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A DESCRIPTIVE STUDY OF COMMERCIAL HERBAL DIETARY SUPPLEMENTS USED FOR DYSLIPIDAEMIA AND BODY WEIGHT LOSS

Doctoral thesis in Pharmacology and Toxicology – XXXIV Cycle

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“Un pezzetto di vita da sola, con il mio nome, con il mio lavoro, senza eredità, sconti o regali
Lavorando sodo, con la massima onestà per conquistare dei muri sui quali appendere pergamene che forse non toglierò mai
Per affacciarmi alla finestra e vedere una distesa di fierezza”

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Summary

Dyslipidaemia and overweight/obesity are two common risk factors of the metabolic syndrome leading to cardiovascular and other chronic diseases. The management of cardiometabolic risk factors with herbal supplementation has become frequent as a prevention. Likewise, hypercholesteraemic and obese individuals who face serious adverse effects and/or intolerance from pharmacological therapies could take advantage using herbal dietary supplements (HDS) though they don't claim therapeutic effects. Prescriptions and counselling of healthcare professionals, therefore, and self-medication are the sources that lead to their use.

According to 5th industry survey of the National Association of Producers and Distributors of Health Products in Italy, in late 2019, the food supplement market reached a value of 3.6 billion euros putting Italy at the top of the European market [1]. However, food supplements include heterogeneous clusters such as: vitamins and minerals; prebiotics and probiotics; other substances with a nutritional or physiologic effect; botanicals. All them are regulated by the Italian Decree 2004/169 which implements the European Directive 2002/46 relating to food supplements.

Botanicals including plants, algae, fungi and lichens, can be marketed as either herbal medicinal products or herbal dietary supplements, cosmetics, etc. Herbal medicinal products which follow the regulations of the European Medicines Agency, include phytotherapics (Dir. 2001/83/CE), herbal medicines of traditional use and herbal medicines of well-established use (Dir. 2004/24/CE). Whereas, herbal dietary supplements do not own therapeutic activity but only health benefits substantiated by a claim. In Italy, they are marketed next to notification addressed to the Ministry of Health. Although it is always mandatory to conduct a quality control on the raw materials, no proof of safety is required.

In the recent years considerable spontaneous reports of suspected adverse reactions collected by the Italian Phytovigilance System, concerned herbal preparations used in dyslipidaemia and body weight loss [2, 3]. Accordingly, the Italian Ministry of Health has paid attention to herbal dietary supplements containing red yeast rice, curcuma, garcinia, etc. A maximum daily intake and/or special warnings have been established for the respective labels.
The purpose of this research was to provide an overview of the number and characteristics of HDS used in dyslipidaemia and body weight loss through a preliminary study of pharmacies sales data. As it is more likely for an obese subject to have hyperlipidaemia than vice versa, HDS with both claims were included in the group of body weight loss.

Reports of suspected adverse reactions potentially related to the use of dyslipidaemia-HDS collected in the interim by Phytovigilance are described. A survey was addressed to the pharmacies of the Lazio region in order to understand pharmacists' awareness about Phytovigilance. The monitoring of pharmacies sales data of HDS, compared to the reports of suspected ARs, serves to contextualize their intrinsic safety and to eventually highlight the real risk profile of these products. This study may help to disseminate the importance of the Italian Phytovigilance System and to increase the knowledge about the safety of use of herbal dietary supplements.

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Chapter 1

A descriptive study of commercial herbal dietary supplements used for dyslipidaemia – Sales data and suspected adverse reactions

1.1 Abstract

Herbal dietary supplements (HDS) used for dyslipidaemia represent a category of concern in Italy for suspected adverse reactions (ARs). However, we cannot estimate the safety, as we don’t know their commercial profile. Sales data of dietary supplements, and in particular those used for dyslipidemia, were monitored for two years in two pharmacies of Rome. Meanwhile, spontaneous reports of suspected ARs potentially related to dyslipidemia supplements were collected by the Italian Phytovigilance System.

The 50% of dietary supplements are herbal-derived; the 9% of HDS are recommended for dyslipidemia. From our data, 113 different brands have claims for improving lipids profile and 91% of them are multi-ingredient preparations. Fifteen spontaneous reports of suspected ARs concerned HDS used for dyslipidemia. The most frequent ARs were joint, abdominal and muscles pain; vomiting; erythema and haematological disorders; asthenia; nausea; rhabdomyolysis.

Our findings point out the limited compliance of commercial dyslipidaemia-HDS and scientific research about their intrinsic safety. A wide range of formulations and the coexistence of many heterogeneous ingredients could not support the risk/benefit profile of the supplement. The variable compositions of HDS do not assure the safety, as they don’t support the reproducibility of their pharmacological activities. This study could contribute to optimise consumers guidance about what they purchase and consume.

1.2 Introduction

In Italy, the use of food supplements containing botanicals is currently regulated by the Ministerial Decree of 10 August 2018 [1]. According to it, herbal dietary supplements (HDS) cannot claim a therapeutic activity, but only nutritional or physiological effects. They can be placed on the market after a simple notification procedure addressed to the Italian Ministry of Health (MoH). Though it is always mandatory to conduct a quality control on the raw materials, no clinical safety trials are required. In light of the current safety issues supported by scientific evidence, the MoH has paid particular attention to herbal supplements containing, for example, curcumin and monacolin K [2,3]. Annex 1 of the Decree-10 August 2018, containing the list of permitted plants and their parts, accompanied where appropriate by additional provisions for use, has already been amended by a directorial decree dated July 26, 2019. The Decree has introduced special warnings concerning *Curcuma* genus [4]. A maximum daily intake of 10 mg has been previously established for monacolin K, but recently a restriction has been proposed and an upcoming regulation of the European Commission (EC) is expected after the conclusions of the European Food Safety Authority (EFSA) about the use of monacolins from red yeast rice (RYR) in food supplements [5]. Indeed, according to EFSA's scientific opinion, there is a significant safety concern of monacolins from RYR, when used as food supplements at the level of 10 mg/day. Moreover, individual cases have reported severe adverse reactions (ARs) even at the 3 mg/day intake [6].

In the European Union (EU), so far there is not a harmonised legislation for botanicals included in food supplements. The safety of HDS is a matter of discussion due to the lack of randomized clinical trials and post-marketing observational evidence [7].

Cardiovascular diseases (CVD) represent a growing global public health issue. As dyslipidemia is one of the risk factors that can lead to CVD, its management is one of the basic approaches to prevent CVD [8]. Thus, clinical benefits are generally determined by lowering low-density lipoprotein cholesterol (LDL-C), total cholesterol, triglycerides (TGs) and increasing high-density lipoprotein cholesterol (HDL-C) plasma levels. According to the Guidelines of the European Society of Cardiology and the European Atherosclerosis Association (2019), healthy lifestyle habits regarding diet, smoking, alcohol, physical activity, etc. contribute to improve the overall lipid profile and should be promoted. Up to date, conversely of the clinical evidence of the pharmacological treatment, data on tolerability/safety of the dietary supplements/functional foods and their possible usefulness are scanty [8].

In Italy, since 2002, the National Institute of Health (NIH), in cooperation with the MoH and the Italian Medicines Agency (AIFA), coordinates the Italian surveillance system (Phytovigilance) that collects spontaneous reports of suspected ARs derived from herbal products and food supplements. The aim of Phytovigilance is to identify, to assess and eventually to prevent adverse effects deriving from dietary supplements, herbal products, galenic preparations, and other botanical-derived products [2].

In the EU as well as Norway, Liechtenstein, Switzerland and Iceland, a centralized post-marketing vigilance approach is not yet implemented for HDS, which often boast pharmacological effects. Meanwhile, EudraVigilance, a large pharmacovigilance database that tracks suspected ARs to au-

thorized medicines including herbal medicinal products, operates on behalf of the EU. However, Eudravigilance allows only the collection of data in aggregated manner. The Rapid Alert System for Food and Feed (RASFF) database detects risks in the food chain on behalf of the EC. Although it provides updated information on food public health warnings, its usefulness for food supplements is limited, as often does not report adverse reactions due to dietary supplements [9].

Facing an overall increase of HDS use, we cannot estimate their safety until we do not know their commercial profile. Hence, the aim of this study is to monitor in territorial pharmacies, sales data of HDS used for dyslipidemia as they represent a category involved in a great number of suspected ARs, at least in Italy [2, 10]. Monitoring sales data of dyslipidemia-HDS would help to highlight the real risk/benefit profile of these products.

1.3 Materials and Methods

1.3.1 *Definition of dietary supplements, HDS and dyslipidemia-HDS*

In our study we consider as dietary supplements, all food supplements containing vitamins, minerals, amino acids, essential fatty acids, fibers, various plants and herbal extracts according to the European Regulation (EC) No 1925/2006 on the addition of vitamins, minerals and of certain other substances to foods [11]. HDS include food supplements having at least one botanical ingredient. Dyslipidaemia-HDS refers to HDS having claims for lowering lipid values, according to the manufacturer labelling.

1.3.2 *Data collection*

Dietary supplement-related sales, from databases of two pharmacies located in Rome (Italy), were monitored for two years. The location of pharmacy 1 is the historic center of Rome, while pharmacy 2 is located in a residential area. Data were collected from October 2018 up to September 2020.

A portable document format (PDF) listing food supplements sold monthly was provided through WINGESFAR software from each pharmacy. In particular, the quantity and the brand names have been recorded. Only data of HDS, having health claims related to dyslipidemia were included in the study.

Meanwhile, through the Italian Phytovigilance System, we collected and analyzed all the spontaneous reports of suspected adverse reactions (ARs) potentially related to anti-dyslipidemia supplements according the “reason of use” indicated in each report. Everyone, such as healthcare professional, patient, manufacturer, who observes a suspected AR, may send the report filling in an “ad hoc” form available on the websites of the involved institutions (NIH, MoH, AIFA). Since December 2018, ARs can be reported online on the website www.vigierbe.it. The collection considered reports from October 2018 to September 2020 which were registered in a database at the NIH.

1.3.3 *Data preparation and descriptive analysis*

Through Microsoft excel, a specific database was created. Data were monthly updated with new results obtained from each pharmacy. In particular, sales of the total dietary supplements, HDS and

dyslipidemia-HDS were recorded and analyzed. Then, for each whole year, trends of sales of dietary supplements, HDS and dyslipidemia-HDS were assembled for both pharmacies and compared to each other. We consider as the first year the period ranging from October 2018 to September 2019 and as second year the period October 2019-September 2020.

Each of the dyslipidemia-HDS has been analyzed for: composition (as described on the label), claims and number of sales. The labels were obtained either from the manufacturer website or, if not available, other websites randomly selected using the product name as a keyword. A statistical descriptive procedure of the composition of each dyslipidemia-HDS was performed. The distribution of the absolute and percentage frequencies of the data was analyzed. In particular, prevalence of the number and type (botanical and non-botanical) of the components was considered. The occurrence of standardization, the plant material and type of extract were also estimated. All the plant species found in the dyslipidemia-HDS were clustered. The physiological functions of the plant materials were examined according to the guidelines of Italian MoH [12], which advise the use in the context of homeostasis model defined by the Council of Europe, as definitions of claims about botanicals are pending. The recurrence of other additional (non-botanical) ingredients like vitamins, coenzymes, amino acids, probiotics, etc., was also recorded. The biological effects claimed for each product were assessed also by interfacing them with scientific literature data.

In relation to Phytovigilance, a descriptive analysis was performed for all data regarding patient, supplement, clinical event, and reporter. The percentage of each HDS, reported for its suspected ARs was carried out. The ARs were coded according to the Medical Dictionary for Regulatory Activities (MedDRA). Referring to the composition stated by the manufacturer, the frequency of each plant species and/or botanical ingredients found in the suspected supplements, was also calculated.

1.4 Results

1.4.1 *Sales data*

During two years of monitoring (see also appendix), 42796 dietary supplements were sold by the two pharmacies selected, and 21484 (50%) of them were HDS. Of the HDS, 1993 (9%) were dyslipidemia-HDS. Referring to both pharmacies, the sales of each year indicate the same percentages of HDS (50%) and dyslipidemia-HDS (9%). In specific, during the first year, out of 22175 dietary supplements sold by both pharmacies, 11075 of them regarded HDS, whereas 1017 of the last ones were dyslipidemia-HDS. During the second year, sales data of both pharmacies indicate 20621 dietary supplements, 10409 HDS, of which 976 dyslipidemia-HDS. Monthly trend sales are described in Figure 1.1.

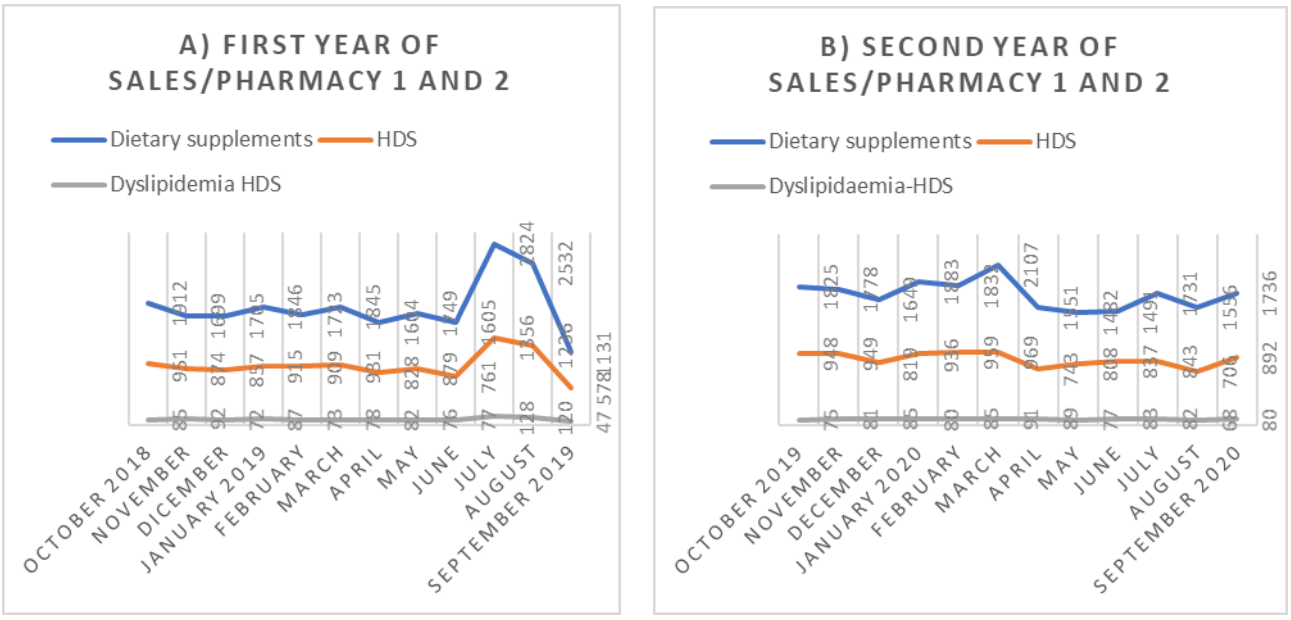

Figure 1.1. Sales from both pharmacies, during the first (A) and second (B) year.

1.4.2 *Description of dyslipidaemia-HDS*

Based on our data, 113 different brands have claims for improving lipids profile. Out of the different dyslipidaemia formulations, 9% (n=10) contain a single ingredient, while 91% (n=103) are multi-ingredient preparations. The number of the ingredients in the same supplement, including botanicals and additional non botanical ones, range from two up to 14. In table 1.1 are listed in alphabetic order all the different formulations of dyslipidaemia-HDS identified in the study. Alongside, the relative sales of each entry, referring to both pharmacies, and the number of the ingredients (botanicals and additional-non-botanicals) are registered. The phytochemical composition is reported without vehicles; daily doses are reported too, when indicated in the label.

Table 1.1. Dyslipidaemia-HDS sold during the study. The phytochemical composition obtained from sources different from the manufacturer website is reported in grey colour.

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
1	Active liver® 30 tablets, New Nordic	Milk thistle (*Silybum marianum* L.) extract (80% of silymarin, 250 mg); artichoke (*Cynara scolimus* L.) extract 13.5:1 (222 mg); curcuma (*Curcuma longa* L.) extract 10:1 (50 mg); choline 85 mg; black pepper (*Piper nigrum* L.) extract (40% of piperine, 10 mg)	5
2	Arkocapsule®Aglio 45 tablets, Arkopharma	Garlic (*Allium sativum* L.) bulb powder 900 mg	1
1	Aglio estratto oleoso® 50 capsules, Aboca	Garlic (*Allium sativum*) bulbs oil extract 1:10	1

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
5	Alares® 20 tablets, Biotema	Lipoic acid, Lyc-o-lutein (lutein 20%, alginates, gum arabic, pea starch, Rosmarinus extract), polygonum (*Polygonum cuspidatum* Siebold & Zucc.) rhizome dry extract (98% of resveratrol)	4
31	Alenil Q® 30 tablets, Revalfarma	Red yeast rice 200 mg (monacolin K 10 mg); betaine 150 mg; coenzyme Q10, 50 mg; vitamin E 12 mg; vitamin B6 1.4 mg, folic acid 200 mcg; vitamin B12 2.5 mcg	7
107	Armolipid® 20, 30 tablets, Rottapharm	Red yeast rice (1.5% of monacolin, 3 mg); microalgae (*Haematococcus pluvialis*) dry extract (2.5% of astaxanthin, 0.5 mg); *Saccharum officinarum* (1.4% of policosanols, 10 mg); coenzyme Q10, 2 mg; folic acid 200 mcg	5
220	Armolipid plus® 20, 30, 60 tablets, Rottapharm	*Berberis aristata* dry extract 588 mg (85% of berberine 500 mg); red yeast rice 200 mg (1.5% of monacolin, 3 mg); microalgae (*Haematococcus pluvialis*) 20 mg (2.5% of astaxanthin, 0.5 mg); *Saccharum officinarum* dry extract (90% of policosanols, 10 mg); folic acid 200 mcg; coenzyme Q10, 2 mg	6
1	Arteractiva® 36 tablets, Studio3farma	Capsicum powder; rosa canina dry extract 70%; *Polygonum cuspidatum* dry extract (98% of resveratrol); black pepper dry extract 95%	4
19	Aterostar® 30 tablets, Stardea	Red yeast rice (1.5% of monacolin K); linear aliphatic alcohols (60% of octacosanol); niacin; green tea (*Camellia sinensis* L. Kuntze leaves) dry extract (40% of total polyphenols); vitamin E acetate (50% of alpha-tocopherol acetate); pyridoxine hydrochloride; vitamin B12 (0.1% of cyanocobalamin); folic acid	8
12	Aterostar forte® 20 tablets, Stardea	Red yeast rice (3% of monacolin K, 10 mg); niacin; linear aliphatic alcohols (60% of octacosanol); green tea (*Camellia sinensis* (L.) Kuntze leaves) dry extract (40% of total polyphenols); vitamin E acetate (50% of alpha-tocopherol acetate), olive (*Olea europaea* L. leaves) dry extract (15% of oleuropein); coenzyme Q10; pyridoxine hydrochloride; vitamin B12 (0.1% of cyanocobalamin); folic acid	10
14	Azelip® 20 sachets, Progine Farmaceutici	Red yeast rice 333.33 mg (monacolin 10 mg); inositol 1.50 g	2
24	Berberol®[1] 30 tablets, PharmExtracta	*Berberis aristata* DC. root dry extract 588 mg (85% of berberine, 500 mg); *Silybum marianum* (L) Gaertn. fruits dry extract (silymarin 105 mg)	2
28	Berberol K®[1] 30 tablets, PharmExtracta	*Berberis aristata* dry extract (berberine 500 mg); milk thistle (*Silybum marianum*) dry extract (silymarin 105 mg); red yeast rice extract(10 mg monacolin K)	3
4	Biostatine forte® 60 tablets, Pharmalife research	Red yeast rice dry extract (1.5% of monacolin K); artichoke (*Cynara scolymus*) leaves dry extract (2.5% of cynarine); citroflavonoids (60% of hesperidin)	3

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
6	Cadired 5® 36 tablets, Cadigroup	L-carnitine 650 mg; red yeast rice 200 mg dry extract (5% of monacolin K, 10 mg); hawthorn (*Crataegus oxyacantha*) leaves 200 mg dry extract (1.8% vitexin, 3.6 mg); niacin 30 mg; microalgae (*Haematococcus pluvialis*) powder 2 mg (5% astaxanthin, 100 mcg); chromium 1.6 mg	6
1	Calip plus® 60 tablets, promopharma	Red yeast rice dry extract 334 mg (3% monacolin K, 10 mg); Biox save® (mixture of *Olea europaea* L. fruit and *Vitis vinifera* L. fruit powder) 100 mg, coenzyme Q10 20 mg	4
16	Captolip® 24 tablets, Chemist's research	Red yeast rice 333.4 (3% monacolin K, 10 mg); policosanols 10 mg; coenzyme Q10 2 mg; thiamine (vit. B1) 1.1 mg; folic acid 200 mcg	5
2	Cardiofol®[1] 30 cpr, Named	Vitamin B6 1.4 mg; folic acid 0.2 mg; vitamin B12 2.5 mcg; *Vitis vinifera* fruit dry extract (titrated in flavonoids, anthocyanins and resveratrol) 40 mg	4
9	Cardiokolester 10® 30 tablets, Dymalife	Red yeast rice dry extract 200 mg (5% of monacolin K, 10 mg); curcuma (*Curcuma longa* L.) rhizome dry extract 100 mg (95% of curcumin, 95 mg); sage (*Salvia miltiorrhiza* Bunge) root dry extract 70 mg; garlic (*Allium sativum* L.) bulb dry extract 40 mg; astaxanthin 0,25 mg; pyridoxine hydrochloride (vitamin B6) 1.4 mg; chromium picolinate 40 mcg.	7
10	Cardiol forte® 30 tablets, U.G.A Nutraceuticals	Fish oil (412 mg), 75% omega-3 (min. 63% EPA and DHA, 231 mg EPA and 115 mg DHA); red yeast rice 350 mg (3% of monacolin K, 10 mg; olive (*Olea europaea* L.) fruit dry extract 50 mg (10% of hydroxytyrosol, 5 mg); coenzyme Q10 (100 mg); natural vitamin E 12 mg; folic acid 300 mcg; vitamin B12 2 mcg; *Piper nigrum* L. fruit dry extract 1 mg (85% of piperine, 0.85 mg)	8
191	Cardiolipid 10® 30 tablets, 20 sachets, Shedir Pharma	Red yeast rice 200 mg (5% of monacolin K, 10 mg); fish oil 60 mg, 65% omega 3 (42% EPA and 27.6% DHA, 19.5 mg); alpha-lipoic acid 30 mg; niacin, 27 mg; policosanol, 13 mg (60% of octacosanol, 7.8 mg; *Polygonum cuspidatum* Siebold & Zucc. rhizome 2.1 mg (98% of resveratrol, 2 mg); pantothenic acid 2 mg; folic acid 200 mcg; chromium picolinate 62 mcg; vitamin B12 2 mcg	10
16	Cardionam® 30, 60 tablets, Named	Artichoke (*Cynara scolymus* L.) leaves dry extract 500 mg (5% of caffeoylquinic acids); red yeast rice 200 mg (5% of monacolin K, 10 mg); banaba (*Lagerstroemia speciosa* L. Pers) leaves dry extract 75 mg (1% of corosolic acid); coenzyme Q10 50 mg; niacin 9 mg; vitamin B6 1.4 mg; vitamin B12 0.83 mcg; folic acid 110 mcg	8
4	Cardioqten 20® tablets, Carepharm	Indian berberi (*Berberis aristata* DC) bark dry extract (85% of berberine); red yeast rice dry extract (5% of monacolin K); coenzyme Q10; folic acid	4
27	Cardiostatin plus® 30 tablets, Criver Farmaceutici	Red yeast rice 200 mg (monacolin K 3 mg); sugar cane (*Saccharum officinarum*) dry extract (policosanols 20 mg); beta-sitosterol 75 mg; niacin 27 mg; zinc 10 mg; coenzyme Q10 10 mg; folic acid 200 mcg	7

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
1	Colber 30® tablets, Esserre Pharma	Bergamot (*Citrus bergamia* Risso & A. Poit) fruit dry extract 200 mg (60% of flavonoids); phytosterols 120 mg, artichoke (*Cynara scolymus* L.) leaves dry extract 80 mg (2.5% of chlorogenic acid), vitamin C (L-ascorbic acid) 20 mg	4
1	Colenorm plus®1 30 tablets Inpha nutraceuticals	*Polygonum cuspidatum* (resveratrol 20 mg); 20 mg policosanols (12 mg octacosanol); 333.3 mg red yeast rice (10 mg of monacolin K); 50 mcg chromium; 3.15 mg black pepper of which 2.99 mg piperine	5
5	Colesia oral gel® 20 sticks, IBSA Farmaceutici	Linseed (*Linum usitatissimum* L. oleum); apple annurcomplex (*Malus pumila* Miller *cultivar Annurca*) fruit dry extract; sterol esters titrated in sterols and stanols; red yeast rice (10% of monacolin K)	4
51	Colesia softgel 30®1 tablets, IBSA Farmaceutici	Sterol esters (59% of sterols and stanols); curcuma (*Curcuma longa* L.) rhizome dry extract; red yeast rice (3% of monacolin K); olive (*Olea europaea* L.) fruit dry extract titrated in polyphenols	4
4	Colesolv® 30 tablets, Glauber Pharma	Red yeast rice 200 mg (1.5% of monacolin); berberis (*Berberis aristata* DC) bark dry extract 150 mg (98% of berberine); green tea (*Camellia sinensis* Kuntze) leaves dry extract 100 mg (50% of polyphenols); artichoke (*Cynara scolymus* L.) leaves dry extract 65 mg (2.5% of caffeoylquinic acids); alpha-lipoic acid 50 mg; black pepper (*Piper nigrum* L.) fruits dry extract 20 mg (95% of piperine), sugar cane (*Saccharum officinarum* L.) dry extract (60% of octacosanol, 10 mg), coenzyme Q10 5 mg	8
11	Colest 500® 60 tablets, OTI (Officine Terapie Innovative)	Berberis (*Berberis aristata* DC.) root dry extract 515 mg (98% of berberine, 505 mg); red yeast rice 334 mg (3% of monacolin K,10 mg); astaxanthin 5 mg; coenzyme Q10, 5 mg; folic acid 200 mcg; vitamin B12, 2 mcg	6
2	ColestaltQ10® 45 tablets, Rima Laboratori	Red yeast rice; gamma-oryzanol; olive (*Olea europaea* L.) leaves dry extract; policosanols from rice (60% of octosanol); coenzyme Q10	5
370	Colestarmony plus® 20, 60 tablets, Biodue Spa	Red yeast rice 333 mg (3% of monacolin K, 10 mg and (2% of total polyphenols, 6.66 mg); berberine Bio-Sol® 236 mg (berberine hydrochloride 47.2 mg); curcuma dry extract 50 mg (95% of curcumin, 47.5 mg); pomegranate dry extract 50 mg (40% of punicosides, 20 mg); coenzyme Q10, 2 mg	5
4	Colestat® 30 tablets, Difass	Red yeast rice 200 mg (1.5% of monacolin K); linear aliphatic alcohols 10 mg (60% of octacosanol); niacin 27 mg; green tea (*Camellia sinensis*) dry extract 144 mg (40% of polyphenols), vitamin E 20 mg; folic acid 300 mcg, vitamin B6 2 mg; vitamin B12 1 mcg	8
2	Colestereg® 24 tablets, Profar	Artichoke (*Cynara scolymus* L.) leaves dry extract (5-6% of caffeoylquinic acid); red yeast rice (3% of monacolin K); resveratrol from the root of *Polygonum cuspidatum* Siebold & Zucc.	3

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
28	Colesterol act plus®2 60 tablets, F&F srl.	Guggul (*Commiphora mukul*) resin 10 mg; *Coleus forskohlii* root 10 mg; red yeast rice 200 mg (5% of monacolin 10 mg); octacosanol 10 mg; beta-sitosterol 50 mg; folic acid 200 mcg; Caigua (*Cyclantera pedata*) fruits 10 mg	7
2	Colestoil omega 3® 100 tablets, Aboca	Fish oil 1.25 g (min. 60% EPA and DHA, 750 mg); linseed oil 600 mg (50% of alpha-linolenic acid, 300 mg); garlic bulb oil extract 150 mg; lemon (*Citrus limon*) essential oil 20.6 mg; vitamin E (12 mg of alpha-tocopherol)	5
1	Colevis liquid analcolic® 500 ml Dr. Giorgini	Walnut (*Juglans regia*) fresh unripe fruits liquid integral extract; red yeast rice (1% of monacolin K), dandelion (*Taraxacum officinale*) root liquid integral extract; boldo (*Peumus boldus*) leaves liquid integral extract; artichoke (*Cynara scolymus*) leaves liquid integral extract; white horehound (*Marrubium vulgare*) aerial parts liquid integral extract; cleavers (*Galium aparine*) aerial parts liquid integral extract; milk thistle (*Silybum marianum*) fruit dry extract (40% of silymarin); rosemary (*Rosmarinus officinalis*) leaves liquid integral extract	9
7	Colex mu® 50 tablets, MU s.r.l.	Red yeast rice 360 mg (1.5% of monacolin, 1.26 mg); artichoke (*Cynara scolymus*) leaves 216 mg; *Plantago ovata* (ispaghula) seeds 71 mg; Algae Klamath 71 mg	4
8	Coltrix®1 30 tablets, Laboratori Legren	Policosanols from sugar cane 20 mg; red yeast rice 200 mg (1.5% of monacolin K); gamma-oryzanol 100 mg; resveratrol 40 mg; coenzyme Q10, 10 mg; folic acid 100 mcg; vitamin E 10 mg	7
1	Corlipid® 30 tablets, Essecore	Red yeast rice 200 mg (1.5% of monacolin, 3 mg), green tea (*Camellia sinensis* Kuntze) leaves dry extract 100 mg (95% of polyphenols, 95 mg), policosanols from rice 10 mg (60% of octacosanol, 6 mg)	3
10	Desimet® 20 sachets, Gofarma	Inositol 1500 mg; red yeast rice 333 mg (3% of monacolin K, 10 mg); Centellin® - centella (*Centella asiatica* L.) leaves dry extract 60 mg; folic acid 200 mcg	4
17	Dislicol® 30 tablets, Deltha Pharma	Red yeast rice 200 mg (1.5% of monacolin, 3 mg); policosanols 5 mg from sugar cane (90% of octacosanol); artichoke 150 mg; resveratrol 20 mg; folic acid 0.20 mg	5
1	Epadx® 40 tablets AVD reform	N-acetyl cysteine 400 mg; *Silybum marianum* Gaertn. fruit dry extract 400 mg (132 mg silymarin fitosoma®; Fumaria dry extract 200 mg; SAMe (S-Adenosyl-methionine) 200 mg; Cultavit®: natural B complex from buckwheat (*Fagopyrum esculentum* Moench) whole fruit 150.5 mg (0.31 mg of B1, 0.5 mg of B2, 5.4 mg of B3, 2 mg of B5, 0.31 mg B6, 68 mcg of folic acid, 0.6 mcg B12, 16.5 mcg of biotin); zinc gluconate 10 mg	6
1	Epatoguna® 32 tablets, Guna	Freeze-dried pork liver; choline bitartrate; green tea (*Camellia sinensis* L. Kuntze) leaves dry extract (40% of epigallocatechin gallate (EGCG)	3

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
5	Equitrig® 30 tablets, Trendfarma	Red yeast rice 334 mg (monacolin K 10 mg); *Cassia nomame* (*Cassia mimosoides* L. *var nomame* Makino) 200 mg (16 mg of catechins); niacin 24 mg; policosanols 10 mg (octacosanol 0.5 mg); folic acid 200 mcg	5
26	Esterol 10®[1], 20 tablets, Laborest	Red yeast rice (5% of monacolin K, 10 mg); green tea (*Camelia sinensis* L. Kuntze) leaves dry extract 100 mg (40% of EGCG); coenzyme Q10 20 mg; microalgae (*Haematococcus pluvialis* Flotow, thallus (astaxanthin 2 mg); resveratrol (*Polygonum cuspidatum* Siebold & Zucc.) rhizome 20 mg; quercetin 50 mg; vitamin D 5 mcg; vitamin K2 75 mcg; folic acid 200 mcg; selenium 83 mcg	10
5	Eufortyn colesterolo® 30 tablets, Scharper	Dried bergamot juice; coenzyme Q10; choline; zinc	4
1	Experid-250®[1] 50 tablets, Biotema	*Citrus sinensis* fruit (hesperidin), pomegranate (*Punica granatum* L.) fruit (20% of ellagic acid); bilberry (*Vaccinium myrtillus* L.) fruit dry extract (1% of anthocyanosides	3
1	Ezimega®[1] 20 tablets, Alfasigma	Fish oil (65% of omega 3 604 mg, 165 mg EPA and 121 mg DHA); red yeast rice 200 mg (1.5% of monacolin, 3 mg); L-carnitine 147 mg; resveratrol 10 mg; coenzyme Q10, 10 mg; policosanols from sugar cane (*Saccharum officinarum*) 10 mg; vitamin B6, 3 mg; vitamin B12 2.5 mcg	8
1	Ezimega 3® 20 tablets, Alfasigma	Red yeast rice (5% of monacolin K), *Lactobacillus plantarum* ECGC 13110402, resveratrol from *Polygonum cuspidatum* Siebold & Zucc. rhizome dry extract, coenzyme Q10, folic acid	5
77	Ezimega plus®[1] 20 tablets, Alfasigma	Fish oil 651 mg of omega 3 (100 mg of DHA, 150 mg of EPA); coenzyme Q10, 10 mg; resveratrol 10 mg; folic acid 300 mcg; vitamin B12 2.5 mcg; vitamin B6 3 mg; red yeast rice 417 mg (3% of monacolin K, 10 mg); policosanols from sugar cane (*Saccharum officinarum* L.) 10 mg	8
29	Faros® 30 tablets, Fidia Farmaceutici	Red yeast rice (5% of monacolin K, 10 mg) Revifast® (*Polygonum cuspidatum* Siebold & Zucc. rhizome extract) (min. 30% of resveratrol)	2
2	Farostin® 20 tablets, Fidia	Berberis (*Berberis aristata* DC) branches bark dry extract (85% of berberine chloride); Revifast® (*Polygonum cuspidatum* Siebold & Zucc. rhizome extract) (min. 30% of resveratrol); Astragalus (*Astragalus microcephalus* Willd.) root dry extract (70% of polysaccharides)	3
1	Fitobiostatin® 30 tablets, Fitobios	Red yeast rice (1.5% of monacolin K); artichoke (*Cynara scolymus* L.) leaves dry extract (5% of chlorogenic acid); Nopal cladodes (*Opuntia ficus-indica* Mill.) powder; vitamin E; gamma oryzanol; coenzyme Q10; folic acid	7
3	Fito-omocisteina® 60 tablets, Solgar	Trimethylglycine (*Beta vulgaris*) 500 mg; vitamin B6 (25 mg of pyridoxin hydrochloride, 3 mg of pyridoxal 5-phosphate); vitamin B12, 250 mcg; folic acid 200 mcg; powder Phyto2x (beta-carotene); vitamin C	6

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
38	Glicemarmony® 30 tablets, Biodue Spa	Berberine Bio-Sol® (*Berberis aristata* DC) bark dry extract 1000 mg (20% of berberine hydrochloride, 200 mg); white mulberry (*Morus alba* L.) dry extract 200 mg (2% of 1-deoxynojirimycin, 4 mg); curcuma (*Curcuma longa* L.) root dry extract 100 mg (95% of curcumin 95 mg)	3
3	Iceflox® 20 tablets, Cetra Italia	Pineapple (*Ananas comosus* Merr.) stem and fruits 2500 GDU/gr (400 GDU of bromelain, 160 mg); quercetin 150 mg; curcuma (*Curcuma longa* L.) root dry extract (95% of curcumin, 200 mg); green tea (*Camellia sinensis* L. Kuntze) leaves dry extract (98% of total polyphenols and 40% of EGCG, 70 mg); black pepper (*Piper nigrum* L.) fruit dry extract (95% of piperine, 2.6 mg)	5
2	Insulipid®[2] 30 tablets, Piemme Pharmatech	Berberine 200 mg; L-arginine 200 mg; L-carnitine 150 mg; *Spirulina platensis* 100 mg; red yeast rice 150 mg; *Euphrasia superba* (krill) 100 mg; chromium 20 mcg	7
12	Kilocal colesterolo®[1,2] 15, 30 tablets, Pool Pharma	Red yeast rice 200 mg (monacolin K, 10 mg); fenugreek 100 mg (*Trigonella foenum graecum* L.) seed dry extract titrated in saponins; lespedeza (*Lespedeza capitata* Mich.) leaves and whole plant dry extract 100 mg, titrated in flavones; olive (*Olea europaea* L.) leaves dry extract 100 mg (oleuropein 6 mg); white mulberry (*Morus alba* L.) leaves dry extract 100 mg; berberine powder (*Berberis aristata* DC.) bark dry extract 50 mg (85% of berberine, 42.5 mg); willow (*Salix alba* L.) bark dry extract 50 mg (20% of salicin, 10 mg); banaba (*Lagerstroemia speciosa* L.) leaves dry extract; coleus (*Coleus forskohlii*) root dry extract 25 mg (10% of forskolin); coenzyme Q10, 5 mg; chromium picolinate 200 mcg; folic acid 200 mcg	12
4	Klamath RX Max® 60, 180 tablets, Nutrigea	Microalgae Klamath RW®max (*Aphanizomenon Flos Aquae*)	1
34	Kogi plus®[1] 24 tablets, Bromatech	Coenzyme Q10, 20 mg; green tea (*Camellia sinensis* L.) leaves dry extract 60 mg; red yeast rice 200 mg (monacolin 10 mg); fruit extra-virgin olive oil (*Olea europea* L.) titrated in spinacetin; DL-alfa tocoferolo	5
16	Koginet® 24 tablets, Bromatech	Annurca apple (*Malus pumila* Mill. *cultivar annurca*) fruit dry extract 400 mg; l-teanina 100 mg; probiotic mixture (*Lactobacillus acidophilus* LA-14, *Lactobacillus plantarum* LP-115); gum Arabic (*Acacia senegal* Wiud.) powder 30 mg; vitamin Bl, 1.1 mg	6
15	Kolestina 10 complex® tablets, Cosval Group	Red rice (*Oryza sativa* L.) seed dry extract fermented with *Monascus purpureus* Went. sporophore (37.3%) 200 mg (10% of monacolin K, 10 mg); Venere black rice 100 mg (*Oryza sativa* L.) seed dry extract 18.5% (25% of anthocyanosides, 25 mg); guggul (*Commiphora mukul* Hook) resin dry extract 13%, 70 mg (10% of guggul sterols, 7 mg); sugar cane (*Saccharum officinarum* L.) juice dry extract 3.7%, 20 mg (60% of policosanols, 12 mg)	4

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
2	Lactoflorene colesterolo® 30 tablets, Montefarmaco	Red yeast rice (3% of monacolin K, 10 mg); *Bifidobacterium longum* BB536® (ATCC BAA-999) 1 billion UFC; coenzyme Q10, 20 mg; niacin 16 mg	4
1	Lecitina di soia® 400 g, Marco Viti	Soya lecithin (*Glycine max*); vitamin E acetate; vitamin B6 hydrochloride	3
8	Lecitina di soia® 45 tablets, Arkopharma	Soya lecithin (*Glycine max* (L.) Merr.)-soya oil 1650 mg	1
8	Levelipduo® 20 tablets, 14 sticks, Laboratori Guidotti	Sterols of vegetal origin 800 mg; red yeast rice 167 mg (3% of monacolin k, 5 mg); niacin 27 mg; policosanols 10 mg (60% of octacosanol)	4
3	LFP colesttab®[1] 30 tablets 5 mg, Unifarco	Red yeast rice 334 mg (3% of monacolin k, 10 mg); coenzyme Q10, 100 mg; *Haematococcus pluvialis* Flotow thallus (2 mg of astaxanthin); policosanols of sugar cane (*Saccharum officinarum* L.) juice 20 mg; folic acid 400 mcg	5
32	Lfp colesttab®[1] 30 tablets 10 mg, Unifarco	Red yeast rice 210 mg (5% of monacolin K, 10 mg); coenzyme Q10, 100 mg; *Haematococcus pluvialis* flotow thallus (1 mg of astaxanthin); policosanols from sugar cane (*Saccharum officinarum* L.) juice 10 mg; folic acid 200 mcg	5
19	Lipalt®[1] 30 tablets, Farmacrimi	*Citrus bergamia* Risso & Poit. fruit 250 mg; red yeast rice 167 mg (3% of monacolin K); policosanols from sugar cane (*Saccharum officinarum* L.) 10 mg; coenzyme Q10, 2 mg	4
18	Lipocol plus® 30 tablets, Laboratori Nutriphyt	Red yeast rice (5% of monacolin K); bergamot dry extract of fruit juice (25%-28% of flavonoids); pine (*Pinus massoniana*) bark dry extract; vitamin E; vitamin B3; vitamin B12; vitamin B6; vitamin B1; folic acid	9
1	Liposan forte® 60 tablets Salugea	Red yeast rice 334 mg (3% of monacolin K, 10 mg); barberry (*Berberis vulgaris* L.) root bark dry extract 266 mg (98% of berberine, 260 mg); milk thistle (*Silybum marianum* Gaertn.) fruits dry extract 100 mg (80% of silymarin, 80 mg); rosemary (*Rosmarinus officinalis* L.) leaves dry extract 1:4, 100 mg	4
2	Liposcudil®[1] 30 tablets, Piam farmaceutici Spa	Policosanols from rice 10 mg; red yeast rice 200 mg (1.5% of monacolin K, 3 mg); phytosterols (95%) 50 mg; Extramel®-melon pulp (*Cucumis melo*) 5 mg, *Vitis vinifera* seeds extract (95% of proanthocyanidins); Olivex®-olive polyphenols 10 mg; folic acid 0.2 mg	7
5	Liposcudil BBR® 30 tablets, Piam Farmaceutici	Red yeast rice 100 mg (3% of monacolin K, 3 mg); *Berberis aristata* 572 mg (87.4% of berberine, 500 mg); chromium 40 mg; coenzyme Q10, 30 mg; folic acid 200 mcg	5
82	Liposcudil plus® 30 tablets, sachets, Piam Farmaceutici	Red yeast rice 333 mg (3% of monacolin K, 10 mg); coenzyme Q10, 30 mg	2
17	Long life olio germe grano® 60 tablets, Longlife	Wheat germ (*Triticum aestivum* L.) oil 1500 mg: 62% of polyunsaturated fatty acids (930 mg), of which 40% of linoleic acid (omega-6, 372 mg) and 10% of oleic acid (omega-9, 150 mg); 0.15% of vitamin E 2.2 mg	1

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
4	Long life riso rosso fermentato® 60 tablets, Longlife	Red yeast rice 334 mg (3% of monacolin K, 10 mg); coenzyme Q10, 30 mg	2
12	Lopiglik®[1] 20 tablets, AkademyPharma	Berberis (*Berberis aristata* D.C.) bark dry extract 531.25 mg (85% of berberine); white mulberry (*Morus alba* L.) leaves dry extract (4 mg of deoxynojirimycin); red yeast rice 220 mg (1.5% of monacolin K, 3.3 mg)	3
11	Lopiglik plus® 20 tablets, Akademypharma	Berberis (*Berberis aristata* DC.) bark dry extract 531.25 mg (85% of berberine); red yeast rice 220 mg (1.5% of monacolin K, 3.3 mg); white mulberry (*Morus alba* L.) leaves dry extract (2% of deoxynojirimycin, 4 mg); cholecalciferol powder (vitamin D3) 15,00 mcg (600 U.I.)	4
1	Lovachole® 30 tablets, Nalkein Pharma	Red yeast rice 200 mg (5% of monacolin K, 10 mg); linseed oil (*Linum usitatissimum* L.) 100 mg; alpha lipoic 50 mg; niacin 20 mg; zinc oxide 12.5 mg; vitamin B12 2.5 mcg; chromium picolinate 50 mcg	7
3	Loxicor® 30 tablets, 20 sachets, Logidex	Pine (*Pinus spp.*) stems (99% of phytosterols); red yeast rice (5% of monacolin K); coenzyme Q10	3
5	Monalip® 30 tablets, Biogroup	Red yeast rice 334 mg (3% of monacolin, 10 mg); coenzyme Q10, 10 mg	2
11	Nocol plus® 30 tablets, Princeps	Red yeast rice 200 mg (monacolin K 10 mg); total sterols 150 mg (beta-sitosterol 112.5 mg); coenzyme Q10, 50 mg; policosanols 10 mg (octacosanol 6 mg)	4
1	Nocolesteno® 30 tablets, Elmafarma srl	Red yeast rice 200 mg (min. 1.5% of monacolin k, 3 mg); coenzyme Q10, 80 mg	2
5	No-colest omegasol formula potenziata®, 40 tablets, Specchiasol	Bergamot fruit dry extract 42 mg (polyphenols 25 mg); red yeast rice 200 mg (5% of monacolin K, 10 mg); algae oil 46 mg (35% of natural DHA, 16 mg); coenzyme Q10, 5mg	4
18	Normolip 5® 30 tablets, Esi	Red yeast rice 200 mg (5% of monacolin K, 10 mg); gamma-oryzanol 90 mg; coenzyme Q10, 10 mg; policosanols 5 mg; chromium 200 mcg	5
6	Nova lipid plus® 30 tablets, Nova Argentia	Red yeast rice (5% of monacolin); olive (*Olea europaea* L.) leaves extract; artichoke (*Cynara scolymus* L.) leaves extract; grapevine (*Vitis vinifera* L.) seeds and leaves extract; coenzyme Q10; calcium pantothenate; vitamin B6; vitamin B2; vitamin B1; folic acid; chromium picolinate; vitamin H (biotin); vitamin B12	13
23	Nurvast® 30 tablets, Coohesion Pharma	Annurca apple (*Malus pumila* Miller) dry extract 800 mg (0.03% of chlorogenic acid, 0.24 mg; 0.15% of phlorizin, 1.2 mg; 0.04% of procyanidin B2, 0.32 mg; 0.5% of ursolic acid, 4 mg)	1
1	Nurvast plus® 30 tablets, Coohesion Pharma	Annurca apple (*Malus pumila* Miller) dry extract 400 mg (0.03% of chlorogenic acid, 0.12 mg; 0.15% of phlorizin, 0.6 mg; 0.04% of procyanidin B2, 0.16 mg; 0.5% of ursolic acid, 2 mg); policosanols from sugar cane (*Saccharum officinarum* L.) 20 mg (60% of octacosanol, 12 mg)	2

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
3	Nutricol®[2] 30, 120 tablets, Nutrigea	Psyllium (*Plantago ovata* Forsk.) husk 450 mg; dandelion (*Taraxacum officinale* DC) root 150 mg; *Bifidobacterium bifidum* (DSM 25565) 16.2 billion UFC; *Aloe ferox* Mill. juice 105 mg; chinese rhubarb (*Rheum palmatum* L. var. *tanguticum* Max) rhizome 105 mg; microalgae Klamath RW® max (*Aphanizomenon Flos Aquae*) 90 mg; EnzyMax® (fermented maltodextrin) 90 mg; *Berberis aristata* DC. bark dry extract (8% of berberine); cascara sagrada (*Rhamnus purshiana* DC) bark dry extract 60 mg (18-20% of cascaroside A, 10.8 mg); *Echinacea purpurea* L. Moench. dry extract 30 mg (4% of total polyphenols, 1.2 mg); milk thistle (*Silybum marianum* L. Gaertn.) fruits dry extract 30 mg (80% of silymarin, 24 mg; 30% of silibinin and isosilibinin, 9 mg); ginger (*Zingiber officinale* Roscoe) rhizome 30 mg; fennel (*Foeniculum vulgare* Miller.) fruits 30 mg; bamboo (*Bambusa spp*.) sprouts dry extract 30 mg (75% of silicium, 22.5 mg)	14
2	Olivis liquido® 50 ml, Dr. Giorgini	Olive (*Olea europaea*) leaves liquid integral extract; hawthorn (*Crataegus oxyacantha*) flowers and leaves liquid integral extract; mistletoe (*Viscum album*) aerial parts liquid integral extract; shepherd's purse (*Capsella bursa-pastoris*) aerial parts liquid integral extract; fumaria (*Fumaria officinalis*) aerial parts liquid integral extract	5
10	Omegadin plus retard® 30 tablets, GD tecnologie interdisciplinari farmaceutiche srl	Ahiflower® oil (*Buglossoides arvensis*) seeds (60% of omega-3, 15% of omega-6, 6% of omega-9); olive oil; red orange complex (R.O.C.) Sicily red orange extract titrated; vitamin C; vitamin E; selenium 25 mcg	6
22	Omega 3 age® 45 tablets, Fitobios	Linseed oil (*Linum usitatissimum* L.); grapevine (*Vitis vinifera* L.) seeds dry extract (75% of polyphenols); olive fruits (*Olea europaea* L.) dry extract (10% of hydroxytyrosol); vitamin E	4
27	Omega formula® 80 tablets, Guna	Baobab (*Adansonia digitata* L.) seed 1500 mg (5.4 mg of omega 3, 89.25 mg of omega 6, 85.95 mg of omega 9, 1.50 mg of polyphenols, 5.10 mg of sterols; red yeast rice powder 666.66 mg (monacolins 10 mg); vitamin B6, 3 mg; folic acid 300 mcg	4
4	Oxolipid® 30 tablets, Sanamedica group	Red yeast rice (5% of monacolin K); mangosteen (*Garcinia mangostana* L.) fruit pulp dry extract (40% of mangostins)	2
1	Pantavis 600 lipoico®, 20 tablets, Biodelta	Alpha lipoic acid; berberine; gymnema (*Marsdenia sylvestris* (Retz.) P.I. Forst.) leaves dry extract (25% of gymnemic acid); chromium picolinate	4
5	Polidal 75®[1] 20 tablets, Ghimas	*Fallopia japonica* (Japanese knotweed) (*Polygonum cuspidatum*) extract (75 mg of polydatin)	1
8	Polidase® 30 tablets, Sherman tree nutraceuticals	*Fallopia japonica* (*Polygonum cuspidatum*) dry extract (98% of polydatin, 160 mg);	1
1	Profito ST® drops 50 ml, Qantiqa	Mistletoe 7.50 mg; rosemary 7.50 mg; rhubarb 7.50 mg; black radish (*Raphanus sativum*) 7.50 mg	4

Table 1.1. (continued)

Number of sales	Brand name, pharmaceutical form, manufacturer	Phytochemical composition without vehicles, daily dose when reported	Number of ingredients
23	Redulip® 60 tablets, ForFarma	Artichoke (*Cynara scolymus* L.) leaves dry extract (5% of chlorogenic acid); red yeast rice (3% of monacolin K); *Fallopia japonica* Houtt Ronse Dec. rhizome (resveratrol); coenzyme Q10; chromium picolinate; vitamin B6; folic acid; vitamin B12	8
4	Resveratrox® 60 tablets, Solgar	*Polygonum cuspidatum* Sieb. et Zucc. rhizome dry extract 400 mg (50% of resveratrol, 200 mg)	1
2	Revidox+® 60 tablets, Paladin Pharma	Stilvid®-grapevine (*Vitis vinifera* L.) fruit and seed dry extract 133 mg titrated; pomegranate (*Punica granatum* L.) fruit dry extract 125 mg; selenium 34 mcg; vitamin C, 12 mg; zinc 1.5 mg; vitamin B2, 1.4 mg	6
2	Riscol 5® 30 tablets, Errekappa euroterapici spa	Red yeast rice 200 mg (monacolin K 10 mg); policosanols 20 mg (octacosanol 12 mg); resveratrol 40 mg	3
15	Riscol plus® 30 tablets, Errekappa Euroterapici	Fish oil 800 mg (40% of EPA, 288 mg and 30% of DHA, 244 mg); Bergavit® (*Citrus bergamia* Risso & Poit) fruit 400 mg, red yeast rice 200 mg (5% of monacolin K, 10 mg); Cromax® (chromium, 20 mcg)	4
2	Ritenil depura® 30 tablets, Syrio	Kale (*Brassica oleracea* L.) juice powder 300 mg; choline bitartrate 90 mg; desmodium (*Desmodium adscendens* Sw. DC.) leaves dry extract 200 mg; milk thistle (*Silybum marianum* L. Gaertn.) fruit dry extract 100 mg	4
3	Sincrolipid® 60 tablets, UP pharma	Policosanols; berberine; red yeast rice; C*assia nomame*; astaxanthin; coenzyme Q10; folic acid	7
2	Tegradoc® 30 tablets, Doc generic	Berberine 200 mg; red yeast rice 100 mg (monacolin K 3 mg); chitosan 100 mg; coenzyme Q10, 10 mg	4
2	Tirecol® 30 tablets, Fera Pharma	Selenium 83mcg; myo-inositol 400 mg; vitamin D3 5 mcg; red yeast rice 334 mg (monacolin K 10 mg)	4
3	Tokaber plus® 30 tablets, Polifarma	*Olea europaea* L. leaves dry extract; Italian bergamot juice; choline; zinc	4
1	Trigofien® 60 tablets, Sarandrea	Fenugreek (*Trigonella foenum-graecum* L.) seeds dry extract 1:4, 2400 mg; fenugreek (*Trigonella foenum-graecum* L.) seeds powder 540 mg	1
2	Trixy® 28 tablets, Nathura	*Berberis aristata* DC. bark dry extract 588 mg (85% of berberine); *Elaeis guineensis* Jacq. oleum dry extract 143 mg (21% of tocotrienols); coffee (*Coffea arabica*) without caffeine seed dry extract 67 mg (45% of chlorogenic acid)	3
1	Viridian EPA&DHA® liquid vegan	Marine algae (*Schizochytrium spp*.) oil; chia seed (*Salvia hispanica*) oil; natural orange oil; vitamin E	4
13	Zeta colest® 30 tablets, Erbozeta	Red yeast rice (3% of monacolin), milk thistle (*Silybum marianum*) fruits dry extract (80% of silymarin); guggul (*Commiphora mukul* Hook) resin dry extract (10% of guggulipids and 2.5% of guggulsterones; sugar cane (*Saccharum officinarum* LJ.) juice (98% of policosanols and 60% of octacosanols)	4

[1] The label reports the active ingredients and/or phytochemicals without percentage.

[2] The label describes only the kind of phytoextract.

1.4.3 *Description of the botanicals and the additional ingredients*

Seventy-one plant species, 17 isolated phytochemicals and 31 additional non-botanical ingredients were clustered from dyslipidaemia-HDS. In table 1.2 are reported all the plant species in decreasing order of prevalence, along with the plant materials and the types of extract found in commercial dyslipidaemia-HDS. Furthermore, the markers with the relative range and the physiological functions (pending claims), according to the MoH, are also stated.

According to Ministerial guidelines, 23% (n=16) of the plant species found in commercial dyslipidemia-HDS have claims for affecting cholesterol/triglycerides/lipids metabolism, while 18% (n=13) claims the improvement of the cardiovascular system. 51% (n=36) of the plant species refers to other physiological effects. A small percentage either (4%, n=3) does not have any claim at all, or (4%, n=3) is not included in the list because clustered as "other nutrients and other substances with a nutritional and physiological effect"/novel food (i.e., RYR, *Salvia hispanica, Schizochytrium spp.*).

Other plant derived ingredients, as pure substances or extracts, were identified in the labels of dyslipidaemia-HDS; their frequency was as follows: policosanols (n=11), resveratrol (n=6), phytosterols (n=5), astaxanthine, gamma-oryzanol (n=4), linear aliphatic alcohols (n=3), beta-sitosterol, quercetin, sterolic esters (n=2), beta-carotene, betaine (trimethylglycine), citroflavonoids, lutein, octacosanol, orange oil, polyphenols, red orange complex, enzymax® (fermented maltodextrin) (n=1).

The occurrence of additional non-botanical ingredients is the following in decreasing order: coenzyme Q_{10} (n=40), folic acid (n=34), vitamin B12 (cyanocobalamin) (n=16), vitamin B6 (pyridoxine) (n=15), vitamin E (tocopherol) (n=14), chromium (n=13), vitamin B3 (niacin) (n=12), omega 3 (EPA&DHA), zinc (n=6), alpha lipoic acid, choline (n=5), selenium, vitamin B1 (thiamine), vitamin C (ascorbic acid) (n=4), inositol (myo-), L-carnitine, vitamin D3 (cholecalciferol) (n=3), vitamin B2 (riboflavin), vitamin B5 (pantothenic acid), *Lactobacillus plantarum* (n=2), chitosan, *Bifidobacterium bifidum*, freeze-dried pork liver, L-arginine, *Lactobacillus acidophilus*, *Bifidobacterium longum*, L-theanine, N-acetyl cysteine, S-adenosyl methionine, vitamin B8 (biotin), vitamin K2 (menaquinone) (n=1).

Table 1.2. Plant species found in dyslipidaemia-HDS, and their relative descriptions.

Plant[1]	**Plant material[2]**	**Type of extract[3]**	**Prevalence in dyslipidaemia-HDS No. (%)[4]**	**Marker/range (%)**	**Physiological function according to the MoH[5]**
Oryza sativa fermented with *Monascus purpureus*	Seed fermented with sporophore	Dry extract	72 (64%)	Monacolin K, 1%-10%	Substance/nutrient[6]

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Berberis aristata DC.	root, bark, branches bark	Dry extract, powder	19 (17%)	Berberine, 8%-98%	*Cortex ex ramis*: regular function of the cardiovascular system. Digestive function. Hepatic functionality. Regularity of intestinal transit. Functionality of the digestive system.
Saccharum officinarum L.	Stem (Cane)	Dry extract, juice	13 (12%)	Policosanols, 1.4%-98% Octacosanol, 60%-90%	*Succus*: digestive function. Fluidity of bronchial secretions
Olea europea L.	Fruit, leaf	Dry extract, powder, oil, liquid integral extract	13 (12%)	Oleuropeina, 6%-15% Hydroxytyrosol, 10% Spinacetin[7]	*Folium*: carbohydrate and lipid metabolism. Normal blood circulation. Regularity of blood pressure. Antioxidant.
Fallopia Japonica (Houtt.) Ronse Dec. (*Polygonum cuspidatum* Siebold & Zucc.)[8]	Rhizome	Dry extract	12 (11%)	Resveratrol, 30%-98% Polydatin, 98%	*Radix*: antioxidant. Fluidity of bronchial secretions. Detoxification of the organism. Body fluids drainage. Regularity of the menstrual cycle. Regular function of the cardiovascular system. Tonic (physical, mental fatigue).
Cynara scolymus L.	Leaf	Dry extract, liquid integral extract	12 (11%)	Cynarine, 2.5% Caffeoylquinic acids, 2.5%-6% Chlorogenic acid, 2.5%-5%	*Folium*: digestive function. Hepatic functionality. Elimination of intestinal gas. Detoxification of the organism. Lipid metabolism. Antioxidant.
Silybum marianum (L.) Gaertn.	Fruit	Dry extract	9 (8%)	Silymarin, 33%-80% Silibin/isosilibin, 30%	*Fructus, tegumen seminis*: digestive function. Hepatic functionality. Detoxification of the organism. Antioxidant. Carbohydrate metabolism.
Camellia sinensis (L.) Kuntze	Leaf	Dry extract	8 (7%)	Polyphenols, 40%-98% Epigallocatechin gallate, 40%	*Folium*: body fluids drainage. Body weight balance. Normal intestinal function. Tonic (physical, mental fatigue). Antioxidant.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Citrus bergamia Risso & Poit. *Citrus aurantium var. bergamia* (Risso) Brandis.[8]	Fruit	Dry extract, juice dry extract	7 (6%)	Flavonoids, 25%-60% Polyphenols, 59.5%	ND[9]
Curcuma longa L.	Rhizome	Dry extract	6 (5%)	Curcumin, 95%	*Rhizoma*: joint function. Antioxidant. Improvement of menstrual cycle disorders.
Haematococcus pluvialis Flotow	Thallus	Dry extract, powder	6 (5%)	Astaxanthin, 2.5%-5%	*Thallus*: antioxidant.
Vitis vinifera L.	Fruit, seed, leaf	Dry extract, powder	6 (5%)	Polyphenols, 75% Proanthocyanidins, 95% Flavonoids[7] Resveratrol[7] Anthocyanins[7]	*Folium, semen*: microcirculation functionality (heavy legs). Antioxidant. Regular function of the cardiovascular system.
Piper nigrum L.	Fruit	Dry extract	6 (5%)	Piperine, 40%-95%	*Fructus, oleum-resina, oleum*: digestive function. Regularity of intestinal transit. Regular gastrointestinal motility and gas elimination. Antioxidant. Regular function of the cardiovascular system.
Allium sativum L.	Bulb	Dry extract, powder, oil extract	4 (4%)	ND	*Bulbus*: regular function of the cardiovascular system. Antioxidant. Triglycerides and cholesterol metabolism. Regularity of blood pressure. Bronchial secretions fluidity. Nose and throat wellness. Digestive function.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Linum usitatissimum L.	Seed	Oil extract	4 (4%)	Alpha-linolenic acid, 50%	*Semen, tegumen seminis*: regularity of intestinal transit. Normalized stool volume and consistency. Emollient and soothing action (digestive system). Modulation/limitation of nutrient absorption. Lipid metabolism. *Oleum*: lipid metabolism. Integrity and functionality of cell membranes.
Malus pumila Mill. cv *annurca*	Fruit	Dry extract	4 (4%)	Chlorogenic acid, 0.03% Phlorizin, 0.15% Procyanidin B2, 0.04% Ursolic acid, 0.5%	ND
Morus alba L.	Leaf	Dry extract	4 (4%)	1-deoxynojirimycin, 2%	*Cortex ex radicibus, folium, fructus*: regularity of the intestinal transit. Body fluids drainage. Fluidity of bronchial secretions. Carbohydrate metabolism. Regularity of blood pressure. Functionality of urinary tract.
Rosmarinus officinalis L.	Leaf	Dry extract, liquid integral extract	4 (4%)	ND	*Aetheroleum, folium*: digestive function. Hepatic functionality. Regular gastrointestinal motility and gas elimination. Antioxidant. Regular function of the cardiovascular system.
Aphanizomenon flos-aquae	ND	ND	3 (3%)	ND	*Bacteria*: mood balance.
Commiphora mukul (Hook. Ex Stocks) Engl.	Resin	Dry extract	3 (3%)	Guggulsterols, 10% Guggulipids, 10% Guggulsterones, 2.5%	*Oleum-gummi-resina*: lipid metabolism. Skin regeneration and functionality. Body weight balance.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Punica granatum L.	Fruit	Dry extract	3 (3%)	Ellagic acid, 20% Punicosides, 40%	*Fructus*: antioxidant. Pericarpum: digestive system functionality. Regularity of intestinal transit
Cassia mimosoides var. nomame (Siebold) Makino *Chamaecrista nomame* (Sieber) H. Ohashi[8]	ND	ND	2 (2%)	Catechins, 8%	*Folium, fructus*: triglycerides and cholesterol metabolism. Body weight balance.
Coleus forskohlii (Willd.) Bricq.	Root	Dry extract	2 (2%)	Forskolin, 10%	*Radix, tuber*: regular functionality of the cardiovascular system. Regularity of blood pressure. Functionality of the upper respiratory tract. Digestive function. Body weight balance.
Crataegus oxyacantha *Crataegus laevigata* (Poir.) DC.[8]	Leaf, flowers	Dry extract, liquid integral extract	2 (2%)	Vitexin, 1.8%	*Folium, flos*: regular functionality of the cardiovascular system. Antioxidant. Relaxation and mental wellness. Regularity of blood pressure.
Fumaria officinalis L.	Aerial parts	Dry extract, liquid integral extract	2 (2%)	ND	*Herba cum floribus, summitas*: hepatobiliary and digestive function. Detoxification of the organism. Skin regeneration and functionality (wellness).
Lagerstroemia speciosa (L.) Pers.	Leaf	Dry extract	2 (2%)	Corosolic acid, 1%	*Folium*: digestive system functionality. Regularity of intestinal transit.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Plantago ovata Forssk.	Seed, husk	ND	2 (2%)	ND	*Semen, tegumentum seminis*: regularity of the intestinal transit. Emollient and soothing effect (digestive system). Modulation/limitation of nutrient absorption. Lipid and carbohydrate metabolism. Stool normal volume and consistency. Prebiotic effect.
Glycine max (L.) Merr.	ND	oil	2 (2%)	ND	*Semen, semen germinatus*: lipid metabolism. Improvement of menopausal symptoms.
Rheum palmatum L.	Rhizome	ND	2 (2%)	ND	*Radix, rhizoma*: digestive function. Regularity of intestinal transit.
Taraxacum officinale (L.) Weber ex F.H.Wigg	Root	Liquid integral extract	2 (2%)	ND	*Herba cum radicibus, radix*: hepatic functionality. Digestive function. Regularity of the intestinal transit. Detoxification of the organism. Body fluids drainage.
Trigonella foenum graecum L.	Seed	Dry extract, powder	2 (2%)	Saponins	*Semen*: triglycerides and cholesterol metabolism. Carbohydrate metabolism. Digestive function. Emollient and soothing effect (digestive system).
Viscum album L.	Aerial parts	Liquid integral extract	2 (2%)	ND	*Folium, herba*: Lipid metabolism. Antioxidant.
Acacia senegal (L.) Willd.	Gum (exudate)	Powder	1 (1%)	ND	*Gummi*: emollient and soothing effect (digestive system). Carbohydrate metabolism. Cholesterol metabolism. *Prebiotic*: intestinal flora balance.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Adansonia digitata L.	Seed	ND	1 (1%)	ND	*Cortex, folium, fructus, radix, semen*: joint function. Improvement of menstrual cycle disorders. Improvement of menopausal symptoms. Supportive and restorative effect. Boosting the immune system. Regularity of blood pressure. Regularity of the intestinal transit. Functionality of the upper respiratory tract.
Astragalus microcephalus Willd.	Root	Dry extract	1 (1%)	Polysaccharides, 70%	*Radix*: cholesterol metabolism. Boosting the immune system.
Bambusa spp.	Sprouts	Dry extract	1 (1%)	Silicium, 75%	*Germen*: digestive function. Intestinal gas elimination. Nails and hair wellness.
Berberis vulgaris L.	Root bark	Dry extract	1 (1%)	Berberine, 98%	*Cortex ex radicibus*: Digestive function. Hepatic functionality. Regularity of intestinal transit. Functionality of the digestive system.
Beta vulgaris L.	ND	ND	1 (1%)	Trimethyglycine (betaine)[7]	*Folium, radix*: antioxidant.
Brassica oleracea L.	ND	Juice powder	1 (1%)	ND	*Folium, flos*: antioxidant. Regular functionality of the cardiovascular system. Digestive function. Joint functionality.
Buglossoides arvensis (L.) I. M. Johnst	Seed	Oil	1 (1%)	Omega-3, 60% Omega-6, 15% Omega-9, 6%	ND

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Capsicum spp.	ND	Powder	1 (1%)	ND	*Fructus, oleum-resina*: digestive function. Regular gastrointestinal motility and gas elimination. Regular functionality of the cardiovascular system. Normal blood circulation. Metabolism stimulation. Antioxidant.
Centella asiatica (L.) Urb.	Leaf	Dry extract	1 (1%)	ND	*Folium, herba*: fight cellulite imperfections. Microcirculation functionality (heavy legs). Memory and cognitive function.
Citrus limon (L.) Osbeck.	ND	Essential oil	1 (1%)	ND	*Pericarpum, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination.
Citrus sinensis (L.) Osbeck.	Fruit	ND	1 (1%)	Hesperidin[7]	*Pericarpum, aetheroleum*: digestive function. Intestinal gas elimination.
Coffea arabica L.	Seed	Dry extract	1 (1%)	Chlorogenic acid, 45%	*Semen*: tonic and metabolic support action. Antioxidant.
Cucumis melo L.	Fruit	ND	1 (1%)	ND	*Fructus*: digestive function. Skin regeneration.
Cyclanthera pedata (L.) Schrad.	Fruit	ND	1 (1%)	ND	*Fructus*: regularity of blood pressure. Carbohydrate and cholesterol metabolism. Digestive function. Mucose wellness and regeneration. Body fluids drainage. Functionality of the urinary tract.
Desmodium adscendens (Sw.) DC.	Leaf	Dry extract	1 (1%)	ND	*Folium*: functionality of the upper respiratory tract. Joint functionality. Hepatic functionality.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Echinacea purpurea (L.) Moench.	ND	Dry extract	1 (1%)	Polyphenols, 4%	*Herba, radix*: boosting the immune system. Functionality of the urinary tract. Functionality of the upper respiratory tract.
Elaeis guineensis Jacq.	ND	Oleum dry extract	1 (1%)	Tocotrienols, 21%	*Fructus, oleum*: joint functionality. Sedative effect. Body fluids drainage. Functionality of the urinary tract.
Fagopyrum esculentum Moench.	Fruit	ND	1 (1%)	B_1, 0.31 mg B_2, 0.5 mg B_3, 5.4 mg B_5, 2 mg B_6, 0.31 mg Folic acid, 68 mcg B_{12}, 0.6 mcg Biotin, 16.5 mcg	*Folium, flos*: functionality of the microcirculation. Functionality of the venous circulation. Regular functionality of the cardiovascular system. Regularity of blood pressure.
Foeniculum vulgare Mill.	Fruit	ND	1 (1%)	ND	*Fructus, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Improvement of menstrual cycle disorders. Body fluids drainage. Bronchial secretions fluidity.
Galium aparine L.	Aerial parts	Liquid integral extract	1 (1%)	ND	*Flos, herba cum floribus, summitas*: body fluids drainage and functionality of the urinary tract. Detoxification of the organism.
Garcinia mangostana L.	Fruit pulp	Dry extract	1 (1%)	Mangostins, 40%	*Pulpa fructus*: antioxidant. Boosting the immune system.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Juglans regia L.	Fresh unripe fruits	Liquid integral extract	1 (1%)	ND	*Pericarpum, semen*: digestive function. Detoxification of the organism. Regularity of the intestinal transit. Functionality of the digestive system. Integrity and functionality of cell membranes. Regular functionality of the cardiovascular system.
Lespedeza capitata Michx.	Leaf, whole plant	Dry extract	1 (1%)	Flavones[7]	*Folium, herba, summitas*: body fluids drainage. Functionality of the urinary tract. Detoxification of organism. Regular functionality of the cardiovascular system. Lipid metabolism.
Marrubium vulgare L.	Aerial parts	Liquid integral extract	1 (1%)	ND	*Folium, herba cum floribus*: bronchial secretions fluidity. Thermoregulation. Digestive function. Intestinal gas elimination.
Marsdenia sylvestris (Retz.) P.I. Forst *Gymnema sylvestre* (Retz) R.Br.[8]	Leaf	Dry extract	1 (1%)	Gymnemic acid, 25%	*Folium*: carbohydrate and lipid metabolism. Appetite control.
Opuntia ficus-indica (L.) Mill.	Cladodes	Powder	1 (1%)	ND	*Cladodium*: body weight balance. Modulation/limitation of nutrients absorption. Emollient and lenitive effect (digestive system). Regularity of the intestinal transit.
Peumus boldus Molina	Leaf	Liquid integral extract	1 (1%)	ND	*Folium*: digestive function. Hepatic functionality. Body fluids drainage. Functionality of the urinary tract. Regularity of the intestinal transit.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Raphanus sativus L.	ND	ND	1 (1%)	ND	*Semen, radix*: digestive function. Body fluids drainage. Functionality of the urinary tract. Bronchial secretions fluidity. Antioxidant.
Rhamnus purshiana DC. *Frangula purshiana* Cooper	Bark	Dry extract	1 (1%)	Cascaroside A, 18-20%	*Cortex*: regularity of the intestinal transit. Digestive function.
Rosa canina L.	ND	Dry extract	1 (1%)	ND	*Fructus, falso fructus*: supportive and restorative effect. Regularity of the intestinal transit. Antioxidant.
Salix alba L.	Bark	Dry extract	1 (1%)	Salicin, 20%	*Cortex, cortex ex ramis, folium*: joint functionality. Thermoregulation. Sedative effect.
Salvia miltiorrhiza Bunge	Root	Dry extract	1 (1%)	ND	*Radix*: functionality of the cardiovascular system. Regularity of blood pressure. Improvement of the menstrual cycle disorders. Antioxidant.
Salvia hispanica	Seed	Oil	1 (1%)	ND	Not included[10]
Schizochytrium spp.	ND	Oil	1 (1%)	ND	Not included[10]
Spirulina platensis (Gomont) Geitler	ND	ND	1 (1%)	ND	*Thallus*: supportive and restorative effect.
Triticum aestivum L.	ND	Oil	1 (1%)	ND	*Fructus*: source of carbohydrate and gluten proteins. *Fructus germinatus (malt)*: supportive and restorative effect. *Oleum germinis*: antioxidant. Lipid metabolism.

Table 1.2. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in dyslipidaemia-HDS No. (%)[4]	Marker/range (%)	Physiological function according to the MoH[5]
Vaccinium myrtillus L.	Fruit	Dry extract	1 (1%)	Anthocyanosides, 1%	*Fructus*: functionality of the microcirculation (heavy legs). Antioxidant. Ocular health. Regularity of the intestinal transit.
Zingiber officinale Rosc.	Rhizome	ND	1 (1%)	ND	*Rhizome, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Antinausea. Regular functionality of the cardiovascular system. Normal blood circulation. Joint functionality. Sedative effect. Improvement of menstrual cycle disorders.

[1] Plant species are in decreasing order of prevalence in the commercial supplements and in alphabetical suborder.
[2, 3] The plant material used and the type of the extract, only when reported in the label.
[4] Plant prevalence calculated as a percentage of commercial supplements that contain it (No./113x100).
[5] Usable, pending definitions of claims about botanicals [12]. Only physiological indications for plant materials found in the commercial supplements, are reported in the table.
[6] According to the Italian MoH, it is included as "other nutrients and other substances with a nutritional and physiological effect" [13].
[7] Marker reported in the label without its titration percentage.
[8] Synonym of the botanical name.
[9] Not determined.
[10] Plants not included in the plant list annex because authorised as novel foods according to the Regulation (EU) 2017/2470 establishing the list of novel foods, in accordance with Regulation (EU) 2015/2283 on novel foods [14].

1.4.4 *Reports from Phytovigilance*

From 01 October 2018 to 30 September 2020, 16 spontaneous reports of suspected ARs were collected by the Italian Phytovigilance System. Only 15 of them were considered because related to HDS (one contained only niacin). The frequency of reporting, in decreasing order, of each dyslipidemia-HDS is the following: Armolipid plus® (27%, n=4); Colesia oral gel® or Colesia® (27%, n=4); Calip plus®, Cardiolipid®, Berbered plus®, Midaqor®, SlimMetabol®, RYR, Colestà® (7%, n=1).

The recurrence of the plant species and isolated botanical ingredients was as follows: *Oryza sativa* fermented with *Monascus purpureus* (n=8); *Olea europea* (n=3); *Berberis aristata*, *Curcuma longa*, sterolic esters, *Haematococus pluvialis (n=2)*; others such as: *Moringa oleifera*, *Polygonum cuspidatum*, *Malus pumila*, *Saccharum officinarum*, *Punica granatum*, *Vitis vinifera*, *Citrus bergamia*, etc. (n=1).

The patients involved in the suspected ARs were 13 women and 2 men, 50-81 years aged (median age 63.35 ± 8.13). Particularly, the median age for men was 75.5 ± 5.5 years, while for women 61.3 ± 6.6 years.

Acute liver failure was reported in one case, where the death of a 71-years old woman occurred. The patient took a HDS called SlimMetabol® in concomitance with the medicine Lobivon®. The outcome of the other patients was: 6 recovers (40%), 6 in progress of recovery (40%), 1 not recovered (7%), 2 not reported (not-known) (13%). All the data refer to the moment of reporting the suspected ARs.

The ARs reported (n=33) were: asthenia (n=2); joint, abdominal, muscles pain (n=10); vomiting (n=5); nausea (n=3); erythema and haematological disorders (n=4); rhabdomyolysis (n=3); hepatitis (n=2, of which one lethal); other ARs like cramps, body weight loss, hyperkalaemia, etc. (n=11).

A "positive" dechallenge was reported in 11 cases; in the remaining reports information was not reported. Although the doses have not been reported correctly, the considered HDS appear to have been taken appropriately without any abuse. The reporters were healthcare professionals (n=10), patients (n=2) and manufacturers (n=3).

1.5 Discussion

To the best of our knowledge, this is the first study that gives an overview, although preliminary, of sales data on HDS. It is a different approach that reflects the existing market and consumer practice on dyslipidaemia-HDS, as well as the challenges to be faced by scientific authorities and regulatory agencies when dealing with the complex correlation between herbal-derived food supplements and human health.

This study describes the characteristics of commercial dyslipidaemia-HDS referring to their sales data, heterogeneity, labelling, claims, and spontaneous reports of suspected ARs.

From our data collection, a constant interest in herbal supplements for the management of metabolic syndrome was found, despite the lockdown period due to Covid-19 pandemic. The number of new formulations of dyslipidemia-HDS using various plant species has increased from one year to the other. A complexity in the formulations of the supplements marketed subsist.

The results evidence scarce standardization in terms of accuracy about plant species, plant material, type of extract, dose of extract, percentage of active ingredient. In particular, the plant material is not reported in the label of all supplements. Though the dosages are reported for all the ingredients, the standardisation lacks in a lot of dyslipidaemia-HDS; even when reported, the composition in terms of percentage of the markers (when known) is extremely variable. Moreover, some labels report the active ingredients and/or phytochemicals without their percentage (table 1, footnote 1); some others describe only the kind of phytoextract (table 1, footnote 2). We can find even the extract with the relative percentage, but missing the pharmacological marker (Arteractiva®, black pepper 95%, despite the marker of black pepper is well-known). In our study, markers of some plant extracts (i.e., *Curcuma longa*, *Camellia sinensis*, *Olea europea*) often have a unique percentage of titration instead of a range as reported in tables 1 and 2. It could be intended as a harmonised stand-

ardisation; on the other hand not all the labels report it. One supplement (Kolestina 10 complex®) has even an erratum standardisation relative to monacolin K on its label reported by the producer website. In every supplement there is at least one lacking element (the name of the species, the plant material used, the type of the extract, the percentage of the titration) that makes it difficult to evaluate the quality and therefore the safety profile of it.

There are also patented extracts (Stilvid®, Centellin®, Extramel®, Biox save®, Bergavit®) whose composition is not reported specifically either in the label or in the package leaflet or the website of the producer; this hinders the assurance of quality and a clear information for the consumers and healthcare professionals.

Two supplements (LFP colesttab® 5mg, LFP colesttab® 10 mg) are difficult to be distinguished from each other, as having the same brand name and almost the same packaging, though different dosage. Frequently, the same producer markets many dyslipidaemia-HDS differing in either one ingredient, or the dosage of a single ingredient, or the pharmaceutical form. It could be strongly indicative of the prevalence of commercial rather than health interest/goals, as neither the efficacy nor the therapeutic effect could make the difference between them. Moreover, it could mislead the consumer. A question arises spontaneously: isn't it better for a producer to have only one good-quality, standardised and fully-studied supplement, rather than having more than one with same claims but a doubtful rationale use?! It seems that "playing" with the complexity of ingredients - generally multicomponent supplements often with unpredictable effects - has become a common marketing strategy.

The websites of the producers often don't show publicly the labels. Healthcare professionals who require information must apply for registration. Considering that internet is a very important tool where the population frequently addresses its needs, a such practice does not support informed choice and consumers protection.

The MoH guidelines recommend some plant species for dyslipidaemia that are not frequent in commercial supplements or vice versa. Furthermore, some of them are not supported by scientific literature. In this context, we were faced with three different situations:

(i) plants that do not occur frequently in dyslipidaemia-HDS though having claims according Ministerial guidelines to improve the lipid profile (*L. speciosa, P. ovata, G. max, T. foenum graecum, C. mimosoides var. nomame, V. album, A. Senegal, A. microcephalus, C. pedata, L. capitata, G. sylvestre, O. ficus-indica, T. aestivum*). Scientific literature about the efficacy/safety of these botanicals is very weak. Preclinical data are often lacking and, when exist, composition and standardisation of extracts are not specified [15, 16]. Despite the beneficial effects claimed, the few clinical trials performed have several limitations that require additional randomized clinical studies [17].

(ii) plants that are quite frequent in the commercial supplements but don't have claims according to Ministerial guidelines (*C. bergamia, M. pumila cultivar. annurca, B. arvensis*). Scientific evidence is also quite inconclusive and/or insufficient [18, 19].

(iii) plants that do not have Ministerial claims specifically for dyslipidaemia. Their claims often correspond to other indications of use of a single supplement (*S. officinarum, C. longa, P. cuspidatum,*

C. sinensis, H. pluvialis, V. vinifera). These botanicals occur frequently in the dyslipidaemia-HDS as well as in scientific literature as agents for lowering plasma lipid levels, even though evidence is inconclusive and conflicting [20, 21]. Given that dyslipidaemia ranks together with diabetes, obesity, hypertension as a CVD risk factor, the effects of the above mentioned plant species could help in reducing CVD risks. Indeed, several studies confirm their anti-inflammatory, antioxidant, hypoglycaemic effects [22, 23, 24]. Nevertheless, scientific literature highlights the risk of toxicity i.e. *Camellia sinensis* [25] and *Curcuma longa* [3], in particular of extracts enriched in a specific phytoconstituent (e.g., curcumin, EGCG).

Our data suggest RYR as the most frequent botanical in dyslipidaemia-HDS and the most reported ingredient for suspected ARs, but it is also more studied in comparison to other plant species. Probably for all these reasons, it remains of higher concern for its safety profile. In different European countries like Germany, Austria, the use of HDS containing monacolin K is strongly recommended under medical supervision. In Switzerland, it is even prohibited in food supplements [26]. In its latest opinion, EFSA considers monacolin K alone of risk for human health [6]. In our study, dosages of 1.5-10 mg of monacolin K are recommended in the dyslipidaemia-HDS. Moreover, monacolin K is frequently associated with other ingredients, which have not been fully studied together. According to the Italian MoH, RYR is not included as a botanical in the plant list annex [12], whereas, monacolin K is classified as "other nutrients and other substances with a nutritional and physiological effect" [13]. In scientific literature, RYR is frequently defined, as "nutraceutical" despite this term does not appear in the legislation. It is indicative of the fact that there is no compliance between regulatory framework, market and scientific literature. The results remain difficult to be evaluated because the same plant/compound might fall in various categories such as that of novel food, botanicals, functional food, etc. Neither efficacy nor safety proofs are required. The first ones are not necessary, given that supplements could not claim any efficacy, while the safety profile is based only on the traditional use.

The coexistence of many botanical and heterogeneous non-botanical ingredients could not support the risk/benefit profile of the supplement. Scientific literature describes some combinations that are sold in the market. *B.aristata* and *S. marianum* together (Berberol®) seem a good choice because of the P-glycoprotein inhibitory effects of silymarin. As the poor oral bioavailability of berberine is due to the P-glycoprotein mediated efflux mechanism, it can be improved by silymarin. Though in meta-analysis they appear safe and well-tolerated as a combination, limited high-quality clinical studies and large patient-populations are underlined [27]. Armolipid plus®, that in our study comes out as one of the most sold supplements and most reported for suspected ARs, is also one of the most studied multi-ingredient formulations. On the contrary, it comes out as a safe alternative in improving the lipids profile in clinical practice. Systematic literature describes no increased risk of neither musculoskeletal nor gastrointestinal disorders of the multi-ingredient preparation made of berberine, policosanols, astaxanthin, monacolin, folic acid, CoQ_{10} [28]. It is therefore difficult to recommend the supplement to the consumer given the contrasting evidence. Levelipduo® a combination of red yeast rice, sterols, policosanols and niacin has undergone to a randomized, doble-blinded, placebo-controlled clinical study demonstrating a good tolerability besides the significant decrease of lipids plasma levels in mild hypercholesterolemia. However, relevant limitations regarding the number of enrolled subject, the short-term duration are underlined. It seems that the combination between RYR and phytosterols could be similar to that of statins and ezetimibe as the

mechanisms of actions are almost the same [29]. Accordingly, it would be important to further investigate its safety profile along with its efficacy. Other combinations of botanicals have been tested in clinical studies: RYR, artichoke and Banaba extract; RYR, artichoke and policosanols; RYR, policosanols and silymarin [30]. Their efficacy comes out with some positive results. Though the safety appears without concerns on the available data, the latter are not enough to draw conclusions. Almost all the combinations require long-term randomized trials, large observational cohort studies, and epidemiological studies.

Referring to the non-botanical ingredients, some of them appear to have claims substantiated by EFSA. Niacin helps the maintenance of normal LDL-C, HDL-C and TGs [31]. Folic acid can be beneficial in reducing the CVD risk because of its functional and regulatory role in the homocysteine metabolism [32]. Although the risk of toxicity seems to be quite low, long-term use of high doses could have important side effects (flushing, stomach irritation, liver toxicity). Therefore, the use should be under the control of a healthcare professional, considering all these multi-ingredient formulations that a single individual can take for health benefits. The excessive intake of trace minerals (zinc, selenium) could be harmful in the CVD prevention [33]. Therefore, the rationale of putting many ingredients together should be carefully evaluated.

All the HDS reported to the Phytovigilance were used for lowering lipid levels, except the case of death in which the supplement was taken in order to improve body weight balance, cholesterol and blood pressure. As the causality assessment was not performed, this report remains only suspect regardless the association between the supplement's intake and the AR. However, it should be noted that the suspected product consists in a complex multi-ingredient preparation (25 ingredients). This composition makes impossible the prediction of the final biological effect of the product. Furthermore, the industrial choice of such composition should be justified in detail by public scientific studies. However, to date, no clinical safety evidence is required on the composition of the finished product, to be marketed as a food supplement.

In our study, we cannot compare directly the reports for suspected ARs with the dyslipidemia-HDS sold, because Phytovigilance collects reports from all the Italian territory and our sales data concern only two pharmacies. However, exactly for this reason comes to attention a gap between the low number of reports and the wide range of dyslipidemia-HDS marketed. Hence, underreporting of suspected ARs about dyslipidaemia-HDS can be evidenced. Moreover, underreporting together with the extreme variability of commercial multi-ingredient HDS make it difficult to evaluate the impact of a single component independently. Taking into account the above safety considerations, a low awareness of the population about the safety of HDS appears obvious. Underreporting could be a signal for implementing programs of counselling and education in order to address the needs of the consumers and to protect their health. Further deeper investigation on sales data of dyslipidemia-HDS of all the Italian territory pharmacies is required.

1.6 Conclusions

Overall, our findings point out the limited compliance of commercial dyslipidaemia-HDS and scientific research about them. What is placed on the market does not match with what does exist in scientific literature, in terms of methodological issues. Lack of a similar and constant biochemical composition of HDS does not support the reproducibility of the biological and pharmacological activities. Hence, the safety cannot be assured. Unmet needs can be underlined because of the lack of concordance between the use of multi-ingredient supplements in real life and regulatory framework. It would not play therefore in favour of the safety profile of HDS.

This study could contribute to increase the importance of Phytovigilance. The risks attributed to the use of dyslipidemia-HDS should be highlighted in order to allow their rationale use, enhance their benefits and prevent alarmism related to botanicals and/or supplements containing them.

Botanicals must be, therefore, appropriately characterised and defined; accuracy and controlled information must be assured in order to provide consumers with guidance about what they purchase and consume. Analysing their label and properties that are claimed, knowledge on HDS would improve. We should never forget that supplements cannot (and must not) boast therapeutic or "miraculous" properties. Supplements can be used to maintain a physiological state of health; accordingly, they should at least guarantee their intrinsic safety.

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Chapter 2

Preliminary sales data of herbal dietary supplements used for body weight loss and pharmacists' awareness about Phytovigilance

2.1 Abstract

Overweight/obesity is a metabolic risk factor contributing to chronic diseases. To improve the body weight, individuals use herbal dietary supplements (HDS) certain of having an healthy attitude. In the light of new warnings of body weight loss-HDS containing garcinia, curcuma, and suspected adverse reactions (ARs) received by the Italian Phytovigilance System concerning them, the purpose of our study was to investigate sales data of body weight loss-HDS in territorial pharmacies, in order to enlarge the entire safety perspective of what is placed on the market. A questionnaire about Phytovigilance addressed to pharmacies explored the awareness of pharmacists about the safety of botanicals.

Hence, sales data of body weight loss-HDS were monitored from October 2018 to September 2020 in two pharmacies of Rome. A survey about Phytovigilance was addressed to community pharmacies of the Lazio region. Overall, the sales of both pharmacies point out that 9% of the HDS sold claim body weight loss; they consist in 122 brands. Among them 76% are multi-ingredient with up to 29 different components. Moreover, 158 plant species with either variable or missing standardisation and 49 non-botanical ingredients are clustered.

In conclusion, given the (i) variety of formulations mostly multi-ingredient without a rationale of use, (ii) the wide range of plant species not strictly claimed for the management of body weight and its burdens, (iii) variable standardisation and/or incomplete label's information of botanicals, (iv) low adherence of pharmacies to report suspected ARs, highlight safety profile uncertainties of body weight loss-HDS. Future efforts involving sales data of all territorial pharmacies, other categories of HDS, and promotion of Phytovigilance are required.

2.2 Introduction

Overweight/obesity jointly to hyperglycaemia, raised blood pressure and hyperlipidaemia are metabolic risk factors that contribute to chronic diseases, such as cardiovascular diseases, diabetes, cancer, and mortality. The global epidemic of overweight/obesity continues its rise affecting about 30% of the world population on both developed and developing countries [1]. Body mass index (BMI) still remains the main parameter for assessing it. Environmental pollutants, extreme level of socioeconomic disparity and genetic/epigenetic susceptibility have led to reduced physical activity, increase of sedentary lifestyle, promotion of low-cost fast foods, low adherence to health-support interventions which are the basis of a high incidence and prevalence of overweight/obesity.

Pathophysiologic mechanisms consist basically in imbalance of calorie intake and energy expenditure. Central homeostatic factors involve hypothalamus- and brain stem-originating circuits, while the peripheral ones include gut-originating signals of satiety and hunger, and adiposity signals of adipocytes and pancreatic β-cells. Moreover, eating behaviour is regulated also by the non-homeostatic system consisting in a reward mechanism circuit of brain, originating on food palatability [2].

Being a multifactorial disease, the targets for prevention and treatment are multiple. However, pharmacotherapy of obesity has still less options respect other chronic diseases. So far, orlistat, naltrexone/bupropion and liraglutide are the anti-obesity drugs approved for long-term use by both Food and Drug Administration (FDA) and European Medicines Agency (EMA). Phentermine/topiramate is approved only by FDA and included as a drug enforcement administration (DEA) controlled substance due to the phentermine. Lorcaserin that had only FDA approval and never from the EMA, was withdrawn in 2020 because of the increase risk of cancer [3]. It is the most recent case of market withdrawal, that has followed numerous previous drugs with cardiovascular severe adverse effects like fenfluramine, sibutramine, dexfenfluramine, etc. Given that pharmacotherapy lacks yet of a long-term safety, of a low-cost of use and willingness of a lifelong management, life style changes consisting in healthy eating, physical activity and behavioural modification constitute the most safe basis to sustain body weight reduction. In the context of a modern world, reluctant individuals of developed countries search for fast and alternative options. Moreover, overweight and leanness are considered often a fashion and esthetical issue rather than a health related hazard. Thus, in order to improve the body weight, individuals search for self-medication supplements certain of having an healthy attitude. Accordingly, other scenarios of public health that concern the use of HDS appear.

Supplements containing botanicals are placed on the market following the regulations of food supplements. Unlike vitamins and minerals which are well defined and regulated, the state-of-the-art regarding botanicals lies in the so called “grey area” which is characterised by a series of safety critical aspects. On one hand, various definitions include them such as food supplements, functional foods, nutraceuticals, phytochemicals, novel foods, etc. Innumerable market sources i.e. grocery stores, websites, organic & natural retailers, etc. can supply them without a professional counselling, approaching all the population subgroups as multimorbidity patients, pregnant and breastfeeding women, elderly people. A profuse economic value outlines a flourishing market [4]. On the oth-

er hand, despite the increasing popularity, the safety issues are still uncontextualized as they continue to be embedded in the traditional use and don't undergo to robust clinical assessments.

Sliding from a global framework to a preliminary Italian perspective, the following representative background describes the topic. In the past years, in the context of HDS, several regulatory revisions have been made by the Italian Ministry of Health (MoH) based on new scientific evidence. The latest regard mandatory warnings to be stated on the labels of supplements containing garcinia and curcuma. Annex I of the Ministerial Decree of 10 August 2018 [5], containing the list of plants and their materials allowed for use with relative physiological functions [6], was updated with the Directorial Decree of 4 August 2021 [7]. MoH removed the physiological functions recommended for *Garcinia gummi-gutta* (L.) Roxb. Now, its supplements must state on the label to interrupt the use in case of arising disorders as of either hepatic or central nervous dysfunctions, and to seek medical advice. The Directorial decree of 26 July 2019 decided to regulate the labels of supplements containing *Curcuma longa* L. with a specific warning [8]. According to it, the use of these supplements is not recommended in case of either alterations of hepatic or biliary functions, or gallstones of the biliary tract. Moreover, in case of concomitant pharmacotherapies, medical advice should be sought. A less recent regulation of 18 July 2002 [9], that if added to the latest increases the safety concerns, includes warnings that must be stated on the supplements containing bitter orange. Supplements with *Citrus aurantium* var. *amara* L. must indicate on the label the titration in synephrine with a limit of 30 mg/die which correspond to ~800 mg of *C. aurantium* standardised in 4% of synephrine. An additional warning does not recommend the use during pregnancy, breastfeeding and under 12 years of age; in case of altered cardiovascular conditions, it is advised to consult the doctor before use. What these botanicals have in common, is the use for body weight loss.

HDS with this claim have been in the focus of the Italian Phytovigilance System, as one of the most concerned category for suspected adverse reactions (ARs). The latest involve the cardiovascular, central nervous, gastrointestinal, cutaneous and other various systems [10]. Despite the limitations due to the lack of a post-marketing surveillance for the "natural products", the causality assessment of spontaneous reporting has judged as possible the association between the product intake and the adverse reactions in most of the cases [11]. However, sales data of HDS with specific claims are not available. Thus, reporting rates and safety profile of what is placed on the market can't be estimated.

The aim of the study was to monitor sales data of HDS with a specific claim in territorial pharmacies, in order to enlarge the entire perspective of the safety of these supplements; for the reasons described above, the focus encompassed body weight loss-HDS. Moreover, a questionnaire about Phytovigilance was addressed to pharmacies, to explore the awareness of healthcare professionals about the safety of botanicals. Hence, in this preliminary descriptive analysis of sales, we may understand if the safety could be guaranteed.

2.3 Materials and Methods

2.3.1 *Definition of dietary supplements, HDS and body weight loss-HDS*

The methodology is described previously in chapter 1. Nevertheless, below, the procedure is reported again. In our study, we take into account body weight loss-HDS, which refer to HDS, having claims for improving the body weight balance, according to the manufacturer labelling. As dietary

supplements include all food supplements containing vitamins, minerals, amino acids, essential fatty acids, botanicals [12], HDS include food supplements having at least one botanical ingredient.

2.3.2 *Data collection*

Sales data of dietary supplements were monitored for two years, in two pharmacies of Rome. The period of data collection was from October 2018 to September 2020. The sites of pharmacy 1 and pharmacy 2 are respectively in the historic center of Rome and in a residential area.

From each pharmacy, an inventory document with brand names and quantity of dietary supplements was provided through Wingesfar® software. The study considered only data of HDS, having health claims related to body weight loss.

A survey about Phytovigilance was addressed to community pharmacies of the Lazio region. The questionnaire was created *ad hoc* through *Google forms*. Then, it was forwarded via *WhatsApp* to pharmacists associated to "Mondo Farmacia" in August 2020 remaining available for one month. The "Mondo Farmacia" is an association of community pharmacists operating in Rome, Lazio. The questionnaire is made up of nine questions as reported in figure 2.1.

2.3.3 *Data preparation and descriptive analysis*

The data assembly consisted in the creation of a dossier through Microsoft excel. Every month, up-to-date information of each pharmacy regarding sales of dietary supplements, HDS and body weight loss-HDS was recorded and analyzed. Next, their trend of sales, for each year were implemented and compared between each other. The period from October 2018 to September 2019 was considered as the first year, while that of October 2019-September 2020 as the second one.

Analyses of the number of sales, composition (as described on the label) and claims were performed for each body weight loss-HDS. The labels and claims were collected conducting an online research. Using the brand name as a keyword, the sources involved were either the manufacturer website or, if not available, other websites randomly selected.

Descriptive statistics of the composition of each body weight loss-HDS summarize the data in terms of absolute and percentage frequencies. In specific, characteristics of the number and type (botanical and non-botanical) of the ingredients are described. Plant species which occur in the body weight loss-HDS are clustered, and their plant materials, type of extracts and standardisation are estimated. As stated by the guidelines of Italian MoH, Annex 1 [6], which advise the use of botanicals in the context of homeostasis model defined by the Council of Europe, given that definitions of claims about botanicals are pending, physiological functions of our plant materials are examined. The occurrence of additional (non-botanical) ingredients like vitamins, coenzymes, amino acids, probiotics, etc., is also recorded. Plant species and supplements are interfaced with scientific literature data for their biological effects claimed.

Relating to the questionnaire, a statistical description was also performed for each question taking into account that not all the respondents answered to all of them.

Figure 2.1. Questionnaire addressed to the pharmacies.

(A) Closed questions	Answers
1. Do you know Phytovigilance?	Yes/No
2. Do you know Vigierbe?	Yes/No
3. Have you received last year reports of suspected ARs of HDS?	Yes/No
4. Have you received last year reports of suspected ARs of HDS used for body weight loss?	Yes/No
5. Have you received last year reports of suspected ARs of HDS used for dyslipidaemia?	Yes/No
6. If you answered "yes" at least to one of the last three questions, did you send the report?	Yes/No
(B) Single-answer multiple choice question	**Answers**
7. If you answered that you didn't send the report, which is the reason that you didn't do it?	○ I didn't know I had to send the report ○ I knew I had to send the report but I didn't know how to do it ○ I had no time to send the report ○ I didn't consider important what was reported to me for the purposes of the surveillance
(C) Open-ended questions	**Answers**
8. Specify the names of the supplements being eventually subject of reporting. 9. Specify the suspected ARs eventually received.	

Origin: Google forms. Previously validated questionnaire.

2.4 Results

2.4.1 Sales Data

Overall, the sales of both pharmacies point out 1915 body weight loss-HDS after two years monitoring. They represent 9% of the HDS (21484) sold. Table 2.1 reports the sales of each year, for each pharmacy (see also appendix). Monthly trend sales of body weight loss-HDS are reported in figure 2.2.

Table 2.1. Cumulative sales data reported annually.

	1° year			2° year		
	Dietary supplements	HDS	Body weight loss-HDS	Dietary supplements	HDS	Body weight loss-HDS
Pharmacy 1	8283	3449 (42%)	335 (10%)	8379	3610 (43%)	291 (8%)
Pharmacy 2	13892	7626 (55%)	623 (8%)	12242	6799 (56%)	666 (10%)

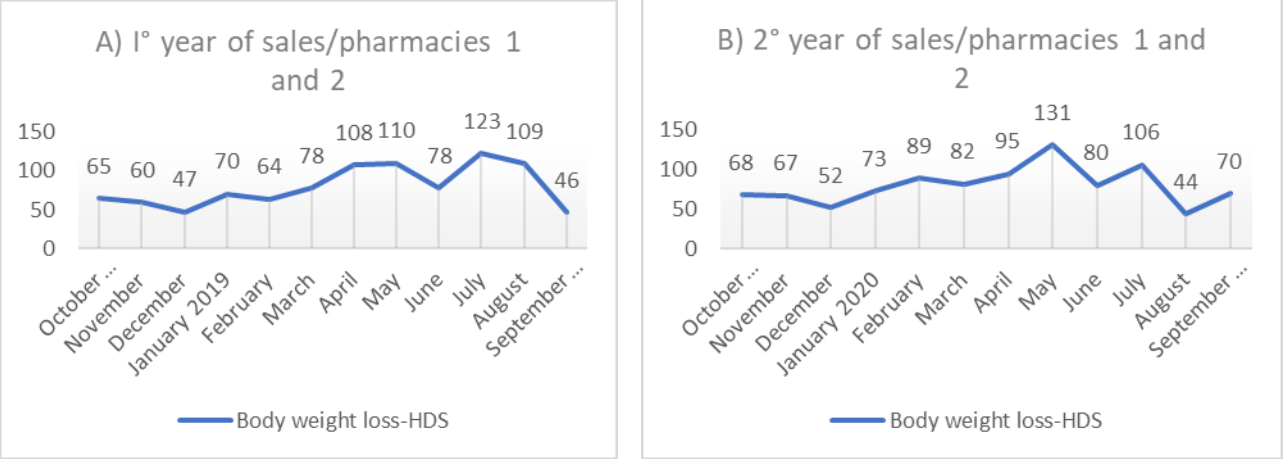

Figure 2.2. Sales of body weight loss-HDS from both pharmacies during the first (A) and second year (B).

2.4.2 Description of body weight loss-HDS

From our results come out 122 brands of HDS sold, with claims for the body weight loss. Among them, 24% (n=29) have a single ingredient composition and 76% (n=93) are multi-ingredient. In the same supplement, up to 29 different ingredients between botanicals and additional non-botanicals are found. Table 2.2 reports the formulations of the body weight loss-HDS sold in both pharmacies, listed in alphabetical order. Likewise, the sales for each entry and the relative number of ingredients (botanical and non-botanical) are documented. The phytochemical composition is reported without vehicles and with daily doses if indicated in the label.

Table 2.2. Body weight loss herbal dietary supplements sold during the study.

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Adipecal® 30 tablets, Fitobios	Cola (*Cola nitida* Schott et Endl.) seeds dry extract (10% of caffeine); Greenselect® Phytosome®-green tea leaves (*Camellia sinensis* L. Kuntze) dry extract (22% of catechins and 13% of EGCG); green coffee (*Coffea arabica* L.) seeds dry extract (45% of chlorogenic acid); Wakame seaweed thallus (*Undaria pinnatifida* Harvey Suringar) dry extract (10% of fucoxanthin); red pepper (*Capsicum annuum* var. *grossum* L. Sendtn.) fruit dry extract (2.5% of capsaicin); vitamin B_6 (33% of pyridoxine chloride), chromium picolinate	7
4	Adipesina Plus dietalinea® 30 tablets, General Dietetics Pharma S.r.l.	LeptiCore® 200 mg-Guar (*Cyamopsis tetragonoloba* L. Taub.) seeds dry extract; carob tree (*Ceratonia siliqua* L.) fruit dry extract; Arabic gum (*Acacia nilotica* Willd Ex Del.) gum; pomegranate (*Punica granatum* L.) fruit dry extract; Klamath algae (*Aphanizomenon flos aquae*) thallus dry extract; Alga Wakame seaweed (*Undaria pinnatifida* Harvey, Suringar) thallus dry extract 100 mg (10% of fucoxanthin, 10 mg); Java tea (*Orthosiphon stamineus* Benth) leaves dry extract 100 mg (0.1% of sinensetin); Guarana (*Paullinia cupana* H.S.K.) seeds dry extract 100 mg (15% of caffeine); Garcinia (*Garcinia cambogia* Gaernt Desr.) fruit dry extract 60 mg (50% of hydroxycitric acid)	9
1	AdipeZaffer dietalinea® 32 tablets, General Dietetics Pharma S.r.l.	Bitter orange (*Citrus aurantium* L. var. bitter) unripe fruit 300 mg (10% of synephrine, 30 mg); Satiereal®-saffron (*Crocus sativus* L) stigmas extract, 176.5 mg; griffonia (*Griffonia simplicifolia* D.C. Baill.) seeds dry extract 102 mg (98% of 5-hydroxytryptophan, 100 mg); chromium picolinate 100mcg	4
10	Adiprox Advanced® 50 tablets, Aboca	AdiProFen MS®-lyophilized coextract, 573 mg (11.5% of cyanidin chloride, 66 mg and 4.2% of silymarin, 24 mg) made of: green tea (*Camellia sinensis*) leaves and grape (*Vitis vinifera*) seeds 300 mg; yerba mate (*Ilex paraguariensis*) leaves lyophilized extract, 182 mg; milk thistle (*Silybum marianum*) fruit powder, 176 mg and fruit pericarp lyophilized extract, 91 mg; green tea leaves powder 463 mg; elderflower (*Sambucus nigra*) concentrated fruit juice. Presence of caffeine 34.6 mg	5

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Adiprox Fitomagra® 20 sachets herbal tea, Aboca	Roselle (*Hibiscus sabdariffa*) flowers, 560 mg; liquorice (*Glycyrrhiza glabra*) root, green tea (*Camellia sinensis*) leaves, 400 mg (6% of epigallocatechin gallate and 3% of caffeine); dandelion (*Taraxacum officinale*) root, 320 mg; grape (*Vitis vinifera*) seeds, 200 mg; AdiProFen®-lyophilized coextract: of green tea (*Camellia sinensis*) leaves and grape (*Vitis vinifera*) seeds (20% of gallic acid and 22% of cyanidin chloride. Presence of caffeine 13.9 mg	5
1	Agamorin plus® 20 sachets, Promopharma	AMLF Complex® 8.7 g-Inulin (*Agave tequilana* F.A.C. Weber); fructo-oligosaccharides (FOS); moringa (*Moringa oleifera* Lam.) seeds dry extract (40% of polysaccharides and 10% of glycosides) and leaves dry extract E:D=1:4; hydrolysed milk proteins	3
19	Algocur® 20 tablets, Pharmextracta	Curcumin phytosome®, 1000 mg (*Curcuma longa* L. extract); *Piper nigrum* L. dry extract, 10 mg (95% of piperine)	2
6	Almetax easy® 30 sachets, Kolinpharma	CurQfen®-*Curcuma longa* L. rhizome dry extract, 140 mg (35% of curcuminoids, 49 mg) and *Trigonella foenum graecum*) seeds 42 mg; L-tryptophan 150 mg; alpha lipoic acid 313 mg; zinc 3 mg; chromium 50 mcg; vitamin C 125 mg; vitamin B_5 9 mg; vitamin B_6 2.375 mg	9
2	Aloe 100% & Caffè verde® 1 liter, Pharmalife research	*Aloe vera* juice dry extract (*Aloe barbadensis*) 200:1, 610 mg; green coffee (*Coffea arabica*) dry extract 480 mg (Caffeine <5%, 24 mg)	2
1	Aloe 100% & Garcinia® 1 liter, Pharmalife research	Garcinia fruit dry extract 1200 mg (*Garcinia cambogia*) (60% of hydroxycitric acid, 720 mg); Aloe vera juice dry extract (*Aloe barbadensis*) 200:1, 610 mg	2
1	Anadepis® 30 tablets, Cortex Italia S.r.l.	Garcinia (*Garcinia cambogia* Gaernt. Desr.) fruit dry extract 1200 mg (60% of hydroxycitric acid, 720 mg); cactus pear (*Opuntia ficus-indica* Mill.) cladodes powder 390 mg; Coleus (*Plectranthus barbatus* Andrews) root dry extract 240 mg (10% of forskolin, 24 mg); horsetail (*Equisetum arvense* L.) aerial parts dry extract 180 mg (2.5% of silicon, 4.5 mg); Betulla (*Betula pubescens* Ehrh) leaves dry extract 150 mg (2.5% of hyperoside, 3.75 mg); milk thistle (*Silybum marianum* Gaertn.) fruit dry extract 150 mg (80% of silymarin, 120 mg); tomato (*Solanum lycopersicum* L.) fruit dry extract 150 mg (5% of lycopene, 7.5 mg); red yeast rice (with *Monascus purpureus*) dry extract 150 mg (5% of monacolin K, 7.5 mg); dandelion (*Taraxacum officinale* Weber) root dry extract 90 mg (2% of inulin, 1.8 mg)	9

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
3	Arkocapsule ananas® 45 tablets, Arkopharma Laboratoires	Pineapple stalk powder (*Ananas comosus* (l.) Merr.) 975 mg, enriched with pineapple bromelain, 6.3 mg	1
4	Androhelp® 60 tablets, OTI	Guar (Cyamopsis tetragonoloba Taub.) seeds powder 300 mg; *Berberis aristata* DC. bark dry extract (98% of berberine, 294 mg); curcuma (*Curcuma longa* L.) rhizome dry extract (95% of curcumin, 285 mg); banaba (*Lagerstroemia speciosa* Pers.) leaves dry extract 150 mg (1% of corosolic acid, 1.5 mg)	4
6	Aros® 60 tablets, Carofarma S.r.l.	pomegranate 200 mg (ellagic acid 40 mg); green tea 200 mg (EGCG 160 mg); garcinia 70 mg (mangostin 28 mg); curcuma 70 mg (curcuminoids 14 mg); polygonum 24 mg (resveratrol 22 mg)	5
1	Bean forte® 30 tablets, Named	Faseomin Max® (*Phaseolus vulgaris*-bean protein concentrate); fennel dry extract; vitamin B_6; vitamin B_1; chromium; *Cassia mimosoides nomame* dry extract (8% of dimer flavans)	6
74	Benefibra® 12 sachets, liquid, powder, Novartis	Fibre-partially hydrolysed guar gum (PHGG) 5g	1
3	Bruciadren fast® 20 tablets, Fitopreparatori italiani	Tamarindus (*Tamarindus indica* L.) fruit dry extract 500 mg (5% of tartaric acid, 25 mg); nopal (*Opuntia ficus-indica* Mill.) cladode powder 400 mg; 3orthoDREN® (*Orthosiphon stamineus* Benth) leaves dry extract 300 mg (0.03% of sinensetin, 0.09 mg and 0.5% of rosmarinic acid, 1.5 mg); ginger (*Zingiber officinale* Roscoe) rhizome dry extract 100 mg (5% of total gingerols, 5 mg)	4
2	Brucia fat 30® tablets, Fitopreparatori italiani (BioDue S.p.a.)	Mixture ADIECG®: *Cassia nomame* dry extract 600 mg (8% of catechins, 48 mg); Tamarindus dry extract 500 mg (5% of tartaric acid, 25 mg); green tea dry extract 320 mg (40% of epigallocatechin gallate, 120 mg); caffeine max 1.28 mg	3
32	Cadicioc® dark chocolate, Cadigroup	Glucomannan (soluble fibres) and cacao (insoluble fibres)	2

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
4	Cartijoint slim® 32 tablets, Fidia	Glucosamine hydrochloride 500 mg; chondroitin sulphate 400 mg; ID-alG® 400 mg: mixture of brown seaweed (*Ascophyllum nodosum* De Jolis.) thallus and grape (*Vitis vinifera* L.) seeds dry extract (35% of tannins-phloroglucinol); griffonia (*Griffonia simplicifolia* DC Baill.) seeds dry extract 306 mg (98% of 5-HTP); bitter orange (*Citrus aurantium* L. subsp. amara) unripe fruit dry extract 300 mg (10% of synephrine (octopamine/synephrine <1/8); vitamin C (L-ascorbic acid) 200 mg	7
1	Citrus® 45 tablets, Arkopharma Laboratoires	Bitter orange (*Citrus aurantium* L.) unripe fruit dry extract 166 mg (6% of synephrine, 10 mg)	1
1	Clinnix Slim® 48 tablets, Abbate Gualtiero S.r.l.	Vitamin C; *Centella asiatica* dry extract; vitamin E; bioflavonoids; pineapple juice and stalk dry extract; restharrow (*Ononis spp.*) root dry extract; orthosiphon leaves dry extract; bilberry fruit dry extract	8
43	Cruscasohn® 20 sachets, 100 tablets, Marco Antonetto Farmaceutici	Wheat *(Triticum spp.*); psyllium (*Plantago ovata*) husk	2
26	Curcuma Gold® 30 tablets, Fitopreparatori italiani	Curcuma Fitosoma® (*Curcuma longa* L.) rhizome dry extract 1000 mg (20% of curcuminoids, 200 mg); ginger (*Zingiber officinale* Roscoe) rhizome dry extract 200 mg (5% of gingerols, 10 mg)	2
9	Curcuma+Piperina® 45 tablets, Arkopharma laboratoires	Curcuma (*Curcuma longa* L.) rhizome powder (560 mg) and dry extract 108 mg (curcumin 103 mg); black pepper fruit dry extract (*Piper nigrum* L.) 16 mg (piperine 15 mg)	2
12	Curcumin® gel sachets, BioenergeticLab	HGC-C® (Hydro Gel Complex-C)-two *Curcuma longa* rhizome dry extracts (45% of curcuminoids and 25% of curcuminoids)	1
1	Curcumina redox® 30 tablets, Solgar	Full Spectrum Curcumin NovaSOL®- *Curcuma longa* L. rhizome extract 800 mg (total curcuminoids 48 mg and curcumin 40 mg)	1
2	Curmax-500® 30 tablets, Biotema	Meriva®-curcuma (*Curcuma longa* L.) phospholipid rhizome dry extract (18% of curcuminoids)	1
2	Dicoplus 100® 60 tablets, AGpharma	Glucomannan 3 g	1
9	Dimalosio complex® 20 sachets, Alcka-Med S.r.l.	Psyllium (*Plantago ovata*) husk; glucomannan; senna (*Cassia angustifoglia*) leaves dry extract 90 mg (20% of sennosides, 18 mg); lactulose 1.92 mg	4

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Dimasal® 60 tablets, Salugea	SelectSIEVE®-rainbow dry extract 300 mg (50% of catechins, 150 mg and 5% of anthocyanins, 15 mg): black rice (*Oryza sativa* L.) seeds, Kiwi (*Actinidia chinensis* Planch.) fruit, red orange (*Citrus sinensis* L. Osbeck. fruit, Ananas (*Ananas comosus* L. Merr.) stalk; Cassia nomame (*Chamaecrista nomame* Sieber, H. Ohashi) leaves and fruits dry extract 200 mg (8% of catechins, 16 mg); Satiereal®-saffron (*Crocus sativus* L.) stigma dry extract 180 mg (0.34% safranal, 0.6 mg); Dermogranate®-pomegranate (*Punica granatum* L.) fruit dry extract 120 mg (20% of polyphenols, 24 mg; 10% of ellagic acid, 12 mg; 7% of punicalagin, 8 mg); green tea (*Camellia sinensis* L. Kuntze) leaves dry extract 100 mg (50% of polyphenols, 50 mg and 30% of catechins, 30 mg)	8
1	Diuresan formula potenziata® 60 tablets, Salugea	Pilosella (*Hieracium pilosella* L.) herb dry extract (1% of vitexin); Betula (*Betula pubescens* Ehrh.) leaves dry extract (2.5% of hyperoside); Orthosiphon (*Orthosiphon stamineus* Benth) leaves dry extract (0.2% of sinensetin), Ash tree (*Fraxinus excelsior* L.) leaves dry extract (2% of chlorogenic acid); Roselle (*Hibiscus sabdariffa* L.) flowers dry extract (2% of anthocyanins)	5
1	Diur Mech® 500 ml, Gianluca Mech	Aqueous extract of bitter herbs 70%: equisetum (*Equisetum arvense* L.) herb; asparagus (*Asparagus officinalis* L.) root; betula (*Betula pendula* Roth.) leaves; cypress (*Cupressus sempervirens* L.) berries; quackgrass (*Agropyron repens* L. P. Beauv.) rhizome; corn (*Zea mays* L.) stigmas; dandelion (*Taraxacum officinale* L. Weber ex F.H.Wigg.) root; bearberry (*Arctostaphylos uva ursi* L. Spreng.) leaves; fennel (*Foeniculum vulgare* Mill.) fruit; elderflower (*Sambucus nigra* L.) flower; roselle (*Hibiscus sabdariffa* L.) flower; anise (*Pimpinella anisum* L.) fruit	12
31	Drena sel forte® 300 ml, 20 sachets, Fitopreparatori Italiani	Dandelion dry extract 500 mg (2% of inulin, 10 mg); betula dry extract 500 mg (2.5% of hyperoside, 12.5%); fennel dry extract 250 mg (0.9-1.1% of essential oil, 2.5 mg); 3orthoDREN® 300 mg (0.03% of sinensetin, 0.09 mg and 0.5% of rosmarinic 1.5 mg); Spirulina algae 50 mg	5

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
46	Drena sel active® tea/peach 500 ml, Fitopreparatori italiani	Bitter orange (*Citrus aurantium* spp. amara) unripe fruit dry extract 300 mg (min. 6% of synephrine, 18 mg); Betula leaves dry extract 250 mg (min. 2.5% of hyperoside); dandelion root dry extract 250 mg (2% of inulin); Pilosella aerial parts dry extract 250 mg (min 0.5% of vitexin); pineapple stalk dry extract (min 250 GDU/g of bromelain); Spirulina algae powder, 50 mg; Gymnema (*Gymnema sylvestre*) leaves dry extract 41.7 mg (min 25% of gymnemic acid)	7
5	Drenanten® 48 tablets, Homeosyn Italia	*Equisetum arvense* herb dry extract 460 mg (2-3% of silicon); *Orthopsihon stamineus* leaves dry extract 300 mg (0.2% of sinensetin); *Urtica dioica* L. root dry extract 300 mg (0.8% of beta-sitosterols; *Crataegus monogyna* Jac. flowers and leaves dry extract 240 mg (1% of total flavonoids); *Silybum marianum* Gartner seeds dry extract 160 mg (80% of silymarin); *Undaria pinnatifida* whole plant 120 mg (10% of fucoxanthin); chromium 60 mcg	7
2	Drenax forte® bilberry 750 ml, Paladinpharma	Aloe vera and bilberry juice; rutin; Orthosiphon; Betula; *Centella asiatica*; *Silybum marianum*; grape; *Ribes nigrum*; artichoke; green tea; curcuma; roundhead lespedeza	12
2	Drenaxil® 500 ml, Biofarmex	Cherry (*Prunus spp.*) dry extract, 612 mg; Orthosiphon dry extract, 408 mg (sinensetin, 0.816 mg); pineapple dry extract, 326 mg (bromelain 16.3 mg); Betula dry extract, 326 mg (hyperosine 9.78 mg); corn dry extract, 204 mg; juniper dry extract, 204 mg; restharrow dry extract, 204 mg; quackgrass dry extract, 204 mg; bearberry dry extract, 164 mg (arbutin 16.4 mg); elderflower dry extract, 164 mg (anthocyanidins 16.4 mg); green tea dry extract, 164 mg (caffeine 8.2 mg)	11
70	Dren diet® bar, Fitobios S.r.l.	Potato proteins; rice proteins; pea proteins; *Betula pendula* leaves dry extract (2.5% of hyperoside); *Ananas sativus* stalk powder (250 GDU/g); *Equisetum arvense* aerial parts (1% of silicon); puffed rice (0.75%); niacin hydrochloride (vitamin B_3); calcium d-pantothenate (vitamin B_5); riboflavin (vitamin B_2); pyridoxine hydrochloride (vitamin B_6); thiamine hydrochloride (vitamin B_1); cyanocobalamin (vitamin B_{12})	12

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
4	Dren Gheos funzionale® 20 sachets, Gheos S.r.l.	Equisetum (*Equisetum arvense* L.) aerial parts dry extract, 150 mg (1% of organic silicon); polyporus (*Polyporus umbellatus* Pers. Fr.) sporophore powder, 200 mg; asparagus (*Asparagus officinalis* L.) root dry extract 4:1, 100 mg; Java tea (*Orthosiphon stamineus* Benth) leaves dry extract 100 mg (0.2% of sinensetin); green tea (*Camellia sinensis* L. Kuntze) leaves dry extract, 100 mg (95% of polyphenols); Betula (*Betula pendula* Roth.) leaves dry extract, 100 mg (2.5% of hyperoside); Pilosella (*Hieracium pilosella* L.) aerial parts dry extract, 100 mg (1% of vitexin); artichoke (*Cynara scolymus* L.) leaves dry extract, 50 mg (5% of chlorogenic acid); burdock (*Arctium lappa* L.) root dry extract 50 mg (20% of inulin); green coffee (*Coffea arabica* L.) seeds dry extract 50 mg (45% of chlorogenic acid); dandelion (*Taraxacum officinalis* Weber) leaves dry extract 25 mg (20% of inulin); acai (*Euterpe oleracea* Mart.) fruits dry extract 4:1, 25 mg	12
2	Drops® drops 50 ml, Named	Fucus thallus aqueous extract 135 mg; Centella aerial parts aqueous extract 135 mg; Pilosella aerial parts aqueous extract 90 mg; Fraxinus leaves aqueous extract 90 mg	4
32	Ecamannan® 36 tablets, powder Cadigroup	Glucomannan (*Amorphophallus konjac* K. Koch) tuber powder 3 g	1
2	Endothyr® 50 tablets, Endocell	Seaweed (*Fucus vesiculosus* L.) thallus dry extract, 400 mg (0.05% of iodine, 200 mcg); selenium methionine 45 mcg; vitamin B_6 1.4 mg; vitamin B_2 1.4 mg	4
8	Enervit power time® peanuts/berries bar, Enervit	peanuts (45%); chopped almonds (12%); Pistachio (6.5%); sweetened cranberries (6%)-cranberries on the bar (3.6%); sweetened blueberries (3%)-blueberries on the bar (2,3%); sesame seeds; rice flakes (rice flour); L-ascorbic acid; D-alfa-tocopherol acetate; nicotinamide; pyridoxine hydrochloride; thiamine hydrochloride	12
1	Enerzona snack super fruit® bar, Enervit	Soy flakes (26.4%); dark chocolate (14%); chopped pomegranate (8.4%); puffed brown rice grain (4.1%); corn flakes (4.1%); oat flakes (3.4%); acacia fiber (1.4%)	7
3	Epaepa® 42 tablets, Natural Bradel	Curcuma Fitosoma®, 800 mg (*Curcuma longa* L.) rhizome dry extract, 160 mg (95% of curcuminoids); black pepper (Piper nigrum L.) fruit dry extract, 8.4 mg (95% of piperine)	2

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Epakur advanced® 50 tablets, Aboca	Neocuphenyl®- (1.23% of rosmarinic acid and 1.20% of hyperoside): artichoke (*Cynara scolymus*) leaves lyophilized extract, 83 mg; rosemary (*Rosmarinus officinalis*) leaves lyophilized extract, 75 mg; yerba mate (*Ilex paraguariensis*) leaves lyophilized extract, 43 mg; hawthorn (*Crataegus monogyna*) flowers lyophilized extract, 41 mg; (caffeine, 2.25 mg)	4
1	Epavin® 50 ml, Erbe Nobili	hydroalcoholic extracts (20% of the plant material): dandelion (*Taraxacum officinale* Web.) root; milk thistle (*Silybum marianum* L. Gaertn.) fruit; artichoke (*Cynara scolymus* L.) leaves; barberry (*Berberis vulgaris* L.) leaves; boldo (*Peumus boldus* Mol.) leaves; radish (*Raphanus sativus* L.) root; chinese rhubarb (*Rheum palmatum* L.) root; chrysantemum (*Chrysanthemum americanum* V.) aerial parts; curcuma (*Curcuma longa* L.) rhizome; kinkeliba (*Combretum micranthum* G. Don.) leaves; peppermint (*Mentha piperita* L.) essential oil; rosemary (*Rosmarinus officinalis* L.) essential oil	12
1	Fame sel® 300 ml, Fitopreparatori italiani	Griffonia soft extract, 800 mg (min. 12% of 5-HTP, 96 mg); banaba dry extract, 150 mg (min. 1% of corosolic acid); gymnema dry extract, 100 mg (min. 25% of gymnemic acid); cinnamon dry extract E/PM 1:4, 50 mg	4
1	Fast drena® 500 ml, Equilibra	Asparagus (*Asparagus officinalis* L.) root fluid extract, 120 mg; burdock (*Arctium Lappa* L.) root fluid extract, 120 mg; boldo (*Peumus boldus* Molina) leaves fluid extract, 120 mg; artichoke (*Cynara scolymus* L.) leaves fluid extract, 120 mg; milk thistle (*Silybum marianum* L. Gaertn.) fruits fluid extract, 120 mg; curcuma (*Curcuma longa* L.) rhizome fluid extract, 120 mg; blackcurrants (*Ribes nigrum* L.) leaves fluid extract, 120 mg; dandelion (*Taraxacum officinale* L. Weber ex. F.H. Wigg.) root fluid extract, 120 mg	8
1	Fibermet® 20 sachets, Pharmextracta	Psyllium 1500 mg; phytosterols 1500 mg; glucomannan 1500 mg; guar gum 500 mg; chromium 40 mcg	5

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Fisiodiur start up® 300 ml, Zuccari	Date palm concentrated juice (*Phoenix dactylifera* L.) fruit; prune concentrated juice (*Prunus domestica* L.) fruit; pilosella (*Hieracium pilosella* L.) whole plant dry extract; betula (*Betula pubescens* Ehrh.) leaves dry extract; quackgrass (*Agropyron repens* P. de Beauvois) rhizome dry extract; orthosiphon (*Orthosiphon stamineus* Benth) leaves dry extract; tamarind (*Tamarindus indica* L.) concentrated fruit juice; dandelion (*Taraxacum officinale* Weber) root dry extract; goldenrod (*Solidago virga-aurea* L.) aerial parts dry extract; equisetum (*Equisetum arvense* L.) aerial parts dry extract; ginkgo (*Ginkgo biloba* L.) leaves dry extract; magnesium gluconate; potassium chloride; sweet clover (*Melilotus officinalis* Pallas) leaves dry extract	14
3	Fisiodren® 240 ml, Laboratori Legren	Betula lymph glycerine macerate 0.50 g; dandelion root dry extract, 0.37 g (5% of inulin); milk thistle fruit dry extract, 0.25 g (65% of silymarin); pilosella flowers dry extract, 0.25 g (0.4% of vitexin); restharrow root dry extract 0.25 g; Phyllanthus flowers and leaves dry extract 0.17 g; roundhead lespedeza leaves dry extract, 0.12 g (4% of rutin); fumitory (*Fumaria spp.*) aerial parts dry extract 0.075 g	8
4	Fitobiogum diet® 24 chewing gum, Fitobios S.r.l.	Griffonia (*Griffonia simplicifolia* DC. Baill.) seeds dry extract (25% of 5-HTP); garcinia (*Garcinia cambogia* Gaernt. Desr.) fruits dry extract (60% of hydroxycitric acid)	2
1	Fitocurcuma® 60 tablets, Solgar	Curcuma (*Curcuma longa* L.) rhizome extract, 400 mg (93% of curcuminoids)	1
4	Fitomagra drena plus ® tea 20 sachets, Aboca	Orthosiphon (*Orthosiphon stamineus*) leaves, 460 mg (≥ 0.04% of sinensetin); liquorice (*Glycyrrhiza glabra*) root; fennel (*Foeniculum vulgare*) fruits; dandelion (*Taraxacum officinale*) root, 250 mg (≥ 0.15% of caffeic acid); sweet peppermint (*Mentha viridis*) leaves; goldenrod (*Solidago virga-aurea*) flowers; dandelion (*Taraxacum officinale*) root lyophilized extract, 50 mg (0.6% of caffeic acid derivatives); orthosiphon (*Orthosiphon stamineus*) leaves lyophilized extract, 30 mg (0.3% of sinensetin)	8

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
9	Fitomagra lynfase® 12 ampoules, Aboca	Apple concentrated juice; red grape concentrated juice; orange concentrated juice; lemon concentrated juice; AdipoDren®, 765 mg (3% of rutin, 22.9 mg): buckwheat (*Fagopyrum esculentum*) lyophilized extract, 180 mg; ruscus (*Ruscus aculeatus*) root lyophilized extract, 75 mg; lyophilized coextract of goldenrod (*Solidago virga-aurea*) flowers and orthosiphon (*Orthosiphon stamineus*) leaves, 300 mg; dandelion (*Taraxacum officinale*) lyophilized root extract, 210 mg	9
1	Fitomagra lynfase® tea sachets, Aboca	Orthosiphon (*Orthosiphon stamineus*) leaves, 500 mg; dandelion (*Taraxacum officinale*) root, 400 mg; liquorice (*Glycyrrhiza glabra*) root; buckwheat (*Fagopyrum esculentum*) flowers, 200 mg; goldenrod (*Solidago virga-aurea*) flowers, 200 mg; sweet orange (*Citrus aurantium* var. *dulcis*) peels; ruscus (*Ruscus aculeatus*) root, 100 mg; Adipodren®, 49.8 mg (3% of rutin,1.5 mg): lyophilized coextract of goldenrod (*Solidago virga-aurea*) flowers and Orthosiphon (*Orthosiphon stamineus*) leaves, 19.5 mg; dandelion (*Taraxacum officinale*) lyophilized root extract, 13.7 mg; buckwheat (*Fagopyrum esculentum*) lyophilized flowers extract, 11.7 mg; ruscus (*Ruscus aculeatus*) lyophilized root extract, 4.9 mg	7
1	Fitomagra ondieta® 100 tablets, Aboca	Curcuma (*Curcuma longa*) rhizome powder, 966 mg (1.1% of essential oil, 10.60 mg), griffonia (*Griffonia simplicifolia*) seeds powder, 450 mg (10% of 5-hydroxytryptophan, 45 mg); rosenroot (*Rhodiola rosea*) root dry extract, 200 mg	3
10	Fucus® 60 tablets, 500 mg, Erbavita	Seaweed (*Fucus vesiculosus* L.) thallus dry extract, 300 mg (0.05 % of iodine, 150 mcg); inulin 500 mg	2
1	Garcinia® 60 tablets, Erba vita	Garcinia (*Garcinia cambogia* Gaertn. Desr.) fruit peel dry extract, 365 mg (60% of hydroxycitric acid, 219 mg)	1
11	Garcinia 100%® juice, Pharmalife	Garcinia (*Garcinia gummi-gutta*, sin. *Garcinia cambogia*) fruits hydro soluble dry extract, 840 mg (60% of hydroxycitric acid, 501 mg); apple juice	2
8	Garcinia Cambogia Bodyspring® 50 tablets, Angelini	Garcinia cambogia (*Garcinia cambogia* Desr.) fruit dry extract, 1200 mg (50% of hydroxycitric acid, 600 mg)	1
24	Garcinia cambogia Arkocapsule® 45 tablets, Arkopharma	Garcinia (*Garcinia cambogia* Desr.) fruit pericarp extract, 1604 mg (min. 50% of hydroxycitric acid, 802 mg)	1
22	Gdue® 30, 60 tablets, Aesculapius farmaceutici	InSea2® (20% of polyphenols): *Ascophyllum nodosum*, 712.5 mg and *Fucus vesiculosus*, 37.5 mg; chromium picolinate, 22.5 mcg	3

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
3	Ginohelp® 60 tablets, O.T.I	Garcinia (*Garcinia cambogia* Desr.) fruits dry extract, 840 mg (60% of hydroxycitric acid, 504 mg); bitter orange (*Citrus aurantium* L. var. amara) unripe fruits dry extract, 600 mg (4% of synephrine, 24 mg); guarana (*Paullinia cupana* Kunt) seeds dry extract, 480 mg (2.5% of caffeine, 12 mg); green tea (*Camellia sinensis* Kuntze) leaves dry extract, 480 mg (5% of caffeine, 24 mg and 20% of polyphenols, 96 mg); sweet clovers (*Melilotus officinalis* Pallas) herb with flowers dry extract, 300 mg (1% of coumarin, 3 mg)	5
2	Glicemir® 30 tablets, Fitobios	Gymnema (*Gymnema sylvestre* R. Br.) leaves dry extract (25% of gymnemic acid); olive (*Olea europaea* L.) leaves dry extract (40% of oleuropein); olive (*Olea europaea* L.) fruit dry extract (10% of hydroxytyrosol and its derivatives); curcuma (*Curcuma longa* L.) rhizome dry extract (23% of curcuminoids); vitamin A (retinyl acetate), chromium ppicolinate; folate (pteroylmonoglutamic acid)	6
4	Glycinet® 24 tablets, Bromatech	*Gynostemma pentaphyllum* Thunb. Makino herb dry extract, 62.5 mg; *Althaea officinalis* root dry extract, 62.5 mg; Cassia nomame (*Cassia mimosoides* L.) fruit dry extract, 125 mg	3
8	Glucomannano Arkocapsule® 45 tablets, Arkopharma	Konjac glucomannan (*Amorphophallus konjac* K. Koch) tuber powder, 3000 mg (glucomannan, 2000 mg)	1
2	Glucomannano plus® 50 tablets, Bodyspring	Glucomannan tuber powder (*Amorphophallus konjac* Koch), 3000 mg	1
7	Isocell forte® 40 tablets, Marco Antonetto Farmaceutici	Rutin, 100 mg; dandelion (*Taraxacum officinalis*) root dry extract, 167 mg; green tea (*Camellia sinensis*) dry extract, 150 mg; *Ginkgo biloba* leaves dry extract, 100 mg (24% of ginkgo-flavone glycosides); *Vitis vinifera* leaves dry extract, 167 mg; *Centella asiatica* herbs dry extract, 150 mg; *Ruscus aculeatus* rhizome dry extract, 150 mg; *Melilotus officinalis* herbs dry extract, 150 mg; vitamin C, 80 mg; vitamin E, 12 mg	10
21	Kilocal® 20 tablets, Pool pharma	Inulin; *Rhamnus frangula* L. cortex dry extract; senna (*Cassia angustifolia* Vahl.) leaves dry extract; seaweed (*Fucus vesiculosus* L. and *A. nodosum*) thallus dry extract (0.1% of iodine); tamarindus (*Tamarindus indica* L.) fruit dry extract; golden shower (*Cassia fistula* L.) fruit dry extract; pineapple (*Ananas comosus* L. Merr.) stalk dry extract; star anise (*Illicium verum* Hook f.) fruit powder; chromium picolinate	9

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
16	Kilocal Age menopausa® 30 tablets, Pool pharma	Soya (*Glycine max* L. Merr.) seeds dry extract (40% of isoflavones); magnolia (*Magnolia officinalis* Rehder & Wilson) bark dry extract (2% of honokiol); moringa (*Moringa oleifera* Lam.) seeds dry extract; Leptinolin®: chromium picolinate - Banaba (*Lagerstroemia speciosa* L. Pers.) leaves dry extract; red clover (*Trifolium pratense* L.) aerial parts with flowers dry extract (8% of isoflavones); Tamarindus (*Tamarindus indica* L.) fruits dry extract; K2VITAL®– Menaquinone (Vitamin K_2); cholecalciferol (vitamin D); melatonin	10
75	Kirocomplex® 20 tablets, S&R Farmaceutici	D-chiro-inositol 500 mg; myo-inositol 200 mg; Revifast® - *Polygonum cuspidatum* root extract, 80 mg (min. 30% of resveratrol, 24 mcg); manganese pidolate 5 mg; folic acid, 200 mcg; vitamin D_3 12.5 mcg	6
68	Klamin® 20 tablets, Nutrigea	Klamin®: microalgae Klamath (*Aphanizomenon flos aquae*) dry extract	1
3	Klamin gocce®, drops, Nutrigea	Klamin®: microalgae Klamath (*Aphanizomenon flos aquae*) dry extract; pummelo and grapefruit (*Citrus grandis* L. Osbeck et *Citrus x paradisi* MacFayden) seeds and pericarp dry extract (40% of naringenin); *Mentha piperita* L. essential oil	4
17	Levomap® 60 tablets, Maharishi Ayurveda	Guggul (*Commiphora mukul* Hook.) resin, 1202 mg; Haritaki (*Terminalia chebula* Retz.) fruit powder, 240 mg; Bibhitaki (*Terminalia bellerica* Roxb.) fruit powder, 240 mg; Amalaki (*Phyllanthus emblica* L.) fruit powder, 240 mg	4
10	LFP curcuma® 20 tablets, Unifarco	Novasol® curcumin: curcuma (*Curcuma longa* L.) rhizome extract, 1332 mg (total curcuminoids, 79.9 mg)	1
6	LFP Drenafluid® 300 ml, Unifarco	Betula (*Betula pendula* Roth) leaves dry extract, 1000 mg (0.3% of hyperoside, 3 mg); pilosella (*Hieracium pilosella* L.) herb dry extract, 600 mg (0.5% of vitexin, 3 mg); (Sunphenon® 90 D): green tea (*Camellia sinensis* L. Kuntze) leaves dry extract, 156.25 mg (80% of catechins, 125 mg); sweet clovers (*Melilotus officinalis* L. Lam.) herb with flowers dry extract, 150 mg (2% of coumarin, 3 mg)	4
6	LFP Psillioregola® 20 sachets, Unifarco	Psyllium (*Plantago ovata* Forsk.) seed husk (98% of cuticula, 10.8 g)	1
244	Lipecal Diet ® bar, Fitobios	Potato protein; rice protein; pea protein; *Garcinia cambogia* fruit dry extract (60% of hydroxycitric acid); puffed rice (0.75%); *Ananas sativus* stalk powder; niacin hydrochloride (vitamin B_3); calcium d-pantothenate (vitamin B5); riboflavin (vitamin B_2); pyridoxin hydrochloride (vitamin B_6); thiamine hydrochloride (vitamin B_1); cyanocobalamin (vitamin B_{12})	11

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Longlife caffe verde® 60 tablets, Longlife	Green coffee (*Coffea arabica*) seed hydroalcoholic dry extract, 1000 mg (50% of chlorogenic acids, 500 mg), (< 5% of caffeine, < 50 mg)	1
1	Longlife Oxy Max® 30 tablets, Longlife	L-ascorbic acid, 500 mg; vitamin E (d-alfa tocopherol succinate), 60 mg; Betatene® D. Salina® - mixture of microencapsulated carotenoids from microalgae *Dunaliella salina*, 4.8 mg and bioflavonoids from citrus fruits, 50 mg; N-acetyl L-cysteine, 25 mg; L-glutathione, 25 mg; *Camellia sinensis* L. leaves, 25 mg (98% of polyphenols and 45% of EGCG); *Tagetes erecta* L. petal (lutein, 1 mg); L-selenomethionine, 55 mcg; coenzyme Q_{10}, 10 mg; alpha lipoic acid, 10 mg; *Polygonum cuspidatum* root (50% of trans-resveratrol, 5 mg); *Vitis vinifera* L. seed, 10 mg (95% of oligomeric proanthocyanidin); tomato oleoresin (50% of lycopene, 1 mg)	14
4	Lympha dren® 12 sachets, BodySpring Angelini	Orthosiphon (*Orthosiphon stamineus* Benth) leaves and flowers hydroalcoholic extract, 200 mg; stinging nettle (*Urtica urens* L.) leaves hydroalcoholic extract, 200 mg; pilosella (*Hieracium pilosella* L.) herb hydroalcoholic extract, 200 mg; blackcurrant (*Ribes nigrum* L.) leaves hydroalcoholic extract, 200 mg; betula (*Betula pendula* Roth.) leaves hydroalcoholic extract, 150 mg; roundhead lespedeza (*Lespedeza capitata* Mich) leaves hydroalcoholic extract, 150 mg; green tea (*Camellia sinensis* L. Kuntze) leaves soft extract, 150 mg	7
1	Meravis® 30 tablets, Naturvis	Carnitine (L-acetyl carnitine) 500 mg; S-adenosyl methionine (SAMe) 150 mg; glutamine (L-glutamine) 120 mg; phenylalanine (L-phenylalanine) 100 mg; tyrosine (L-tyrosine) 100 mg; griffonia (*Griffonia simplicifolia* DC. Baill.) seeds dry extract, 100 mg (10% of 5-HTP); lemon balm (*Melissa officinalis* L.) leaves dry extract, 100 mg (2% of rosmarinic acid, 2 mg); vitamin B_6 (pyridoxine hydrochloride) 0.8 mg; vitamin B_1 (thiamine hydrochloride) 0.3 mg	9
1	Mico-five® 70 tablets, Freeland	*Ganoderma lucidum* dry extract, 316.8 mg; *Agaricus blazei* Murrill dry extract, 158.4 mg; *Inonotus oblquus* dry extract, 158.4 mg; *Grifola frondosa* dry extract, 158.4 mg; *Lentinula edodes* dry extract, 158.4 mg: all standardized in: polysaccharides 486 mg; alpha-glucans 124 mg; beta-glucans 252 mg; triterpenes 24 mg; ergosterol 283 mcg; ganoderic acid* 196 mcg; grifolan* 3.51 g; lentinan* 6.48 g *refers to 100 g of extract	5

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Micotherapy Glico® 90 tablets, AVD Reform	*Coprinus comatus* sporophores, 600 mg; Gymnema dry extract, 300 mg (75% of gymnemic acid, 225 mg); Banaba dry extract, 300 mg (1% of corosolic acid, 3 mg); *Rosa canina* dry extract, 90 mg (70% of vitamin C, 63 mg); methylsulfonylmethane (MSM), 30 mg; chromium picolinate, 200 mcg	6
1	Moringa Unicis® 30 tablets, Biogroup	Moringa (*Moringa oleifera* Lam.) leaves and seeds, 400 mg	1
33	Noglic® 30 tablets, Esi	*Momordica charantia* dry extract, 300 mg (3%); Gymnema dry extract, 300 mg (25%); cinnamon dry extract, 250 mg (4/1); alpha lipoic acid, 200 mg; chromium 200 mcg	5
73	Norflo® 30 tablets, EyePharma	Iphytoone®- phytosomal curcuminoids and phosphatidylserine (2%), 500 mg	2
4	Nutramet Fibra® powder, Esserre Pharma	Nutriose FB06®-Wheat (*Triticum* spp.) soluble dietary fiber, 24 g	1
10	Nutriva gliceval® 30 tablets, Cabassi e Giuriati Group	*Cinnamomum zeylanicum* Blume bark dry extract (1.6% of Methylhydroxychalcone polymer-MHCP), 150 mg; Banaba leaves dry extract (1% of corosolic acid), 150 mg; Gymnema leaves dry extract (25% of gymnemic acid), 150 mg; alpha lipoic acid 150 mg; chromium picolinate 200 mcg	5

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
18	Olimap® 60 tablets, Maharishi Ayurveda	Guggul (*Commiphora mukul* Hook.) resin, 549 mg; Vasa (*Adhatoda vasica* Nees) leaves powder, 96 mg; ginger (*Zingiber officinale* Rosc.) rhizome powder, 48 mg; long pepper (*Piper longum* L.) fruit powder, 48 mg; wormwood (*Artemisia absinthium* L.) aerial parts with flowers powder, 48 mg; black pepper (*Piper nigrum* L.) fruit powder, 48 mg; vidarikand (*Pueraria tuberosa* Roxb. ex Willd., DC.) rhizome powder, 25 mg; cinnamon (*Cinnamomum zeylanicum* Blume) bark powder, 24 mg; Jatamansi (*Nardostachys jatamansi* DC.) root powder, 12 mg; Cardamom (*Elettaria cardamomum* White et Mason.) seeds powder, 12 mg; Vanslochan (*Bambusa arundinacea* Willd.) manna lymph powder, 12 mg; grape (*Vitis vinifera* L.) fruit dry extract, 6 mg; Gokshura (*Tribulus terrestris* L.) aerial parts dry extract, 5 mg; Shatavari (*Asparagus racemosus* Willd. Oberm.) root dry extract, 4 mg; Yavani (*Trachyspermum ammi* Sprague) fruit dry extract, 3 mg; liquorice (Glycyrrhiza glabra L.) root dry extract, 3 mg; garlic (*Allium sativum* L.) bulb dry extract, 3 mg; Katuka (*Picrorhiza kurroa* Royle) rhizome powder, 2 mg; chinese smilace (*Smilax china* L.) root powder, 2 mg; caraway (*Carum carvi* L.) fruit powder, 2 mg; Meshasringi (*Gymnema sylvestre* R. Br.) leaves powder, 1 mg; cumin (*Cuminum cyminum* L.) fruit powder, 1 mg; Ashvagandha (*Withania somnifera* L. Dunal.) root powder, 1 mg; Sigru (*Moringa oleifera* Gaertn.) seeds powder, 1 mg; Vidarikand (*Pueraria tuberosa* Roxb. ex Willd., DC.) rhizome powder, 1 mg; Bibhitaki (*Terminalia bellerica* Roxb.) fruit powder, 1 mg; Kankola (*Piper cubeba* L.f.) fruit powder, 1mg; Bilva (*Aegle marmelos* Correa) bark powder, 1 mg; Musta (*Cyperus rotundus* L.) root powder, 1 mg; Amalaki (*Phyllanthus emblica* L.) fruit powder, 1mg	29
1	Ondefence® 30 tablets, Baif International	Curcuma (*Curcuma longa*) rhizome dry extract, 1000 mg (95% of curcumin, 950 mg); Bioperina®-black pepper (*Piper nigrum*) fruit dry extract, 2.2 mg (95% of piperine, 2 mg)	2

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
9	Pelvimap® 60 tablets, Maharishi Ayurveda	Guggul (*Commiphora mukul* Hook.) resin, 198 mg; Aragvadha (*Cassia fistula* L.) fruit pulp powder, 15 mg; Ajowan (*Trachyspermum ammi* Sprague) fruit powder, 15 mg; cinnamon (*Cinnamomum zeylanicum* Blume) bark powder, 15 mg; Vanslochan (*Bambusa arundinacea* Willd.) manna lymph powder, 15 mg; long pepper (*Piper longum* L.) fruit powder, 8 mg; Senna of Tinnevelly (*Cassia angustifolia* Vahl.) leaves powder, 4 mg; Zedoaria (*Curcuma zedoaria* Rosc.) rhizome powder, 4 mg; Musta (*Cyperus rotundus* L.) root powder, 4 mg; Gokshur (*Tribulus terrestris* L.) fruit powder, 4 mg; Curcuma (*Curcuma longa* L.) rhizome powder, 4 mg; *Quercus infectoria* Oliv. galls, 4 mg; cardamom (*Elettaria cardamomum* White et Mason.) seeds powder, 4 mg; Coriander (*Coriandrum sativum* L.) fruit powder, 4 mg; Haritaki (*Terminalia chebula* Retz.) fruit powder, 4 mg; Bibhitaki (*Terminalia bellerica* Roxb.) fruit powder 4 mg; Amalaki (*Phyllanthus emblica* L.) fruit powder, 4 mg; chasteberry (*Vitex agnus-castus* L.) fruit powder, 4 mg; ginger (*Zingiber officinale* Rosc.) rhizome powder, 4 mg; black pepper (*Piper nigrum* L.) fruit powder, 4 mg; iron, 16.85 mg	21
24	Pesoforma Drenante Liquido®, Nutrition & Sante' Italia	Green tea (*Camellia sinensis*) leaves fluid extract, 200 mg; pineapple (*Ananas comosus*) stalk fluid extract, 200 mg; violet tricolor (*Viola tricolor*) aerial parts fluid extract, 200 mg; Betula (*Betula alba*) leaves fluid extract, 200 mg; orthosiphon (*Orthosiphon stamineus*) leaves fluid extract, 200 mg; asparagus (*Asparagus officinalis*) root fluid extract, 200 mg; fig (*Ficus carica*) fruit fluid extract, 200 mg; guarana (*Paullinia cupana*) seeds fluid extract, 200 mg	8
8	Pesoforma Nature Raw Fruits® snack, Nutrition & Sante' Italia	Date 39.8%; walnut flower 22%; raisin 21.5%; raw cocoa butter; grated coconut 4.7%; apricot 1.9%; Mosqueta rose seed flower; apricot powder 0.2%	7
107	Plantalax 3® ace, prune/kiwi, peach/lemon, Sofar	Psyllium (*Plantago ovata*) husk fibre (98%), 12 g; β-galactosidase (lactase) 135 mg; α-galactosidase 30 mg	3

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Profem plus® 20 sachets, Guna	Fructo-oligosaccharides (FOS); soya (*Glycine max* L. Merr.) seeds dry extract, 360 mg (10% of isoflavones, 37.3 mg); green tea (*Camellia sinensis* L. Kuntze) leaves dry extract, 150 mg (50% of polyphenols); kudzu (*Pueraria lobata* Willd. Ohwi) root dry extract, 100 mg (40% of isoflavones, 41.8 mg); B*ifidobacterium lactis* Bb1 (DSM17850) tindalyzed rich of zinc, 4.3 mg; griffonia (*Griffonia simplicifolia* M. Vahl ex DC. Baill.) seeds dry extract, 50 mg (> 20% of L-5-HTP); zinc gluconate; chasteberry (*Vitex agnus castus* L.) fruit dry extract, 40 mg (> 0.6% of aucubin and > 0.5% of agnoside); micro-encapsulated probiotics: *Bifidobacterium lactis* BS01 (LMG P-21384), *Lactobacillus acidophilus* LA02 (DSM 21717), *Lactobacillus paracasei* LPC00 (LMG P-21380), *Lactobacillus rhamnosus* LR06 (DSM 21981), *Lactobacillus plantarum* LP02 (LMG P-21020), *Lactobacillus salivarius* LS03 (DSM 22776); Trifolium (*Trifolium pratense* L.) leaves and flowers dry extract, 5 mg (8% of isoflavones, 0.45 mg)	14
1	Profito End® drops, Qantiqa	Wild radicchio (chicory) 7.50 mg; maple (*Acer campestre*) 7.50 mg; fucus 7.50 mg; guarana 7.50 mg	4
4	Prometabol® 30 tablets, Confarm	*Garcinia cambogia*; guarana*;* green tea*;* bitter orange; burdock; chromium	6
13	Psillio e acido ialuronico® 20 sachets, Teva	Psyllium (*Plantago ovata* Forsk.) seed husk, 9.0 g; sodium hyaluronate, 20 mg	2
410	Psyllogel Fibra® red orange, lemon tea 20 sachets, Nathura	Psyllium (*Plantago ovata* Forsk.) fibre seeds husk (84.40%)	1
35	Psyllogel megafermenti® ACE 24 sachets, Nathura	Psyllium (*Plantago ovata* Forsk.) fibre seeds husk; mixture of probiotics: *Lactobacillus paracasei* SD5275 (4 billions), *Bifidobacterium animalis* subsp. *lactis* SD5219 (1 billion), *Lactobacillus acidophilus* SD5221 (1 billion)	4
3	Psylloplus® 40 sachets, Pool Pharma	Psyllium (*Plantago ovata* Forsk.) seeds husk	1
4	Pufacur® 30 sachets, Vanda omeopatici	Oil fish, 2 g (EPA, 546 mg and DHA, 358.8 mg); curcuma (*Curcuma longa* L.) rhizome, 1.5 g; black pepper dry extract 15.79 mg (piperine 15 mg); vitamin A 0.63 mg; vitamin C 90 mg; vitamin D_3 5 mcg; vitamin E 20 mg; zinc 5 mg; selenium 20 mcg	9
1	Realim® 20 sachets, AG Pharma	Glucomannan 4 g; myo-inositol 1.75 g; D-chiro-inositol 0.25 g	3

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Resveratrox® 60 tablets, Solgar	*Polygonum cuspidatum* Sieb. et Zucc. root extract, 400 mg (50% of resveratrol, 200 mg	1
1	Semi di Chia bio® seeds 400 g, Fior Di Loto	Chia (*Salvia hispanica*) seeds (fibres 38 g, proteins 16 g, alpha-linoleic acid 22 g)	1
1	Spirulife® 100 tablets, Natural Point	Spirulina (*Spirulina platensis* Gomont. Geitler) thallus powder, 1500 mg	1
8	Spirulina® 50 tablets, Body Spring	Spirulina (*Spirulina platensis*) thallus powder (50% of proteins)	1
8	Spirulina Marcus Rohrer® 60, 180 tablets, Cabassi&Giurati	Spirulina	1
4	Super ananas slim® 25 sachets, Zuccari	Pineapple (*Ananas comosus* L. Merr.) fruit concentrated juice; pineapple (*Ananas comosus* L. Merr.) stalk dry extract (bromelain 250 GDU/g); yerba mate (*Ilex paraguariensis* A. St.-Hill.) leaves dry extract (2% of caffeine); Garcinia (*Garcinia cambogia* Gaernt. Desr.) fruit dry extract (60% of hydroxycitric acid); pineapple (*Ananas comosus* L. Merr.) stalk dry extract (bromelain 2500 GDU/g) *(caffeine, 6 mg)	3
3	Tepigal 300® 30 tablets, Sherman tree nutraceuticals	*Camellia sinensis* L. Kuntze leaves dry extract, (95% of epigallocatechin gallate, 300 mg)	1
1	Termodren evo® 30 tablets, Shedir Pharma	Ortosiphon, *Garcinia cambogia;* dandelion; milk thistle; Centella; Rhodiola; chromium	7
10	Termodren® 30 tablets, Shedir Pharma	Betula, dandelion; orthosiphon; bitter orange; green tea; *Undaria pinnatifida*	6
1	Termodren sciroppo®, Shedir Pharma	Stinging nettle; quackgrass; dandelion; orthosiphon; bitter orange; green tea; *Undaria pinnatifida;* liquorice; pantothenic acid; vitamin B_6	10
2	Xanadren Plus® 30 tablets, Promopharma	Pilosella (*Hieracium pilosella* L.) aerial parts dry extract (1% of vitexin); Betula (mixture of *Betula pendula* Roth leaves 90% and *Betula pubescens* Ehrh. Leaves 10%) dry extract (1% of hyperoside); hawthorn (*Crataegus oxyacantha* Auct.) flowers and leaves dry extract (3% of vitexin); milk thistle (*Silybum marianum* Gaertn.) fruit dry extract (80% of silymarin); green coffee (*Coffea arabica* L.) seeds dry extract (45% of chlorogenic acid); tryptofan sulphate; chromium picolinate	7

Table 2.2. (continued)

Sales	Brand name, pharmaceutical form, producer	Phytochemical composition without vehicles, daily dose when reported	Number of components
1	Xls drena® 10 ampoules, Perrigo Italia	Betula (*Betula pendula*) leaves extract, 300 mg; quackgrass (*Agropyron repens* L., radici) 300 mg; pilosella (*Hieracium pilosella* L.) aerial parts extract, 200 mg; Java tea (*Orthosiphon stamineus*) leaves extract, 200 mg; equisetum (*Equisetum arvense* L.) aerial parts extract, 200 mg	5
3	Ymea Silhouette® 64 tablets, Perrigo Italia	Maca extract (*Lepidium spp.*) 100 mg; sage extract 300 mg; green tea 100 mg; vitamin D 5 mcg; vitamin B_6 1.4 mg; vitamin B_{12} 2.5 mcg; zinc 10 mg; copper 1 mg; chromium 40 mcg	9
3	Zerolip Dren® 30 sachets, Oti	Inulin (extracted from *Cichorium intybus* L.) 8 g; dandelion (*Taraxacum officinale* Weber) root dry extract, 1.8 g (2% of inulin); pineapple (*Ananas comosus* Merr.) stalk dry extract, 1.8 g (0.1% of bromelain)	3
1	Zuccarin® 60 tablets, New Nordic	Japanese mulberry (*Morus alba* L.) leaves dry extract, 1200 mg *(the producer refers to 100 g of extract and not to daily dose (3 tablets)	1

*The phytochemical composition reported in grey colour was obtained from different sources of the manufacturer website.

2.4.3 Description of the botanicals and the additional ingredients

In body weight loss-HDS, 158 plant species and 49 non botanical components were clustered. Table 2.3 describes each plant species in decreasing order of prevalence with relative plant materials and types of extracts identified. Alongside, the markers range together with Ministerial guidelines about physiological functions are also reported.

Table 2.3. Plant species found in body weight loss-HDS, markers range and relative ministerial guidelines about physiological effects.

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in body weight loss-HDS No.(%)[4]	Marker/range (%)	Physiological function according to the Ministry of Health[5]
Camellia sinensis (L.) Kuntze	Leaves	Dry extract, powder, soft extract, fluid extract	21 (17%)	Polyphenols, 20%-98% EGCG, 6%-95% Catechins, 22%-80% Caffeine, 3%-5%	*Folium*: body fluids drainage. Body weight balance. Normal intestinal function. Tonic (physical, mental fatigue). Antioxidant.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Curcuma longa L. *Curcuma zedoaria* (Christm.) Roscoe	Rhizome	Dry extract, powder, fluid extract	20 (16%)	Curcuminoids, 6%-95% Curcumin, 5%-95% Essential oil, 1.1%	*Rhizoma*: antioxidant. Joint functionality. Improvement of the menstrual cycle disorders.
Taraxacum officinale (L.) Weber ex F.H.Wigg	Root, leaves	Dry extract, fluid extract, lyophilized extract, aqueous extract	18 (15%)	Inulin, 2%-20% Caffeic acid, 0.15%	*Herba cum radicibus, radix*: liver function. Digestive function. Regularity of the intestinal transit. Detoxification of the organism. Body fluids drainage. *Folium*: body fluids drainage. Functionality of the urinary tract.
Betula pendula Roth *(alba)* *Betula pubescens* Ehrh.	Leaves, lymph	Dry extract, hydroalcoholic extract, fluid extract, glycerine macerate, aqueous extract	17 (14%)	Hyperoside, 0.3%-3%	*Folium*: body fluids drainage. Urinary tract functionality. Detoxification of the organism.
Orthosiphon stamineus Benth	Leaves, flowers	Dry extract, hydroalcoholic extract, lyophilized extract, fluid extract	17 (14%)	Sinensetin, 0.03%-0.3% Rosmarinic acid, 0.5%	*Folium, herba cum floribus*: body fluids drainage. Functionality of the urinary tract.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Garcinia cambogia (Gaernt) Desr. *Garcinia gummi-gutta*[7] (L.) Roxb. *Garcinia spp*.[8]	Fruit	Dry extract	14 (11%)	Hydroxycitric acid, 50%-60% Mangostin, 40%	ND[6]
Hieracium pilosella L. *Pilosella officinarum*[7] Vaill.	Herb, aerial parts, flowers	Dry extract, aqueous extract, hydroalcoholic extract	10 (8%)	Vitexin, 0.4%-1%	*Herba*: body fluids drainage. Fluidity of bronchial secretions
Ananas comosus (L.) Merr. *(sativus)*	Stalk, fruit	Dry extract, fluid extract, powder, juice dry extract	9 (7%)	Bromelain, 0.1%; 250 GDU/g-2500 GDU/G	*Fructus, stipites*: digestive function. Body fluids drainage (heavy legs). Functionality of the microcirculation. Fight cellulite imperfections.
Citrus aurantium var. *amara* L.	Unripe fruit, peels	Dry extract	9 (7%)	Synephrine, 4%-10%	*Fructus*: digestive function. Elimination of intestinal gas. *Fructus immaturus*: body weight balance. Metabolic stimulation and lipid metabolism. Digestive function. Regular gastrointestinal motility and gas elimination. *Pericarpum, aetheroleum ex pericarpo*: Digestive function. Regular gastrointestinal motility and gas elimination.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Plantago ovata Forssk. *Plantago ispaghula*[7] Roxb. Ex Fleming	Seed husk	ND	9 (7%)	ND	*Semen, tegumentum seminis*: regularity of the intestinal transit. Emollient and soothing action (digestive system). Modulation/limitation of nutrient absorption. Lipids and carbohydrates metabolism. Normal volume and consistency of stool. Prebiotic effect.
Silybum marianum (L.) Gaertn.	Fruit, seeds, fruit pericarp	Dry extract, fluid extract, powder, lyophilized extract	9 (7%)	Silymarin, 4.2%-80%	*Fructus, tegumen seminis*: digestive function. Liver function. Detoxification of the organism. Antioxidant. Carbohydrate metabolism.
Amorphophallus konjac K. Koch	Tuber	Powder	8 (7%)	ND	Substance/nutrient[9]
Vitis vinifera L.	Seeds, leaves, fruit	Dry extract, lyophilized extract	8 (7%)	Cyanidin chloride, 11.5%-22% Oligomeric proanthocyanidin, 95%	*Folium, semen*: microcirculation functionality (heavy legs). Antioxidant. Regular function of the cardiovascular system.
Cassia angustifolia M. Vahl. *Cassia fistula* L. *Cassia mimosoides var. nomame* (Siebold) Makino	Leaves, fruit	Dry extract, powder	7 (6%)	Dimer flavans, 8% Catechins, 8% Sennosides, 20%	*Folium, fructus*: regularity of the intestinal transit. *Folium, fructus*: body weight balance. Triglycerides and cholesterol metabolism.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Equisetum arvense L.	Aerial parts, herb	Dry extract, aqueous extract	7 (6%)	Silicon, 1%-3%	*Herba*: body fluids drainage. Functionality of the urinary tract. Trophism of the connective tissue. Nails and hair wellness.
Griffonia simplicifolia (DC.) Baill.	Seeds	Dry extract, powder	7 (6%)	5-hydroxytryptopane, 10%-98%	*Semen*: improvement of the mood. Relaxation and mental well-being. Control of appetite.
Gymnema sylvestre (Retz) R.Br.	Leaves	Dry extract, powder	7 (6%)	Gymnemic acid, 25%-75%	*Folium*: carbohydrates and lipids metabolism. Control of appetite.
Piper nigrum L. *Piper longum* L. *Piper cubeba* L.	Fruit	Dry extract, powder	7 (6%)	Piperine, 94%-95%	*Fructus, oleum-resina, oleum*: digestive function. Regularity of the intestinal transit. Regular gastrointestinal motility and gas elimination. Regular functionality of the cardiovascular system. Antioxidant. *Fructus*: tonic-adaptogen. Antioxidant. *Fructus*: body fluids drainage. Functionality of the urinary tract. Regular gastrointestinal motility and gas elimination. Fluidity of the bronchial secretions.
Fucus vesiculosus L.	Thallus	Dry extract, aqueous extract	6 (5%)	Iodine, 0.05%-0.1% Polyphenols[7]	*Thallus*: body weight balance. Metabolism stimulation. Regularity of the intestinal transit.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Agropyron repens (L.) P. Beauv. *Elymus repens*[7] (L.) Gould	Rhizome	Dry extract	5 (4%)	ND	*Rhizoma*: body fluids drainage. Functionality of the urinary tract. Detoxification of the organism.
Asparagus officinalis L. *Asparagus racemosus* Willd.	Root	Dry extract, fluid extract, aqueous extract	5 (4%)	ND	*Radix, rhizoma*: body fluids drainage. Functionality of the urinary tract. Detoxification of the organism. *Radix*: tonic (physical, mental fatigue). Digestive function. Regularity of the intestinal transit.
Centella asiatica (L.) Urb.	Herb, aerial parts	Dry extract, aqueous extract	5 (4%)	ND	*Folium, herba*: fight cellulite imperfections. Microcirculation functionality (heavy legs). Memory and cognitive functions.
Cinnamomum verum J. Presl *Cinnamomum zeylanicum*[7] Blume *Cinnamomum zeylanicum*[7] Nees	Bark	Dry extract, powder	5 (4%)	Methylhydroxychalcone polymer, 1.6%	*Cortex, folium, aetheroleum*: digestive function. Intestinal gas elimination. Regularity of the intestinal transit. Antioxidant. Carbohydrate metabolism.
Coffea arabica L.	Seeds	Dry extract, hydroalcoholic extract	5 (4%)	Chlorogenic acid, 45%-50% Caffeine, < 5%	*Semen*: tonic action and metabolic support. Antioxidant.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Cynara scolymus L.	Leaves	Dry extract, lyophilized extract, fluid extract	5 (4%)	Chlorogenic acid, 5%	*Folium*: digestive function. Liver function. Elimination of intestinal gas. Detoxification of the organism. Lipids metabolism. Antioxidant.
Glycyrrhiza glabra L.	Root	Dry extract	5 (4%)	ND	*Radix, rhizoma*: functionality of the digestive system. Bronchial secretions fluidity. Nose and throat wellness. Joint functionality.
Lagerstroemia speciosa (L.) Pers.	Leaves	Dry extract	5 (4%)	Corosolic acid, 1%	*Folium*: functionality of the digestive system. Intestinal transit regularity.
Paullinia cupana Kunth	Seeds	Dry extract, fluid extract	5 (4%)	Caffeine, 2.5%-15%	*Semen*: tonic (physical, mental fatigue). Metabolism stimulation. Lipids metabolism. Body weight balance.
Spirulina maxima (Setchell & Gardner) Geitler *Spirulina platensis* (Gomont) Geitler	Thallus	Powder	5 (4%)	Proteins, 50%	*Thallus*: supportive and restorative action.
Tamarindus indica L.	Fruit	Dry extract, concentrated juice	5 (4%)	Tartaric acid, 5%	*Fructus, pulpa fructis, succus*: intestinal transit regularity. Stool normal volume and consistency.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Undaria pinnatifida Harvey (Suringar)	Thallus, whole plant	Dry extract	5 (4%)	Fucoxanthin, 10%	*Thallus*: nails and hair wellness. Trophism and functionality of the skin. Body weight balance. Detoxification of the organism.
Cyamopsis tetragonoloba (L.) Taub.	Seeds, gum	Dry extract, powder	4 (3%)	ND	*Semen*: modulation/limitation of the nutrient absorption. Satiety promotion.
Foeniculum vulgare Mill.	Fruit	Dry extract, aqueous extract	4 (3%)	Essential oil, 0.9%-1.1%	*Fructus, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Body fluids drainage. Improvement of menstrual cycle disorders. Bronchial secretions fluidity.
Melilotus officinalis (L.) Pall.	Leaves, herb with flowers, herb	Dry extract	4 (3%)	Coumarin, 1%-2%	*Herba cum floribus:* functionality of the venous circulation (functionality of the hemorrhoidal plexus). Microcirculation functionality. Body fluids drainage.
Moringa oleifera Lam.	Seeds, leaves	Dry extract, powder	4 (3%)	Polysaccharide, 40% Glycosides, 10%	*Semen, oleum*: digestive function. Bronchial secretions fluidity. Regularity of the sweating process. Normal blood circulation. Lipids metabolism. Body weight balance.
Phyllanthus emblica L.	Fruit, flowers, leaves	Powder, dry extract	4 (3%)	ND	*Fructus*: carbohydrates metabolism. Antioxidant. Gastric acidity control. Tonic-adaptogen. Boosting immunity system. Liver function.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Polygonum cuspidatum Siebold & Zucc *Fallopia japonica*[7] (Houtt.) Ronse Dec.	Root	ND	4 (3%)	Resveratrol, 30%-92%	*Radix*: antioxidant. Fluidity of bronchial secretions. Detoxification of the organism. Body fluids drainage. Menstrual cycle regularity. Regular function of the cardiovascular system. Tonic (physical, mental fatigue).
Punica granatum L.	Fruit	Dry extract	4 (3%)	Polyphenols, 20% Ellagic acid, 10%-20% Punicalagin, 7%	*Fructus*: antioxidant. *Pericarpum*: regularity of the intestinal transit. Functionality of the digestive system.
Solidago virgaaurea L.	Flowers, aerial parts	Dry extract, lyophilized extract	4 (3%)	ND	*Herba cum floribus*: body fluids drainage. Functionality of the urinary tract. Functionality of the upper respiratory tract.
Zingiber officinale Rosc.	Rhizome	Dry extract, powder	4 (3%)	Gingerols, 5%	*Rhizoma, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Anti-nausea. Regular functionality of the cardiovascular system. Normal blood circulation. Joint functionality. Improvement of the local tensions. Improvement of the menstrual cycle disorders.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Aloe vera (L.) Burm. F. *Aloe barbadensis*[7] *Mill.*	ND	Juice dry extract	3 (2%)	ND	*Succus ex foliis:* regularity of the intestinal transit. Digestive function. Liver function. *Gel sine cute*: emollient and soothing action (digestive system). Detoxification of the organism. Throat wellness.
Aphanizomenon flos aquae	Thallus	Dry extract	3 (2%)	ND	*Bacteria*: improvement of the mood.
Arctium lappa L.	Root	Dry extract, fluid extract	3 (2%)	Inulin, 20%	*Herba, radix*: detoxification of the organism (hair wellness). Body fluids drainage. Joint functionality.
Commiphora mukul (Hook. Ex. Stocks) Engl.	Resin	ND	3 (2%)	ND	*Oleum-gummi-resina*: lipids metabolism. trophism and functionality of the skin. Body weight balance.
Crataegus monogyna Jacq. *Crataegus oxycantha* auct. *Crataegus laevigata*[7] (Poir.) DC.	Flowers, leaves	Dry extract, lyophilized extract	3 (2%)	Flavonoids, 1% Vitexin, 3%	*Flos, folium*: regular functionality of the cardiovascular system. Relaxation and mental wellness. Antioxidant. Regularity of blood pressure.
Hibiscus sabdariffa L.	Flowers	Dry extract, aqueous extract	3 (2%)	Anthocyanins, 2%	*Flos*: regularity of the intestinal transit. Body fluids drainage. Antioxidant. Blood pressure regularity. Functionality of the urinary tract.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Ilex paraguariensis A. St.-Hil.	Leaves	Lyophilized extract, dry extract	3 (2%)	Caffeine, 2%-5%	*Folium*: antioxidant. Body fluids drainage. Body weight balance. Tonic (physical, mental fatigue). Metabolism stimulation. Lipids metabolism.
Lespedeza capitata Michx.	Leaves	Dry extract, hydroalcoholic extract	3 (2%)	Rutin, 4%	*Folium, herba, summitas*: body fluids drainage. Functionality of the urinary tract. Detoxification of the organism. Regular functionality of the cardiovascular system. Lipids metabolism.
Mentha x piperita L. *Mentha viridis* auct. *Mentha spicata*[7] L.	Leaves	Essential oil, hydroalcoholic extract	3 (2%)	ND	*Folium, aetheroleum*: digestive function. Liver function. Regular gastrointestinal motility and gas elimination. Functionality of the upper respiratory tract. Balsamic effect.
Ononis spp.[8]	Root	Dry extract	3 (2%)	ND	
Ribes nigrum L.	Leaves	Fluid extract, hydroalcoholic extract	3 (2%)	ND	*Folium*: body fluids drainage. Functionality of the urinary tract. Joint functionality. Nose and throat wellness.
Ruscus aculeatus L.	Root	Dry extract, lyophilized extract	3 (2%)	ND	*Radix, rhizoma*: microcirculation functionality (heavy legs). Functionality of the venous circulation (functionality of the hemorrhoidal plexus).

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Sambucus nigra L.	Fruit, flowers	Concentrate juice, dry extract, aqueous extract	3 (2%)	Anthocyanidins, 10%	*Cortex, flos, folium, fructus*: bronchial secretions fluidity. Functionality of the upper respiratory tract. Regularity of the sweating process. Body fluids drainage. Boosting the immunity system.
Terminalia bellerica (Gaertn.) Roxb.	Fruit	powder	3 (2%)	ND	*Fructus*: liver function. Regularity of the intestinal transit. Lipids metabolism.
Urtica dioica L. Urtica *urens* L.	Root, leaves	Dry extract	3 (2%)	Beta-sitosterols, 0.8%	*Folium, summitas*: joint functionality. Detoxification of the organism. Body fluids drainage. Functionality of the urinary tract. Functionality of the upper respiratory tract. Nails and hair wellness. *Radix*: prostate functionality.
Zea mays L.	Stigmas	Dry extract	3 (2%)	ND	*Stigmata*: body fluids drainage and functionality of the urinary tract. Prostate functionality.
Acacia nilotica (L.) Delile *Acacia arabica*[7] (Lam.) Willd. *Acacia spp.*[8]	Gum	ND	2 (2%)	ND	*Gummi*: emollient and soothing action (digestive system). Carbohydrate metabolism. Cholesterol metabolism.
Arctostaphylos uva ursi L. Spreng.	Leaves	Aqueous extract, dry extract	2 (2%)	Arbutin, 10%	*Folium*: body fluids drainage. Urinary tract functionality.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Ascophyllum nodosum (L.) Le Jolis	Thallus	Dry extract	2 (2%)	ND	*Thallus*: body weight balance. Joint functionality.
Bambusa arundinacea (Retz.) Willd. *Bambusa bambos*[7] (L.) Voss	Manna lymph	Powder	2 (2%)	ND	*Germen*:
Berberis aristata DC. *Berberis vulgaris* L.	Bark, leaves	Dry extract, hydroalcoholic extract	2 (2%)	Berberine, 98%	*Cortex ex ramis, cortex ex radicibus*: digestive function. Liver function. Regularity of the intestinal transit. Functionality of the digestive system. Regular functionality of the cardiovascular system.
Cichorium intybus L.	ND	ND	2 (2%)	ND	*Radix*: digestive and hepatobiliary function. Body fluids drainage. Urinary tract functionality. Intestinal transit regularity; normal volume and consistency of stool. Prebiotic: intestinal flora balance. *Folium*: digestive and hepatobiliary function. Body fluids drainage. Carbohydrate metabolism. *Summitas*: digestive function.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Citrus sinensis L. *Citrus aurantium*[7] var. *dulcis* Hayne	Fruit	ND	2 (2%)	ND	*Pericarpum, aetheroleum*: digestive function. Intestinal gas elimination.
Crocus sativus L.	Stigma	Dry extract	2 (2%)	Safranal, 0.34%	*Stigmata*: digestive function. Improvement of the mood. Improvement of the menstrual cycle disorders.
Cyperus rotundus L.	Root	Powder	2 (2%)	ND	*Radix*: improvement of the menstrual cycle disorders. Digestive function.
Elettaria cardamomum (L.) Maton.	Seeds	Powder	2 (2%)	ND	*Semen, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Fluidity of the bronchial secretions.
Fagopyrum esculentum Moench. *Polygonum fagopyrum*[7] L.	Flowers	Lyophilized extract	2 (2%)	ND	*Folium, flos*: microcirculation functionality. Functionality of the venous circulation. Regular functionality of the cardiovascular system. Regularity of the arterial blood pressure.
Fraxinus excelsior L. *Fraxinus spp.*[8]	Leaves	Dry extract, aqueous extract	2 (2%)	Chlorogenic acid, 2%	*Folium*: joint functionality. Body fluids drainage. Functionality of the urinary tract. Regularity of the intestinal transit.
Ginkgo biloba L.	Leaves	Dry extract	2 (2%)	Ginkgoflavone glycosides, 24%	*Folium*: antioxidant. Memory and cognitive function. Normal blood circulation. Functionality of the microcirculation.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Glycine max (L.) Merr.	Seeds	Dry extract	2 (2%)	Isoflavones, 10%-40%	*Semen, semen germinatus*: improvement of the menopausal disorders. Lipids metabolism.
Malus spp.[8]	Fruit	Juice	2 (2%)	ND	
Opuntia ficus-indica (L.) Mill.	Cladodes	Powder	2 (2%)	ND	*Cladodium*: Body weight balance. Modulation/limitation of the nutrient absorption. Emollient and soothing action (digestive system). Regularity of the intestinal transit.
Peumus boldus Molina	Leaves	Fluid extract	2 (2%)	ND	*Folium*: digestive function. Liver function. Body fluids drainage. Urinary tract functionality. Intestinal transit regularity.
Prunus domestica L. *Prunus spp.*[8]	Fruit	Dry extract	2 (2%)	ND	*Fructus*: regularity of the intestinal transit.
Pueraria tuberosa (Willd.) DC. *Pueraria montana* var. *lobata* (Willd.) Sanjappa & Pradeep	Rhizome	Dry extract, powder	2 (2%)	Isoflavones, 40%	*Rhizoma*: emollient and soothing action (digestive system, urinary tract). Functionality of the upper respiratory tract. Joint functionality. *Radix, rhizoma*: joint functionality. Regularity of the arterial blood pressure. Regularity of the intestinal transit. Regular functionality of the cardiovascular system.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Rhodiola rosea L. *Sedum roseum*[7] (L.) Scop.	Root	Dry extract	2 (2%)	ND	*Radix*: tonic-adaptogen. Tonic (physical, mental fatigue). Improvement of the mood.
Rosmarinus officinalis L.	Leaves	Essential oil, lyophilized extract	2 (2%)	ND	*Aetheroleum, folium*: digestive function. Liver function. Regular gastrointestinal motility and gas elimination. Antioxidant. Regular functionality of the cardiovascular functionality.
Salvia hispanica[11] *Salvia spp.*[8]	Seeds	ND	2 (2%)	ND	ND
Terminalia chebula Retz.	Fruit	Powder	2 (2%)	ND	*Fructus*: regularity of the intestinal transit. Digestive function. Liver function. Regularity of the sweating process.
Trachyspermum ammi (L.) Sprague	Fruit	Dry extract, powder	2 (2%)	ND	*Aetheroleum*:
Tribulus terrestris L.	Aerial parts, fruit	Dry extract, powder	2 (2%)	ND	*Fructus*: tonic action and metabolic support. Tonic (physical and mental fatigue). Functionality of the urinary tract. Digestive function.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Trifolium pratense L.	Flowers, leaves	Dry extract	2 (2%)	Isoflavones, 8%	*Flos, herba*: functionality of the upper respiratory tract. Improvement of the menopausal disorders. Physiological functionality of the skin. Detoxification of the organism.
Triticum spp.[8]	ND	ND	2 (2%)	ND	
Vitex agnus castus L.	Fruit	Dry extract, powder	2 (2%)	Aucubin, 0.6% Agnoside, 0.5%	*Fructus*: improvement of the menstrual cycle disorders.
Acer campestre L.	ND	ND	1 (1%)	ND	*Gemma*: digestive function. Liver function. Cholesterol metabolism. Rugular functionality of the cardiovascular system.
Actinidia chinensis Planch.	Fruit	ND	1 (1%)	ND	*Fructus*: supportive and restorative action. Boosting the immunity system. Antioxidant.
Adhatoda vasica Nees *Justicia adhatoda*[7] L.	Leaves	Powder	1 (1%)	ND	*Folium*: fluidity of the bronchial secretions. Throat wellness.
Aegle marmelos Correa	Bark	Powder	1 (1%)	ND	*Cortex, folium, radix, semen*: regularity of the intestinal transit. Functionality of the digestive system.
Agaricus blazei Murrill	ND	Dry extract	1 (1%)	ND	*Sporophorum*: boosting the immunity system. Carbohydrates metabolism.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Agave tequilana F.A.C. Weber	ND	ND[9]	1 (1%)	Inulin[10]	*Folium*: boosting the immunity system.
Allium sativum L.	Bulb	Dry extract	1 (1%)	ND	*Bulbus*: regular functionality of the cardiovascular system. Triglycerides and cholesterol metabolism. Arterial blood pressure regularity. Bronchial secretions fluidity. Nose and throat wellness. Digestive function. Antioxidant.
Althaea officinalis L.	Root	Dry extract	1 (1%)	ND	*Flos, folium, radix*: functionality of the mucosa's respiratory system. Throat wellness. Emollient and soothing action (digestive system, urinary tract). Intestinal transit.
Capsicum annuum L.	Fruit	Dry extract	1 (1%)	Capsaicin, 2.5%	*Fructus, oleum-resina*: digestive function. Regular gastrointestinal motility and gas elimination. Regular functionality of the cardiovascular system. Normal blood circulation. Stimulant of the metabolism. Antioxidant.
Carum carvi L.	Fruit	Powder	1 (1%)	ND	*Fructus, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Bronchial secretions fluidity.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Ceratonia siliqua L.	Fruit	Dry extract	1 (1%)	ND	*Fructus*: regularity of the intestinal transit. Emollient and soothing action (digestive system). Modulation/limitation of the nutrient absorption and satiety promotion.
Chrysanthellum americanum (L.) Vatke	Aerial parts	Hydroalcoholic extract	1 (1%)	ND	*Herba*: regular functionality of the cardiovascular system. Digestive function. Liver function.
Citrus paradisi Macfad. *Citrus grandis* (L.) Osbeck *Citrus maxima*[7] (Burm.) Merr.	Seeds, pericarp	Dry extract	1 (1%)	Naringenin, 40%	*Pericarpum, semen*: antioxidant. Functionality of the microcirculation. Body fluids drainage
Cola nitida (Vent.) Schott. et Endl.	Seeds	Dry extract	1 (1%)	Caffeine, 10%	*Semen*: tonic (physical, mental fatigue). Metabolism stimulant.
Coleus forskholii (Willd.) Bricq. *(Plectranthus barbatus)*	Root	Dry extract	1 (1%)	Forskolin, 10%	*Radix, tuber*: regular functionality of the cardiovascular system. Regularity of blood pressure. Functionality of the upper respiratory tract. Digestive function. Body weight balance.
Combretum micranthum G.Don	Leaves	Hydroalcoholic extract	1 (1%)	ND	*Folium*: digestive and hepatobiliary function.
Coprinus comatus (O.F. Mull.)	Sporophores	ND[9]	1 (1%)	ND	ND

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Coriandrum sativum L.	Fruit	Powder	1 (1%)	ND	*Fructus*: digestive function. Regularity of the gastrointestinal motility and gas elimination. Carbohydrates metabolism. Antioxidant.
Cuminum cyminum L.	Fruit	Powder	1 (1%)	ND	*Fructus, aetheroleum*: digestive function. Regularity of the gastrointestinal motility and gas elimination. Improvement of the menstrual cycle disorders.
Cupressus sempervirens L.	Berries	Aqueous extract	1 (1%)	ND	*Galbuli, aetheroleum*: fluidity of the bronchial secretions. Digestive function. Liver function.
Dunaliella salina (Dunal) Teodoresco	ND	ND[9]	1 (1%)	Carotenoids[10]	*Thallus*: ocular wellness. Supportive and restorative action. Skin trophism and wellness.
Euterpe oleracea Mart.	Fruit	Dry extract	1 (1%)	ND	*Fructus, germen*: antioxidant. Lipids and carbohydrates metabolism. Regularity of the intestinal transit.
Ficus carica L.	Fruit	Fluid extract	1 (1%)	ND	*Folium, latex*:
Fumaria spp.[8]	Aerial parts	Dry extract	1 (1%)	ND	
Ganoderma lucidum (Curtis) P.	ND	Dry extract	1 (1%)	ND	*Sporophorum*: boosting the immunity system.
Grifola frondose (Dicks.) Gray	ND	Dry extract	1 (1%)	ND	*Sporophorum*: boosting the immunity system.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Gynostemma pentaphyllum (Thunb.) Makino	Herb	Dry extract	1 (1%)	ND	*Herba*: carbohydrates and lipids metabolism. Liver function. Functionality of the upper respiratory tract. Regular functionality of the cardiovascular system.
Illicium verum Hook. f.	Fruit	Powder	1 (1%)	ND	*Fructus, aetheroleum*: digestive function. Regularity of the gastrointestinal motility and gas elimination. Fluidity of bronchial secretions. Nose and throat wellness.
Juniperus spp.[8]	ND	Dry extract	1 (1%)	ND	
Lentinula edodes (Berk.) Pegler	ND	Dry extract	1 (1%)	ND	*Sporophorum*: boosting the immunity system.
Lepidium spp.[8]	ND	ND	1 (1%)	ND	
Magnolia officinalis Rehder & Wilson	Bark	Dry extract	1 (1%)	Honokiol, 2%	*Cortex*: digestive function. Regularity of the gastrointestinal motility and gas elimination. Body fluids drainage. Fluidity of bronchial secretions. Re-balance of the oral bacterial flora.
Melissa officinalis L.	Leaves	Dry extract	1 (1%)	Rosmarinic acid, 2%	*Folium, herba cum floribus, aetheroleum*: digestive function. Regularity of the gastrointestinal motility and gas elimination. Relaxation and mental wellness. Improvement of the mood. Antioxidant.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Momordica charantia L.	ND	Dry extract	1 (1%)	3% ND	*Fructus*: carbohydrates metabolism. Functionality of the upper respiratory tract. Regularity of blood pressure. Digestive function. Intestinal transit regularity.
Monascus purpureus fermented with *Oryza sativa*	ND	Dry extract	1 (1%)	Monacolin K, 5%	Substance/nutrient[9]
Morus alba L.	Leaves	Dry extract	1 (1%)	ND	*Cortex ex radicibus, folium, fructus*: regularity of the intestinal transit. Body fluids drainage. Urinary tract functionality. Carbohydrates metabolism. Bronchial secretions fluidity. Regularity of the arterial blood pressure.
Nardostachys jatamansi (D. Don) DC.	Root	Powder	1 (1%)	ND	*Folium, radix*: regular intestinal motility and gas elimination. Intestinal transit regularity. Body fluids drainage. Menstrual cycle regularity. Relaxation and mental wellness. Regular functionality of the cardiovascular system.
Olea europaea L.	Leaves, fruit	Dry extract	1 (1%)	Oleuropein, 40% Hydroxytyrosol, 10%	*Folium*: carbohydrates and lipids metabolism. Normal blood circulation. Arterial blood pressure regularity. Antioxidant.
Oryza sativa L.	Seeds	ND	1 (1%)	ND	*Semen*: emollient and soothing action (digestive system). Gastric acidity control.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Phaseolus vulgaris L.	ND	ND	1 (1%)	ND	*Fructus, semen*: body fluids drainage. Carbohydrates metabolism.
Phoenix dactylifera L.	Fruit	Juice	1 (1%)	ND	*Fructus*: fluidity of the bronchial secretions. Functionality of the upper respiratory tract. Body fluids drainage. Urinary tract functionality. Emollient and soothing action (digestive system).
Picrorhiza kurroa Royle	Rhizome	Powder	1 (1%)	ND	*Radix, rhizoma*: digestive function. Liver function. Boosting the immunity system. Fluidity of the bronchial secretions.
Pimpinella anisum L.	Fruit	ND	1 (1%)	ND	*Fructus, aetheroleum*: digestive function. Regular gastrointestinal motility and gas elimination. Fluidity of the bronchial secretions. Nose and throat wellness.
Polyporus umbellatus (Pers.) Fr. *Grifola umbellata*[7] (Pers.) Pilàt	Sporophore	Powder	1 (1%)	ND	*Sporophorum*: boosting theimmunity system.
Quercus infectoria G. Olivier	Galls	ND	1 (1%)	ND	*Galla*: regularity of the intestinal transit. Mucosa's trophism and wellness.

Table 2.3. (continued)

Plant[1]	**Plant material**[2]	**Type of extract**[3]	**Prevalence in body weight loss-HDS No.(%)**[4]	**Marker/range (%)**	**Physiological function according to the Ministry of Health**[5]
Raphanus sativus L.	Root	ND	1 (1%)	ND	*Semen, radix*: digestive function. Body fluids drainage. Functionality of the urinary tract. Fluidity of the bronchial secretions. Antioxidant.
Rhamnus frangula L. *Frangula alnus*[7] Mill.	Cortex	Dry extract	1 (1%)	ND	*Cortex*: regularity of the intestinal transit. Digestive function.
Rheum palmatum L.	Root	ND	1 (1%)	ND	*Radix, rhizoma*: regularity of the intestinal transit. Digestive function.
Rosa canina L.	ND	Dry extract	1 (1%)	Vitamin C, 70%	*Fructus, false fructus*: supportive and restorative action. Regularity of the intestinal transit. Antioxidant.
Smilax china L.	Root	Powder	1 (1%)	ND	*Radix*: detoxification of the organism (skin wellness). Joint functionality.
Tagetes erecta L.	Petal	ND	1 (1%)	Lutein[10]	*Capitula*: antioxidant. Ocular wellness.
Trigonella foenum graecum L.	Seeds	ND	1 (1%)	ND	*Semen*: digestive function. Emollient and soothing action (digestive system). Carbohydrates metabolism. Tryglycerides and cholesterol metabolism.
Vaccinium macrocarpon Aiton	Fruits	ND	1 (1%)	ND	*Fructus*: body fluids drainage. Functionality of the urinary tract. Antioxidant. Intestinal transit regularity.

Table 2.3. (continued)

Plant[1]	Plant material[2]	Type of extract[3]	Prevalence in body weight loss-HDS No.(%)[4]	Marker/range (%)	Physiological function according to the Ministry of Health[5]
Viola tricolor L.	Aerial parts	Fluid extract	1 (1%)	ND	*Flos, herba cum floribus*: bronchial secretions fluidity. Detoxification of the organism (skin wellness). Joint functionality.
Withania somnifera (L.) Dunal	Root	Powder	1 (1%)	ND	*Radix*: tonic-adaptogen. Tonic (physical, mental fatigue). Relaxation and mental wellness. Boosting immunity system.

[1] Plant species are in decreasing order of prevalence in the commercial supplements and in alphabetical suborder. Species of the same genera are counted as one in the prevalence calculation and their physiological functions according the Ministry of Health are reported together.
[2, 3] The plant material used and the type of the extract, only when reported in the label.
[4] Plant prevalence calculated as a percentage of commercial supplements that contain it (No./122x100).
[5] Usable, pending definitions of claims about botanicals [6]. Only physiological indications for plant materials and specified species found in the commercial supplements, are reported in the table.
[6] ND-not determined.
[7] Synonym of the botanical name.
[8] Species not determined.
[9] According to the Italian Ministry of Health, it is included as "other nutrients and other substances with a nutritional and physiological effect" [13].
[10] marker reported in the label without its titration percentage or as a percentage that refers to a mixture of botanicals and not to the specific plant species.
[11] Plants not included in the plant list annex because authorised as novel foods according to the Regulation (EU) 2017/2470 establishing the list of novel foods, in accordance with Regulation (EU) 2015/2283 on novel foods [14].
*Patented phytoextracts where the standardisation refers to the mixture of different plants without a specific one for each plant extract were not considered.

According to the guidelines of the Italian MoH, 25% (n=40) of plant species have claims regarding body weight balance, lipids and carbohydrates metabolism, modulation/limitation of nutrient absorption, control of appetite, satiety promotion. 20% (n=31) of them claim body fluids drainage. About 42.5% (n=67) have other claims not related to the body weight loss. In 11.5% (n=18), the claims are not determined either because of unknown species, or because the plant material to which the ministerial claims refer does not correspond to that found in the supplement, or because clustered as novel food (*S. hispanica*). 1% (n=2) of the species are not included in the plant list annex because clustered as "other nutrients and other substances with a nutritional and physiological effect" (i.e. *O. sativa* fermented with *M. purpureus, A. konjac*). However, their physiological effects are not reported anywhere.

The recurrence of additional non-botanical ingredients is in the following decreasing order: chromium (n=17); vitamin B_6 (n=10); vitamin C (n=8); vitamin B_1 (n=5); alpha lipoic acid, zinc, vitamin E, vitamin D, vitamin B_5 (n=4); vitamin B_2, vitamin B_3, vitamin B_{12}, selenium (n=3); vitamin A, folic acid, D-chiro-inositol, myo-inositol, *Bifidobacterium lactis*, *Lactobacillus acidophilus*, *Lactoba-*

cillus paracasei, copper (n=2); L-tryptophan, glucosamine hydrochloride, chondroitin, sulphate, lactulose, magnesium gluconate, potassium chloride, vitamin K_2, melatonin, manganese, N-acetyl L-cysteine, L-glutathione, coenzyme Q_{10}, L-acetyl carnitine, L-glutamine, L-phenylalanine, L-tyrosine, methylsulfonylmethane, phosphatidylserine, β-galactosidase, α-galactosidase, S-adenosyl methionine, *Lactobacillus rhamnosus*, *Lactobacillus plantarum*, *Lactobacillus salivarius*, sodium hyaluronate, omega 3 (DHA&EPA), hydrolysed milk proteins, iron (n=1).

2.4.4 Questionnaire about Phytovigilance addressed to pharmacies

29 pharmacies answered the questionnaire. Out of the nine questions, the first six closed questions with the relative answers are reported in figure 2.3.

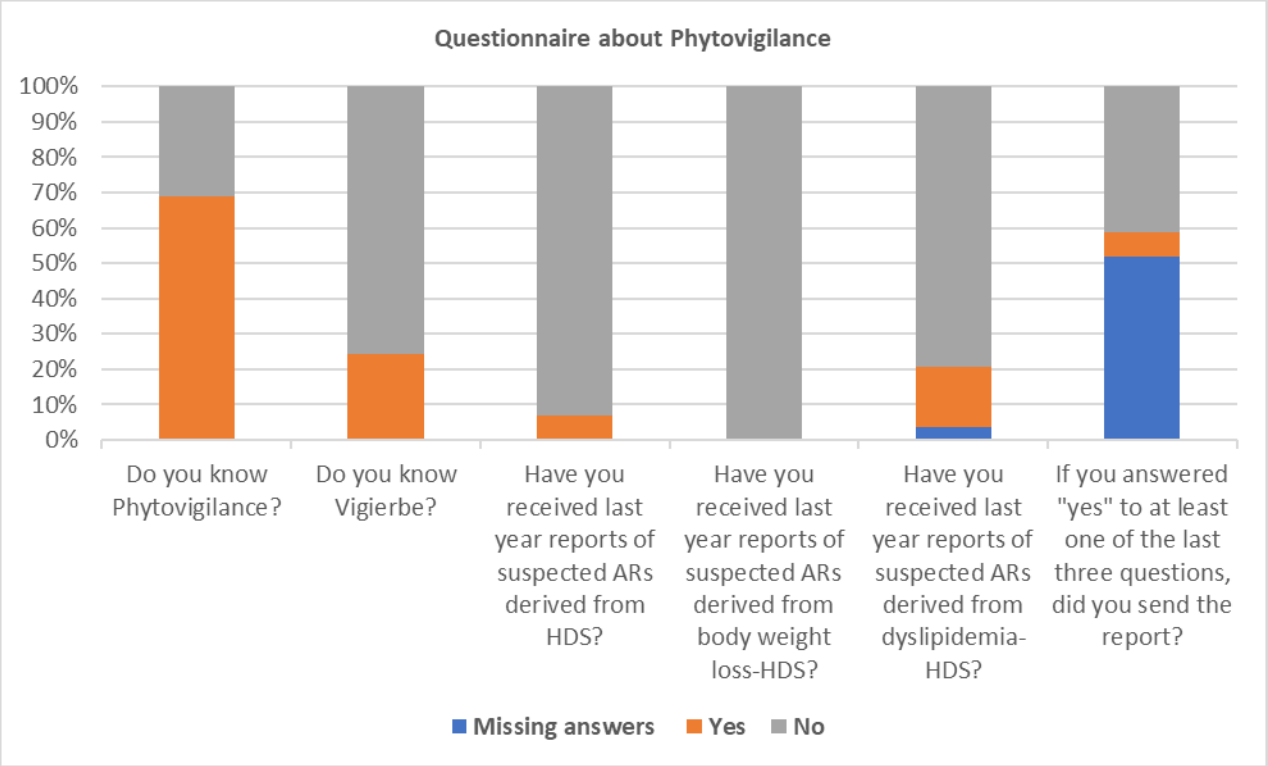

Figure 2.3. Graphical description of the first six closed questions

The distribution of the seven respondents to the single-answer multiple choice question “if you answered that you didn’t send the report, which is the reason why you didn’t do it?” was: (i) I didn’t know I had to send the report (n=3); (ii) I knew I had to send the report but I didn’t know how to do it (n=1); (iii) I had no time to send the report (n=0); (iv) I didn’t considered important what was reported to me for the purposes of the surveillance (n=3).

Five respondents specified red yeast rice (n=2); Armolipid plus® (n=2); Armolipid® (n=1) as supplements being eventually subject of reporting. Whilst muscles pain (n=4); gastrointestinal disorders (n=2); swelling lower limbs with pain (n=1); cramps (n=1) were specified by respondents (n=5) as suspected ARs eventually received.

2.5 Discussion

For the first time, our work aims to give a preliminary overview of sales and types of body weight loss-HDS from territorial pharmacies in Italy. It weighs up the safety of commercial body weight loss-HDS based on scientific literature, and regulations of governments Authorities. Through a survey, it investigates the awareness and pragmatism of pharmacists about Phytovigilance.

Cumulative sales data of both pharmacies indicate the same percentage, during the first and the second year, of HDS and body weight loss-HDS. The highest point of dietary supplements sales is reached during the second year and overlaps the beginning of the lockdown due to Covid-19 pandemic. During each year, the trend of body weight loss-HDS sales has a slight increase close to the summer. Seasonality might be related to the leanness as an aesthetic conception rather than a pathologic condition.

Labelling available to consumers does not guarantee the qualitative and quantitative content of the supplements in various examples. In specific, the manufacturer's website does not describe correctly the composition of Drenanten®. Indeed, hawthorn (*C. monogyna*) reports the standardisation of the milk thistle (*S. marianum*), while the later together with chromium are missing ingredients. Therefore, we report the correct label according other websites. Frequently, botanicals are described in the labels with common names as it can be seen in the cases of Aros®, Drops® Noglic®, Nutriva gliceval®, Micotherapy Glico®. The marker mangostin next to the common name of garcinia, leads to a specific species such as *G. mangostana* that however is not reported. Thus, it can be confused with *G. gummi-gutta*. By analogy, it is like confusing *Allium cepa* with *Allium sativus* which have different bio pharmacological activities. Consequently, it does not witness for the safety of the supplements. Prometabol® could be absolutely the supplement which has less online information. There is not even a manufacturer website whereas other websites describe only the ingredients with common names. Cases of manufacturer's website that report only a photo of the supplement (Clinnix Slim®) without any description of the composition can be evidenced. Meanwhile, the same supplement is sold in other different websites without any support of information and choice for the consumers. Although Spirulina Marcus Rohrer® is a patented phytoextract, the manufacturer does not report any detail about the quality/quantity profile of the product. Well-kept websites, that describe everything except the detailed profile of the supplement which could assure direct clear information for healthcare professionals and consumers, are noticed frequently. Almost the same phenomenon is repeated for Termodren evo®, Termodren®, Termodren sciroppo®, Garcinia® 60 tablets, Xls drena®, where there is only a photo of the supplement. Detailed description about the composition is either difficult or quite impossible to find even in other websites. Therefore, questions about the accuracy of the information found in internet, arise.

Episodes of disappeared supplements (Fitomagra ondieta®) in the manufacturer website, could be probably due to eventual marketing suspension since the "curcuma case" [15]. In addition, specimens of manufacturer's websites that report either the extract's doses of only some ingredients (Fitomagra drena plus ®), or that describe the ingredients but don't report the doses (Kilocal®, Kilocal Age menopausa®) occur frequently. Moreover, labels (Profem plus®) that describe the standardisation of all the botanicals but don't report all the doses of the relative markers, are found. Micofive® represents an example where the manufacturer reports a cumulative standardisation for the multi-ingredient composition and not for each ingredient.

About twenty-six patented extracts can be identified from the marketed supplements such as: Greenselect®; Phytosome®; LeptiCore®; Satiereal®; AdiProFen MS®; AMLF Complex®; Curcumin phytosome®; CurQfen®; Faseomin Max®; 3orthoDREN®; ADIECG®; HGC-C®; NovaSOL®; Meriva®; SelectSIEVE®; Dermogranate®; AdipoDren®; InSea2®; Leptinolin®; Sunphenon®; Betatene®; D. Salina®; Iphytoone®; Nutriose FB06®; Bioperina®; Revifast®. Although in a few cases the standardisation of the phytoextract refer to the mixture of different plants (AdiProFen MS®), almost all of them have a clear description of the standardisation providing better quality. However, it serves more as advertise and as a marketing goal as they don't own a solid clinical recognition in terms of efficacy and/or safety. Although, a few observational studies describe positive results in the management of body weight, further clinical studies with a longer duration, different population groups, are warranted to establish optimal doses and consequently efficacy and safety [16, 17, 18].

There are a number of uncertainties regarding botanicals such as (i) the widely variety of the chemical composition due to plant's environment and season, (ii) the marker's content due to manufacturing conditions and procedures, and (iii) their dose–response evidence after oral exposure due to limited pharmacokinetics data. All these intrinsic uncertainties added to the extrinsic ones related to the incomplete labelling, information and compliance between marketed supplements and scientific evidence, lead up to safety concerns that require urgent efforts for general population. Indeed, in our study, Super ananas slim® is an example of a supplement that has in its composition different types of extracts of the same plant species with different standardisations without understanding which could be the rationale. In the case of Zuccarin®, the manufacturer's website does not report the daily dose extract but 100 g dose extract though it recommends 3 tablets/day. Obviously, it becomes difficult to understand the equivalence between the declared dose extract and the recommended daily dose. Hereby, how can a pharmacist or a doctor evaluate and recommend the supplement to the patient with a specific clinical situation?!

The other topic to discuss are the multi-ingredient preparations that emerge as the majority of our body weight loss-HDS. Up to twenty-nine botanical ingredients are marketed together just as the Ayurveda supplements Olimap® and Pelvimap®. Although Ayurveda is embedded in the Indian National Health System, neither efficacy nor safety are clinically proven. Hereby, in times where science and technology have made giant progress and the population lifestyle has changed the threshold exposure, we should no longer rely on mythological concepts and merely consider as healthy the traditional medicine. In terms of effectiveness, as a multifactorial disease, overweight/obesity could be treated better with a multi-target approach. On the other hand, safety becomes a matter of debate as scientific literature is so far unable to explain the rationale of putting many ingredients together. In our study, each of the botanicals like *G. cambogia*, *C. aurantium*, *C. sinensis*, *P. cupana*, part of the same supplement (Ginohelp®) have specific warnings if taken alone. Yet we don't know neither what warnings could have a mixture like this one nor if they are additive or exponential, as long as there are not randomized clinical studies compliant to the commercial supplement.

The heterogeneity of plant species contained in the body weight loss-HDS interrogates for the real balance benefit/risk in terms of public health. If we consider the most frequent plant species in our study, some are in line with the guidelines of the Italian MoH about the physiologic functions, and also with scientific literature about purported mechanisms of action. As a matter of fact, *C. sinensis*, *C. aurantium*, *P. ovata*, *S. marianum*, *C. mimosoides* var. *nomame*, *G. simplicifolia*, *G. sylvestre*, *F. vesiculosus*, *C. verum*, *C. scolymus*, *P. cupana*, *U. pinnatifida* coincide with the targets suggested

even for pharmacological therapies ranging from the nutrient absorption reduction, appetite regulation, satiety promotion, energy expenditure increase, lipids and carbohydrates metabolisms, etc. [19, 20]. However, up to date, the causality assessment between suspected ARs and use of body weight loss-HDS, reported to Phytovigilance, is judged as possible [11]. Despite no conclusions can be drawn for each single plant, in the reported supplements, green tea, bitter orange, curcuma, *G. cambogia*, aloe, red yeast rice, are often recurrent in the involved adverse reactions [21, 22]. In our study, green tea appears as the most frequent botanical in marketed body weight loss-HDS. Indeed, less than three years ago, European Food Safety Authority (EFSA) delivered recommendations regarding existing uncertainties about hepatotoxicity of catechins and pyrrolizidine alkaloids of green tea supplements [23]. The concern persists more, given that the use of concomitant therapies is underlined in the majority of the cases reported for ARs due to the body weight loss-HDS [10].

Plant species that claim body fluids drainage and beneficial effects on the liver function are frequently included in the marketed body weight loss-HDS. So far, neither efficacy nor safety are totally proved by real world studies for *T. officinale, B. pendula, O. stamineus, H. pilosella, A. comosus, E. arvense, A. repens, A. officinalis, C. asiatica,* etc. Moreover claims like detoxification of the organism, improvement of cellulite imperfections lead individuals to use them more for beauty and aesthetic matters rather than health problems. That could be explained also by the peak of sales close to the summer season. Misconception of the population about HDS constitutes at present a real public health issue. It derives also from missing and/or incompliant information as can be seen in cases of plant species like *G. cambogia, A. konjac, A. flos aquae, A. vera, M. purpureus* fermented with O. *sativa*, etc. where either MoH doesn't report physiologic functions, or the plant material contained in the marketed supplement does not correspond to the plant material whose physiological functions are recommended by the MoH, or even the supplement's label doesn't report the plant material used.

On the other hand in our study emerge plant species frequently marketed that are reported in scientific literature for their beneficial effects on body weight management and its burden in the context of metabolic syndrome like *C. longa, V. vinifera, G. glabra, S. maxima, P. cuspidatum*. Yet the Italian MoH does not recommend them for body weight loss. Conversely, the ministry recommends others such as *C. tetragonoloba, M. oleifera, P. emblica, C. mukul, I. paraguariensis, L. capitata, T. bellerica, A. nilotica, A. nodosum, C. intybus, G. max, O. ficus-indica, A. campestre, A. sativum, C. annuum, C. siliqua, C. nitida, C. forskholii, C. sativum, E. oleracea, G. pentaphyllum, M. charantia, M. alba, O. europaea, P. vulgaris, T. foenum graecum*, for functions that improve at least one of the chronic diseases related to the metabolic syndrome. Nevertheless, a few of them are reported in critical reviews for purported mechanisms of action that still remain unconfirmed for scanty studies [19, 20]. Almost all of them occur poorly in the commercial body weight loss-HDS.

A large part of the remaining plant species identified, own other physiological effects. Beyond increasing the number of claims for the same supplement, they have nothing to do with body weight loss. It leads to speculate that the commercial purpose might be the reason, except any case where the combination of active ingredients helps to maximise the bioavailability. *P. nigrum* is often associated with *C. longa* because of synergistic effects. Due to the content in piperine, it enhances the absorption and reduces the fast degradation and instability of curcumin from chemical and oxidative reactions in the gastrointestinal tract. However, to resume the safety concern, black pepper and piperine improve also the bioavailability of other phytochemicals and drugs like green tea, carbamaze-

pine, phenytoin [24]. Although it becomes of importance in improving delivery systems of pharmaceuticals in terms of efficacy, on the other side the inhibition of cytochrome P450 enzymes, like CYP3A4 isoform, by both curcumin and piperine is thought to be a risk factor for drug interaction, driving therefore to toxicity [15]. As expected, in our study almost all HDS containing *P. nigrum*, have also *C. longa* in association with, despite EFSA has evaluated as safe the use of curcumin alone at an acceptable daily intake of 3 mg/kg/day given its low bioavailability [25]. In the majority of the body weight loss-HDS, curcuma is associated with other ingredients and its use is not as a food additive.

Additional ingredients, not just botanicals, should be taken in consideration as they occur frequently in association with botanicals, notwithstanding they are regulated separately and better than botanicals, because of intrinsic factors. Some of them like chromium, carnitine, alpha lipoic acid pertain challenges for the management of body weight, though exacts mechanisms of action are still unknown [19]. Thus, in the context of inconclusive evidence, contrasting clinical studies, highly variable supplementation, strong causality between the use and suspected ARs [26], it becomes difficult to recommend or discourage the use of body weight loss-HDS containing them.

In relation to the survey addressed to pharmacies, we remark a low awareness of community pharmacists to implement territorial Phyto-surveillance. Although data are preliminary, it is obvious the scarce reporting receipt from individuals as well as the reduced transmission of the reports from the pharmacies. Precisely, out of twenty-nine participants, five-seven (17%-24%) have received suspected ARs due to the use of HDS in the last year, and only two (7%) of them have sent the report to the Italian Phytovigilance System. The reasons of the missing reporting indicate that regulators are not aware of the factual safety profile of HDS in the “real world”. Concerted efforts should be done in order to increase the territorial enactment of Phytovigilance and hence real world data about safety.

2.6 Conclusions

Overall, our preliminary overview of sales highlights a series of elements that conduct to safety concerns of body weight loss-HDS. In specific: (i) the variety of different formulations mostly multi-ingredient without clinical evidence and thus usually without any rationale of use, (ii) plant species contained in marketed supplements not in accordance either with Ministerial guidelines about physiological effects or observational randomized clinical trials, (iii) variable standardisations and incomplete label's information in order to assure a good qualitative and quantitative supplement. Hence, lack of a reproducible bio-pharmacological action leads to uncertain safety profile. In addition, low adherence to the Phytovigilance reporting system from the pharmacies means that stakeholders are not aware of the risk profile of the marketed HDS. Future efforts involving sales data of all territorial pharmacies, other categories of HDS and promotion of Phytovigilance, are required.

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Appendix

Chapter 1 - Dyslipidaemia-HDS sales data

Table 1.3. First year of sales/pharmacy 1

Month	Dietary supplements	HDS (n)	HDS (%)*	Dyslipidaemia HDS (n)	Dyslipidaemia HDS (%)**
October 2018	858	343	40%	14	4%
November	683	293	43%	26	9%
December	644	269	42%	23	9%
January 2019	698	274	39%	34	12%
February	677	255	38%	21	8%
March	721	300	42%	25	8%
April	665	287	43%	26	9%
May	710	293	41%	18	6%
June	668	282	42%	19	7%
July	774	336	43%	24	7%
August	482	182	38%	16	9%
September 2019	703	335	48%	21	6%

*Data are reported as percentage of the dietary supplements
** Data are reported as percentage of the HDS

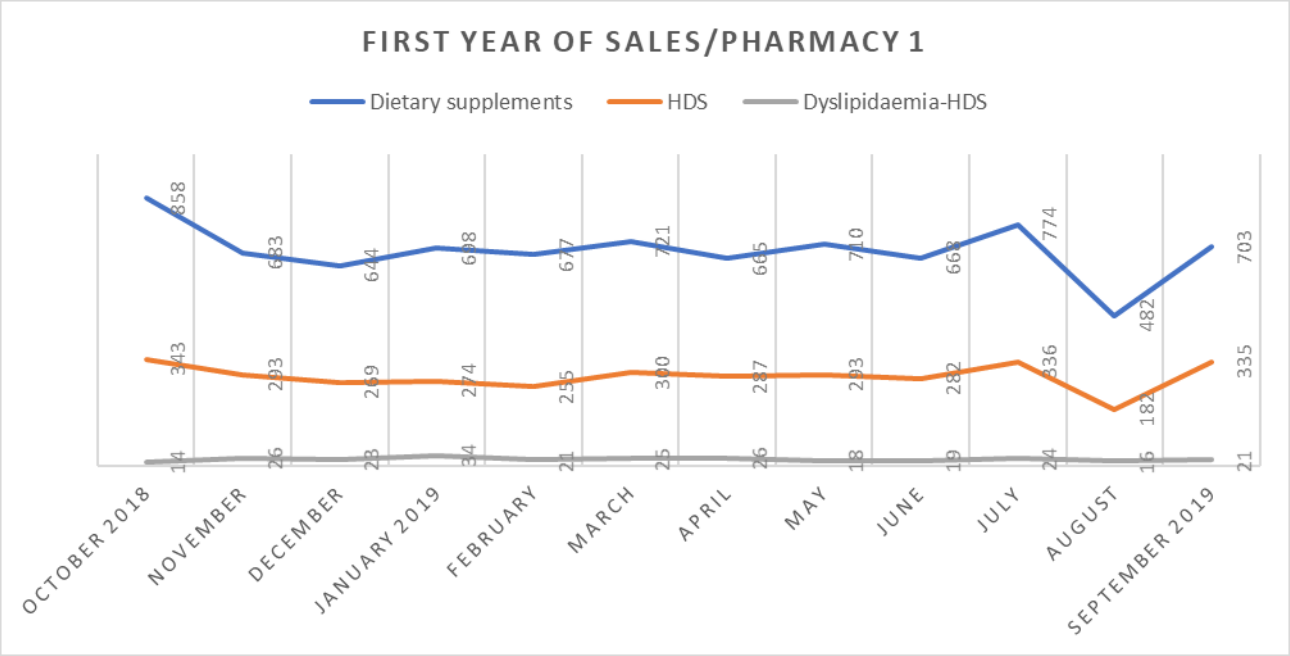

Figure 1.3. Sales data of pharmacy 1 during the first year

Table 1.4. Second year of sales/pharmacy 1

Month	Dietary supple-ments	HDS (n)	HDS (%)*	Dyslipidae-mia HDS (n)	Dyslipidaemia HDS (%)**
October 2019	826	357	43%	23	6%
November	782	364	47%	26	7%
December	694	306	44%	33	11%
January 2020	865	354	41%	30	8%
February	748	348	47%	31	9%
March	843	313	37%	29	9%
April	532	222	42%	28	13%
May	530	241	45%	26	11%
June	569	293	51%	24	8%
July	683	280	41%	28	10%
August	673	252	37%	22	9%
September 2020	634	280	44%	14	5%

*Data are reported as percentage of the dietary supplements
** Data are reported as percentage of the HDS

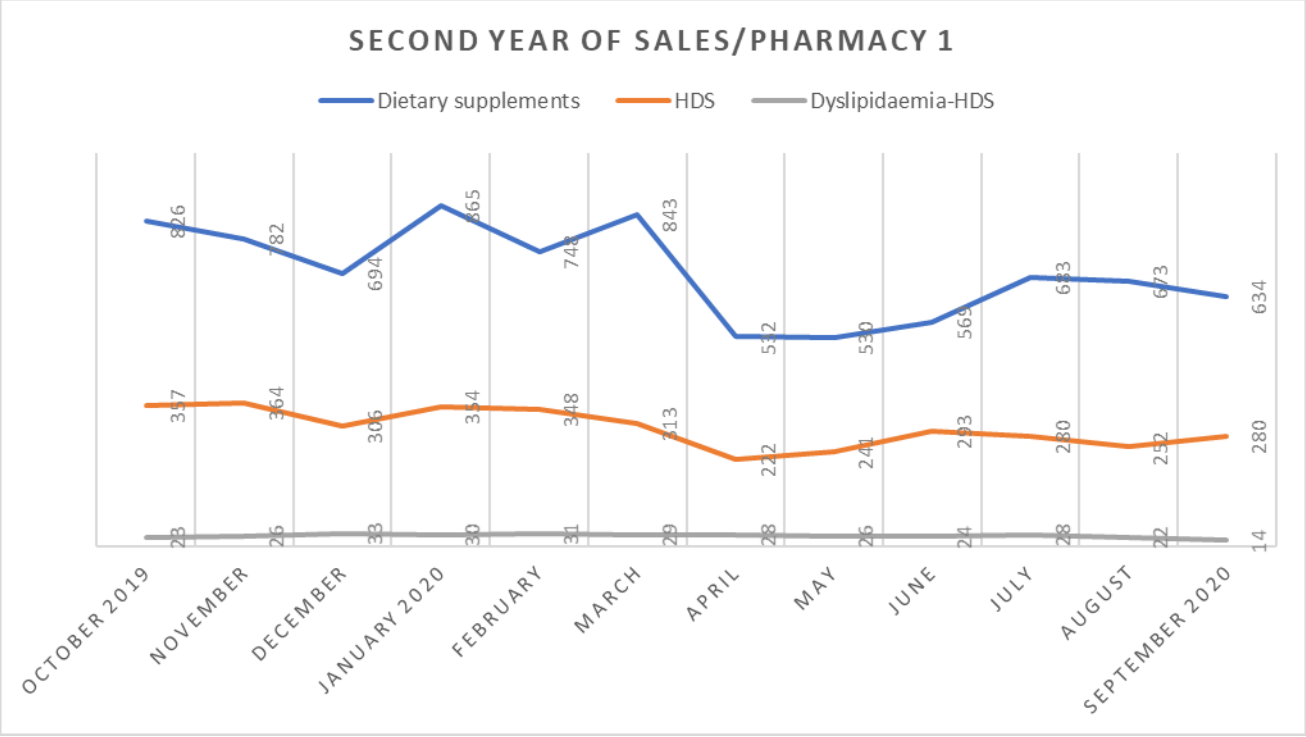

Figure 1.4. Sales data of pharmacy 1 during the second year

Table 1.5. First year of sales/pharmacy 2

Month	Dietary supplements	HDS (n)	HDS (%)*	Dyslipidaemia HDS (n)	Dyslipidaemia HDS (%)**
October 2018	1054	608	58%	71	12%
November	1016	581	57%	66	11%
December	1061	588	55%	49	8%
January 2019	1148	641	56%	53	8%
February	1046	654	63%	52	8%
March	1124	631	56%	53	8%
April	939	541	58%	56	10%
May	1039	586	56%	58	10%
June	937	479	51%	58	12%
July	2050	1020	50%	104	10%
August	2050	1054	51%	104	10%
September 2019	428	243	57%	26	11%

*Data are reported as percentage of the dietary supplements
** Data are reported as percentage of the HDS

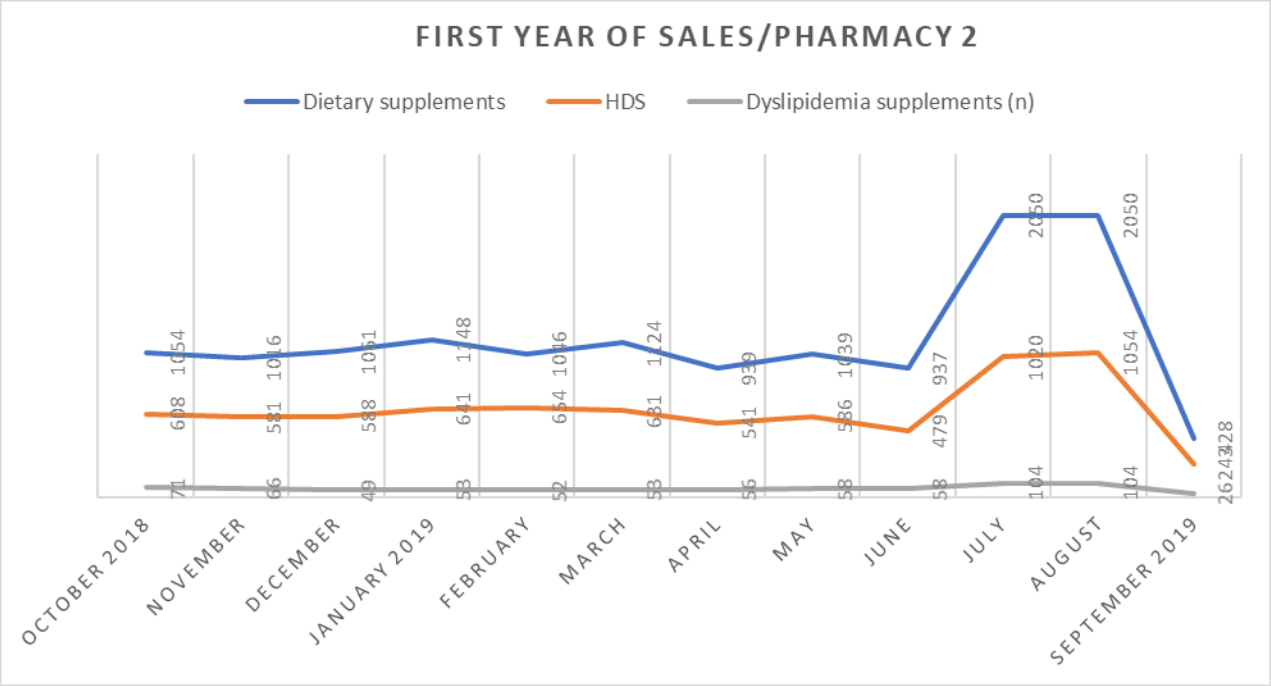

Figure 1.5. Sales data of pharmacy 2 during the first year

Table 1.6. Second year of sales/pharmacy 2

Month	Dietary supplements	HDS (n)	HDS (%)*	Dyslipidaemia HDS (n)	Dyslipidaemia HDS (%)**
October 2019	999	591	59%	52	9%
November	996	585	59%	55	9%
December	955	513	54%	52	10%
January 2020	1018	582	57%	50	9%
February	1084	611	56%	54	9%
March	1264	656	52%	62	9%
April	1019	521	51%	61	12%
May	952	567	60%	51	9%
June	922	544	59%	59	11%
July	1048	563	54%	54	10%
August	883	454	51%	46	10%
September 2020	1102	612	56%	66	11%

*Data are reported as percentage of the dietary supplements
** Data are reported as percentage of the HDS

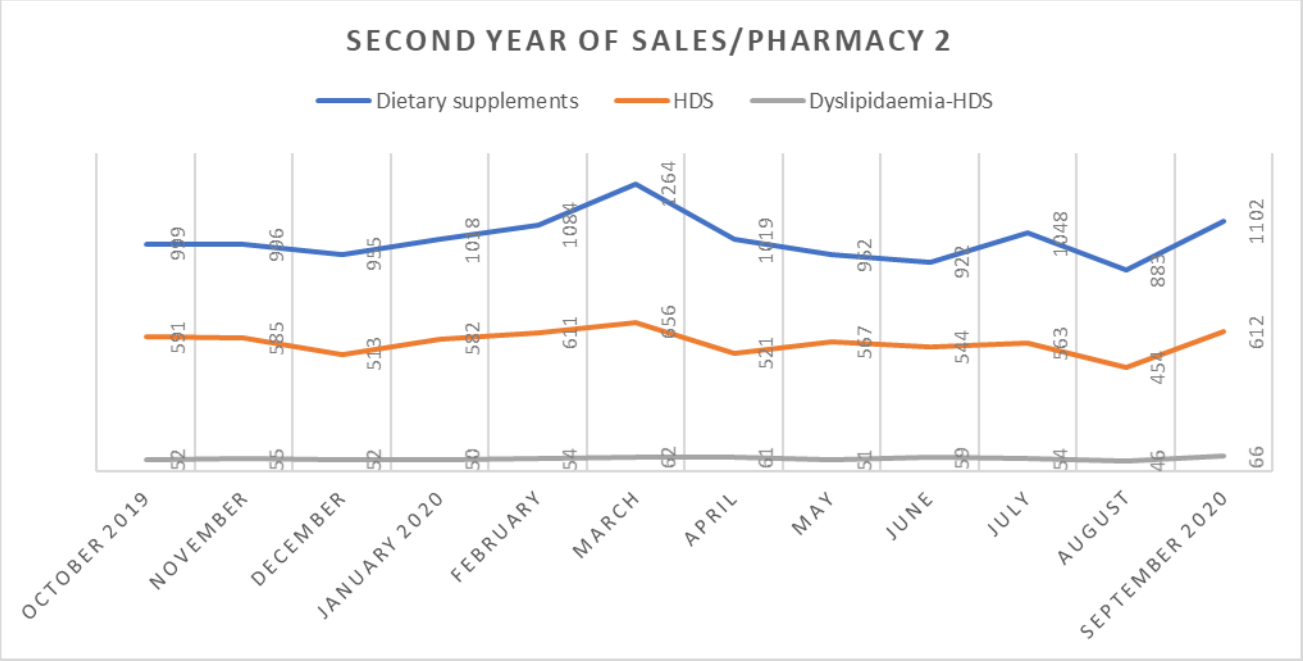

Figure 1.6. Sales data of pharmacy 2 during the second year

Table 2.4. First year of sales/pharmacy 1

Month	Dietary supplements	HDS (n)	HDS (%)*	Body weight loss HDS (n)	Body weight loss HDS (%)**
October 2018	858	343	40%	32	9%
November	683	293	43%	30	10%
December	644	269	42%	20	7%
January 2019	698	274	39%	32	12%
February	677	255	38%	33	13%
March	721	300	42%	24	8%
April	665	287	43%	27	9%
May	710	293	41%	38	13%
June	668	282	42%	26	9%
July	774	336	43%	31	9%
August	482	182	38%	16	9%
September 2019	703	335	48%	26	8%

*Data are reported as percentage of the dietary supplements
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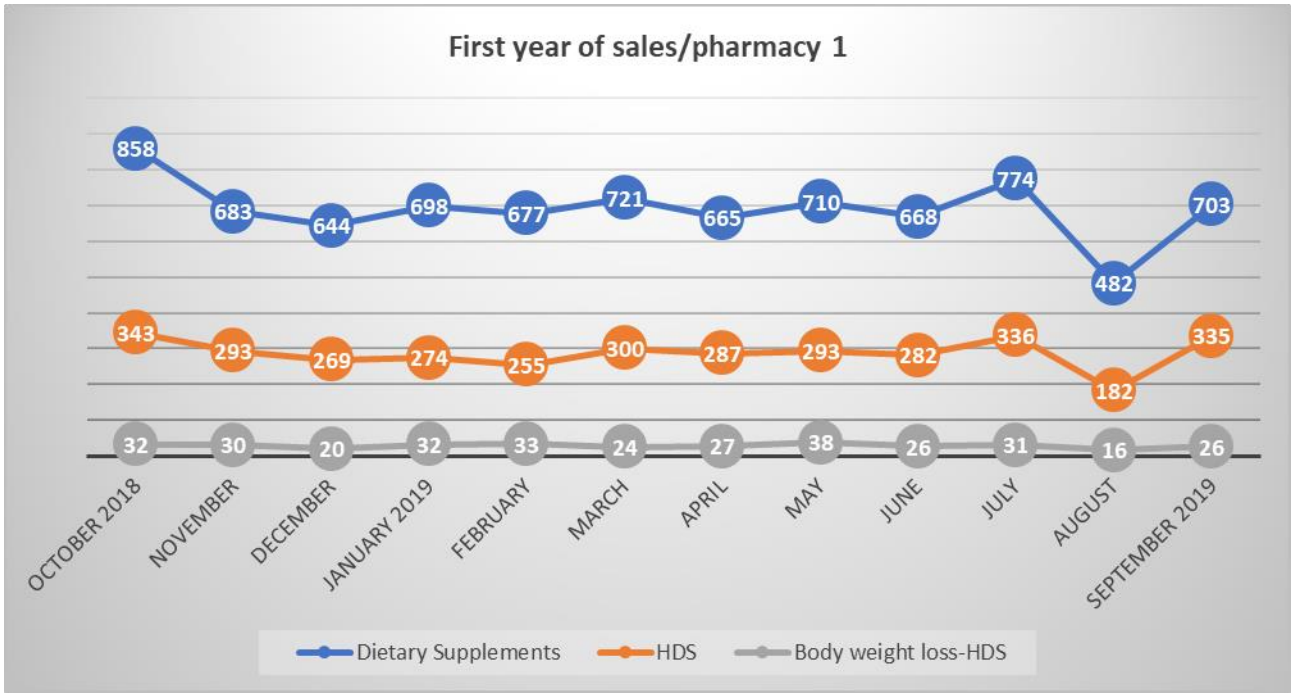

Figure 2.4. Sales data of pharmacy 1 during the first year

Table 2.5. Second year of sales/pharmacy 1

Month	Dietary supplements	HDS (n)	HDS (%)*	Body weight loss HDS (n)	Body weight loss HDS (%)**
October 2019	826	357	43%	28	8%
November	782	364	47%	28	8%
December	694	306	44%	20	7%
January 2020	865	354	41%	26	7%
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August	673	252	37%	14	6%
September 2020	634	280	44%	27	10%

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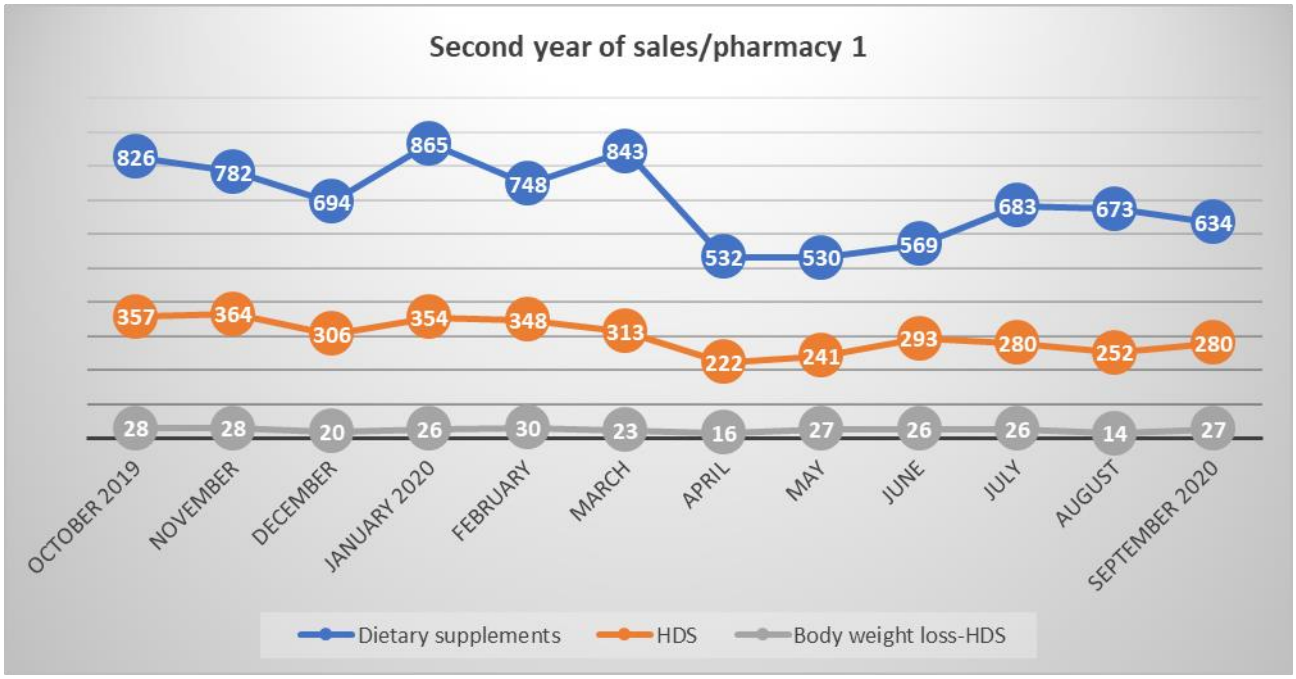

Figure 2.5. Sales data of pharmacy 1 during the second year

Table 2.6. First year of sales/pharmacy 2

Month	Dietary supplements	HDS (n)	HDS (%)*	Body weight control HDS (n)	Body weight loss HDS (%)**
October 2018	1054	608	58%	33	5%
November	1016	581	57%	30	5%
December	1061	588	55%	27	5%
January 2019	1148	641	56%	38	6%
February	1046	654	63%	31	5%
March	1124	631	56%	54	9%
April	939	541	58%	81	15%
May	1039	586	56%	72	12%
June	937	479	51%	52	11%
July	2050	1020	50%	92	9%
August	2050	1054	51%	93	9%
September 2019	428	243	57%	20	8%

*Data are reported as percentage of the dietary supplements
** Data are reported as percentage of the HDS

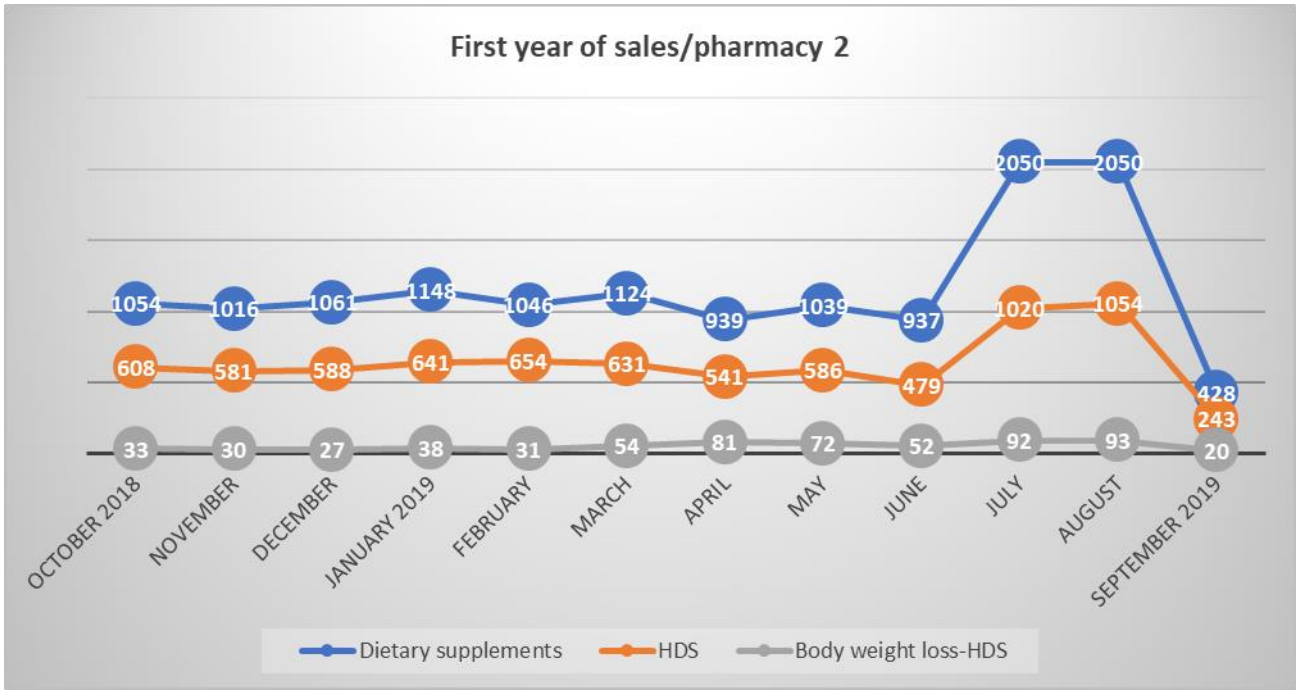

Figure 2.6. Sales data of pharmacy 2 during the first year

Table 2.7. Second year of sales/pharmacy 2

Month	Dietary supplements	HDS (n)	HDS (%)*	Body weight loss HDS (n)	Body weight loss HDS (%)**
October 2019	999	591	59%	40	7%
November	996	585	59%	39	7%
December	955	513	54%	32	6%
January 2020	1018	582	57%	47	8%
February	1084	611	56%	59	10%
March	1264	656	52%	59	9%
April	1019	521	51%	79	15%
May	952	567	60%	104	18%
June	922	544	59%	54	10%
July	1048	563	54%	80	14%
August	883	454	51%	30	7%
September 2020	1102	612	56%	43	7%

*Data are reported as percentage of the dietary supplements
** Data are reported as percentage of the HDS

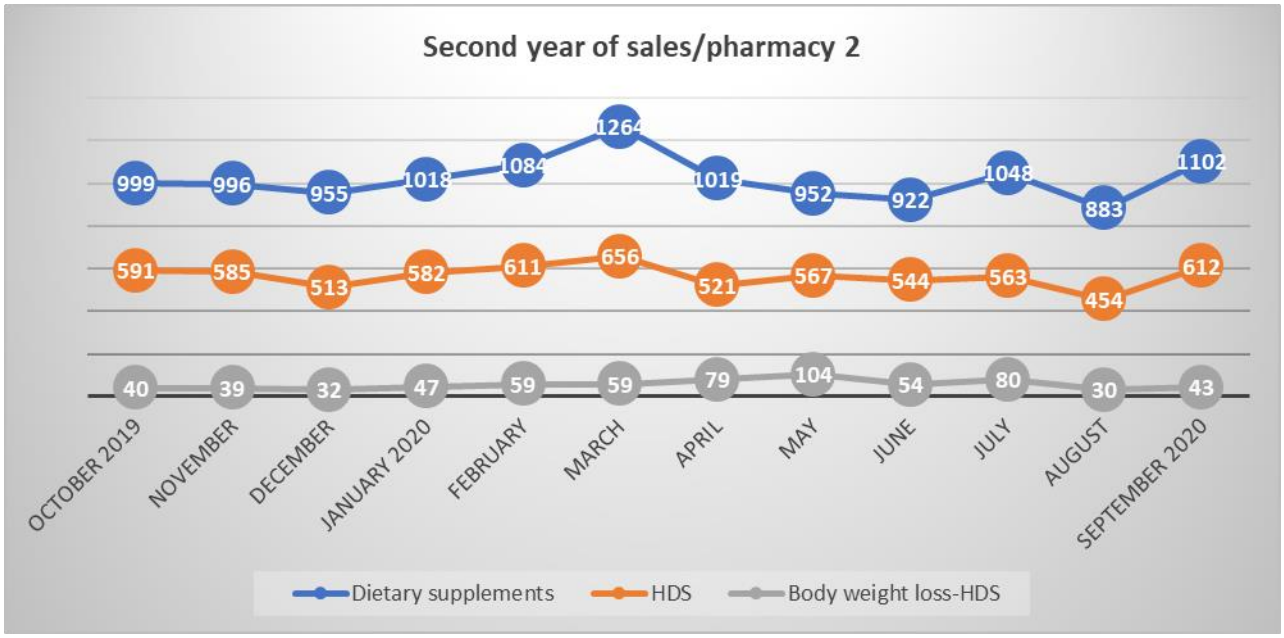

Figure 2.7. Sales data of pharmacy 2 during the second year

Research products

Publications in indexed journals

Allkanjari O, Menniti-Ippolito F, Ippoliti I, Di Giacomo S, Piccioni T & Vitalone A (2022) A descriptive study of commercial herbal dietary supplements used for dyslipidemia—Sales data and suspected adverse reactions. *Phytotherapy Research*. 1–22. https://doi.org/10.1002/ptr.7473

Allkanjari O (2021) The safety concern of plant-based supplements: A public health topic. *International Journal of Health Planning and Management*. 36(4):1370-1372.

Vitalone A, Allkanjari O, Durazzi F, Guizzetti M, & Aleandri V (2021) The use of herbal products during pregnancy: which is the risk perception? *American Journal of Phytomedicine and Clinical Therapeutics*. 9 No.1:1

Cicero A, Allkanjari O, Busetto GM, Cai T, Larganà G, Magri V, Perletti G, Robustelli Della Cuna F, Russo G, Stamatiou K, Trinchieri A & Vitalone A (2019) Nutraceutical treatment and prevention of benign prostatic hyperplasia and prostate cancer. *Archivio Italiano Di Urologia E Andrologia*, 91(3).

Vitalone A & Allkanjari O (2019) Studi preclinici su piante medicinali utilizzate nel trattamento delle patologie prostatiche. *Archivio Italiano di Urologia e Andrologia*. 91:3, pp. 3-8.

Vitalone A & Allkanjari O (2018) Epilobium spp: Pharmacology and Phytochemistry. *Phytotherapy Research*. 32(7):1229-1240.

Allkanjari O & Vitalone A (2015) What do we know about phytotherapy of benign prostatic hyperplasia? *Life Science*. 126:42-56.

Summaries/posters at national or international congresses

Allkanjari O, Di Giacomo S; Mazzanti G, Menniti-Ippolito F, Piccioni T, & Vitalone A. Herbal dietary supplements used in weight control and dyslipidemia: preliminary study of pharmacies sales data. (04f Poster). pp. 91-91. 39° *Congresso Nazionale della Società Italiana di Farmacologia – SIF*, 20-23 Novembre 2019, Firenze.