food meets the criteria for "low fat." A "100 % fat free" claim may be made only on foods that meet the criteria for "fat free," that contain less than 0.5 g of fat per 100 g, and that contain no added fat

(*continued*)

Table 80.3 (continued)

"Saturated fat free," "free of saturated fat," "no saturated fat," "zero saturated fat," "without saturated fat," "trivial source of saturated fat," "negligible source of saturated fat," or "dietarily insignificant source of saturated fat"	The food contains less than 0.5 g of saturated fat and less than 0.5 g trans fatty acid per reference amount customarily consumed and per labeled serving and
	The food contains no ingredient that is generally understood by consumers to contain saturated fat (unless the listing of the ingredient in the ingredient statement is followed by an asterisk that refers to the statement below the list of ingredients which states, "adds a trivial amount of saturated fat," "adds a negligible amount of saturated fat," or "adds a dietarily insignificant amount of saturated fat," and
	If the food meets these conditions without the benefit of special processing, alteration, formulation, or reformulation to lower saturated fat content, it is labeled to disclose that saturated fat is not usually present in the food.
"Low in saturated fat," "low saturated fat," "contains a small amount of saturated fat," "low source of saturated fat," or "a little saturated fat"	The food contains 1 g or less of saturated fatty acids per reference amount customarily consumed and not more than 15 % of calories from saturated fatty acids.
	If a food meets these conditions without benefit of special processing, alteration, formulation, or reformulation to lower saturated fat content, it is labeled to clearly refer to all foods of its type and not merely to the particular brand to which the label attaches (e.g., "raspberries, a low saturated fat food").
"Reduced saturated fat," "reduced in saturated fat," "saturated fat reduced," "less saturated fat," "lower saturated fat," or "lower in saturated fat"	The food contains at least 25 % less saturated fat per amount customarily consumed than an appropriate reference food
"Cholesterol free," "free of cholesterol," "zero cholesterol," "without cholesterol," "no cholesterol," "trivial source of cholesterol," "negligible source of cholesterol," or "dietarily insignificant source of cholesterol"	The food contains less than 2 mg of cholesterol per reference amount customarily consumed and per labeling serving and
	The food contains no ingredient that is generally understood by consumers to contain cholesterol (unless the listing of the ingredient in the ingredient statement is followed by an asterisk that refers to the statement below the list of ingredients, which states "adds a trivial amount of cholesterol," "adds a negligible amount of cholesterol," or "adds a dietarily insignificant amount of cholesterol") and
	The food contains 2 g or less of saturated fatty acids per reference amount customarily consumed
	If the food contains less than 2 mg of cholesterol per reference amount customarily consumed without the benefit of special processing, alteration, formulation, or reformulation to lower cholesterol content, it is labeled to disclose that cholesterol is not usually present in the food (e.g., "applesauce, a cholesterol-free food").

(*continued*)

Table 80.3 (continued)

"Low in cholesterol," "low cholesterol," "contains a small amount of cholesterol," "low source of cholesterol," or "little cholesterol"	The food contains 20 mg or less of cholesterol per reference amount customarily consumed
	The food contains 2 g or less of saturated fatty acids per reference amount customarily consumed and
	If the food meets these conditions without the benefit of special processing, alteration, formulation, or reformulation to lower cholesterol content, it is labeled to clearly refer to all foods of that type and not merely to the particular brand to which the label attaches (e.g., "low fat cottage cheese, a low cholesterol food").
"Reduced cholesterol," "reduced in cholesterol," "cholesterol reduced," "less cholesterol," "lower cholesterol," or "lower in cholesterol"	The food has been specifically formulated, altered, or processed to reduce its cholesterol by 25 % or more from the reference food it resembles and
	The food contains 2 g or less of saturated fatty acids per reference amount customarily consumed
"Lean" and extra lean claims	
"Lean"	The food is a seafood or game meat product and as packaged contains less than 10 g total fat, 4.5 g or less saturated fat, and less than 95 mg cholesterol per reference amount customarily consumed and per 100 g
"Extra lean"	The food is a discrete seafood or game meat product and as packaged contains less than 5 g total fat, less than 2 g saturated fat, and less than 95 mg cholesterol per reference amount customarily consumed and per 100 g

Table 80.4 Nutrition claims approved in UE

Nutrition claims for energy	
"Low Energy"	The product does not contain more than 40 kcal (170 kJ)/100 g for solids or more than 20 kcal (80 kJ)/100 ml for liquids. For table-top sweeteners the limit of 4 kcal (17 kJ)/portion, with equivalent sweetening properties to 6 g of sucrose (approximately 1 teaspoon of sucrose), applies.
"Energy-reduced"	The energy value is reduced by at least 30 %, with an indication of the characteristic(s) which make(s) the food reduced in its total energy value
"Energy-free"	The product does not contain more than 4 kcal (17 kJ)/100 ml. For table-top sweeteners the limit of 0,4 kcal (1,7 kJ)/portion, with equivalent sweetening properties to 6 g of sucrose (approximately 1 teaspoon of sucrose), applies.
Nutrition claims for fat	
Low fat:	The product contains no more than 3 g of fat per 100 g for solids or 1.5 g of fat per 100 ml for liquids (1.8 g of fat per 100 ml for semi-skimmed milk).
Fat-free:	The product contains no more than 0.5 g of fat per 100 g or 100 ml. However, claims expressed as "X % fat-free" shall be prohibited.
Nutrition claims for saturated fat	
Low saturated-fat:	The sum of saturated fatty acids and trans-fatty acids in the product does not exceed 1.5 g per 100 g for solids or 0.75 g/100 ml for liquids and in either case the sum of saturated fatty acids and trans-fatty acids must not provide more than 10 % of energy.

(*continued*)

Table 80.4 (continued)

Saturated fat-free:	The sum of saturated fat and trans-fatty acids does not exceed 0.1 g of saturated fat per 100 g or 100 ml.
Nutrition claims for omega-3 fatty acids	
Source of:	The product contains at least 0.3 g alpha-linolenic acid per 100 g and per 100 kcal, or at least 40 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal.
High:	The product contains at least 0.6 g alpha-linolenic acid per 100 g and per 100 kcal, or at least 80 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal.
Nutrition claims for monounsaturated fat	
High:	At least 45 % of the fatty acids present in the product derive from monounsaturated fat under the condition that monounsaturated fat provides more than 20 % of energy of the product.
Nutrition claims for polyunsaturated fat	
High:	At least 45 % of the fatty acids present in the product derive from polyunsaturated fat under the condition that polyunsaturated fat provides more than 20 % of energy of the product.
Nutrition claims for unsaturated fat	
High:	At least 70 % of the fatty acids present in the product derive from unsaturated fat under the condition that unsaturated fat provides more than 20 % of energy of the product
Nutrition claims for sugar	
Low Sugar:	The product contains no more than 5 g of sugars per 100 g for solids or 2.5 g of sugars per 100 ml for liquids.
Sugars-free:	The product contains no more than 0.5 g of sugars per 100 g or 100 ml.
With no added sugar	The product does not contain any added mono- or disaccharides or any other food used for its sweetening properties. If sugars are naturally present in the food, the following indication should also appear on the label: "CONTAINS NATURALLY OCCURRING SUGARS."
Nutrition claims for sodium/salt	
Low sodium/salt:	The product contains no more than 0.12 g of sodium, or the equivalent value for salt, per 100 g or per 100 ml. For waters, other than natural mineral waters falling within the scope of Directive 80/777/EEC, this value should not exceed 2 mg of sodium per 100 ml.
Very low sodium/salt:	The product contains no more than 0.04 g of sodium, or the equivalent value for salt, per 100 g or per 100 ml. This claim shall not be used for natural mineral waters and other waters.
Sodium-free or salt-free	The product contains no more than 0.005 g of sodium, or the equivalent value for salt, per 100 g.
Nutrition claims for fiber	
Source of fiber:	The product contains at least 3 g of fiber per 100 g or at least 1.5 g of fiber per 100 kcal.
High fiber:	The product contains at least 6 g of fiber per 100 g or at least 3 g of fiber per 100 kcal.
Nutrition claims for protein	
Source of protein:	At least 12 % of the energy value of the food is provided by protein.
High protein:	At least 20 % of the energy value of the food is provided by protein.

(*continued*)

Table 80.4 (continued)

Nutrition claims for vitamins/minerals	
Source of:	The product contains at least a significant amount as defined in the Annex to Directive 90/496/EEC or an amount provided for by derogations granted according to Article 6 of Regulation (EC) No 1925/2006 of the European Parliament and of the Council of 20 December 2006 on the addition of vitamins and minerals and of certain other substances to foods
High:	The product contains at least twice the value of "source of [NAME OF VITAMIN/S] and/or [NAME OF MINERAL/S]."
Nutrition claims for nutrients or other substances	
Contains:	The product complies with all the applicable provisions of this Regulation, and in particular Article 5. For vitamins and minerals, the conditions of the claim "source of" shall apply.
Increased:	The product meets the conditions for the claim "source of" and the increase in content is at least 30 % compared to a similar product.
Reduced:	The reduction in content is at least 30 % compared to a similar product, except for micronutrients, where a 10 % difference in the reference values as set in Directive 90/496/EEC shall be acceptable, and for sodium, or the equivalent value for salt, where a 25 % difference shall be acceptable.
Nutrition claims for omega-3 fatty acids	
Source of:	The product contains at least 0.3 g alpha-linolenic acid per 100 g and per 100 kcal, or at least 40 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal.
High:	The product contains at least 0.6 g alpha-linolenic acid per 100 g and per 100 kcal, or at least 80 mg of the sum of eicosapentaenoic acid and docosahexaenoic acid per 100 g and per 100 kcal.
Nutrition claims for monounsaturated fat	
High:	At least 45 % of the fatty acids present in the product derive from monounsaturated fat under the condition that monounsaturated fat provides more than 20 % of energy of the product.
Nutrition claims for polyunsaturated fat	
High:	At least 45 % of the fatty acids present in the product derive from polyunsaturated fat under the condition that polyunsaturated fat provides more than 20 % of energy of the product.
Nutrition claims for unsaturated fat	
High:	At least 70 % of the fatty acids present in the product derive from unsaturated fat under the condition that unsaturated fat provides more than 20 % of energy of the product.
Other Nutrition claims	
Light/lite	Shall follow the same conditions as those set for the term 'reduced'; the claim shall also be accompanied by an indication of the characteristic(s) which make(s) the food "light" or "lite."
Naturally/Natural	Where a food naturally meets the condition(s) for the use of a nutritional claim, the term "naturally/natural" may be used as a prefix to the claim.

References

1. Eussen SRBM, Verhagen H, Klungel OH, Garssen J, Van Loveren H, Van Kranen HJ, Rompelberg CJM (2011) Functional foods and dietary supplements: products at the interface between pharma and nutrition. Eur J Pharmacol 668:S2–S9
2. Smith R (2004) Let food be thy medicine. . .. BMJ, 328:0.8
3. Kwak N-S, Jukes DJ (2001) Functional foods. Part 1: the development of a regulatory concept. Food Control 12(2):99–107
4. Williams M, Pehu E, Ragasa C (2006) Functional foods: opportunities and challenges for developing countries. Agricultural and rural development notes, 19 Sept 2006. World Bank, Washington, DC. https://openknowledge.worldbank.org/handle/10986/9594
5. Siró I et al (2008) Functional food. Product development, marketing and consumer acceptance. A review. Appetite 51(3):456–467
6. ILSI (1999) Scientific concepts of functional foods in Europe – consensus document. Br J Nutr 81:S1–S27
7. Health Canada – Health Protection Branch, Therpaeutic Products Programme and Food Directorate (1998) Nutraceuticals/functional foods and health claims on foods final policy. http://www.hc-sc.ca/hpb-dgps/therapeut/htmleng/ffn.html
8. Dietary Supplement Health and Education Act (1994) Pub. L. No.103–417, 108 Stat. 4325, Washington, DC, 8 Oct 1994
9. European Parliament and the Council (2002) Directive 2002/46/EC on the approximation of the laws of the member states relating to food supplements, 10 June 2002
10. European Parliament and Council (2009) Directive 2009/39/EC on foodstuffs intended for particular nutritional uses, 6 May 2009
11. European Parliament and Council (2004) Directive 2004/24/EC amending, as regards traditional herbal medicinal products, Directive 2001/83/EC . . . relating to medicinal products for human use, 31 March 2004
12. Hosoya N (1998) Health claims in Japan. Jpn J Nutraceuticals, Funct Med Foods 1(3/4): 1–11
13. Menrad K (2003) Market and marketing of functional food in Europe. J Food Eng 56:181–188
14. Zeisel SH (1999) Regulation of nutraceuticals. Science 285:1853–1855
15. Espín JC, García-Conesa MT, Tomás-Barberán FA (2007) Nutraceuticals: facts and fiction. Phytochemistry 68:2986–3008
16. Bröring S, Cloutier M, Leker J (2006) The fornt end of innovation in an era of industry convergence: evidence from nutraceuticals and functional foods. R&D Manag 36(5):487–498
17. Gulati OP, Berry Ottaway P (2006) Legislation relating to nutraceuticals in the European Union with a particular focus on botanical-sourced products. Toxicology 221:75–87
18. Brandt FS, Cazzaniga A, Hann M (2011) Cosmeceuticals: current trends and market analysis. Sem Cutan Med Surg 30:141–143
19. Millikan LE (2001) Cosmetology, cosmetics, cosmeceuticals: definitions and regulations. Clin Dermatol 19:371–374
20. American Diabetes Association. http://www.diabetes.org/food-and-fitness/food/what-can-i-eat/diabetes-superfoods.html
21. Gianetti V, Testani E, Recchia L (2009) Food consumption and innovation: functional foods. J Commod Sci Technol Qual 48(3):213–225
22. Green MR, van der Ouderaa F (2003) Nutrigenetics: where next for the foods industry? The Pharamcogenom J 3:191–193
23. Bleiel J (2010) Functional foods from the perspective of the consumer: how to make it a success? Int Dairy J 20(4):303–306
24. The Cluster Competitiveness Group (2007) Biotechnology's applications to nutrition and functional foods. Forum euro-latinoamericano di Torino.; 2007 Conference. Public-private partnerships for knowledge-based regional development. 24–26 October 2007, Castello del Valentino, Turin, Italy. http://www.forumtorino.org/download.php?fileID=272&lang=enf

25. Mozaffarian D, Wilson PWF, Kannel WB (2008) Beyond established and novel risk factors: lifestyle risk factors for cardiovascular disease. Circulation 117:3031
26. Mc Carthy M, Aitsi-Selmi A, Bánati D, Frewer L, Hirani V, Lobstein T, McKenna B, Mulla Z, Rabozzi G, Stefcu R, Newton R (2011) Research for food and health in Europe: themes, needs and proposals. Health Res Policy Syst 9(37):1–13
27. Patel D, Dufour Y, Domingan N (2008) Functional food and nutraceutical registration process in Japan and China: similarities and differences. J Pharm Pharmaceut Sci 11(4):1–11
28. Hellyer NE, Fraser I, Haddock-Fraser J (2012) Food choice, health information and functional ingredients: an experimental auction employing bread. Food Policy 37:232–245
29. Verbeke W (2005) Consumer acceptance of functional foods: socio-demographic, cognitive and attitudinal determinants. Food Qual Prefer 16:45–57
30. Bech-Larsen T, Scholderer J (2007) Functional foods in Europe: consumer research, market experiences and regulatory aspects. Trends Food Sci Technol 18:231–234
31. Webb GP (2011). Dietary supplements and functional foods, 2nd edn, s.l. Blackwell Publishing Ltd, Oxford, UK
32. International Food Information Council Foundation (2011) Food & Health survey: consumer attitudes towards food safety, nutrition & health. (En línia). http://www.foodinsight.org/Content/3840/2011%20IFIC%20FDTN%20Food%20and%20Health%20Survey.pdf
33. Gilbert L (2000) The functional food trend: what's next and what Americans think about eggs. J Am Coll Nutr 19(5):507S–512S
34. Kapsak WR et al (2011) Functional foods: consumer attitudes, perceptions, and behaviors in a growing market. J Am Diet Assoc 111(6):804–810
35. Hilliam M (1999) Functional foods. The world of food ingredients, vol (3/4), pp 46–49
36. Annunziata A, Vecchio R (2011) Functional foods development in the European market: a consumer perspective. J Funct Foods 3:223–238
37. Krygier K (2007) Functional foods in Poland. Proceedings of the 4th international FFnet meeting on functional foods, s.n, Budapest
38. Jones PJ, Jew S (2007) Functional food development: concept to reality. Trends Food Sci Technol 18(7):387–390
39. Biström M, Nordström K (2002) Identification of key success factors of functional dairy foods product development. Trends Food Sci Technol 13(11):372–379
40. Lamberti L, Lettieri E (2011) Gaining legitimacy in converging industries: evidence from the emerging market of functional food. Eur Manag J 29(6):462–475
41. Angus F (2008) Functional Foods Market Overview. s.n., Geneve. Vitafoods 2008
42. Nutraingredients- US (2006) US Functional food market up 31 % since 2006, says new report. (En línia) 2011/6/13. http://www.nutraingredients-usa.com/Industry/US-Functional-food-market-up-31-since-2006-says-new-report
43. Leatherhead Food International (2009) Antioxidants market report. http://www.leatherheadfood.com/antioxidants-market-report
44. Barreiro-Hurlé J, Colombo S, Cantos-Villar E (2008) Is there a market for functional wines? Consumer preferences and willingness to pay for resveratrol-enriched red wine. Food Qual Prefer 19(4):360–371
45. Pricewaterhouse Coopers (2009) Leveraging growth in the emerging functional foods industry: trends and market opportunities. http://www.pwc.com/us/en/transaction-services/publications/functional-foods.jhtml
46. Nutraingredients-US. US leads in healthy food product launches. (En línia), 27 Aug 2009. http://www.nutraingredients-usa.com/Consumer-Trends/US-leads-in-healthy-food-product-launches
47. Leatherhead Food (2011) Future directions for the global functional foods market. http://www.leatherheadfood.com/functional-foods
48. Nutraingredients-USA (2011) Leatherhead: Japan lead under threat in global €16.75 bn functional foods market. (En línia) 14 June 2011. http://www.nutraingredients.com/Consumer-Trends/Leatherhead-Japan-lead-under-threat-in-global-16.75bn-functional-foods-market

49. Nutraingredients US (2012) Global nutraceutical ingredient market worth €18.5bn in 2015. (En línia) 06 Jan 2012. http://www.nutraingredients.com/Consumer-Trends/Global-nutraceutical-ingredient-market-worth-18.5bn-in-2015
50. Analysts Global Industry (2010) Nutraceuticals: a global strategic business report. http://www.strategyr.com/Nutraceuticals_Market_Report.asp
51. Szakály Z, Szente V, Kövér G, Polereczki Z, Szigeti O (2012) The influence of lifestyle on health behavior and preference for functional foods. Appetite 58:406–413
52. PWC (2009) Leveraging growth in the emerging functional foods industry. Trends and market opportunities. PrivewaterhouseCoopers, pp 1–22
53. Chadwick R et al. (2003) Functional foods. Springer, Berlin/Heidelberg/New York, p 61
54. Agriculture and Agri-Food Canada (2011) Polyphenol antioxidants in Japan © Her Majesty the Queen in Right of Canada, 2011. ISSN 1920–6615. Market indicator report, p 3
55. Nutraingredients-US (2009) 'Cheap' functional foods set to grow, says Euromonitor. (En línia) 18 Sep 2009. http://www.nutraingredients-usa.com/Consumer-Trends/Cheap-functional-foods-set-to-grow-says-Euromonitor
56. Nutraingredients US. Digestive health products are No.1 functional food, global study. (En línia) 01 Sep 2009. http://www.nutraingredients-usa.com/Consumer-Trends/Digestive-health-products-are-No.1-functional-food-global-study
57. Nutraingredients-US (2010) US functional beverage growth slows: Mintel. (En línia) 18 Feb 2010. http://www.nutraingredients-usa.com/Consumer-Trends/US-functional-beverage-growth-slows-Mintel
58. Hasler CM (2008) Health claims in the United States: an aid to the public or a source of confusion? J Nutr 138(6):1216S–1220S
59. Ellwood KC, Trumbo PR, Kavanaugh CJ (2009) How the US food and drug administration evaluates the scientific evidence for health claims. Nutr Rev 68(2):114–121
60. European Parliament and the Council (2006) Regulation 1924/2006/CE on nutrition and health claims made on foods, 20 Dec 2006
61. Verhagen H, Vos E, Francl S, Heinonen M, van Loveren H (2010) Status of nutrition and health claims in Europe. Arch Biochem Biophys 501:6–15
62. Gilsenan MB (2011) Nutrition & health claims in the European Union: a regulatory overview. Trends Food Sci Technol 22:536–542
63. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2010) Scientific Opinion on the substantiation of health claims related to various food(s)/food constituent(s) and protection of cells from premature aging, antioxidant activity, antioxidant content and antioxidant properties, and protection of DNA, proteins an. EFSA J 8(2):1489
64. Byrne D (2003) Health Nutrition and labelling. Food Sci Technol 17:26–28
65. Moher D, Hopewell S, Schulz KF et al (2010) CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 340:c869
66. Welch RW, Antoine J-M, Berta J-L, Bub A et al (2011) Guidelines for the design, conduct and reporting of human intervention studies to evaluate the health benefits of foods. Br J Nutr 106(S2):S3–S15
67. Marston A (2007) Role of advances in chromatographic techniques in phytochemistry. Phytochemistry 68:2785–2797
68. Dai D, He J, Sun R, Zhang R, Aisa HA, Abliz Z (2009) Nuclear magnetic resonance and liquid chromatography-mass spectrometry combined with an incompleted separation strategy for identifying the natural products in crude extracts. Anal Chim Acta 632: 221–228
69. De la Cruz AA, Hilbert G, Rivière C, Mengin V, Ollat N, Bordenave L, Decroocq S, Delaunay J-C, Delrot S, Mérillon J-M, Monti J-P, Gomès E, Richard T (2012) Anthocyanin identification and composition of wild Vitis spp. accessions by using LC–MS and LC–NMR. Anal Chim Acta 732:145–152
70. Valls J, Millán S, Martí MP, Borràs E, Arola L (2009) Advanced separation methods of food anthocyanins, isoflavones and flavanols. J Chromatogr A 1216(43):7143–7172

71. Guillarme D, Schappler J, Rudaz S, Veuthey J-L (2010) Coupling ultra-high-pressure liquid chromatography with mass spectrometry. Trends Anal Chem 29(1):15–27
72. Martinez-Mayorga K, Medina-Franco JL (2009) Chemoinformatics – applications in food chemistry. Adv Food Nutr Res 58:33–56
73. Kussmann M, Raymond F, Affolter M (2006) OMICS- driven biomarker discovery in nutrition and health. J Biotechnol 124:758–787
74. Weber LF, Peter B (2009) Emerging technologies for efficacy demonstration. s.l., ILSI. Summary report of a workshop held in February 2009 in Brussels
75. Kussman M, Affolter M (2009) Proteomics at the center of nutrigenomics: comprehensive molecular understanding of dietary health effects. Nutrition 25:1085–1093
76. Jové M, Serrano JC, Ortega N, Ayala V, Anglès N, Reguant J, Morelló JR, Romero MP, Motilva MJ, Prat J, Pamplona R, Portero-Otín M (2011) Multicompartmental LC-Q-TOF-based metabonomics as an exploratory tool to identify novel pathways affected by polyphenol-rich diets in mice. J Proteome Res 10(8):3501–3512