9. LEGAL TRADE OF FOOD SUPPLEMENTS

As a general rule, food business operators must notify national authorities when a food supplements is first placed on the market. In certain Member States prior marketing approval is necessary, in other countries the notification is done latest on the day when the product was placed on the market but there are also countries where notification is not compulsory (Austria). Notification has to be sent to the competent authority, such as the Ministry of Health (Italy, Slovenia, Croatia, UK), Ministry of Food, Agriculture and Fisheries (Denmark), Ministry of Agriculture, Food Production and Legislation Department (Czech Republic), National Institute for Food and Nutrition Science (Hungary, Romania), Food Safety Agency (Finland, Bulgaria), Federal Office of Consumer Protection and Food Safety (Germany), National Food and Veterinary Risk Assessment Institute (Lithuania), Chief Sanitary Inspectorate (Poland), General Directorate for Competition Policy, Consumer Affairs and Fraud Control (France), Federal Public Service-Health, Food Chain Safety and Environment (Belgium) or other national authorities responsible for monitoring, control and market surveillance. Online notification is also practiced, in Poland or Belgium, respectively, where FOODSUP digital notification system was implemented since 2012.

9.1. Notification procedure and marketing approval

Considering certain botanicals under particular use, Member states have a long tradition of regulating botanicals, imposing requirements onto domestic producers to follow these rules but also aiming to protect their markets against products not complying originating from other Member states or non-UE countries.

The notification and registration procedures could be more or less different as approach, but the criteria of food safety evaluation are similar in European countries. According to Directive 2002/46/EC, a particular reference to composition (ingredients and levels) and compliance to European regulation regarding food safety, novel food ingredients, food additives and specific requirements for labelling, nutrition and health claims have to be taken into account.

The safety assessment (public health and nutrition point of view) and risk management measures are based on the examination of data provided by the food business operator: type and amounts of active ingredients, chemical forms of minerals, vitamins and recommended daily dose, plant species and their parts used, conditions of use, botanical preparation (drug or plant extract: ratio, active substance, maximum levels), specific warning statements, etc.

Because it has been noticed an important share of botanical food supplements in EU (big intra-Union market) and the growing internet sale (usually reaching markets of more member states), mutual recognition has to be applied on the case by case basis. In principle, a member state is obliged to accept on its territory a product lawfully marketed in another Member State. If there is a danger for health, the Member state can impose restrictions but has to demonstrate and justify the need for this. Medicinal status of botanical species is most of the time used as argument to restrict marketing, while protection of consumers is therefore a frequent argument for imposing restrictions of use.

Positive lists of non harmonised botanicals (plant species and their parts that can be used in food supplements) are regulated under national legislation and are common in many countries, such as: Italy, Hungary, Germany, Belgium, France, Check Republic, and Romania. Botanical Advisory Boards or Expert Committees which members are coming from the universities, academy of sciences, research institutes of food and nutrition, professional associations, ministries, etc. are responsible in each country for evaluation of botanicals and other active substances intended for use in food supplements.

There are also negative lists (in: Sweden, Netherlands, Lithuania, Bulgaria, and Netherlands) as well as restricted botanicals (maximum levels), which are used as national guidance in the absence of a harmonised list on EU level.

Some of the secondary metabolites of safety concern are: the alkaloids (especially pyrrolizidin content), anthraquinones, coumarins and furanocoumarins. They could have hepatotoxic, genotoxic, neurotoxic, carcinogen, and mutagen, drastic emetic, laxative or abortive effects. In connection with the scientific progress and new discoveries, negative lists as well as conditions of use are revised continually.

Derogation possibility and exemptions to the prohibition have to be supported by toxicological studies and analytical tests that prove the final product is free of toxic properties and do not contain the toxic substances synthesized by the plant used as raw material.

In case of safety concerns or other serious problems identified during the product examination, the market enforcement authorities are alerted.

An initiative of Belgium, France and Italy started some years ago (in 2011) aiming to harmonize evaluation of botanicals in food supplements and to accelerate mutual recognition on a scientific basis. There were combined three lists of authorized plants used in Belgium (645 species), France (548 species) and Italy (1182 species) which resulted in a harmonized list (a common positive list)

of about 1000 species called “BELFRIT list”. The involved experts verified the accepted botanical names and synonyms of plant species, edible mushrooms, algae and lichens, but also chemo-taxonomic relation, traditional used plant parts, as well as chemicals (substances, markers) of concern. Further information regarding botanical preparation, essential oils, nutrition and physiological effects were collected from a relevant list of references.

Food business operators, competent authorities and other stakeholders were invited to apply for the up-grade of the list by forwarding a supportive scientific dossier and proofs about traditional use at national level of other species (potential new entries on the list which is a no exhaustive ‘living’ list).

EU harmonisation for botanicals in food supplements is still a goal to achieve because there is a common interest to have on the European market safe products with plausible physiological effects. Harmonisation is possible when coherent policies based on scientific advice and pragmatic approach is implemented, taking traditional use into account and assure safety and consumer information.

In conclusion, the four pillars of sustainable regulatory framework should be:

1. A common list of plants (based on a common methodology for assessing the safe use of plants, to facilitate mutual recognition);
2. A harmonised notification system (based on common requirements to judge the nature of the botanical preparations and the labelling);
3. Verification of product quality (based on HACCP: Risk-based approach complemented by market control);
4. Monitoring (Rapid Alert System-for safety-related incidents and nutravigilence - to cover adverse effect).

9.1. 1. Notification dossier. Quality and safety evaluation

All characteristics of the product should be evaluated technical and scientific point of view. The food business operators must prepare the notification dossier and supply the competent authority with details about the product: technical specifications, list of ingredients (plant name, part used, galenic form, amount, % active substances, function), preparation/processing method (% solvent, Drug-Extract-Ratio), quality and safety test reports (chemical and biological contaminants) labelling (nutritional analysis, qualitative and quantitative data of nutrients, health claims), additional information for imported food supplements, etc.

The competent authority has to check all information provided by food business operator as well as product conformity with vertical and horizontal legislation. Usually there are registered: rewording of the label, need for more specific information, expert advice when necessary, certain recommendation, etc.

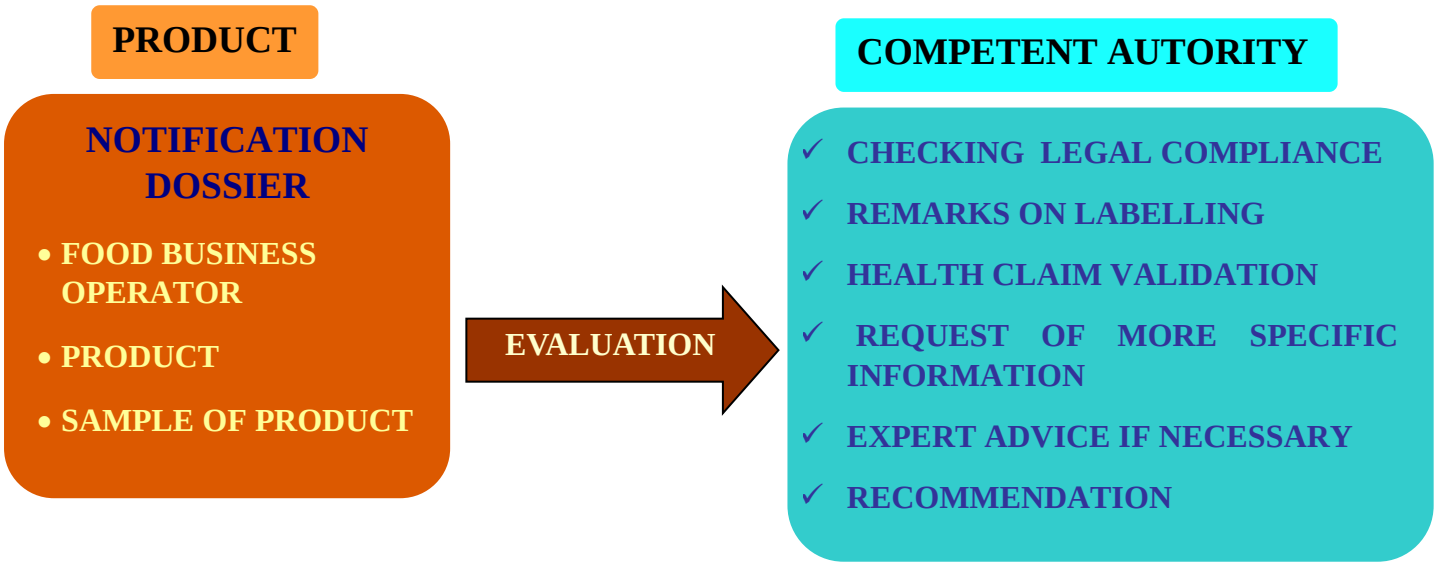
Within month a letter of receipt (possibly with remarks) and a decision of compliance/non-compliance are communicated to the food business operator.

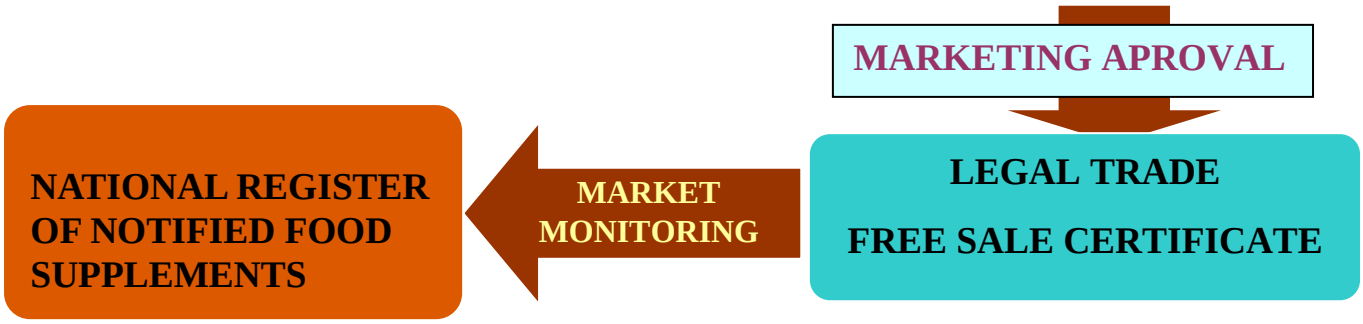
For botanical preparation the scientific safety evaluation focuses on dangerous substances known to be present in plant (as mentioned in EFSA Compendium). Both food business operators and competent authorities must ensure that such substances are not present in the botanical preparation. Certain information are relevant, such as: characterization of the plant, collection of bibliographic data, information on traditional use, analytical reports, maximum levels and warnings, side effects, registered incidents.

To ensure a high but proportional level of consumer protection and information it is also important to respect always precautionary principle for daily recommended dose, to inform specific target group and to label the product with safety warnings.

Borderline issues and distinction between food and medicine products have to be based on case-by-case risk assessment, available scientific data, EMA and WHO monographs. If necessary, for "ambivalent" plants the maximum level (% of minimal daily therapeutic dose obtained after evaluation of clinical trials for well defined indication) have to be taken into account. The claims legislation should be helpful in establishing the status of the product (traditional herbal medicine product versus herbal food supplement) but in case of botanicals a huge number of health claims were not yet evaluated or are still on hold.

Fig.1. The schedule of notification procedure and marketing approval for a food supplement (Romanian experience)





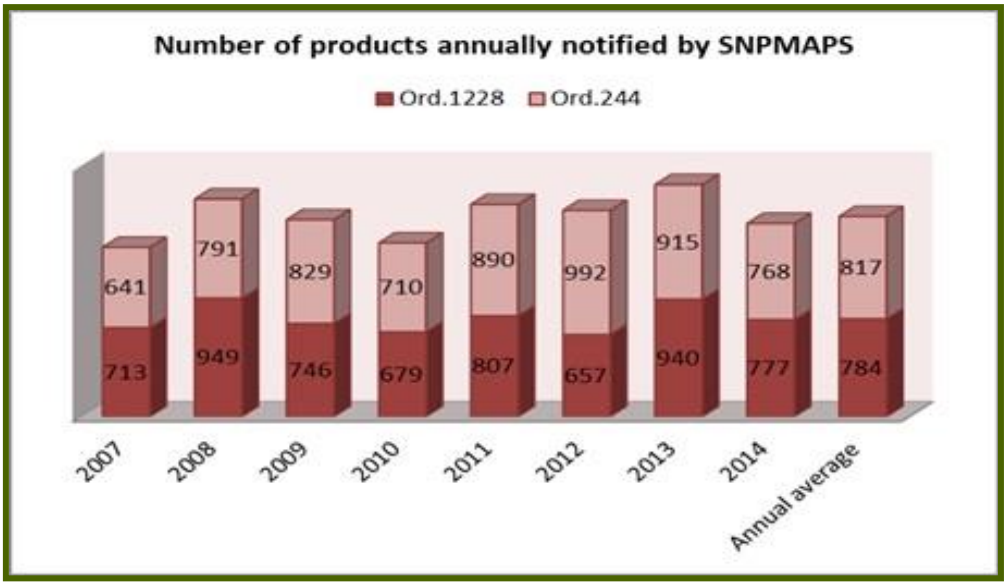
9.2. Distribution channels and legal trade

Botanical food supplements involve various actors, from plant cultivation (agriculture) to product distribution. EUROPAM has shown that in 2005 over 100,000 ha were cultivated in EU, more than 21, 000 people (growers and collectors) being involved in cultivation and harvesting of medicinal and aromatic plants. A number of 150 business operators were registered as extract manufacturers (near 15,000 people working in the field) and more than 1500 enterprises were involved in final product manufacturing, out of which 95% were SME-s. A number of approximately 35,000 people were involved in production activities (mainly botanical food supplements manufacturing), while in distribution were involved 10 times more. The statistical data showed in 2012 about 10,000-15,000 distribution companies of food supplements at EU level, and a number of 75,000-100,000 people involved in botanical food supplements distribution. Food Supplements Europe organization remarked that these data could be underestimated because of combination products, which number have increased during last time.

The EU market of botanical food supplements (retail-direct sales-internet) was estimated to 2, 1 billion euro. Actually 75% of the sales are registered in France, UK, Italy, and Germany, which are considered the biggest markets. The herbal food supplement markets are really dynamic: thousands of new products are notified each year, for example 3,000 in Belgium or 4,500 in Italy. Since 2006 up to 2015, a number of 25,000 products were notified in France, 20,000 in Italy, and 16,000 in Hungary (EHPM EBF, 2012).

Joining the EU in 2007 and opening the local market, the number of food supplements notified in Romania reached, at the end of 2014, near 21,150 products (manufactured all over the world), out of which approximately 70% have in their composition botanicals or plant extracts. Less than half of them (graphic 1) have as ingredients exclusively botanicals (43%), while the rest are mixtures of botanicals or plant extracts combined with vitamins and minerals, or any other substances with nutritional and physiological effect (57%).

Graphic 1- Herbal food supplements notified in Romania during 2005-2014 periods



The herbal food supplements annual monitoring showed that every year approximately 1,860 new products enter the Romanian market and a significant number are coming from other countries.

As compared to food supplements, traditional herbal medicine products market is considerably smaller: since 2004 about 1,300 applications were granted EU wide, covering 150 plant species. It could be noticed that 77% of applications were submitted in only 6 countries (EHPM EBF, 2012).

The distribution of botanical food supplements involves various distribution channels (table 1).

Table 1- EU distribution channels of food supplements (data compiled by EHPM EBF, 2012).

Shops	**Estimated number**	**Employment**	**% of botanical food supplement sales**
Food and health shops/herbalists	50,000	50,000-100,000	5-10%
Grocery/Supermarket/Retail	460,000	5,000,000	10-30%
Pharmacies	120,000	120,000-180,000	50-60%
Direct sales	-	3,000-4,000 850,000-900,000 independent sellers	20-30%
Internet sale	-		5-10%

Markets are different from a Member State to another. Herbalists, health care practitioners, pharmacies (as shown in table 2) are involved in herbal food supplements distribution, protecting their market structure against sales of products through other channels.

Table 2. Distribution channels used in EU member states (PlantLIBRA, 2012)

% of sales	**UK**	**FR**	**DE**	**CZ**	**PL**	**RO**	**FI**	**IT**	**NL**	**ES**
Pharmacies		65	85	87	64	90	32	70	15	40
Groceries	46	11	7	4			32	29	65	
Health shops	19	10		4			33	18	7	60
Direct sales	31		8	4	28		15		7	
Others	4						25	10	6	

The online channel has become a popular platform for manufacturers in their efforts to reach a diverse and broad set of customers. Products are sold via online pharmacies, dedicated health platforms, retailers' and manufacturers' websites and not least via Amazon (one of the largest online retailers), which and are often offer significant discounts. Beyond easy price comparisons, the online channel also facilitates consumers' research of products' ingredients and benefits prior to purchase.

Retailers have taken note that internet is often the first port of call when in need of information on health and have focused efforts on improving the online shopping experience through better online education and targeted marketing. Online pharmacies are required by German law, for example, to provide the option of personal advice via telephone or email and some websites now have live chat options to help instantly address specific consumer questions. Such methods have increased consumers' comfort level for buying dietary supplements online.

9.3. Herbal products' control and market surveillance

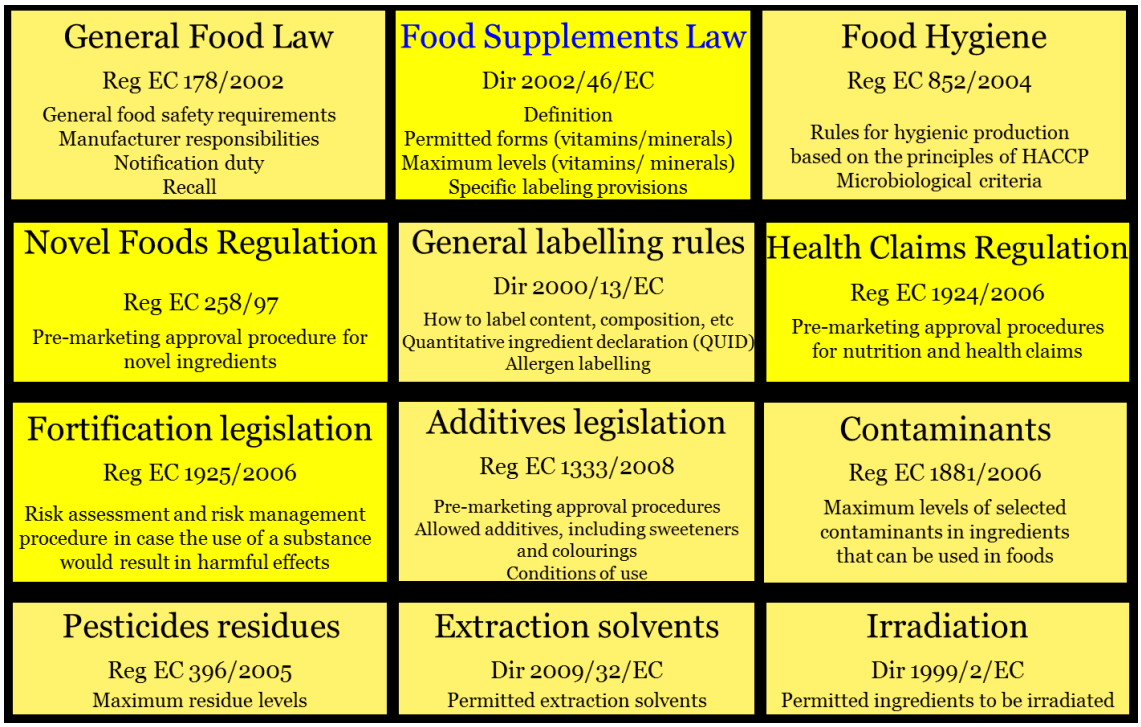
Control and surveillance of the botanical food supplements market seems to be a challenge for the regulators which feel powerless to keep under control this sector. It is underlined the fragmented legislation between the Member states, the difficulty to overview and control all players in the sector. A real problem seems to be to make enforcement actions respected (there are actors that close down and restart again, as well as websites which are moved abroad). Unfortunately the lack of nutravigilence, few unscrupulous importers/ producers responsible for most of the issues, the

difficulty to police the internet as well as illegal products (often advertised and sold via internet) give the impression of an unregulated market, while some gaps in the legislation create feeling of lack of control.

Even if the vast majority of botanicals is not disputed (safety and quality concerns focus on a limited number of species), the EU legislation is not so well equipped to address the specificity of botanicals, while the national approaches are too focused on consolidating historic situations.

EFSA is emphasizing the difficulty of herbal food supplements control due to the enormous diversity of products. The huge number of plant species and their combination, different matrices (solid, liquid) and forms of presentation, methods of preparation (from traditional to modern and sophisticated techniques) are listed as serious issues for competent authorities, which are involved not only in raw material quality and safety control, but also in food supplements fabrication process, which is more severe controlled. All ingredients and products must comply with the general regulations regarding foodstuff, as well as with the specific regulation regarding food supplements (fig. 2).

Figure 2. EU general and specific regulation used in control and surveillance of herbal food supplements



In USA, the FDA regulates both finished dietary supplement products and dietary ingredients. FDA regulates dietary supplements under a different set of regulations than those covering

"conventional" foods and drug products. Under the Dietary Supplement Health and Education Act of 1994 (DSHEA):

- Manufacturers and distributors of dietary supplements and dietary ingredients are prohibited from marketing products that are adulterated or misbranded. That means that those companies are responsible for evaluating the safety and labelling of their products before marketing to ensure that they meet all the requirements of DSHEA and FDA regulations;
- FDA is responsible for taking action against any adulterated or misbranded dietary supplement product after it reaches the market.

Product conformity (compliance with quality and safety requirements) is checked during the current controls (one-two times/year) or when a non-compliance suspicion is expressed (during the notification dossier evaluation or sample examination), but also when a consumer complaint (safety concern, lack of effect, side effects), an alert (expressed by another competent authority, including EFSA) or a specific demand (other food business operators, Customs Authority, lawyers) was registered.

The novel European concept "integrated benefit–risk assessment" as well as the American concept of "multidisciplinary approach of food supplement fraud" calls for additional research support, educational activities and harmonisation of regulation.

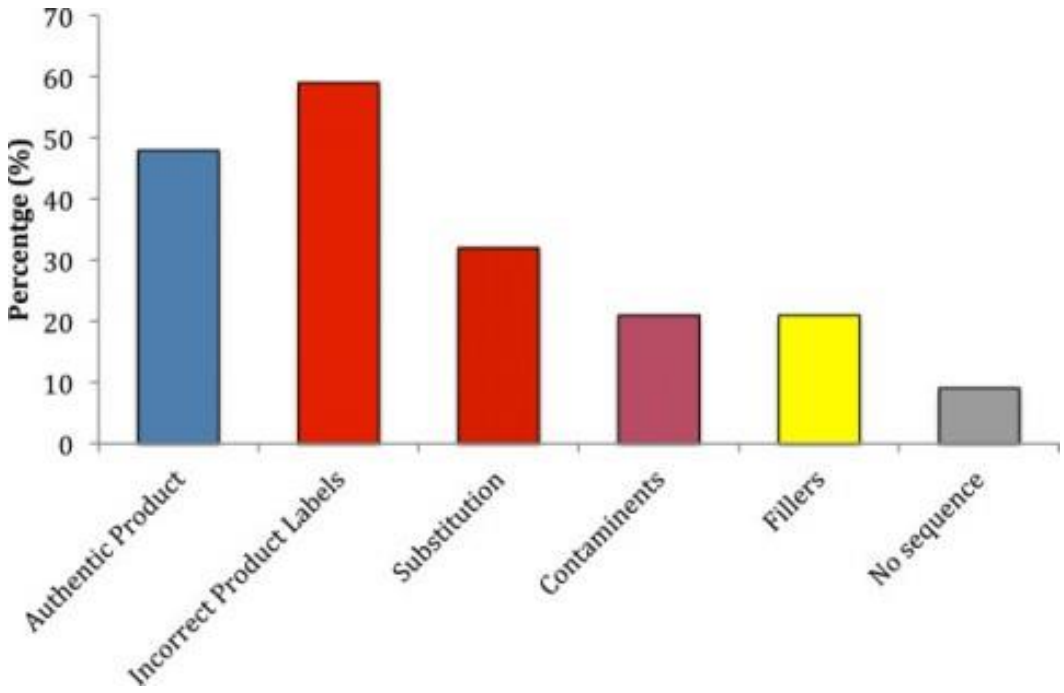
9.4. Main risks and health threats of illegal trade

The control authorities are faced during the last period to an increasing phenomenon which affect both the governments (financial point of view), and the population/food supplements consumers (health point of view). The phenomenon is called "herbal food supplement fraud" and has been characterized as the "deliberate and intentional substitution, addition, tampering or misrepresentation of food, food ingredients or food packaging, false or misleading statements made about a product for economic gain" (Wheatley et Spink, 2013).This intentional act can lead to adverse public health consequences, such as "counterfeit, poor quality or food adulteration", which are, according to WHO a real "threat to consumer safety". Fortin (2011) assumed that adulteration of food supplements could be a potential "terrorist weapon" and a serious problem for the security of any country.

Newmaster et al. (2013) have tested herbal products by DNA bar-coding (which essentially treats DNA strands like UPC codes, examining and distinguishing between different species) and reported that 59% of the analyzed products contained plants not listed on the label. In the same time, in 33%

of the authentically herbal products were detected contaminants and/or fillers in their composition (graphic 2).

Graphic 2 -Results of herbal food supplements authenticity analysis (Newmaster et al, 2013)



Currently, there is a gap in our understanding to the extent of herbal products substitution, contamination and use of fillers. Over the last years, studies on Chinese plant medicine have documented the potential scope and magnitude of market substitution using the biotechnology to mix in the herbal products phenotypically similar species (Li et al., 2011).

9.4.1. Adulteration

Food supplements could be deliberately or accidentally contaminated by different ways (Tseng et Lin, 2002). Contamination ways can be diverse: contaminating substance is present in the raw material; the manufacturing process (cross-contamination); transport, packaging and storage; different concentrations in the product as compared to those stated on the label. The most dangerous one is the deliberate contamination (known as intentional adulteration) or ‘spiking’, which may be maliciously used to increase the effectiveness of the supplement product, and thus to hence the sales (Zhu et al, 2005). Adulterations can be classified in: *i)* addition of orthodox drugs to herbal

medicines, *ii)* substitution (use of fake or inferior plant materials), and *iii)* addition of foreign materials (non-official/forbidden herb parts, sand, metals) (Zou et al., 2006). In this sense food supplements are suitable vehicles for adulteration with drug substances. In most countries food supplements are loosely regulated compared to medicines. Consumers buying place a high trust in natural remedies and probably are less likely to attribute adverse effects to the product. The most frequent intentional adulterated food supplements are those categories of products for which the market demand is increasing: body-building, slimming, sexual performance enhancers, anti-diabetic or fatigue relief products.

Table 3 summarised 210 products recalled by FDA from the market during January 2010 to September 2013: sexual performance enhancers (45%), strength enhancer (39%) and weight loss (16%), which proves that adulteration of finished products is a real problem for the major products categories (Shi et al, 2011).

Table 3. The adulterated food supplements recalled by FDA from the USA market during 2010-2013 periods

Products Recalled	Year of Recall Notice	No. of Products Recalled	Adulterant
Strength enhancer	2010	82	Steroids
Weight loss	2010	1	N-Desmethyl sibutramine
	2011	6	Sibutamine
	2012	8	Sibutamine
	2013	16	Sibutamine+N-Desmethyl sibutramine+N-di-desmethyl sibutramine; Sibutamine+Phenolphthalein; 1,3 dimethylamylamine (DMAA)
Sexual performance enhancer	2010	55	Sildenafil; Sulfoaildenafil; Hydroxythiohomosildenafil; Aminotadalafil
	2011	7	Sulfoaildenafil methane sulfonate + Sulfosildenafil + Dimethylsildenafil; Tadalafil; Tadalafil + Sildenafil +Sibutramine; Sildenafil; Sulfoaildenafil
	2012	15	Sildenafil; Sulfoaildenafil; Sulfoaildenafil+Thioaildenafil; Sildenafi + Hydroxythiohomosildenafil; Tadalafil; Tadalafil+Sildenafil
	2013	16	Sildenafil; Sulfohydroxyhomosildenafil+ Aminotadalafil; Desmethyl carbodenafil+Dimethylsildenafil+ Dapoxetine; Tadalafil; Tadalafil+ Sildenafil

Sexual performance enhancers

Many dietary supplements advertised as all natural, have in contrast been found to contain synthetic PDE-5 inhibitors (Gratz et al., 2004). These kinds of commercially available herbal products have been spiked with legal drugs or mainly their analogues, which have not been subjected to formal pharmacokinetic or other pharmacological testing (Ge et al., 2008). In this sense, the steady stream of new analogues provides an additional challenge and their unclear status as drug substances, may soften any penalties.

The discovery of PDE-5 inhibitors (sildenafil, tadalafil and vardenafil) revolutionised the management of erectil disfunction and oral drug therapy -independent of the disorder etiology- is currently the first therapy option [18-22]. Sildenafil and vardenafil are shorter-acting agents, while tadalafil has a longer half-life allowing the user more flexibility in sexual activity (Langtry et Markham, 1999; Meuleman, 2003; Keating et Scott, 2003).

These drugs are only available with prescription and must be used under medical control. PDE-5 inhibitors are not recommended for patients who ingest medicines based on organic nitrates (e.g. nitroglycerin, isosorbide dinitrate, isosorbide mononitrate, amyl nitrite, or nitrate) for diabetes treatment, hypertension, hyperlipidemia and ischemic heart disease, because may result in marked and unpredictable decreases in blood pressure, accompanied by symptoms of hypotension. The most common adverse reactions given by the three PDE-5 inhibitors are summarised in table 4 (Lee, 2011).

Table 4. Adverse effects of PDE-5 inhibitors

Adverse event*	**Sildenafil**	**Tadalafil**	**Vardenafil**
Headache	12.8%	14.5%	16%
Flushing	10.4%	4.1%	12%
Dyspepsia	4.6%	12.3%	4%
Nasal congestion	1.1%	4.3%	10%
Dizziness	1.2%	2.3%	2%
Abnormal vision	1.9%	-	<2%
Back pain	-	6.5%	-
Myalgia	-	5.7%	-

**European Medicine Evaluation. Association statements on product characteristics.*

The adulteration of dietary supplements has become a major problem for both public health and control authorities because the number of PDE-5 inhibitors analogues grows rapidly. To date, from 46 unapproved analogues of prescription PDE-5 inhibitors found in 2012, there was moved to 57 adulterants in 2013, as described in the literature. The safety and toxicity profile of these unapproved analogues is often not known and hence consumers of such products are exposed to higher health risks, because their physiological effects are not sufficiently studied and supplements that contain such substances are not properly labelled. In order to detect these substances new analytical methods for rapid screening are needed to be developed as well as new strategies for structural elucidation of unknown analogues. Our efforts focused last years on the development of rapid methods for screening of herbal food supplements and early detection of adulterants (Popescu et al., 2014).

Quite recently, Venhuis et al. (2012) found the erectile dysfunction drug tadalafil in capsule shell of a food supplement at levels of 2.85 mg. The adulteration was probably made by adding tadalafil powder to a gelatine jelly during the manufacturing process of the capsule shell.

Slimming and weight management products

Obesity has become one of the diseases of modern civilization, having a negative impact on quality of life and consequently on lifetime (Stypułkowska et al., 2011). Effects of herbal food supplements, designed to reduce body weight are much slower as compared to synthetic drugs (Ariburnu et al., 2012). For this reason, in order to increase efficiency, weight loss supplements are commonly adulterated with pharmaceutically active substances such as sibutramine and its analogues (Song et al., 2014), rimonabant, benzodiazepine, fluoxetine, furosemide, phenolphthalein (Deconinck et al., 2012).

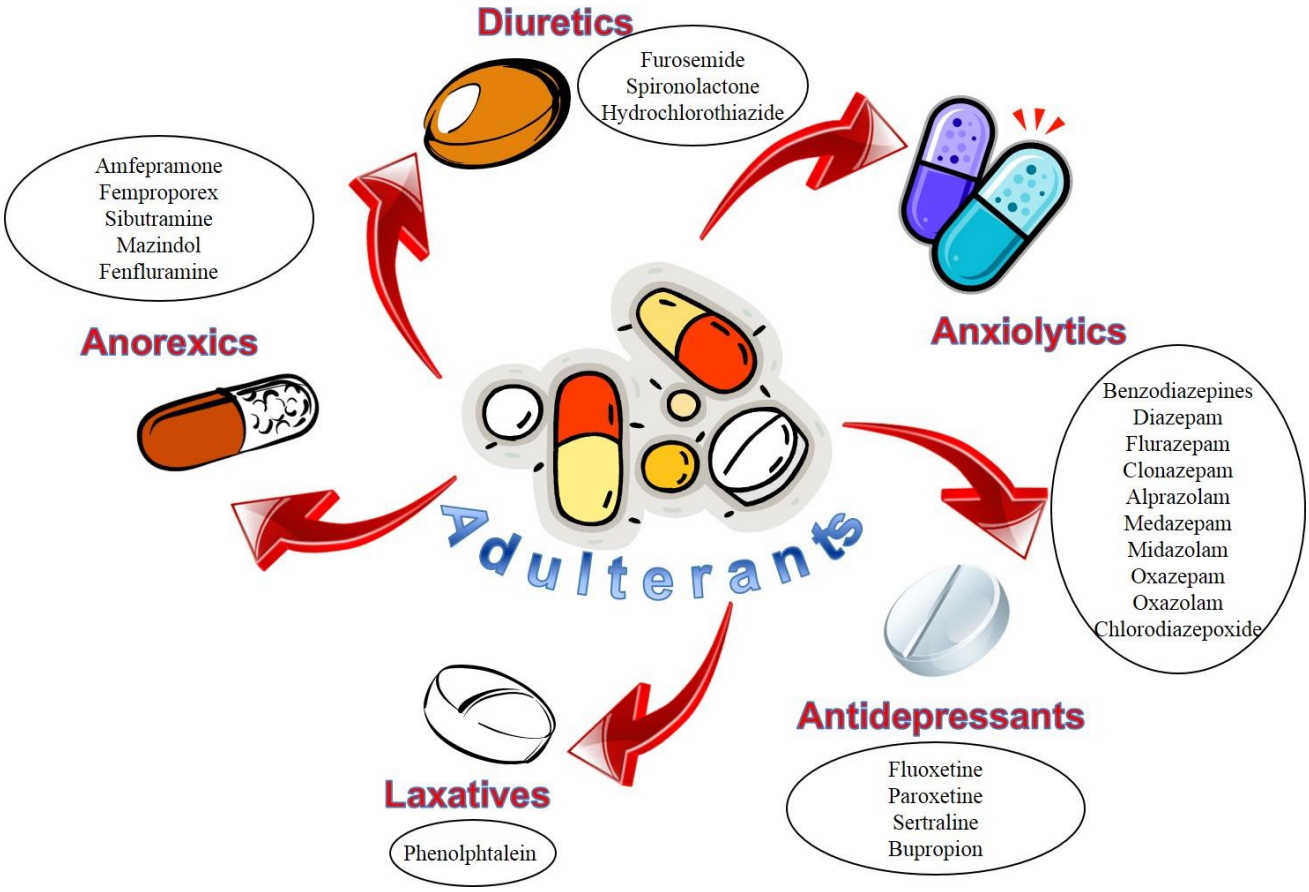
Sibutramine was approved in 1997 by FDA as a drug for treating obesity (manufactured by Abbott's Meridia). Due to side effects it was withdrawn by EMA in January 2010 (Ariburnu et al., 2012), and in September, 2010 by the FDA.

A quantity of 2-5 times higher than in Reductil® or Meridia® authorized drugs was find in slimming capsules (Vanhuis et al, 2014). In addition, the same authors have detected in food supplements for the management of body weight a number of six analogues of sibutramine, respectively: N-desmethyl-sibutramine, N, N-didesmetil, sibutramine, benzyl, sibutramine, N-formyl-didesmetil, sibutramine, N-formyl -benzyl-desmethyl-sibutramine, desmethyl-sibutramine and benzyl.

In other studies, there were detected dietary supplements adulterated with: N-nitrozofenfluramine, fenfluramine, propanolol, dobutamine, rimonabant, efedrine (alcaloid derivat din diverse plante din genul *Ephedra*), norpseudoefedrine (natural compound of *Catha edulis*), furosemide, orlistat, fentermine, clopamid (diuretic de tip piperidin), emodine, crisofanol și reine (compuși antrachinonici proveniți din *Rheum rhabarbarum* ce induc diareea and have carcinogenic potential) (Yuen et al., 2007; Carvalho et al.,2011).

Carvalho et al. (2011) classified the different types of adulterants found in food supplements in five pharmacological classes (Fig. 3): anorexics (amfepranone, femproporex, sibutramine, mazindol, fenfluramine); anxiolytics (benzodiazepine, diazepam, flurazepam, clonazepam, alprazolam, medazepam, midazolam, oxazepam, oxazole, chlordiazepoxide); antidepressants (fluoxetine, paroxetine, sertraline, bupropion); diuretics (furosemide, spironolactone, hydrochlorothiazide) and laxatives (phenolphthalein).

Fig. 3- Pharmacological classes of adulterants found in dietary supplements for weight control (Carvalho și colab., 2011)



The most common side effects caused by the adulterants found in food supplements used for reducing body weight are shown in Table 5.

Table 5- Side effects caused by pharmaceutically active substances found in adulterated slimming products (Haneef et al., 2013)

Adulterants	Adverse Effects	References
Sibutramine	Severe headaches, vertigo, cardiovascular disease, palpitations, tremors, insomnia, dizziness, heart attack, hypertension, generalized weakness, constipation, nausea, dry mouth, psychotic episodes and manic, panic attacks	Haneef et al., 2013; Khazan et al., 2014; Yuen et al., 2007; Ariburnu et al., 2012
N-didesmetil, sibutramine	Hepatotoxic acute psychosis, supraventricular tachycardia, hepatic impairment	Haneef et al., 2013
Fenfluramine	Valvular heart disease, pulmonary hypertension, cardiac fibrosis, hypokalaemia	Shi et al., 2011; Yuen et al., 2007; Haneef et al., 2013
N-nitrozofenfluramine	Hepatotoxic acute psychosis, paralysis hypocalcemia, abnormal functioning of the thyroid gland	Haneef et al., 2013; Yuen et al., 2007
Phenolphthalein	Pulmonary hypertension, heart failure, hypokalemia	Haneef et al. 2013
Emodine, Crisofanol and Reine	Diarrhea, carcinogenic potential, renal toxicity	Shi et al., 2011
Fenproporex, amfepranone	Headaches, depression, irritability and chemical dependency	Carvalho et al., 2011
Fenproporex, Fluoxetine	Headache, chest pain, palpitations, insomnia, nausea and fatigue	Carvalho et al., 2011

Therefore, detection and identification of pharmaceutically active substances or banned substances that are not permitted to be used in food supplements is a serious issue which need sensitive and selective analytical methods.

To protect the health of consumers it is necessarily not only the control and surveillance of the food supplement markets, but also to increase the awareness of all stakeholders and the level of education and information of the consumers.

9.4.2. Substitution

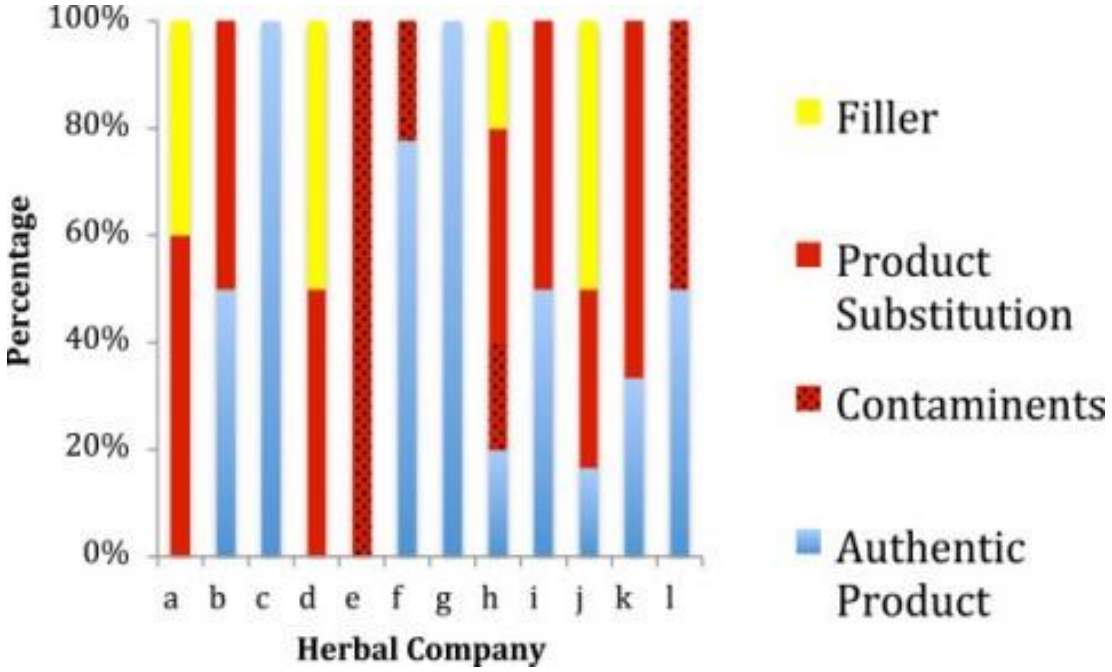
Currently best practices in place for identifying the various ingredients are used in herbal products. This is because the diagnostic morphological features of the plants on which the current Linnaean taxonomic system is based cannot typically be assessed from powdered or otherwise processed biomaterials. As a result, the marketplace is prone to contamination and possible product substitution, which dilute the effectiveness of otherwise useful remedies, lowering the perceived value of all related products because of a lack of consumer confidence in them.

Newmaster et al. (2013) purchased herbal products for sale in Toronto, Canada and via mail order from the United States. Twelve manufacturers were involved, representing 44 products (41 capsules, 2 powders, 1 tablet). In total there were 30 herbal species, and these were studied against a barcoded "library" of over 100 species. Their definitions were as follows:

- **Authentic***:* a product contained the DNA barcode for a species that was the main ingredient on the label
- **Contaminated***:* contains labelled ingredient and also the DNA barcode for a species that was ***not*** on the label
- **Substitution***:* a product contained the DNA barcode for a species that was not on the label, but in the mean time, there was ***no trace*** of the labelled ingredient.

The findings were dismal and quite discouraging for consumers and health professionals alike. Only 48% of products were authentic. Of the 12 companies sampled, only two had authentic products without any substitution, contaminants, and fillers (graphic 3). Unlabelled fillers including wheat, soy, and rice, were found in 20% of products. Three companies had products for which no product could be authenticated.

Graphic 3. Results of authenticity analysis of 44 herbal products (samples provided by 12 companies (Newmaster et al., 2013)



Some of the products were of such poor quality that harms could be expected. One sample was labelled as containing St. John's worth (used to treat depression) but actually only contained senna, a laxative. Another product was contaminated with black walnut, which has a nasty side effect profile. And there's also the undisclosed wheat in some products, which would be harmful to those with Celiac disease or a wheat allergy. Other studies have raised similar concerns: a study of 131 herbal teas revealed only 58% of products could be authenticated, and 33% were contaminated; half of the ginseng products examined in one study contained other forms of ginseng than the labelled *Panax ginseng*, etc.

9.4.3. Mislabelling

Also the frequency of product mislabelling in herbal products became a safety problem and has been estimated at 14-33% (Baker et al., 2012).Whilst the online market for dietary supplements is flourishing, different institutes for risk assessment and consumer protection agencies have been increasing their efforts to warn customers about its particular challenges. With thousands of products available to buy online, not only from domestic, but also non-EU suppliers, customers are considered to be at increased risk from non-licensed ingredients, misleading advertising and missing health warnings.

Increasing public education about possible risks poses a minor threat to the development of the online market for health products, but at the same time represents a chance for trusted and established brands to shine.

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