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SIDE EFFECTS AND TOXICITY OF SOME VEGETAL PRODUCTS INCLUDED IN NUTRITIONAL SUPPLEMENTS

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The inconsistency between the legal bases for "Food and Nutritional Supplements" attributed by the FDA (which states "are food, not medicines") and the EU - Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002, completed in 2004 ("are vitamins and minerals or their mixture") and the one in force in Romania (Order no. 1069/2007 of the Minister of Health published in the Official Gazette of Romania, Part I, no. 455/05.07.2007 ("products of plant and animal origin and/or their mixture with vitamins, minerals and other nutrients"), has led to their confusion with the "api-, phyto- and aromatherapeutic products" or with the gemoderivates products. *Objectives*. Thus, it is necessary to delimit these product categories, among which frequent adverse reactions are met and sometimes even toxic products, by the products of apitherapeutic, phytotherapeutic and aromatherapeutic use. *Material and method*. We consulted several catalogs of nutritional supplements that are admitted to the Romanian market, we analyzed their prospectuses, we correlated the pharmacological action with the chemical composition and we evaluated the consequences.Results**.** For most of the products in our commercials broadcasted at radio or TV and in many printed publications, we noticed the presence of some active principles inducing adverse reactions, including: • hypokalaemia, at long-term administration of anthracenozide products (*Frangulae cortex, Rhei rhizoma, Aloe*), products recommended in slimming cures without noticing about the consequences;• hepatotoxicity - pyrolizidine alkaloids present in some species of families Asteraceae (in *Farfarae folium, Symphyti radix, Senecio herba*) and Boraginaceae (*Boraginis flores*), sporadic in *Fabaceae, Poaceae et al.* a.; glucosinolates (glucocohearoside, gluconaposide, glubobrasicin, gluconasturtioside, progoitrin) - from *Brassica oleracea L.* var. capitata *L.*, *ssp.* capitata (*L.*) Duchene, frequently used in slimming cures (inhibits growth and induces hepatic hypertrophy, hepatocyte fibrosis, biliary hyperplasia and hypothyroidism through the nitriles resulting from hydrolysis); volatile oils containing thymol and carvacrol (Thymi herba et al etheroleum, Origani herba et al etheroleum);• thyroid hypofunction by inhibiting the iodine uptake by the hydrolysis products of glucosinolates from Brassicaceae (*Brassica oleracea* L. variety capitata L., ssp. capitata (L.) *Duchene* = cabbage, *Brassica nigra* = mustard, *Capsella bursa pastoris* = shepherd grass, *Cochlearia officinalis* L. and *C. armoracia* L. = hrean, *Capsella buesa -pastoris Moench* = Shepherd's Shepherd);• dermal irritation at cataplasms obtained from Brassica sp., Cochlearia armoracia, Raphanus sativus, in colds and rheumatic pain due to glucosinolates; volatile oils with limonene, α- and β-pinen (*Pini aetheroleum*), neral, geranial (*Cymbopogon citratus, C. flexuosus citraliferum*), methyl salicylate (*Gaultheria procumbens*);• mutagenicity and carcinogenicity (liver tumors) induced by N-oxides of pyrolizidine alkaloids (phenomena observed in animals that have consumed contaminated feed with different species belonging to the Asteraceae, Boraginaceae, Fabaceae families**.** *Conclusions*. Vegetal products which, by their active principles or by their hydrolysis products, have different therapeutic actions can not be admitted as nutritional supplements. These products should be included in api-, phyto- and aromatherapeutic products.

Keywords: phytotherapy, toxicity, aromatherapy, apitherapy, Nutritional Supplement, vitamins, minerals.

INTRODUCTION

The influence of environmental pollution and of the modern life daily stress on people's health have led to the need of counteracting their consequences. As a result, chronic consumers of medical remedies appeared, on the one hand, and on the other – producers and distributors of "food supplements". The quality of products is often Because their quality control is not as rigorous as the one included in the drug registration regime, the quality of the products often leaves much to be desired.

That's how we came to a "paradox": we feed ourselves with drugs (prescribed or not by a specialist, usually invariably at chronic patients, no matter how effective) and we treat our sufferings with food supplements (nutritional supplements) or with gemoderivates.

The import, then the production and the marketing of food supplements in the EU (mostly of vegetal origin) from where they were exported to most EU member countries, including Romania, required the elaboration of internal normative acts, with the participation of the specialists involved mainly into the fields of legislation and production, less specialists in phytochemistry and phytotherapy, who lost sight of the fact plants, as well as humans, have hidden vices.

That's why it is good to know them in their privacy and be objective when classifying them as food, medicinal, ornamental or toxic plants. Let us not forget that beneath the pleasant beauty of a plant or under the seductive scent of her flowers can hide a friend, a malefactor or an enemy.

Let us remember that the provision is the mother of wisdom!

The **objectives** of this paper are to argue for the *necessity to differentiate* food supplements (nutritive supplements) frequently used in diet, api-, phyto- and aromatherapeutic products used in *integrative medicine*[9], with which they are often confused and the quality of which must be expressed in the content of active principles.

The **purpose** of this plea is to raise awareness of the amendment of the food supplements law by removing from this category products containing active principles of vegetal nature, rarely animal, and used for curative or preventive purposes in various diseases, respectively in *the legal recognition of api- , phyto- and aromatherapeutics products*, as well as gemoderivates; expressing their quality in the content of active principles.

The **criteria for choosing this subject** were:

- the multitude of *side effects* and the acute or chronic *toxicity* (DL_{50}) of active principles found in many products commonly used as dietary supplements in order to treat various conditions, often in long-term cures – a contributory factor for the side effects and toxicity onset;
- the lack of discernment in the selection of products included in some formulas of dietary supplements, confusing them with teas;
- unfair commercials broadcast through radio and television stations.
- the lack of qualitative and quantitative aspects of the active principles of these products, as qualitz markers.

All of these, alone or together, can have dangerous effects on the health and life of patients.

MATERIAL AND METHOD

Because in the latest years "nutritional supplements" have invaded the Romanian market by fraudulently replacing medicines, by the profession profile that I have practiced for more than 50 years (pharmacacognost), I thought it was my duty to bring arguments for amending the legislation *in force* in this domain. I put particular emphasis on side effects and on the acute or chronic toxicity of some plant products present in various dietary supplements formulas and, of course, on their therapeutic action.

For this purpose I have appealed to the legislation in force in Romania, which I carefully analyzed in order to identify the place where errors could have been encountered. Unfortunately, I found a "*serious confusion between dietary supplements and apitherapeutic, phytotherapeutic and aromatherapeutic products*". That is why I insist on the *necessity of amending their legislation*. I have often wondered where this confusion comes from and if it also has a financial substrate ?! That is why I considered it necessary to go through the legislation of these products, from its appearance until now.

1. Definition. Nutrient supplements are defined as *oral administration products by healthy people* who require a higher exogenous intake due to *specific nutritional requirements* related to physiological status (pregnancy, lactation), age (children, adolescents, adults, old people), intense physical activity (performance athletes, requiring physical exercise).

2. Their role consists in the intake of nutrients (vitamins, mineral salts, carbohydrates, proteins, lipids).

3. Differences. While *dietary supplements* come with *nutrients intake*, *the apitherapeutic, phytotherapeutic and aromatherapeutic products* bring *active principles*: plants - polyholoside, phenol-carboxylic acids, proanthocyans, tannins, heterosides (flavonosides, anthocyanosides, anthracenozides, saponins), bitter principles, volatile oils, alkaloids with different chemical structures etc; royal jelly - essential amino acids, proteins, vitamin C, complex B, enzymes and hormones. But bee venom contains

peptides (of which 40–60% melitin), enzymes (hyaluronidase, phospholipase A2), biologically active amines (histamine, dopamine, norepinephrine etc). Is it a dietary supplement?

Unlike nutrients, active principles have *pharmacodynamic action* (dependent on active ingredient content), some of which also have **severe side effects** (*the bee venom has a strong allergen impact and can produce anaphylactic shock*), or **toxicity**, *depending on the dose, on the individual sensitivity and on the duration of treatment*.

4. Legislation. The Romania's entry into the European Union (January 2007) was a decisive step for the *compliance with EU normative acts* in the domain of processing food and nutritive supplements. They make the field of excellence of *food science* (*not to be confused with the medicines*).

The first legislative act (referring to the traditional herbal medicinal products) – "Directive 2002/46 EC of the European Parliament and of the Council" of 10 June 2002[1] – was transferred to the European and pan-European area. This led to controversial discussions in the US between the Food Drugs Administration (FDA) and manufacturers. However, this Directive was transposed almost entirely in Romania, where it was gradually regulated by laws and orders:

• Law no. 491/2003 and Law no. 412/2004 of the Ministry of Public Health (MSP)[2];

• Orders no. 1214/2003 and no. 622/2004 of Public Health Ministry[3];

• Common Order 244/401/2005 of the Ministry of Agriculture, Forestry and Rural Development (MAPDR) and Ministry of Public Health (MS) about the processing and the marketing of medicinal and aromatic plants, partially processed or processed in the form of pre-added food supplements, published in the Official Gazette of Romania, Part I, no. 474 / 03.06.2005)[4];

• Common Order no. 1228/2005, 244/63/2006 of the MAFRD, MSP and the National Sanitary Veterinary and Food Safety Authority (ANSVSA) referring to the approval of the Technical Norms and the Marketing of Predicted Food or Animal Food Supplements and / or their mixtures with vitamins, minerals and other **nutrients**, published in Official Gazette of Romania, Part I, no. 253 / 21.03.2006[5], **subsequently abrogated**.

Specific legislation on dietary supplements, **in force** in Romania, includes Ministry Of Public Health Order no. 1069/2007, published in Official Gazette of Romania, part I, no. 455 / 05.07.2007[6] referring to the approval of the *Norms concerning the vitamin and mineral food supplements or their mixture* and *transposes EC Directive 46/2002*.

In contrast, in the "*Dietary Supplement Helth and Education Act of 1994" it is explicitly stated that dietary supplements are food and not medication*.

So, we are wondering how this **compromise** has been reached in our legislation?

5. Notifications of supplements are made at different institutions, depending on the content of supplements:

• Ministry of Health (MS) – vitamins and minerals;

• National Institute of Public Health (INSP) through Public Health Centers in Cluj, Iaşi, Timişoara (belonging to MS);

• Institute of Food Bioresources (IBA) of the Ministry of Agriculture and Rural Development (MADR) - vitamins and / or minerals + nutritional substances;

• The National Agency for Medicines and Medical Devices – medical devices and medicines, but on the basis of quality standards, from which the content in active principles, the results of some pharmacological experiments on animals – to establish the pharmacological profile, the effective dose and the acute toxicity (DL50), as well as any side effects.

We include in **side effects** the dermal allergies, the mucosal and skin irritation, the photosensitivity, the electrolyte imbalances and in the group of **toxic substances** those substances with neurotoxic, hepatotoxic, hematotoxic, mutagenic or carcinogenic potential.

RESULTS AND DISCUSSION

1. The brief analysis of these laws and **orders** allows us to observe that most food supplements, pre-dosed or not, *are in fact therapeutically products predominantly derived from medicinal or aromatic herbs without specifying the active principles and their quantity*.

Thus, *they have no place in the dietary supplements*.

2. Another aspect of this subject is the so-called medical device, of which we have selected products "A" and "B" – capsules.

Product "A" contains an extract obtained from plant X, characterized by acid Y (without specifying the core and the radicals), magnesium oxide and polyholoside from aloe (without specifying the pharmacological active constituents).

Product "B" contains unsaturated fatty acids obtained from coconut oil, coconut oil, olives, palm and other unsaturated vegetable oils, sodium ascorbate. It is recommended for combating discomfort of the spine and other joints (probably anti-inflammatory).

According to the Romanian Language Explanatory Dictionary, the "*device*" is defined as the "assembly of interconnected parts, usually a building, which performs a well-defined function in a technical system, but also a layout of combat troops on the ground, or a final part of a judgments which show the solution to the dispute"[7].

Here we have a great dilemma: is the *gelatin capsule* an integral part of any invisible *technical system*, any *layout of combat troops on the ground*, or the *conclusion of any court decision* ?!

That's why I wonder: how could these errors go unnoticed by those who registered the products? If they had been registered with the National Medicines Agency, an institution that controls and warrants the quality of the products to be placed on the market, I hope these confusions would have been eliminated, and patients would be protected from forgery and unnecessary expenses.

I am afraid that this practice is in fact a gateway for unfair business and a mean of manipulating the personnel who prescribes, releases or consumes such products, their quality being often desirable because they escape from the quality control imposed to pharmaceuticals.

3. Most of the commercials broadcasted at radio and TV, which are recommended for use in the long-term cures, contain active principles, some of them inducing side effects or toxic phenomena. For example, some TV commercials are about formulas consisting of anthracenosides (active purgative active) products intended for the maintenance of silhouette. Their administration for a long time attracts body dehydration, the decrease of potassium ions (K +) and the establishment of hypokalaemia, manifested by heart rhythm disorders (arrhythmias = adverse reactions). The examples are numerous.

4. Some publicity does not match reality. For example product "C" contains an important amount of bioactive collagen. False are both statements: I assure you that a portion of the patch contains more collagen than product "C" and collagen (complex protein) gets into the stomach, is split into constitutive amino acids; some of them are absorbed at the duodenal level and then metabolized. Only partially can come back collagen - a component of tendons, dermis, blood vessels, as biosynesthetic precursors. Perhaps more effective would be a flavon-based product, as they are inhibitors of collagenase, an enzyme involved in collagen degradation.

5. The practice of using the term "dietary supplements" is based on the avoidance from the active substances and adverse drugs content requirements and from the payment of the registration fee as a medicine at the National Medicines Agency (NMA), fee which is above the financial possibilities of some producers. They are supposed to carry out numerous research to **specify** the concentration *in active principles* (not in the amount of vegetal product or extract, if it is not standardized), the therapeutic action, the adverse reactions, the counter indications, the measures of combating adverse reactions) etc.

In order to support the producers, we propose that the *registration fee for such products be lower than the registration fee for synthetic medicines* obtained with much lower production costs than the extracts from vegetal products. Maybe that's how we get into *normal legislation*.

6. Unnatural associations of vegetal products whose pharmacological properties are annihilated: Passiflorae herba – sedative through C-flavonoids (vitexin, isovitexin, orientin, isooregin, saponarin) = benzodiazepine receptor ligands with Hyperic herba – hyperdepressant antidepressant = mono-amino-oxidase type A (A type IMAO) in a product for the treatment of insomnia (8). The actions of the associated products are annihilated.

7. The frequency of **side effects** and **toxicity** (acute or chronic) to many plant products used as food supplements are other factors to which we must give due weight. This goal is not required for food supplements. So the practice of transposing foodstuffs in the field of phyto- and aromatherapy is a form of avoiding the quality standards of medicinal products.

Allergic reactions (side effects) include: dermal allergies, mucous and skin irritation, photosensitivity, electrolyte imbalances, and toxic, neurotoxic, hepatotoxic, haematotoxic, mutagenic, and carcinogenic potential[14].

Dermal allergies are the most common adverse reactions. They were noticed at some plant products, including volatile oils containing hydrocarbons (especially polyines), phenolic compounds, quinones, sesquiterpenic lactones, have been observed. All act as *haptens* and are listed below.

• Monoterpenes (α- and β-pinen, camphan, limonene) present in many volatile oils (derived from Abies, Pinus, Citrus, etc.) are dermal irritants.

• Phenolic (aromatic) compounds: urusiols - from the juice of trees of the Toxicodendron sin genus. Rhus (sumach); anacardic acid and alkyl phenols (cardol, cardanol) of cashew nut (*Anacardium occidental*) can induce dermis; cinnamic aldehyde - Cinnamomi cortex et aetheroleum; benzoate / cinnamate in quinone form, Benzo resin, balsamum Tolutanum, balsamum Peruvianum, can trigger allergic reactions.

• Simple *benzochinones* (1,4-diketone derivatives of benzene substituted by alkylic or arylic, sometimes oxygenated radicals), of which we mention: primina (2-methoxy-6-pentyl-1,4-benzoquinone) of *Primula* species grown as ornamental plants; Dalbergion, Dalbergion, Methoxy-dalbergion from *Dalgerbia* species (*D. latifolia Roxb*., *D. melanoxilon* Gill. et Perr., *D. nigra* Allem., *D. retusa* Hemsl.) used in traditional Asian medicine (MTC) and in England for the content of 1-dioxo-phenylalanine (DOPA) as tonics, bronchodilators (asthma), febrifuge and antidysenterics[10].

• *Naftoquinone* - lapachol (2-dimethyl-allyl, 3-hydroxy-, 1,4- naphthoquinone) and 2-deoxypalacol (2-dimethylallyl- 1,4-naphthoquinone) of the wood of African tropical species of Tectona grandis = tec (Verbenaceae), *Tabebuia sp.* and *Tecoma (Bignoniaceae)*, *Diospyros* (*Ebenaceae*); their wood is used in the manufacture of furniture or musical instruments; contact with wood or sawdust has a risk of conjunctivitis, rhinitis, erythema and dermatitis (on the eyelids, face, neck, hands, forearms).

Mechanism of action: phenolic compounds oxidation to electrophilic quinones, capable of reacting with nucleophilic groups of proteins, becoming immunogenic.

• Naftodiantrone - hypericin, pseudohipericin from *Hypericum perforatum* (St. John's wort) are photosensitizers.

• Sesquiterpenic lactones (achiline, alantolactone, isoalantolactone, cinaropicrin, costunolida, cryptocaria-lactone, matricin, matricarin, nobilin, partnerolida etc.) are constituents of vegetal products with or without volatile oils (*Achilea millefolium, Apium graveolens, Arnica montana, Inula helenium, Cynara scolymus, Matricaria chamomilla, Levisticum officinalis, Tanacetum partnerium, Laurus nobilis, and the like*). They have mucolytic and expectorant, antifungal, anthelmintic, antibacterial properties. In long-term treatment it favors allergy because it acts as a hapten: it binds to proteins, forming a complete antigen capable of inducing leukocyte sensitization.

• *Poliins* (acetylenic derivatives with two or more triple bonds - falcarinol, falcarindiol, oenantotoxin) encountered in the families Apiaceae, Araliaceae, Asteraceae, Campanulaceae, rarely in Fabaceae and Solanaceae; in leaves of Sheflera species and Hedera helix), at repeated skin contact they produce erythematous and vesicular reactions of the face, hands and arms, 24 hours after the contact with the plant, contact areas becoming edematous and painful[8].

Photosensitizers are coumarins (simple or dimers), glycosidated or not, sometimes welded to other heterocycles (furanocoumarins)[8, 11, 12].

Neurotoxicity is induced by products containing:

• ketones (carvone, cryptone, mentone, piperitone, pinocamphora, thujone present in *Carvi fructus*, *Pini aetheroleum*, *Menthae folium et etheroleum*, *Menthae piperitae folium et aetheroleum*, etc.); these are mucolytic, but in high dose they become neurotoxic[11, 12];

• lactones (alantolactone, isoalantolactone, cryptocarialactone) are mucolytic, antifungal, anthelmintic, antibacterial at low doses and short-term treatment.

Hematotoxicity occurs as a result of hemolysis of erythrocytes under the influence of steroidal saponosides (Trigonella foenum graecum commonly used as hypocolesterolemia and antidiabetes, the pharmacologically active fraction is represented by steroidic saponosides.

Some triterpenic saponoside products are restrictively used in phytotherapy as dietary supplements (*Herniariae h*erba from H. *glabra* L. and *H. hirsuta* L.); (*Medicaginis herba*), since saponosides (heterosides of soiasapogenol) can induce hemolysis of erythrocytes by emulsifying membrane lipids, respectively by lowering the superficial surface tension of erythrocyte membranes.

Hederae folium is traditionally used to relieve cough as an expectorant, prevents acetylcholine spasm in lab mice, action determined by saponosides; *Herbaria herba*, *Liquiritiae radix*, *Saponariae radix* (used as diuretics, depuratives, expectorants), *Gypsophillae radix* (used in cosmetology as a degreasing), *Quillaja saponaria* bark Molina = Panama wood (hypocholesterolemia)[8].

• Cianhydrides (amygdaloside from *Amygdali semen, Lini semen*, prunazosida - *Amygdali semen, Laurocerasi folium, Sambuci flores*, Sambunigrozide - *Sambuci flores*, Vicianozide - *Vicia faba*), by hydrolysis, release hydrogen cyanide that combines with hemoglobin; the resulting cyanhemoglobin is irreversible.

Hepatotoxicity – was observed at vegetal products containing:

• pyrolizidine alkaloids present in some products obtained from Asteraceae species (*Farfarae folium, Senecio herba*) and Boraginaceae species (*Boraginis flores*, *Symphyti radix*), sporadically in Fabaceae, Poaceae etc;

• glucosinolates (glucocorticoids, gluconasuride, progoitrine) - from *Brassica* species commonly used in slimming belts (glucosinolates inhibit growth and induce hepatic hypertrophy, hepatocyte fibrosis, biliary hyperplasia through nitriles resulting from hydrolysis);

• volatile oils containing thymol and carvacrol (*Thymi herba et aetheroleum*, *Origani herba et aetheroleum*) (8).

Nephrotoxicity at monoterpenic hydrocarbons (α- and β-pinen - *Pini aetheroleum, Abies aetheroleum, Terebinthinae aetheroleum, Lignum Santali*) used as antiseptics.

Mutagenicity and **carcinogenicity** (hepatic tumors) induced by N-oxides of pyrolizidinic alkaloids (phenomena observed at animals which consumed feedingstuffs contaminated with various species belonging to Asteraceae, Boraginaceae and Fabaceae families;

• □-s-asarone present in Asarum europaeum has gastrointestinal toxicity;

• myristica - present in *Petroselinum crispum* (leaves) = creamy parsley and *Myristica fragrans* = nutmeg, walnut and pericarp, induces hallucinations and convulsions; by transamination leads to the formation of amphetamine derivatives;

• safrole, dihydrosafrol - hepatic carcinomas in rats, non-reproducible in humans.

Hypokalemia at long-term administration of products with anthracenozide (*Frangulae cortex, Rhei rhizoma, Aloe*) recommended in slimming cures and delayed intestinal transit (constipation) without notice about the consequences.

Irritations of mucous membranes and dermis at cataplasms obtained from Cruciferae (*Brassica spp., Cochlearia armoracia, Raphanus sativus, Sinapis nigrae semen*), administrated in colds and rheumatic pains, produced by glucosinolates, which, by hydrolysis, releases senevoli - pharmacologically active substances (dermocotics);

• volatile hydrocarbon oils - limonene, α- and β-pinene (Pini aetheroleum), p-cimen (*Thymi herba et aetheroleum*); aldehyde neral, geranial (volatile oils from *Cymbopogon citratus*, *C. flexuosus cv. citraliferum*); esters - methyl salicylate (*Gaultheriae procumbensis aetheroleum*), lactones (*Inulae radix et al etheroleum, Petasitidis radix, Levistici folium et radix*);

• furanocumarines (*Ammi visnagae fructus et al etheroleum*) are photosensitizers.

Reduction of intestinal transit (constipation) when administering tannin-based vegetal products.

Electrolyte imbalances – induced by all products with laxative action (anthracenozide) and diuretics at long term administration).

Allergic and hypersensitizing (contact dermatitis) are cinnamaldehyde (*Cinnamomi cortex et aetheroleum*), anicardic acid (*Gingko biloba*), sesquiterpenic lactones - alantolactone, isoalantolactones, helenanine - Arnica montana, poliines - *Echinacea purpuraea*)

Fotosensitization induces furanocoumarins (C*itri aurantii aetheroleum* ssp. *Bergamia, Ammi visnagae aetheroleum*, hypericina - *Hyperici herba*[8, 11].

Vesicant properties resulting from hydrolysis of glucosinolates (*Sinapis nigrae semen*)[8, 11].

It must also have in mind that some active principles have an effect on central nervous system, namely benzodiazepine receptor ligands (C-flavones from *Crataegi folium et flores*) and therefore have a sedative effect[8].

Examples can continue.

Another aspect of the product categories used in the treatment of patients is the confusion of medical devices with **medical devices**.

CONCLUSIONS

As a result of the arguments mentioned above, I request the Ministry of Health:

1. Modification of Order no. 1069/2007 of the Minister of Health, published in the Official Gazette of Romania, Part I, no. 455 / 05.07.2007 and of the Common Order no. 1228/2005, 244/63/2006 of the Ministry of Agriculture, Forests and Rural Development, of the Ministry of Health and of the National Sanitary Veterinary and Food Safety Authority, regarding the approval of the Technical Norms and the Marketing of prediluted food supplements of animal or vegetal origin and/or of their mixtures with vitamins, minerals and other nutrients, published in the Official Gazette of Romania, Part I, no. 253 / 21.03.2006

2. Inclusion of a special category called Apitherapeutic, Phytotherapeutic and Aromatherapeutic Use Products for products used to treat certain diseases (diseases);

3. Expression of their quality by content in active principles or by their hydrolysis products (excluding expression in powder or extract).

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