

## **8. HERBAL FOOD SUPPLEMENTS**

The food supplements are a special category of products that legally are considered unambiguously as food, although they possess some unique characteristics and are specific regulated.

### **8.1. Distinctive features of food supplements**

According to the definition adopted by EU (Directive 2002/46/CEE), ASEAN, USA and New Zealand, the food supplements are “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” (1).

As defined in 1994 by the Dietary Supplement Health and Education Act (approved by US Congress), a dietary supplement is a product that:

- Is intended to supplement the diet;
- Contains one or more dietary ingredients (including vitamins, minerals, herbs or other botanicals, amino acids, and certain other substances or their constituents);
- Is intended to be taken by mouth, in forms such as tablet, capsule, powder, softgel, gelcap, or liquid;
- Is labeled as being a dietary supplement.

Due to their composition and recommendation of use, herbal food supplements could be placed at the borderline between herbal traditional medicine products and food. These products have a large addressability and claiming health benefits for the consumers.

#### **8.1.1. Main ingredients and categories of products**

In the specific category of food supplements could be included a large range of products: plants as a whole, divided or crushed plants (simple or combined tea, bulk or dose), liquid extracts (tinctures, juices, syrups, energizing drinks), oils (fat or volatile), powders and granules (in packets or encapsulated), tablets (filmed/ non-filmed), capsules (soft or hard), drinkable ampoule, jelly, pasta, bonbons or bars etc.

Different kinds of companies are present on the market of food supplements, such as: large pharmaceutical companies, foods and beverage companies, local manufacturers as well as direct sellers. Manufacturers are continuously extending their brand portfolios across different categories of products, that address to different categories of consumers and their specific needs.

Contrary to the traditional medicine products which focus on disease treatments, food supplements are designed with the beneficial aim in mind of ensuring the maintenance and metabolic physiological functioning of an individual in good health.

The food supplements may contain as active ingredients one or a combination of several substances such as:

- vitamins, minerals, amino acids, fatty acids, enzymes, probiotics or other bioactive substances;
- substances originating from natural sources (animal/plant origin, such as concentrated or fractioned botanical extracts, primary or secondary metabolites, beehive products);
- synthesis or semi-synthesis substances belonging to previously mentioned category, whose use is permitted by valid legislation.

There are a lot of different bioactive substances originating in plant species (whole plant, certain parts/ organs, seeds) considered valuable compounds that could be used in food supplements, such as:

- vitamins: fruits of *Rosa canina*, *Hippophae rhamnoides*, *Malpighia glabra* (vitamin C), roots of *Daucus carota* (caroten, provitamin A); germs of *Triticum aestivum* (vitamin A, E);
- colour agents: flowers of *Tagetes erecta* (lutein, zeaxanthin); petals of *Hibiscus sabdariffa*; roots of *Beta vulgaris var rubra* (anthocyanins); *Daucus carota* (Beta-caroten);
- enzymes: fruits of *Ananas comosus* (bromelaine), *Carica papaya* (papaine);
- fibers: roots/rhizoma of *Cichorium intybus* (inulin), husks of *Plantago ovata* (psyllium);
- fat oils and fatty acids: seeds of *Cucurbita species*, *Linum ussitatissimum*, *Canabis sativa*, *Nigella sativa* (Omega-3, 6, 9) *Charthamus tinctorius* (fatty acids), fruits of *Serenoa repens*, *Olea europaea*;
- flavour and essential oils: bark of *Cinnamomum zeylanicum*; leaves/herba of *Mentha piperita*; seeds of *Foeniculum vulgare*, *Pimpinella anisum*, *Carum carvi*; fruits (orange, grape fruit, peach, apple);
- chlorofile: leaves of *Morus alba*, *M. nigra*;
- sweeteners: leaves of *Stevia rebaudiana* (plant extracts standardized in stevioglicosides).

Taking into account the physiological effects of the main active ingredients, there are special categories of food supplements which address to different target organs/system of human body. Depending of the consumer specific needs, there are products which are supporting: bones and joints; blood, heart and circulatory system; immunity; liver activity and digestion; nervous system; weight control; eye view, etc. A large range of products are promoted due to their properties such as: probiotics, antioxidants, stimulants, depurative/detoxification, diuretics. During the last time such “natural products” became very popular and the use of food supplements has been included in the current life habits of many people.

### **8.1.2. Distribution channels and consumer’s access to food supplements**

Scientific evidence demonstrated that certain food supplements have genuine health benefits and may be effective in managing some health issues. Calcium and vitamin D supplements assist in maintaining bone strength; folic acid decrease the incidence of birth defects in newborns; omega-3 fatty acid supplements may benefit heart disease patients; Asian ginseng improve mental and physical performance; ginkgo can assist patients suffering from Alzheimer’s disease, etc. Numerous other supplements have been used historically in traditional medicine and are still utilized today to relieve a wide range of health issues or to assist in health prevention regimes (2).

It is often difficult to study the use of supplements in disease prevention and health promotion in epidemiologic research, because supplement use cannot be disentangled from other health-seeking behaviors.

However, most food supplements are used in USA, for example, by personal choice (77%) rather than by the recommendation of a health care provider (23%). These data lend credence to the “inverse supplement hypothesis” that many supplement users are healthy individuals who want to take an active role in their own health, and who perceive supplements as a type of “insurance” against poor health (3).

The easy access to the food supplements, which are sold using various channels (pharmacies, herbalists, natural food and body care shops, company-owned retail stores, supermarkets, sex-shops, direct sales, e-commerce) could be one of the reason for the increasing consumption of dietary supplements at global level, as well as the intense promotion by mass-media and the consumers’ perception of these category of products.

One single example of the dimension/size of a successful network of distribution is relevant: the well known American company GNC (which is focused on premium, value-added nutritional

products) has sold, at the end of 2014 (under proprietary brands and nationally recognized third party brands) in more than 8,900 locations (of which more than 6,600 retail locations are in the United States) and franchise operations in more than 50 countries. Main GNC proprietary brands include Mega Men (R), Ultra Mega (R), Total Lean (TM), Pro Performance (R), Pro Performance (R) AMP, Beyond Raw (R), GNC Puredge (TM), GNC Genetix HD (R), Herbal Plus (R).

### 8.1.3. Regulation and legal frameworks

The relevant legislation applicable to food supplements includes the Regulation (EC) no. 178/2002 (General Food Law) (4), the specific Directive 2002/46/CEE (Food supplements), Regulation (EC) no. 1924/2006 (claims) (5), Regulation (EU) no. 432/2012 (authorized health claims in food) (6), Regulation (EC) no. 1925/2006 (Addition of other substances) (7), Regulation no. 1169/2011 (Food information for consumers) (8), Regulation (EU) no. 2283/2015 (Novel foods) (9).

When there are no harmonised rules at EU level regarding the safety of botanical substances used in foods, for example, relevant national rules may apply.

## 8.2. Size and dynamics of food supplements markets

The food supplements were being within the last decade the subject of a spectacular diversification and market increase in most of the developed countries.

In table 1 are shown the main European markets and their estimated growing rate till 2020 (10).

Table 1. European food supplement markets evolution (2014-2019)

No.	Country	Sales (mil. EUR)		Estimated Growing (2014-2019)
		2015	2020	
1	Italy	1,424.2	1,601.5	12.40%
2	Germany	966.6	967.2	0.10%
3	Russia	887.7	1,079.9	21.70%
4	United Kingdom	737	755.2	2.59%
5	France	683.8	724.8	6%
6	Poland	353.4	407.5	15.30%
7	Norway	231.5	220.4	-4.80%
8	Finland	201.2	207.4	3.10%
9	Belgium	193.6	194	0.20%
10	Spain	182.6	193.5	6%
11	Sweden	181.5	199.3	9.80%

12	The Netherlands	142.1	169.2	19.10%
13	Hungary	116.6	136.3	16.80%
14	Denmark	96.5	98.7	2.20%
15	Turkey	96	121.7	26.70%
16	Switzerland	93	92.7	-0.30%
17	Czech Republic	84.7	96.1	13.40%
18	Austria	81.7	91.9	12.40%
19	Ukraine	75.7	87.1	15%
20	Romania	72,2	101,8	41%

From 2013-2018, the Western Europe regional market is expected to grow by 13%, reaching €5.65 billion in 2018 (11). Countries leading the market in terms of market size and dynamics are:

- Italy (€ 1.2 billion)
- Germany (€ 935 million)
- France (€ 611 million)
- the UK (€ 538 million)

The rest of Western Europe recorded sales of \$2.8 billion/€2.1 billion in 2013 (12).

Although Italy posted the highest sales of food supplements, herbal supplements represent a relatively small part of sales.

Eastern Europe regional market is estimated to grow substantially; in 2018, the region is projected to reach a market size of €3.2 billion (from €2 billion in 2013), of which the Russian market makes up around two thirds (11). Part of this Russian market is supplied by producers in Latvia and Lithuania adding to industrial demand in these countries. Other fast growing East European countries include Turkey, the Ukraine and Belarus.

Sales of food supplements in Central European countries grew substantially from 2012-2014, especially in Romania, Bulgaria, Slovakia and Poland. To illustrate, Poland is estimated to post sales of almost € 500 million in 2014, € 100 million more than in 2013. The Czech Republic was estimated to grow the slowest, but may still be interesting for developing country suppliers as the country had the highest per capita spending (12).

Romania was included in 2011 on the list of the most important 17 European pharmaceutical markets because it's a real potential of development in connection to rural space development and increasing of consumers' awareness and level of information. As compared to other Central European countries (fig. 1), Romania had the fastest rate of development during last years being

considered one of the most attractive markets from the region, due to the continuous ascendant trend since 2008 up to 2014.

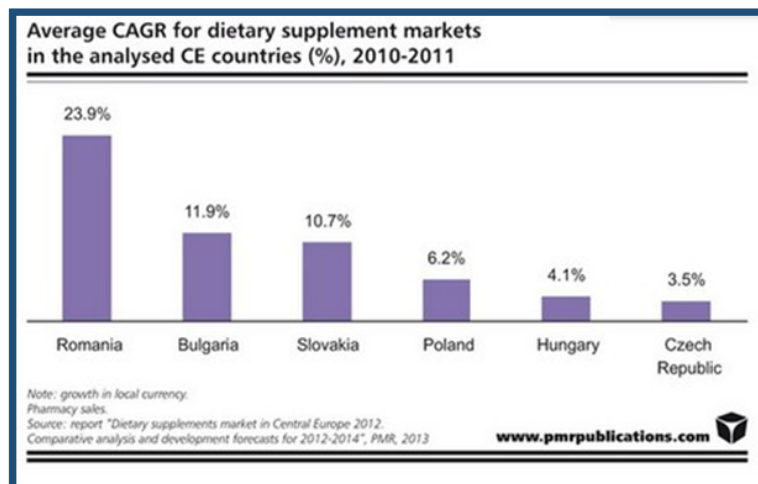


Figure 1. Growing rate of some food supplement markets of Central Europe (2010-2011)

In USA vitamins and dietary supplements continued to see current value growth of 4% to reach US\$ 27.2 billion in 2015, while in Canada it increased by 4% in current value terms in 2015, which was slightly slower than the growth seen in 2014. It is expected a sustained growth, with a value CAGR of 1% at constant 2015 prices over the forecast period, to reach C\$1.8 billion in 2020.

In Japan current value sales of vitamins and dietary supplements increased by 1% to reach ¥1.1 trillion. Value sales of vitamins and dietary supplements are expected to rise at a 1% CAGR at constant 2015 prices over the forecast period to stand at ¥1.2 trillion in 2020.

With improving standards of living and rising disposable incomes and increasing health awareness, the consumption of vitamins and dietary supplements will also become increasingly important in Chinese consumers' daily lives.

### 8.2.1. Trends and prospects in the European food supplements markets

A synthesis of the data published by Euromonitor International concerning the market research on vitamins and dietary supplements in 2015, is offering interesting information about the competitive landscape and prospects in some of the most important European markets (11).

#### Market development

There were observed two direction in the European markets development. On the one hand, in most of the countries it was registered a positive trend and an increasing interest of users in naturally

positioned consumer health products. This was explained by different socio-economic and behavioural reasons:

- people are living longer, are more educated, have wider access to information and feel more responsible as individuals and more active as consumers, becoming the managers of their health capital; it has increased the awareness about healthy ageing, the desire of individuals to feel good, which is reflected in a proactive and preventive approach to health and wellness; people became interested to invest in their long-term health and to improve their underlying health conditions rather than merely treating symptoms;
- it was increasing the preference of use, when possible only natural products, free of chemicals, in order to maintain the physical and intellectual health; during the last decades it was observed a strong emphasis on nutrition (natural ingredients, healthy diets) and lifestyle; strong media has also influenced the perception of the food supplements as products which can improve health and wellness without any potential risks related to their intake; this encouraged self-medication and the new regulation from EFSA had as result the consumers' trust in quality and safety of such products; it was also registered an increasing number of doctors that have started to advise their patients to take vitamins and dietary supplements to help them cope with minor health issues, often in combination with Rx-medicine based therapies.

On the other side, in those countries where it was registered a fairly slow value development of the market (Germany, Belgium) or a decrease of the growing rate (Norway, Switzerland) as compared to previous year, the motivation was found in the high level of market fragmentation and the competition among manufacturers, as well as distribution channels. In Germany, for example, every year a growing number of brands and products are being launched in order to attract consumers' attention, and consequently increased the manufacturing company's share. Amongst these new product launches, private label versions of existing products continued to become more common, putting extra pressure on overall unit prices.

More than this, due to the strong mainstream of alternative medicine and the new concept of health and wellbeing, a part of the consumers are shunning vitamins and dietary supplements in favour of natural foods such as fruit and vegetables, with green drinks and smoothies notably proving increasingly popular as breakfast options among health-conscious consumers.

### **Competitive landscape**

Regarding the competitive landscape of vitamins and dietary supplements in European countries, there are certain specific differences from a state to another:

- in Italy, the competitive landscape of vitamins and dietary supplements is quite fragmented (comprising numerous small domestic companies categorised under others, which accounted for 26% of value sales in 2015), but Whitehall (Multicentrum and Polase brands), followed by Aboca (specialized in herbs) and Bayer (thanks to Supradyn) remained the leading companies in vitamins and dietary supplements;
- MCM Klosterfrau Vertriebsgesellschaft was able to maintain and strengthen its leading position in Germany in 2015 (due to the vast product and brand portfolio, represented in almost all categories within vitamins and dietary supplements, as well as high level of continuous innovation);
- Laboratoires Arkopharma led the category of supplements in France, with a natural and herbal portfolio of highly recognised brands (Arkogélules, Naturland and Cys-Control), strong image and quality of its products, excellent price positioning, along with a very popular merchandising presence in chemists/pharmacies;
- Retailers are strong in vitamins and dietary supplements in United Kingdom, with leading healthcare retailers Holland & Barrett and Boots, which benefit from offering a wide range and attractive prices, in addition to enjoying strong consumer trust;
- Laboratórios Pfizer continued to lead vitamins and dietary supplements in Portugal (well-established brand Centrum), due to aggressive marketing campaigns (including mass media advertising); it was followed by Bayer Portugal also thanks to its good performance in vitamins (Redoxon and Becozyme brands). This shows the strength of multinationals in the category, particularly in vitamins. Nevertheless, local players such as Natiris-Centro Dietetico have a noticeable presence in dietary supplements, and managed to gain ground over the review period;
- Walmark Romania is the leading player within vitamins and dietary supplements in Romania in 2015. The company was followed by Fiterman Pharma and Krka Romania;
- Walmark is also the clear leader in vitamins and dietary supplements in Slovakia, due to the strong brand recognition, consumers' trust and a wide product range. This company is the only player with a wide distribution reach in many niches; it notably accounted for over 70% value share in products including evening primrose oil, ginseng, guarana, co-enzyme Q10 and glucosamine, while also dominating sales in eye health supplements, probiotic supplements and lecithin. Walmark also dominates paediatric vitamins and dietary supplements, where it accounted for 73% value share in 2015.



- no major changes took place in 2015 within the competitive landscape in vitamins and dietary supplements in Spain, where it was maintained a high level of fragmentation. In vitamins and dietary supplements more than a 40% share of total sales is in the hands of small regional companies, which in most cases produce limited portfolios.

### **Prospects**

- The ageing population will be a major contributor to the development of this category of products over the forecast period; people want to live longer and stay in shape, so they are increasingly adopting healthy lifestyles; they also are able to afford higher budgets for their healthcare, which is expected to motivate them to dedicate more of their budgets for food supplements;
- static performance in certain countries is explained by the growing number of alternatives and the increasing pressure on average unit prices;
- sales decline was associated to consumer scepticism (about health claims) and confusion over the benefits offered by certain herbal food supplements; evening primrose oil, echinacea, ginseng, garlic, St John's Wort, starflower oil and vitamin E; all set to see double-digit value decline at constant 2015 prices in United Kingdom, while around 3% volume decline each was registered during the forecast period as a whole in Slovakia;
- Although the size of the category and per capita consumption is still low in Spain, for example, this allows further room for growth in the near future;
- Many areas will continue to see competition from combination dietary supplements and multivitamins; this will also impact the domain of single vitamins, for example of glucosamine and minerals, which registered 1-2% decline in 2015;
- Affordable products with well-proven benefits are expected to prove most successful, with price-sensitive consumers seeking good value-for-money in addition to health benefits.

### **8.2.2. Other important markets**

The huge number of users, the improved economic conditions and level of incomes, as well as the science progress and innovation in the field of dietary supplements transformed USA and Canada or China and Japan in very attractive markets.

### **Trends**

Similar to the European market, the demand for vitamins and dietary supplements remains positive in the US, despite recent debates about the health benefits and efficacy of vitamins and dietary

supplements. Due to improved economic conditions and rising household wealth, consumers are willing to spend on vitamins and dietary supplements in addition to their regular foods to maintain their health.

Other factors such as the ageing population, increasing consumer interest in health and wellness, new product launches, and the improved accessibility of products through various distribution channels is also supporting the growth of vitamins and dietary supplements consumption.

In Canada, new product developments, new ingredients, health and wellness, the ageing population and self-care were the main factors contributing to the growth of the food supplements sale and consumption.

The category of vitamins and dietary supplements is seeing further segmentation in China, offering products for specific conditions and different demands, such as memory boosting, post-operative recovery and immunity enhancement.

In Japan, combination dietary supplements saw the fastest growth, thanks to the robust growth of those products targeting the middle-aged and the elderly. Supplement nutrition drinks posted the strongest retail value growth, up by 3% in 2015, thanks to the increasing demand by senior consumers.

### **Competitive landscape**

In USA, the vitamins and dietary supplement market is very competitive, no company accounted for more than a 5% share of value sales in 2015. Manufacturers are continuously extending their brand portfolios across different categories, hoping to increase brand shares in the market.

Vitamins and dietary supplements market is also fragmented in Canada, although Jamieson Laboratories led with an 18% value share in 2015. A number of players, such as Wyeth Consumer Healthcare (Pfizer), Valeant Pharmaceuticals, Abbott Laboratories, Genuine Health, WN Pharmaceuticals and a few private label lines from well-established drugstore operators such as Shoppers Drug Mart and Jean Coutu, all claimed shares of less than 10% in 2015.

Amway Co Ltd retained its leading position in China, in 2015, commanding a retail value share of 11%. The company's first flagship "experience store" opened in Shanghai in October 2014, offering customers more than a traditional retail experience. The centre enables consumers to sample products and learn more about Amway's science and product development.

In Japan, Taisho Pharmaceuticals continued to lead sales in vitamins and dietary supplements with a retail value share of 9% in 2015, thanks to the continuing strong presence of its major tonics and bottled nutritive drinks brand Lipovitan. Premiumised products, mainly in mini tonics of less than

50ml, saw robust performance compared to other types of tonics containing more than 100ml. The company conducted a lot of promotion over the review period, such as collaboration with popular animation, a new TV commercial, and exposure in fashion and sports events.

### **Prospects**

Vitamins and dietary supplements is expected to see in USA a sustained growth between 2015 and 2020. Middle-aged and elderly consumers will invest in vitamins and dietary supplements to support their immunity system. Manufacturers will extend their research in order to develop new formulations and delivery formats that cater to consumers' specific needs and preferences. For younger consumers, natural ingredients may become a more attractive proposition as they are driving the increasing consumer demand for healthier and more natural ingredients. The market, however, will still face several issues such as negative research questioning the value of vitamins and dietary supplements and an increasing preference for functional and healthy foods over supplements.

In Canada vitamins and dietary supplements is set to see sustained growth, while in China a change in the registration system, along with the continuous development of new herbal/traditional dietary supplements, will inject new energy into this category.

Tonics and bottled nutritive drinks is expected to see a slight decline over the forecast period in Japan, with a declining younger population and competition from new entries of energy drinks from another industry. Vitamins is expected to sustain robust growth, but the speed of that growth is subjective depending on how well FFC products develop in Japan.

Dietary supplements and supplement nutrition drinks will see positive constant value in line with increasing demand from the aging population.

### **8.3. Interest of consumers in food supplements**

Supplement users are making a greater effort to seek health and wellness. They try to consume a better diet, to have somewhat higher intakes of nutrients; they participate in physical exercise, avoidance of obesity, moderate alcohol use and abstinence from smoking. Thus the users of dietary supplements tend to incorporate these food stuffs into their lifestyles as part of a broader focus on healthy living.

Age and sex differences were evident in motivations for use. Older adults were more likely to use supplements for site-specific health reasons (bone, heart, eye), whereas younger adults were more likely to use products with short-term effect, such as enhanced energy or to boost immune function.

Women were more likely to report use for bone health (calcium and vitamin D among for the purpose of maintaining bone health throughout the lifespan and preventing the onset of osteoporosis during aging) and men for heart health. However, men were also more likely to report use of products to improve and maintain health (vitamin D, botanical supplements, vitamin B12, omega-3 and fish oils) or for mental health, whereas women were more likely to report use of products to enhance energy (vitamin B12 and vitamin B6) or for colon health (botanical supplements) (13). The results of the 2013 CRN (Council for Responsible Nutrition) survey, show that 68% of Americans take dietary supplements (Figure. 2). Out of those, 53% say that their intake is frequent, 12% consider themselves to be occasional users, and 4% use supplements on a seasonal basis.

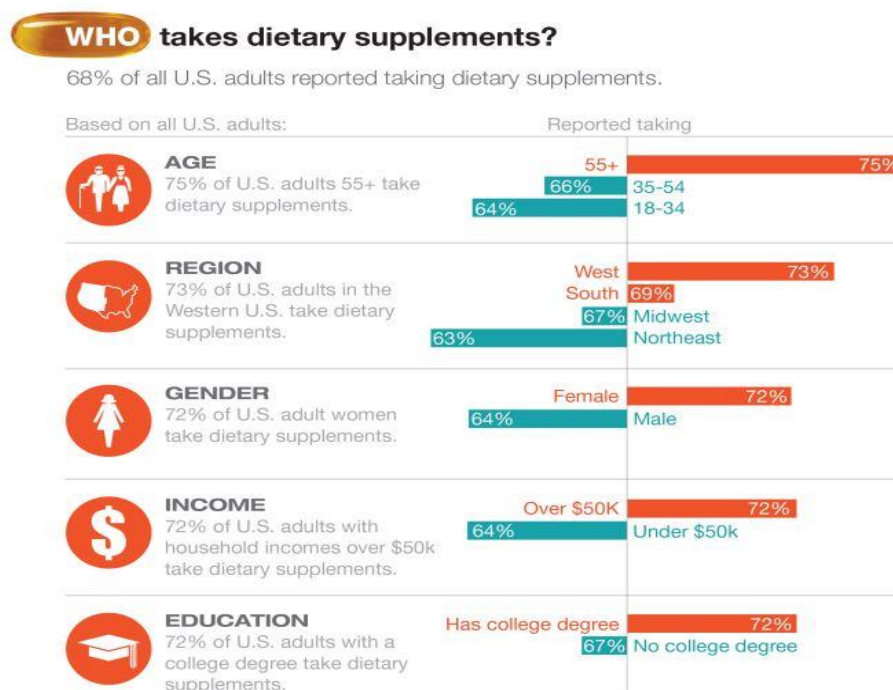


Figure 2. Demographic profile of US adults reporting taking dietary supplements (14).

The survey consistently showed that in USA dietary supplements usage is higher in people with more education than in people with less and the level of income is positive correlated with the food supplements consumption (13).

There was no simple to answer what are the reasons for use of food supplements: the primary reason was to improve or maintain overall health, which may or may not include the prevention or treatment of disease. It is interesting to note that dietary supplements were reported to be used to “supplement the diet” in only 22% of users. Most of the consumers expect to feel better (41%) or to improve the overall energy levels (40.8%), but also to boost the immune system (35.9%), to treat

digestive issues (28.4%), to relieve pain (25.5%), to lower cholesterol (20.6%), to lower blood pressure (15.7%), to improve mood or alleviate depression (11.9%) (15).

## **8.4. Herbal food supplements - a particular category of dietary supplements**

The motivations behind botanical supplement use have been studied more extensively than for other types of dietary supplements. In adults, the use of herbs and botanical supplements has been related to being uninsured, using more prescription and over-the-counter medications, and for certain health conditions (16; 17).

National survey data find that in USA most botanical supplement users do not report this information to their health care providers (16). This may be cause for concern because some botanical supplements have the potential to interact negatively with prescription medications. While some have suggested that botanical supplements are increasing in popularity to replace costly prescription medications (18; 19)

Furthermore, patients' freedom of choice of a practitioner is also encouraging their utilization of alternative treatments and herbal remedies, although many select herbal medicines from a deductive approach based on anecdotal information, that is, "it worked for my friend or relative" (20). So also, because of the influence of religion and greater level of spiritual consciousness, many individuals tend to be increasingly disposed to accepting therapeutic value of a treatment based on faith or intuition rather than scientific reasoning (21; 22).

This situation is similar in most of the European countries: people are looking to new sources of food, functional ingredients and to diseases prevention by a holistic approach including diet, life style, organic products. It is also noticed that herbal food supplement market development was also correlated to the increasing of the category of 55-64 years old in the population. This age group is more susceptible to chronic and degenerative diseases, so is positively correlated to the need for food supplements and their usage.

### **8.4.1. Herbal composition as advantage versus safety concern**

The use of herbal remedies has also been widely embraced in many developed countries with complementary and alternative medicines now becoming a mainstream not only in Europe, but also in North America and Australia (23). In fact, while places like the UK or Italy have a historical

tradition of using herbal medicines (24), their use is also widespread and well established in some other European countries (25). In these developed countries, the most important among many other reasons for seeking herbal therapy is the belief that it will promote healthier living (26).

The knowledge of plant usage rests very largely on tradition, which varies from a country to another. In practice, tradition mainly concerns the methods of preparing the plant and the usual forms in which it is used, including the dosage. If the plant has a „history of use”, this provides information about safety and its physiological effect. In this situation it can be assumed the product to be effective as a result of long experience. But the problem is that ingredients once used some time ago for symptomatic management in traditional healing are now used in developed countries as part of health promotion or disease prevention strategies. Thus the acute treatment (of certain health issues) has been replaced by chronic exposure to herbal products (used for health maintaining). As a result, the statement of „thousands of years of evidence that a product is safe” may not be valid for the way the product is now used (27).

Generally, herbal products are classified as traditional medicine products (if they claim therapeutically or prophylactic indication), but in most cases they belong to the food or cosmetic areas, although they sometimes contain plants which have pharmacological properties. For example, senna pods (from *Cassia* plants, used as laxatives) can be marketed as food in Belgium. In general, market regulators in France, the Netherlands, Belgium and especially Italy are more open to new herbal products than in Germany and the UK.

Specific categories of non-medicinal products could exist in some member states, such as “therapeutic supplement products” in Austria, for example or “medicinal products” which are under specific conditions exempt from licensing requirement in Spain, Ireland or UK (27). In Germany, where herbal products are sold as ‘phytomedicines’, they are subject to the same criteria for efficacy, safety and quality as are other drug products. In the USA, by contrast, most herbal products in the market place are marketed and regulated as dietary supplements, a product category that does not require pre-approval of products on the basis of any of these criteria.

A plant-based food supplement is intended for a person with a normal physiological profile and aimed at keeping that person in a state of homeostasis. The borderline between ‘therapeutic effect’ and “physiological effect“ is not always easy to be pinpoint, mainly because some constituents are present both in plants used for food and food supplements and in plants used as herbal medicine. These plants are called “ambivalent herbs” and the dosage is an important criterion to distinguish between both application fields.

The scientific justification for the safety and purpose of the supplement must be based on all available data, including experimental studies, but also referring to clinical and epidemiological findings. Especially when the product moves away from traditional usage, the level of scientific, toxicological and clinical requirements must be higher, as much for the safety in use, as for the physiological effects and consequently for the health claims.

#### **8.4.2. Reasons of worry for human health**

European Commission together with EFSA have started a sustained activity of evaluation of plant-based food supplements, which are under different regulation in member states (they have specific national rules and procedures for marketing authorisation, positive and negative lists, maximum levels of certain biochemical compounds, specific condition of use, etc.).

The main purpose of the risk assessment was to identify any potential danger involved in using the plant, not only the species or the part of the plant, but also the type of extract chosen, as well as the chemical composition of the finished product and should refer to pharmaco-toxicological and clinical data. All these data are important in order to provide the consumers with correct information regarding the consequences of consumption of such a product. Molecular interactions with other botanical components (especially for the mix of many plant species or the combination of herbals with vitamins and minerals) or with medicines are also possible. The precautionary principle must be the rule in all cases to ensure health consumer protection.

On the other side, such knowledge will be helpful for the manufacturers who must apply mandatory standards of plant processing to ensure the quality and safety of their products aiming to protect the public health.

The reasons for worry reviewed in a report elaborated by Scientific Committee of EFSA in 2004 (EFSA SC/26 Final) (28) are based on vast numbers of scientific communications, press warnings and attitudes of responsible national and international authorities and organizations, regarding the following aspects:

- **toxicity** of certain plants and substances extracted from them, which could be found in the composition of herbal food supplements; pyrrolizidine alkaloids from *Symphytum officinale* and *Tussilago farfara*; aristolochic acids from *Aristolochia species*, active pyrones constituents from *Piper methysticum*; ephedrine from *Ephedra sinica* proved to have hepatotoxic and nephrotoxic effects, induced permanent damage of liver or kidney tissues, stroke and heart attack or cancer and even (29); as consequence, all these plants were forbidden for human use (30; 31); The

“Compendium of Botanicals reported to contain natural occurring substances of possible concern for human health when used in food and food supplements” was published in EFSA Journal (32);

- **adverse reactions** in case of consumption of herbal food supplements simultaneously with synthesis medicines (6% of patients have had serious problems), even if they are common species: *Ginkgo* (cautious use must be advised in individuals on anticoagulant therapy); *Hypericum* (interaction with antidepressants and anticoagulants; allergic reactions, dizziness, headache, fatigue, nausea, photosensitivity); *ginseng* (insomnia, headache, elevation of blood pressure, epistaxis, vaginal bleeding in large excessive doses);
- **misidentification** of plant species with similar vernacular names and mislabelling of the herbal products) in case of *Stephania tetrandia* (Fang-Ji) and the confusion with *Aristolochia fangchi* (Guang-Fang-Ji) produced dramatic adverse reactions which led to nephrotoxic and carcinogenic events (33);
- **the content of secondary metabolites** could register high variations especially in the wild-crafted species (concentration above permitted limits until the quasi-total inexistence) that dramatically influence the efficacy of the herbal products;
- **lack of stability** of the quality end efficacy indicators, especially in case of certain plant extracts, fat oils, herbal teas;
- **contamination** with heavy metals (As, Hg, Pb) of herbal products resulted in toxic effects on children, who reported learning disabilities and behavioural problems;
- **adulteration** of herbal food supplements with active pharmaceuticals have been observed with Sexual Enhancement or Men’s Virility products (PDE-5 inhibitors); Sports Nutrition supplements (steroids); Diet and Weight Management supplements (anorectics like Sibutramine and Phentermine; diuretics like Bumetanide and Furosemide); stimulant adulteration (Caffeine, Methamphetamine, Amphetamine or Methylphenidate), etc;
- **substitution** of some useful plants with similar species as aspect, sold as raw materials proved to be inefficient or dangerous surrogates for public health, which may affect an increasing part of population, as the sales volume of food supplements in continuously increasing.

Although the herbal food supplements has shown promising health supporting potential due to the huge number of bioactive substances clearly identified and characterized, many others remain not tested and their use are poorly monitored or not even monitored at all. The consequence of this is an inadequate knowledge of their mode of action, adverse reactions, interactions with existing



orthodox pharmaceuticals and functional foods. Nevertheless, given the widespread use of dietary supplements for health promotion and maintenance, increased clinical research efforts are warranted to address safety and efficacy. Also, more investigation on the complex interplay of social, psychological, and economic determinants that motivate supplement choices are needed (34).

### **8.4.3. Quality and safety requirements for herbs and herbal food supplements**

Since safety continues to be a major issue with the use of herbal food supplements and botanical remedies, it becomes imperative, therefore, that relevant regulatory authorities put in place appropriate measures to protect public health by ensuring that all herbal products are safe and of suitable quality.

For herbal food supplements as final products of plant processing, quality management system implementing is extremely important. Hygienic rules, employees qualification and health, equipments maintenance, biochemical and microbiological analyses of raw material before manufacturing, packaging and labelling are some of the main issues aiming to ensure quality and safety products on the market.

As Guidelines on the quality, safety and marketing of plant-based food supplements (2005) stipulate, each product have to be prepared according to precise specifications covering all stages in the process, from the description of raw material to release of finished batches of the products. The description of the various stages must be sufficiently detailed to serve as basis for industrial production and must be accompanied by a description of the in-house verifications that will be performed at each stage to enable the manufacturer to monitor and assess the product's quality (35).

Markers of tracers must be taken into account as there are essential tools able to provide proof of:

- quality (a tracer is a chemically-defined constituent of a plant that can be very useful in calculating the quantity of plant or preparation in finished product);
- physiological effect (the biochemical nature of a marker allows an objective evaluation of any influences on organic functions associated with the consumer's psychological and physical performance);
- absence of toxicity (a relevant indicator of chemical, biological, clinical or epidemiological nature to explain the benefit to health);
- the daily amount to be taken must be planned as precisely as possible since plant constituents (which may be highly concentrated in certain extracts) can reach intake levels

causing pharmacological effects. In herbal food supplements, the daily intake of plant substances must take account of normal traditional usage;

- complex mixtures of plants should be limited in the number of different plants or plant preparations in one product in order to allow a correct chemical analysis;
- particular attention have to be given to the characteristics and differences between matrices, whose effect may alter digestive absorption and the bio-availability of active substances, or could induce molecular interactions which may enhance the risks;
- health claim evaluation must be consistent with the recognized physiological effect and the degree to which the claimed effect is demonstrated;
- the proofs required in support of a claim must be internally consistent; where based on tradition must relay on generally recognised knowledge; must be experienced *in vitro* and *in vivo*; may be obtained from several sources, including human intervention studies or even epidemiologic studies, when available;
- scientific assessment means that the fullest possible information must be available.

Public information and communication concerning these products must be fair, supported by scientific data or studies and make it possible to guarantee safety of use, so that the products' consumption is risk-free.

In order to inform the public, the manufacturer must be able to provide information about the anticipated uses of a product and the purpose for use; he should have knowledge about the population at risk (vulnerable categories of consumers, to which the product must not be recommended) and geographic limitation of use (when appropriate).

Regarding the conditions of a product use, the consumer must be informed clear and with the maximum transparency about the product formula, the nature of the plant used, the period of use, the maximum permitted daily amount, the adverse effects and possible interaction with certain medicines or food.

Apart from labelling obligations, there is useful to include detailed instructions concerning the product in the packaging.

In conclusion, with pragmatism, common sense and scientific rigour it should be possible, in the interest of European public and the consumer, to market increasingly reliable, risk-free plant-based food supplements.

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