Title: FORMULATION BASED ON MICRONIZED ZEOLITE, GREEN TEA EXTRACT, AND GENISTEIN AS A THERAPEUTIC AGENT FOR REDUCTION OF BODY WEIGHT AND CELLULITE

Abstract: This invention relates to a pharmaceutical formulation based on variable portions of: (i) micronized zeolite (MZ) of general formula: \(\text{Me}^{x+}\cdot_{y}\left[(\text{Al}_{x-1}\text{Si}_{x}\text{O}_{2x+1})\cdot_{y}\text{H}_{2y}\right]\) (MZ) wherein Me= Na, K, Mg, Ca; whereas ratio of silicon to aluminum, y:x is between 6:1 to 1:1; number of crystalline water m is from 0 to 20, which is characterized by particles size < 5 μm; in concentrations from 1-50%, most preferably from 3-30%; (ii) Green tea extract containing at least 30% of epigallocatechin gallate (EGCG), and 5% of caffeine; in concentrations from 0.1-90%, most preferably from 20-90%; (iii) genistein; in concentrations from 0.05-20%, most preferably from 1-10%; and (iv) one or more excipients which yield in desired pharmaceutical or cosmetic form: tablets, capsules, ointments, creams, gels, lotions, shampoos, powders, liquid powders, syrups, suspensions, and therapeutic pastes; in concentrations from 1-98.85%, most preferably from 10-75%; which is useful for highly effective reduction of body weight and cellulite.
FORMULATION BASED ON MICRONIZED ZEOLITE, GREEN TEA EXTRACT, AND GENISTEIN AS A THERAPEUTIC AGENT FOR REDUCTION OF BODY WEIGHT AND CELLULITE

DESCRIPTION

THE FIELD OF THE INVENTION

The present invention relates to a formulation comprising micronized zeolite, green tea extract, genistein, and one or more optional ingredients which is used as an effective therapeutic agent for reduction of body weight and cellulite.

THE SUMMARY OF THE INVENTION

The present invention solves technical problem of efficient reduction of body weight and cellulite, based on formulation consisting of variable portions of:

(i) micronized zeolite (MZ) of general formula:

\[(\text{Me}^{n+})_{x/\alpha}[\text{AlO}_2\alpha\text{SiO}_2\beta]\cdot m\text{H}_2\text{O} \quad \text{(MZ)}\]

wherein Me= Na, K, Mg, Ca, Fe, Zn, Mn, Cr; whereas ratio of silicon to aluminium, y:x is between 6:1 to 1:1; number of crystalline water \( m \) is from 0 to 20, which is characterized by particles size < 5 \( \mu \)m; in concentrations from 1-50%, most preferably from 3-30%;

(ii) Green tea extract containing at least 30% of epigallocatechin gallate (EGCG; 1), and 5% of caffeine (2); in concentrations from 0.1-90%, most preferably from 20-90%;
(iii) genistein (3); in concentrations from 0.05-20%, most preferably from 1-10%;

and

(iv) one or more excipients which yield in desired pharmaceutical or cosmetic form: tablets, capsules, ointments, creams, gels, lotions, shampoos, powders, liquid powders, syrups, suspensions, and therapeutic patches; in concentrations from 1-98.85%, most preferably from 10-75%.

PRIOR ART

Obesity condition is one of the major risk factors for a numerous diseases of modern people such as hypertension, increased blood triglycerides and cholesterol, atherosclerosis, diabetes, etc. Increased body weight also causes several cosmetic disadvantages in both female and male subjects. One of the most known conditions within female population is enhanced occurrence of cellulite.

The obesity and accompanied condition of cellulite (in female subjects) can be treated with numerous commercial herbal and over-the-counter preparations. Some of them are based on natural substances which physically adsorbs fatty substances in the gastrointestinal (GI) tract. In this manner they impair absorption of fats in GI tract, and help to eliminate them by feces.
Other active substances act at some levels of metabolism by speeding-up the catabolism of triglycerides.

Among them, Green tea extract [S. Sang, J. D. Lambert, C-T. Ho, C. S. Yang: Green Tea Polyphenols, Encyclopedia of Dietary Supplements, Marcel&Dekker (2005) 327-336] due to its content of epigallocatechin gallate (1), and caffeine (2) has been used for treatment of obesity, cellulite, and associated metabolic syndrome both as single ingredient or in combinations with kidney bean extracts [G. S. Birketvedt, CA2627314 (2007)], pregnane glycosides [R. Kamala, R. Ramaswamy, CA2563952 (2005)], pine needle extract [J. Y. Kim, KR20040089258 (2004)], etc.

EGCG (1) is effective in treatment of obesity due to its strong lipolytic and antioxidative effects:

(i) antioxidative effect; In isolated myocytes it inhibited ouabain-induced reactive oxygen species (ROS) production and cell proliferation;

(ii) it reduces the levels of cholesterol, triglycerides, and lipid peroxides in serum; and


Caffeine (2) promotes lipolysis upon metabolic conversion to paraxanthine (under the action of cytochrome P450 oxidase). In this manner it can raise concentration of triglycerides lipolytic products: glycerol and higher fatty acids.

In conclusion, Green tea extract helps reduction of body weight and cellulite by combination of the following pathways:

(i) preventively, by strong antioxidative action of EGCG and related polyphenols; and
(ii) curatively, by lipolytic action of both EGCG (1) and caffeine (2) or its main metabolite paraxanthine.


(i) decreased food intake;
(ii) reduced body weight;
(iii) decreased fat pad weight; and
(iv) causes adipose tissue apoptosis.

(i) by significant reduction of glucose conversion to total lipids (confirmed in experiments with both in presence and absence of insulin);
(ii) by reduction of fatty acids synthesis; and
(iii) by their esterification to lipids.

Due to the fact that cellulite formation is basically inflammatory process, observed effects of genistein are responsible for its anti-cellulite action. Moreover, by inhibiting blood glucose concentration (hypoglycemic effect), genistein also contributes to lowering of fatty acids level and thus subsequently triglycerides biosynthesis [S. Y. Cheng, N. S. Shaw, K. S. Tsai, C. Y. Chen: The hypoglycemic effects of soy isoflavones on postmenopausal women, J. Womens Health (Larchmt) 13 (2004) 1080-1086; E. A. Pop, L. M. Fischer, A. D. Coan, M. Gitzinger, J. Nakamura, S. H. Zeisel: Effects of a high daily dose of soy isoflavones on DNA damage,

In this manner, genistein acts not only on reduction of biosynthesis of lipids, but also on elimination (adipocite apoptosis) of already present fat deposits.

Technical problem of effective reduction of body weight and treatment of cellulite is solved on a new and more efficient manner as will be demonstrated in detailed description of the invention.

**DETAILED DESCRIPTION OF THE INVENTION**

The present invention relates to the formulation consisting of variable amounts of:

(i) micronized zeolite (MZ) of general formula:

\[
(\text{Me}^{n+})_{2n}[\text{Al}\text{O}_2]_n\text{(Si}\text{O}_2)_y\text{]•mH}_2\text{O} \quad (\text{MZ})
\]

wherein Me= Na, K, Mg, Ca, Fe, Zn, Mn, Cr; whereas ratio of silicon to aluminum, y:x is between 6:1 to 1:1; number of crystalline water m is from 0 to 20, which is characterized by particles size < 5 µm; in concentrations from 1-50%, most preferably from 3-30%;

(ii) Green tea extract containing at least 30% of epigallocatechin gallate (EGCG; 1), and 5% of caffeine (2); in concentrations from 0.1-90%, most preferably from 20-90%;
(iii) genistein (3); in concentrations from 0.05-20%, most preferably from 1-10%;

and

(iv) one or more excipients which yield in desired pharmaceutical or cosmetic form: tablets, capsules, ointments, creams, gels, lotions, shampoos, powders, liquid powders, syrups, suspensions, and therapeutic patches; in concentrations from 1-98.85%, most preferably from 10-75%.

The formulation from the present invention provides highly effective reduction of body weight and cellulite.

We have been found that micronized zeolite clinoptilolite, or similar zeolites like zeolite A, when administered orally with Green tea extract and genistein surprisingly does act as very effective composition for treatment of obesity and cellulite.

In comparison to several persons of both sexes suffering from obesity, who consumed (3x2 cps/day) control capsules containing Green tea extract (390 mgs/cps) and genistein (50 mgs/cps), those consuming the formulation of the present invention in the form of the same kind of capsules (see Example 2) containing also micronized zeolite clinoptilolite (MZ; 50 mgs/cps) reached significantly greater reduction in body weight.
In addition several female subjects during this study reported a profound reduction of intensity of cellulite condition. Moreover several women who used topical variant of the formulation of the present invention in the form of hydrophilic (O-W) cream containing 2% of micronized zeolite clinoptilolite (MZ), 2% of Green tea extract and 0.25% of genistein (see Example 4), also reported significant reduction of cellulite in comparison to women which used a control cream of the same composition but without MZ.

Possible mechanism of action

Silicon as essential microelement with a number of roles in human organism is biologically available in the form of ortho-silicic acid (H₄SiO₄). Among others, silicon acts as anti-inflammatory in various conditions and diseases such as seborrheic dermatitis, neurodermitis, atopic dermatitis, skin irritations, disorders connected with decubitus, accelerates wound healing, and stimulates biosynthesis of skin building proteins collagen and elastin. [C. D. Seaborn, F. H. Nielsen: Silicon deprivation decreases collagen formation in wounds and bone, and ornithine transaminase enzyme activity in liver, Biol. Trace Element Res. 89 (2002) 251; M. R. Calomme, D. A. V. Berghe: Supplementation of calves with stabilised orthosilicic acid effect on the Si, Ca, Mg and P concentration in serum and the collagen concentration in skin and cartilage, Biol. Trace Element Res. 56 (1997) 153].


Recently, we have described that micronized zeolite clinoptilolite (MZ) acts as effective pharmaceutically-acceptable source of highly bioavailable silicon. MZ is capable of releasing soluble silicon even in neutral water, presumably in the form of ortho-silicic acid, as
demonstrated by quantitative analyses of aqueous supernatants obtained after trituration of MZ in pure redistilled water [Novatech, PCT7HR2008/000030].

Preparations and characterization of micronized zeolite clinoptilolite in all suitable pharmaceutical forms (Na\(^+\), K\(^+\), Mg\(^{2+}\), Ca\(^{2+}\), Fe\(^{2+}/Fe^{3+}\), Zn\(^{2+}\), Mn\(^{2+}\), Cr\(^{3+}\)) were performed in the same manner as shown in our mentioned previous application. Alternatively commercially available zeolite A can be used after micronization.

According to our best knowledge, herein described synergistic effect of micronized zeolite (MZ) with Green tea extract and genistein in the treatment of obesity and cellulite conditions is a result of at least two possible mechanisms:

(i) Highly bioavailable silicon (from MZ) acts anti-inflammatorically what subsequently helps basic pharmacological actions of both EGCG (1) and caffeine (2; from Greefi tea extract) as well as of genistein (3); and

(ii) ortho-Silicic acid (from MZ) forms relatively stable complexes with ortho-diphenols like EGCG, and \(\beta\)-diketons or \(\beta\)-keto-enols (or analogous \(\beta\)-keto-phenols) such as genistein. In this manner it might enhance biological activity of these polyphenols by keeping their at sufficient concentrations in body fluids. This might occur due to decreased rate of their metabolism in liver through known polyphenols-elimination pathway by glucuronidation or sulfate-conjugation.

**Composition of the formulation according to the invention**

The formulation of the present invention is consisting of the mentioned components in the following concentrations:

(i) micronized zeolite (MZ) of general formula:

\[
(\text{Me}^{n+})_{\text{y/n}}[(\text{AlO}_2)_x(\text{SiO}_2)_y]\cdot m\text{H}_2\text{O} \quad \text{(MZ)}
\]

wherein Me\(=\) Na, K, Mg, Ca, Fe, Zn, Mn, Cr; whereas ratio of silicon to aluminum, y:x is between 6:1 to 1:1; number of crystalline water \(m\) is from 0 to 20, which is characterized by particles size < 5 \(\mu\)m; in concentrations from 1-50%, most preferably from 3-30%;
(ii) Green tea extract containing at least 30% of epigallocatechin gallate (EGCG; 1), and 5% of caffeine (2); in concentrations from 0.1-90%, most preferably from 20-90%;

![Chemical structure of EGCG](image)

(iii) genistein (3); in concentrations from 0.05-20%, most preferably from 1-10%;

![Chemical structure of genistein](image)

and

(iv) one or more excipients which yield in desired pharmaceutical or cosmetic form: tablets, capsules, ointments, creams, gels, lotions, shampoos, powders, liquid powders, syrups, suspensions, and therapeutic patches; in concentrations from 1-98.85%, most preferably from 10-75%.

Tablets, capsules, syrups, suspensions and therapeutic patches are preferred pharmaceutical forms for oral administration in treatment of obesity conditions, whereas forms such as ointments, creams, gels, lotions, shampoos, powders, liquid powders, and therapeutic patches are more suitable for topical treatment of cellulite.

Excipients are selected from the groups consisting of fillers, binders, disintegrants, lubricants, emollients, emulsifiers, tensides, humectants, solvents, thickeners, preservatives, antioxidants, stabilizers, and other functional additives which may help basic therapeutic action of above-defined main active substances.
In solid dosage forms such as tablets, fillers are selected from the group consisting of microcrystalline cellulose, lactose monohydrate, calcium hydrogenphosphate, sorbitol, starch, modified starches, etc. As fillers in powders and liquid powders, the following substances can be used: talc, kaolin, bentonite, montmorillonite, precipitated calcium carbonate, basic magnesium carbonate, calcium silicate, aluminum hydroxide, silicon dioxide, or mixtures of these substances.

In solid dosage forms, binders are selected from the group consisting of gelatin, lactose monohydrate, sorbitol, saccharose, xylitol, maltitol, mannitol, starch, modified starches, methylcellulose, 2-hydroxyethylcellulose, 2-hydroxypropylcellulose, sodium carboxymethylcellulose, polyethyleneglycols, polyglycerols, polyvinylpyrrolidone, polyvinylpyrrolidone co-polymers, carrageenans, or mixtures of these substances.

Disintegrants in solid dosage forms are selected from the group consisting of starch, modified starches, sodium starch glycolate, methylcellulose, sodium carboxymethylcellulose, 2-hydroxyethylcellulose, 2-hydroxypropylcellulose, polyvinylpyrrolidone, polyvinylpyrrolidone co-polymers, or mixtures of these substances.

Lubricants in solid dosage forms and powders are selected from the group consisting of: metal soaps such as magnesium stearate, calcium stearate, and zinc stearate; higher fatty acids like stearic acid; talc; silicon dioxide; or mixtures of these substances.

Emollients in semi-solid and liquid forms of the formulation for topical treatment of cellulite such as ointments, creams, and lotions, are selected from the group consisting of: paraffin wax; mineral oil; petroleum jelly; ozokerite; synthetic esters of higher fatty acids like isopropyl myristate, isopropyl palmitate, trimethylolpropane tristearate, glyceryl tricaprylate; natural waxes such as beeswax or spermaceti; liquid natural waxes such as jojoba oil; synthetic waxes such as lauryl laurate; plant oils such as soybean oil, sweet almond oil, sunflower seed oil, fish oil, olive oil, wheat germ oil, corn germ oil, avocado oil, palm oil, coconut oil; semi-solid or liquid silicones; higher fatty alcohols such as cetyl alcohol, stearyl alcohol, oleyl alcohol; or mixtures of these substances.
Emulsifiers in creams, ointments, and other forms of the formulation such as lotions and shampoos, are selected from the group consisting of: metal salts of sulphates of higher fatty alcohols like sodium laurylsulphate, sodium lauryl ethyleneglycol sulphate, sodium lauryl diethylene glycol sulphate; ethoxylates of higher fatty alcohols such as polyoxyethylene(2) lauryl ether, polyoxyethylene(l θ) lauryl ether, polyoxyethylene(23) lauryl ether, and others, where 2, 10 and 23 represent average number of ethyleneglycol units bounded on higher fatty alcohol; ethoxylates of higher fatty acids such as polyoxyethylene(2) laurate, polyoxyethylene(l θ) laurate, polyoxyethylene(23) laurate, and others, wherein 2, 10 and 23 represent average number of ethyleneglycol units bounded on higher fatty acid; esters of sorbitan such as polyoxyethylene sorbitan monolaurate; lanolin; ethoxylated lanolins; glyceryl monostearate; beeswax ethoxylates; or mixtures of these substances.

Tensides in liquid forms of the formulation like shampoos, are selected from the group consisting of: metal salts of sulphates of higher fatty alcohols such as sodium laurylsulphate, sodium lauryl ethyleneglycol sulphate, sodium lauryl diethylene glycol sulphate, potassium laurylsulphate, potassium lauryl ethyleneglycol sulphate, potassium lauryl diethylene glycol sulphate, ammonium laurylsulphate, ammonium lauryl ethyleneglycol sulphate, ammonium lauryl diethylene glycol sulphate, sodium or potassium cocoamphodipropionate; disodium or dipotassium cocoamphodiacetate; polyoxyethylene(l θ) lauryl ether, polyoxyethylene(23) lauryl ether, polyoxyethylene(l θ) stearyl ether, polyoxyethylene(23) stearyl ether, polyoxyethylene(l θ) oleyl ether, polyoxyethylene(23) oleyl ether, and other ethoxylates of higher fatty alcohols with H.L.B. value >10; polyoxyethylene(l θ) laurate, polyoxyethylene(23) laurate, polyoxyethylene(l θ) stearate, polyoxyethylene(23) stearate, polyoxyethylene(l θ) oleate, polyoxyethylene(23) oleate; or other ethoxylates of higher fatty acids with H.L.B. value >10; esters of sorbitan such as polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyoxyethylene sorbitan monooleate, or other sorbitan derivatives with H.L.B. value >10; mono- or diethanolamides of higher fatty acids; cocoamidopropyl betaine; glycosides of higher fatty alcohols like cocogluicoside; sodium or potassium di(2-ethylhexyl)sulfosuccinate; disodium or dipotassium 2-ethylhexylsulfosuccinate; cationic tensides such as cetyltrimethylammonium bromide, didecyl dimethylammonium chloride, benzalkonium chloride, cetlybenzyl dimethylammonium bromide, cetylpyridinium chloride; metal salts of
higher fatty acids such as sodium or potassium salts of lauric, myristic, palmitic, stearic, oleic, or ricinoleic acid; or mixtures of these substances.

Humectants are selected from the group consisting of glycerol, 1,2-propyleneglycol, 1,3-propyleneglycol, hexyleneglycol, 1,3-butanediol, polyethyleneglycols, polyglycerols, sorbitol, xylitol, saccharose, urea, sodium hyaluronate, or mixtures of these substances.

Solvents in liquid forms of the formulation like lotions are selected from the group consisting of purified water, ethanol, 1-propanol, isopropanol, isosorbide dimethylether, diethyleneglycol monomethylether, diethyleneglycol dimethylether, diethyleneglycol monoethylether, diethyleneglycol diethylether, triethyleneglycol monomethylether, triethyleneglycol dimethylether, triethyleneglycol monoethylether, triethyleneglycol diethylether, ethyl lactate or other lactate esters with lower aliphatic alcohols, triethylhexanoin, or mixtures of these substances.

Thickeners in the formulation are selected from the group consisting of: polyacrylic acid, its co-polymers, or their sodium, potassium, or triethanolamine salts; methylcellulose; sodium carboxymethylcellulose; 2-hydroxyethylcellulose; 2-hydroxypropylcellulose; starch; modified starches; polyglycerols; polyethyleneglycols; gelatin; pectin; agar agar; carrageenans; gum arabic; alginic acid; sodium alginate; montmorillonite; bentonite; or mixtures of these substances.

Preservatives are selected from the group consisting of: methyl 4-hydroxybenzoate; ethyl 4-hydroxybenzoate; propyl 4-hydroxybenzoate; butyl 4-hydroxybenzoate; triclosan; chlorhexidine or its dihydrochloride, diacetate, or digluconate salts; sorbic acid; potassium sorbate; benzoic acid; sodium benzoate; 2-bromo-2-nitropropane-1,3-diol; 2-hydroxybiphenyl; 2-phenoxyethanol; 4-chloro-m-cresol; thymol; eugenol; methyl salicylate; or mixtures of these substances.

Antioxidants are selected from the group consisting of 2,6-di-terc-butyl-4-hydroxytoluene (BHT), terc-butylhydroxyanisole (BHA), tocopherol, tocopherol acetate, ascorbic acid, ascorbyl palmitate, or mixtures of these substances.
Stabilizers are selected from the group consisting of disodium ethylenediamine tetraacetate (Na₂EDTAx2H₂O), disodium N-(2-hydroxyethyl)ethylenediamine triacetate [Na₂H(HEDTA)], disodium diethylenetriamine pentaacetate [Na₂H₃(DTPA)], disodium citrate [Na₂(C(OH)(COOH)(CH₂COO)₂], or mixtures of these substances.

It is well known to those skilled in the art that several mentioned excipients can play two-or-more roles in the formulation of the present invention. Therefore numerous combinations are possible but still remain within the scope of this invention.

Other functional additives which may help basic therapeutic action of above-defined main active substances are selected from the group known to those skilled in the art as anti-inflammatory and/or antiphlogistic agent, antioxidant, astringent, and various skin tonifying agents.

Anti-inflammatory and/or antiphlogistic agent is selected from the group consisting of: paracetamol; metamizol sodium; acetylsalicylic acid and its salts with pharmaceutically acceptable bases; salicylic acid and its salts with pharmaceutically acceptable bases; salicylamide; phenylbutazone sodium; propyphenazone; oxyphenbutazone; mofebutazone; bumadizon calcium; phenazone; ethenzamide; ketoprofen, ibuprofen, naproxen, flurbiprofen, pirprofen, mefenamic acid, fluphenamic acid, thiaiprolen acid or their salts with pharmaceutically acceptable bases; diaclofenac sodium; indomethacin; piroxicam; meloxicam; codeine; caffeine; extract of St John's wort (Hypericum perforatum); azulene; extract of Chamomile (Matricaria recutita); extract of Marigold (Calendula officinalis); extract of Arnica (Arnica montana); extract of White Willow (Salix alba); extract of Spiny Restharrow (Ononis spinosa); menthol; essential oil or extract of Mint (Mentha piperita); eucalyptol; essential oil or extract of Rosemary (Rosmarinus officinalis); essential oil or extract of Lavender (Lavandula officinalis); purified turpentine oil; camphor; pinene; bornyl acetate; terpineol; terpenyl acetate; eugenol; essential oil of Lemon (Citrus limonum); essential oil of Orange (Citrus aurantium); essential oil of Common Juniper (Juniperus communis); essential oil of Clove (Syzygium aromaticum); extract of Green Tea (Camellia sinensis); extract of Rooibos (Aspalathus linearis); extract of Nettle (Urtica dioica); extract of Horse-Chestnut (Aesculus hippocastanum); extract of Mullein (Verbascum phlomoides); extract of European Holly (Ilex
aquifolium); extract of Borage (Borago officinalis); extract of Burdock (Arctium lappa); extract of Ribwort Plantain (Plantago lanceolata); extract of Century Plant (Agave americana); extract of Ground Pine (Lycopodium clavatum); methyl nicotinate; benzyl nicotinate; glucosamine sulfate; L-histidine; chondroitin sulfate; hyaluronidase; heparin sodium; coumarin; choline and its salts; sulphur; extracts of plants with significant content of silicic acid (H₄SiO₄) such as Field Horsetail (Equisetum arvense), Lungwort (Pulmonaria officinalis), Common Knotgrass (Polygonum aviculare), Couch Grass (Agropyron repens), Common Agrimony (Agrimonia eupatoria), Oat (Avena sativa); cortisone; hydrocortisone; dexamethasone; betamethasone; alclometasone; fluprednidene; prednisone; prednisolone; triamcinolone; methylprednisolone; paramethasone; clobetasol; diflorasone; fluocinolone; clocortolone; flumetasone; halometasone; fluocortolone; diflucortolone; mono- or diesters of mentioned synthetic steroids at 17- and/or 21-positions, or 16,17-acetonide derivatives such as hydrocortisone acetate, hydrocortisone-17-butyrate, betamethasone-17-valerate, betamethasone-17,21-dipropionate, alclometasone-17,21-dipropionate, triamcinolone-16α,17α-acetonide; or mixtures of these substances.

Antioxidant is selected from the group consisting of: extract of Rooibos (Aspalathus linearis); extract of Nettle (Urtica dioica); extract of Bilberry (Vaccinium myrtillus); extract of Orange (Citrus aurantium); silymarin; extract of Milk Thistle (Silybum marianum); ascorbic acid, its salts, and esters such as ascorbyl palmitate; tocoferol; tocoferol acetate; niacinamide; rutin; quercetin; extracts of plants with significant content of rutin and/or quercetin; cyanidin; hesperidin; diosmin; lycopene; extracts of plants with significant contents of lycopene; resveratrol; tetrahydrocurcumin; rosmarinic acid; extract of Rosemary (Rosmarinus officinalis); hypericin; extract of St John's wort (Hypericum perforatum); ellagic acid; chlorogenic acid; 3,4-dihydroxycinnamic acid; oleuropein; extract of Olive leaves (Olea europea); extract of Grape seed; pycnogenol; carnosine; α-lipoic acid; glutathione; extracts of plants with significant content of silicic acid (H₄SiO₄) such as Field Horsetail (Equisetum arvense), Lungwort (Pulmonaria officinalis), Common Knotgrass (Polygonum aviculare), Couch Grass (Agropyron repens), Common Agrimony (Agrimonia eupatoria), Oat (Avena sativa), Silverweed (Potentilla anserina), Common Bistort (Polygonum bistorta), Common Sage (Salvia officinalis); or mixtures of these substances.
Astringent is selected from the group consisting of: zinc oxide; zinc stearate; zinc tannate; zinc acetate; zinc sulphate; zinc chloride; iron(III) chloride; aluminum sulphate; potassium aluminum sulphate; aqueous basic aluminum acetate; aluminum acetotartrate; bismuth subnitrate; bismuth subcarbonate; bismuth phosphate; bismuth tannate; calamine; copper(II) sulphate; silver nitrate; silver-proteine; aescin; extract of Horse-Chestnut (*Aesculus hippocastanum*); Balsam of Peru; silica gel; kaolin; talc; titanium dioxide; tannic acid; albumin tannate; methylene ditannate; extracts with significant content of tannins such as extracts of Oak bark (*Cortex Quercus ruber, Quercus sessiliflora*), Bearberry leaves (*Arctostaphylos uvae ursi*), Common Agrimony (*Agrimonia eupatoria*), Silverweed (*Potentilla anserina*), Common Bistort (*Polygonum bistorta*), Common Sage (*Salvia officinalis*), etc.; or compatible mixtures of these substances.

Skin tonifying agents are selected from the group consisting of: vitamins and pro-vitamins like retinol palmitate, β-carotene, niacinamide, d-panthenol, calcium pantothenate, folic acid, riboflavin, pyridoxine, thiamine, biotin, cyanocobalamin, ascorbic acid its salts and esters such as ascorbyl palmitate, cholecalciferol, tocopherol, tocopherol acetate, phylloquinone, menaquinone, menadione; animal and plant oils with high contents of omega-3 higher fatty acids such as fish or linseed oil; choline chloride; protein hydrolysates; algae extracts; extract of Witch-hazel (*Hamamelis virginiana*); extract of Centaurium (*Erythraea centaurum*); extract of Mullein (*Verbascum phlomoides*); extract of European Holly (*Ilex aquifolium*); extract of Common Ivy (*Hedera helix*); chlorophyll; α-hydroxyacids like glycolic, lactic, malic, citric, and tartaric acid; urea; co-enzyme Q10; or mixtures of these substances.

The formulation of the present invention can be in the form of tablets, capsules, ointments, creams, gels, lotions, shampoos, powders, liquid powders, syrups, suspensions, and therapeutic patches. The formulations are produced by common procedures known to those skilled in the art of cosmetic and/or pharmaceutical technology [S. C. Gad (Ed.): *Pharmaceutical Manufacturing Handbook: Production and Processes*, Wiley (2008)]. Several possible variations are possible but which essentially remain under the scope of this invention.
EXAMPLES

General information

Preparations and characterizations of micronized zeolite (MZ) in all possible forms (Na, K, Mg, Ca, Fe, Zn, Mn, Cr) were carried out in our R&D department according to procedures previously described in our recent patent application [Novatech, PCT/HR2008/000030]. Zeolite A and natural clinoptilolite were purchased and micronized in our laboratory. The term room temperature means: 20-25 °C.

Example 1

Preparation of the formulation in the form of 1000 mg tablets for reduction of body weight

Content (100 g of tablet mixture): (a) Micronized zeolite A (MZ; 10.00 g; 10%), (b) Green tea extract (40.00 g; 40%), (c) genistein (3; 10.00 g; 10%), (d) microcrystalline cellulose (15.00 g; 15%), (e) lactose monohydrate (20.00 g; 20%), (f) sodium starch glycolate (2.00 g; 2%), (g) polyvinylpyrrolidone (2.00 g; 2%), (h) magnesium stearate (1.00 g; 1%).

Procedure: Ingredients (a), (b), (c), (d), (e), (f) and (g) were homogenized in dry homogenizer during 15 minutes. Then, (h) was added and homogenization was continued for 15 minutes. Then, homogeneous mixture was milled, and compressed into tablets yielding approx. 100 tablets (1000 mg). Average tablet weight 993 mg.

Example 2

Preparation of the formulation in the form of capsules for reduction of body weight

Content (1000 g of capsules mixture): (a) Micronized zeolite clinoptilolite (MZ; natural, 100.00 g; 10%), (b) Green tea extract (740.00 g; 74%), (c) genistein (3; 100.00 g; 10%), (d) microcrystalline cellulose (50.00 g; 5%), (e) magnesium stearate (10.00 g; 1%).
Procedure: Previously milled ingredients (a), (b), (c), and (d) were homogenized in a homogenizer during 15 minutes. Then milled (e) was added and homogenization was continued for 15 minutes. Then the homogeneous mixture was capsulated into hard-gelatine capsules ("0") using a laboratory capsule filling machine yielding approx. 1850 cps. Average weight of capsules: 620 mgs brutto; 530 mgs netto.

Composition per cps: 500 mgs of genistein; 390 mgs of Green tea extract (corresponds to 175 mgs of EGCG and 40 mgs of caffeine); and 50 mgs of micronized clinoptilolite.

Example 3

Preparation of the formulation in the form of a syrup for reduction of body weight

Content (100 g of syrup): (a) Micronized zeolite clinoptilolite (MZ; Ca-form, 5.00 g; 5%), (b) Green tea extract (5.00 g; 5%), (c) genistein (3; 1.00 g; 1%), (d) sorbitol (70% solution in water; 60.00 g; 60%), (e) xylitol (1.00 g; 1%), (f) 1,2-propyleneglycol (10.00 g; 10%), (g) methyl cellulose (Ph. Eur. grade; 0.30 g; 0.3%), (h) methyl 4-hydroxybenzoate (0.20 g; 0.2%), (i) ethanol (0.60 g; 0.6%), 0) artificial strawberry arome (1.00 g; 1.0%); (k) purified water (15.90 g; 15.9%).

Procedure: Ingredient (g) was slowly added into previously prepared mixture of (d), (f), and (k) and vigorously stirred for 2 hrs. Then (a), (b), (c), (e), and (j) were added and homogenization was continued for 30 minutes. Then, separately prepared solution of (h) in (i) was added, and finally homogenized for 15 minutes, giving 100 gms of strawberry-coloured viscous syrup.

Example 4

Preparation of the formulation in the form of a cream for topical treatment of cellulite

Content (100 g of cream): (a) Petroleum jelly (18.00 g; 18%), (b) cetyl alcohol (16.00 g; 16%), (c) lanolin (2.00 g; 2%), (d) isopropyl myristate (2.00 g; 2%), (e) sodium laurylsulphate (1.00 g; 1%), (f) methyl 4-hydroxybenzoate (0.10 g; 0.1%), (g) ethyl 4-hydroxybenzoate (0.05 g; 0.05%), (h) propyl 4-hydroxybenzoate (0.025 g; 0.025%), (i) butyl 4-hydroxybenzoate
(0.025 g; 0.025%), G) sorbitol (7.00 g; 7%), (k) glycerol (3.00 g; 3%), (l) micronized zeolite clinoptilolite (MZ; natural; 2.00 g; 2%), (m) Green tea extract (2.00 g; 2%), (n) genistein (3; 0.25 g; 0.25%), (o) isosorbide dimethylether (1.00 g; 1%), (p) purified water (44.75 g; 44.75%), (q) fragrance (0.80 g; 0.8%).

Procedure: Ingredients (a) and (b) were carefully melted, and further heated to 80 °C with stirring. Then (c), (d), (e), (f), (g), (h), and (i) were added. The mixture was stirred at this temperature for 30 min. Water phase was prepared by dissolution of (j) and (k) in (p), and added drop-wise during 30 min into hot fatty-phase with vigorous stirring. Thus obtained emulsion was further stirred at temperatures between 80 °C and 50 °C during additional 30 minutes, and then (o), (l), (m), (n), and (q) were added. The cream was stirred at 50 °C for 30 minutes, and then carefully cooled to room temperature with constant stirring. The product was additionally homogenized by mixing at room temperature during 15 min. The product was orange-brown, fine, semi-solid cream with slight scent of fragrance employed.

Example S

Preparation of the formulation in the form of an ointment for topical treatment of cellulite

Content (100 g of ointment): (a) Petroleum jelly (40.00 g; 40%), (b) heavy mineral oil (21.10 g; 21.1%), (c) soyben oil (20.00 g; 20%), (d) sweet almond oil (10.00 g; 10%), (e) yellow beeswax (0.30 g; 0.3%), (f) micronized zeolite clinoptilolite (MZ; Ca-form; 3.00 g; 3%), (g) Green tea extract (3.00 g; 3%), (h) genistein (3; 0.50 g; 0.5%), (i) isosorbide dimethylether (1.00 g; 1%), G) d-panthenol (0.25 g; 0.25%), (k) tocoferol acetate (0.10 g; 0.1%), (l) lavender oil (0.75 g; 0.75%).

Procedure: Ingredients (b), (c), and (d) were slowly heated to 60 °C, and then (a) and (e) were added with stirring until clear oily liquid was formed. Then (f), (g), (h), (i), G), (k), and (l) were added, and stirring was continued for 15 minutes. Thus obtained mixture was carefully poured into small (25 mL) plastic jars. The product was in the form of fine, slightly orange-brown, semi-solid ointment of agreeable lavender scent.
Example 6

Preparation of the formulation in the form of a gel for topical treatment of cellulite

Content (100 g of gel): (a) 1,2-Propyleneglycol (25.00 g; 25%), (b) glycerol (3.00 g; 3%), (c) sorbitol (70% solution in water; 5.00 g; 5%), (d) ethanol (96%; 10.00 g; 10%), (e) Carbopol 934P (1.00 g; 1%), (f) triethanolamine (q.s.), (g) micronized zeolite clinoptilolite (MZ; Mg-form; 3.00 g; 3%), (h) Green tea extract (2.00 g; 2%), (i) genistein (3; 0.2 g; 0.2%), (j) methyl 4-hydroxybenzoate (0.15 g; 0.15%), (k) propyl 4-hydroxybenzoate (0.05 g; 0.05%), (l) purified water (49.10 g; 49.1%), (m) mixture of essential oils of lemon and cinnamon (2:1 w/w; 1.50 g; 1.5%).

Procedure: To vigorously stirred (1), (e) was added in small portions over 15 minutes. Obtained mixture was stirred at room temperature during 2 h giving clear colourless viscous liquid. Then other ingredients were added in the following order: (a), (b), (c), (d), (g), (h), (i), (j), and (k), and the mixture was stirred at room temperature for additional 30 minutes. Then (m) was added and stirred for 10 minutes, followed by (f) until the pH between 6-6.5 was reached, and mixed until the formation of orange-brown turbid gel of fine top-lemon, cinnamon-undertone scent. Finally the product was homogenized by stirring at room temperature for 15 minutes.

Example 7

Efficacy of capsule form of the formulation in reduction of body weight

Several persons of both sexes suffering from obesity were consumed (3x2 cps/day) control capsules containing Green tea extract (390 mgs/cps) and genistein (50 mgs/cps). Those persons which consumed the formulation of the present invention in the form of capsules containing, beside mentioned active substances, also micronized zeolite clinoptilolite (MZ; 50 mgs/cps) reached significantly greater and faster reduction in body weight.

In addition several female subjects during this study reported a profound decreasing of cellulite.
Example 8

Efficacy of cream form of the formulation for the topical treatment of cellulite

Several women which used the topical variant of the formulation of the present invention in the form of hydrophilic (O-W) cream containing 2% of micronized zeolite clinoptilolite (MZ), 2% of Green tea extract and 0.25% genistein (see Example 4), reported significant reduction of intensity of cellulite appearance in comparison to women which used a control cream of the same composition but without MZ.
CLAIMS

1. The formulation based on micronized zeolite (MZ) as therapeutic agent for reduction of body weight and cellulite, characterised by the variable portions of:

(i) micronized zeolite (MZ) of general formula:

\[
(\text{Me}^n\text{V} [(\text{AlO}_2)_x(\text{SiO}_2)_y]^\cdot m\text{H}_2\text{O}) \quad \text{(MZ)}
\]

wherein \( \text{Me}= \text{Na}, \text{K}, \text{Mg}, \text{Ca}, \text{Fe}, \text{Zn}, \text{Mn}, \text{Cr} \); whereas ratio of silicon to aluminum, \( y:x \) is between 6:1 to 1:1; number of crystalline water \( m \) is from 0 to 20, which is characterized by particles size < 5 \( \mu \text{m} \); in concentrations from 1-50%, most preferably from 3-30%;

(ii) Green tea extract containing at least 30% of epigallocatechin gallate (EGCG; 1), and 5% of caffeine (2); in concentrations from 0.1-90%, most preferably from 20-90%;

(iii) genistein (3); in concentrations from 0.05-20%, most preferably from 1-10%;

and
(iv) one or more excipients which yield in desired pharmaceutical or cosmetic form: tablets, capsules, ointments, creams, gels, lotions, shampoos, powders, liquid powders, syrups, suspensions, and therapeutic patches; in concentrations from 1-98.85%, most preferably from 10-75%.

2. Formulation according to claim 1, characterized by that the excipients are selected from the groups consisting of fillers, binders, disintegrants, lubricants, emollients, emulsifiers, tensides, humectants, solvents, thickeners, preservatives, antioxidants, stabilizers, and other functional additives which may help basic therapeutic action of main active substances.

3. Formulation according to claims 1 and 2, characterized by that the excipient is filler selected from the group consisting of microcrystalline cellulose, lactose monohydrate, calcium hydrogenphosphate, sorbitol, starch, modified starches, talc, kaolin, bentonite, montmorillonite, precipitated calcium carbonate, basic magnesium carbonate, calcium silicate, aluminum hydroxide, silicon dioxide, or mixtures of these substances.

4. Formulation according to claims 1-3, characterized by that the excipient is binder selected from the group consisting of gelatin, lactose monohydrate, sorbitol, saccharose, xylitol, maltitol, mannitol, starch, modified starches, methylcellulose, 2-hydroxyethylcellulose, 2-hydroxypropylcellulose, sodium carboxymethylcellulose, polyethyleneglycols, polyglycerols, polyvinylpyrrolidone, polyvinylpyrrolidone co-polymers, carrageenans, or mixtures of these substances.

5. Formulation according to claims 1-4, characterized by that the excipient is disintegrant selected from the group consisting of starch, modified starches, sodium starch glycolate, methylcellulose, sodium carboxymethylcellulose, 2-hydroxyethylcellulose, 2-hydroxypropylcellulose, polyvinylpyrrolidone, polyvinylpyrrolidone co-polymers, or mixtures of these substances.

6. Formulation according to claims 1-5, characterized by that the excipient is lubricant selected from the group consisting of: metal soaps such as magnesium stearate, calcium...
stearate, zinc stearate; higher fatty acids such as stearic acid; talc; silicon dioxide; or mixtures of these substances.

7. Formulation according to claims 1-6, characterized by that the excipient is emollient selected from the group consisting of: paraffin wax; mineral oil; petroleum jelly; ozokerite; synthetic esters of higher fatty acids like isopropyl myristate, isopropyl palmitate, trimethylolpropane tristearate, glyceryl tricaprylate; natural waxes such as beeswax or spermaceti; liquid natural waxes such as jojoba oil; synthetic waxes such as lauryl laurate; plant oils such as soybean oil, sweet almond oil, sunflower seed oil, fish oil, olive oil, wheat germ oil, corn germ oil, avocado oil, palm oil, coconut oil; semi-solid or liquid silicones; higher fatty alcohols such as cetyl alcohol, stearyl alcohol, oleyl alcohol; or mixtures of these substances.

8. Formulation according to claims 1-7, characterized by that the excipient is emulsifier selected from the group consisting of: metal salts of sulphonates of higher fatty alcohols like sodium laurylsulphonate, sodium lauryl ethyleneglycol sulphate, sodium lauryl diethyleneglycol sulphate; ethoxylates of higher fatty alcohols such as polyoxyethylene(2) laurylether, polyoxyethylene(l 0) laurylether, polyoxyethylene(23) laurylether, and others, where 2, 10 and 23 represent average number of ethyleneglycol units bounded on higher fatty alcohol; ethoxylates of higher fatty acids such as polyoxyethylene(2) laurate, polyoxyethylene(l 0) laurate, polyoxyethylene(23) laurate, and others, wherein 2, 10 and 23 represent average number of ethyleneglycol units bounded on higher fatty acid; esters of sorbitan such as polyoxyethylene sorbitan monolaurate; lanolin; ethoxylated lanolins; glyceryl monostearate; beeswax ethoxylates; or mixtures of these substances.

9. Formulation according to claims 1-8, characterized by that the excipient is tenside selected from the group consisting of: metal salts of sulphonates of higher fatty alcohols such as sodium laurylsulphonate, sodium lauryl ethyleneglycol sulphate, sodium lauryl diethyleneglycol sulphate, potassium laurylsulphonate, potassium lauryl diethyleneglycol sulphate, ammonium laurylsulphonate, ammonium lauryl ethyleneglycol sulphate, ammonium lauryl diethyleneglycol sulphate, sodium or potassium cocoamphodipropionate; disodium or dipotassium cocoamphodiacetate; polyoxyethylene(l 0) laurylether, polyoxyethylene(23)
lauryl ether, polyoxyethylene(1θ) stearyl ether, polyoxyethylene(23) stearyl ether, polyoxyethylene(1θ) oleylether, polyoxyethylene(23) oleylether, and other ethoxylates of higher fatty alcohols with H.L.B. value >10; polyoxyethylene(1θ) laurate, polyoxyethylene(23) laurate, polyoxyethylene(1θ) stearate, polyoxyethylene(23) stearate, polyoxyethylene(1θ) oleate, polyoxyethylene(23) oleate; or other ethoxylates of higher fatty acids with H.L.B. value >10; esters of sorbitan such as polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyoxyethylene sorbitan monooleate, or other sorbitan derivatives with H.L.B. value >10; mono- or diethanolamides of higher fatty acids; cocoamidopropyl betaine; glycosides of higher fatty alcohols like cocoglucoiside; sodium or potassium di(2-ethylhexyl)sulfosuccinate; disodium or dipotassium 2-ethylhexylsulfosuccinate; cationic tensides such as cetyltrimethylammonium bromide, didecyldimethylammonium chloride, benzalkonium chloride, cetylbenzyldimethylammonium bromide, cetylpyridinium chloride; metal salts of higher fatty acids such as sodium or potassium salts of lauric, myristic, palmitic, stearic, oleic, or ricinoleic acid; or mixtures of these substances.

10. Formulation according to claims 1-9, characterized by that the excipient is humectant selected from the group consisting of glycerol, 1,2-propyleneglycol, 1,3-propyleneglycol, hexyleneglycol, 1,3-butanediol, polyethyleneglycols, polyglycerols, sorbitol, xylitol; saccharose, urea, sodium hyaluronate, or mixtures of these substances.

11. Formulation according to claims 1-10, characterized by that the excipient is solvent selected from the group consisting of purified water, ethanol, 1-propanol, isopropanol, isosorbide dimethylether, diethylene glycol monomethylether, diethylene glycol dimethylether, diethylene glycol monoethylether, diethylene glycol diethylether, triethylene glycol monomethylether, triethylene glycol dimethylether, triethylene glycol monoethylether, triethylene glycol diethylether, ethyl lactate or other lactate esters with lower aliphatic alcohols, triethylhexanoin, or mixtures of these substances.

12. Formulation according to claim 1-11, characterized by that the excipient is thickener selected from the group consisting of: polyacrylic acid, its co-polymers, or their sodium, potassium, or triethanolamine salts; methylcellulose; sodium carboxymethylcellulose; 2-hydroxyethylcellulose; 2-hydroxypropylcellulose; starch; modified starches; polyglycerols;
polyethylene glycols; gelatin; pectin; agar agar; carrageenans; gum arabic; alginic acid; sodium alginate; montmorillonite; bentonite; or mixtures of these substances.

13. Formulation according to claims 1-12, characterized by that other functional additives which help basic therapeutic action of main active substances are selected from the group consisting of anti-inflammatory and/or antiphlogistic agent, antioxidant, astringent, and skin tonifying agent, or mixtures of these substances.

14. Formulation according to claims 1-13, characterized by that other functional additive which helps basic therapeutic action of main active substances is anti-inflammatory and/or antiphlogistic agent selected from the group consisting of: paracetamol; metamizol sodium; acetylsalicylic acid and its salts with pharmaceutically acceptable bases; salicylic acid and its salts with pharmaceutically acceptable bases; salsalate; methyl salicylate; ethyl salicylate; benzyl salicylate; 2-hydroxyethyl salicylate; salicylamide; phenylbutazone sodium; propyphenazone; oxyphenbutazone; mofebutazone; bumadizon calcium; phenazone; ethenzamide; ketoprofen, ibuprofen, naproxen, flurbiprofen, pirprofen, mefenamic acid, fiuphenamic acid, thiaprofenic acid or their salts with pharmaceutically acceptable bases; diclofenac sodium; indomethacin; piroxicam; meloxicam; codeine; caffeine; extract of St John's wort (Hypericum perforatum); azulene; extract of Chamomile (Matricaria recutita); extract of Marigold (Calendula officinalis); extract of Arnica (Arnica montana); extract of White Willow (Salix alba); extract of Spiny Restharrow (Ononis spinosa); menthol; essential oil or extract of Mint (Mentha piperita); eucalyptol; essential oil or extract of Rosemary (Rosmarinus officinalis); essential oil or extract of Lavender (Lavandula officinalis); purified turpentine oil; camphor; pinene; bornyl acetate; terpineol; terpenyl acetate; eugenol; essential oil of Lemon (Citrus limonum); essential oil of Orange (Citrus aurantium); essential oil of Common Juniper (Juniperus communis); essential oil of Clove (Syzygium aromaticum); extract of Green Tea (Camellia sinensis); extract of Rooibos (Aspalathus linearis); extract of Nettle (Urtica dioica); extract of Horse-Chestnut (Aesculus hippocastanum); extract of Mullein (Verbascum phlomoides); extract of European Holly (Ilex aquifolium); extract of Borage (Borago officinalis); extract of Burdock (Arctium lappa); extract of Ribwort Plantain (Plantago lanceolata); extract of Century Plant (Agave americana); extract of Ground Pine (Lycopodium clavatum); methyl nicotinate; benzyl nicotinate; glucosamine sulfate; L-histidine; chondroitin sulfate;
hyaluronidase; heparin sodium; coumarin; choline and its salts; sulphur; extracts of plants with significant content of silicic acid (H₄SiO₄) such as Field Horsetail (Equisetum arvense), Lungwort (Pulmonaria officinalis), Common Knotgrass (Polygonum aviculare), Couch Grass (Agropyron repens), Common Agrimony (Agrimonia eupatoria), Oat (Avena sativa); cortisone; hydrocortisone; dexamethasone; betamethasone; alclometasone; fluprednidene; prednisone; prednisolone; triamcinolone; methylprednisolone; paramethasone; clobetasol; diflorsone; fluocinolone; clocortolone; flumetasone; halometasone; fluocortolone; diflucortolone; mono- or diesters of mentioned synthetic steroids at 17- and/or 21-positions, or 16,17-acetonide derivatives such as hydrocortisone acetate, hydrocortisone-17-butyrate, betamethasone-17-valerate, betamethasone-17,21-dipropionate, alclometasone-17,21-dipropionate, triamcinolone-16α,17α-acetonide; or mixtures of these substances.

15. Formulation according to claims 1-14, characterized by that other functional additive which helps basic therapeutic action of main active substances is antioxidant selected from the group consisting of: extract of Rooibos (Aspalathus linearis); extract of Nettle (Urtica dioica); extract of Bilberry (Vaccinium myrtillus); extract of Orange (Citrus aurantium); silymarin; extract of Milk Thistle (Silybum marianum); ascorbic acid, its salts, and esters such as ascorbyl palmitate; tocoferol; tocoferol acetate; niacinamide; rutin; quercetin; extracts of plants with significant content of rutin and/or quercetin; cyanidin; hesperidin; diosmin; lycopene; extracts of plants with significant contents of lycopene; resveratrol; tetrahydrocurcumin; rosmarinic acid; extract of Rosemary (Rosmarinus officinalis); hypericin; extract of St John's wort (Hypericum perforatum); ellagic acid; chlorogenic acid; 3,4-dihydroxycinnamic acid; oleuropein; extract of Olive leaves (Olea europea); extract of Grape seed; pycnogenol; carnosine; α-lipoic acid; glutathione; extracts of plants with significant content of silicic acid (H₄SiO₄) such as Field Horsetail (Equisetum arvense), Lungwort (Pulmonaria officinalis), Common Knotgrass (Polygonum aviculare), Couch Grass (Agropyron repens), Common Agrimony (Agrimonia eupatoria), Oat (Avena sativa), Common Agrimony (Agrimonia eupatoria), Silverweed (Potentilla anserina), Common Bistort (Polygonum bistorta), Common Sage (Salvia officinalis); or mixtures of these substances.
16. Formulation according to claims 1-15, characterized by that other functional additive which helps basic therapeutic action of main active substances is astringent selected from the group consisting of: zinc oxide; zinc stearate; zinc tannate; zinc acetate; zinc sulphate; zinc chloride; iron(III) chloride; aluminum sulphate; potassium aluminum sulphate; aqueous basic aluminum acetate; aluminum acetonitrate; bismuth subnitrate; bismuth subcarbonate; bismuth phosphate; bismuth tannate; calamine; copper(II) sulphate; silver nitrate; silver-proteine; aescin; extract of Horse-Chestnut (*Aesculus hippocastanum*); Balsam of Peru; silica gel; kaolin; talc; titanium dioxide; tannic acid; albumin tannate; methylene ditannate; extracts with significant content of tannins such as extracts of Oak bark (*Cortex Quercus ruber, Quercus sessiliflora*), Bearberry leaves (*Arctostaphylos uvae ursi*), Common Agrimony (*Agrimonia eupatoria*), Silverweed (*Potentilla anserina*), Common Bistort (*Polygonum bistora*), Common Sage (*Salvia officinalis*); or mixtures of these substances.

17. Formulation according to claims 1-16, characterized by that other functional additive which helps basic therapeutic action of main active substances is skin tonifying agent selected from the group consisting of: vitamins and pro-vitamins like retinol palmitate, β-carotene, niacinamide, d-panthenol, calcium pantothenate, folic acid, riboflavin, pyridoxine, thiamine, biotin, cyanocobalamin, ascorbic acid its salts and esters such as ascorbyl palmitate, cholecalciferol, tocopherol, tocopherol acetate, phylloquinone; animal and plant oils with high contents of omega-3 higher fatty acids such as fish or linseed oil; choline chloride; protein hydrolysates; algae extracts; extract of Witch-hazel (*Hamamelis virginiana*); extract of Centaurium (*Erythraea centaurum*); extract of Mullein (*Verbascum phlomoides*); extract of European Holly (*Ilex aquifolium*); extract of Common Ivy (*Hedera helix*); chlorophyll; α-hydroxyacids like glycolic, lactic, malic, citric, and tartaric acid; urea; co-enzyme Q10; or mixtures of these substances.

18. The use of the formulation according to claims 1-17, for reduction of body weight.

19. The use of the formulation according to claims 1-17, for reduction of cellulite.
A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K47/02 A61K9/10 A61K9/48
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, EMBASE, BIOSIS, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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<td>WO 97/40699 A1 (UNILEVER PLC [GB]; UNILEVER NV [NL]) 6 November 1997 (1997-11-06) the whole document</td>
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X Further documents are listed in the continuation of Box C

X See patent family annex

Special categories of cited documents

- 'A' document defining the general state of the art which is not considered to be of particular relevance
- 'E' earlier document but published on or after the international filing date
- 'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- 'O' document referring to an oral disclosure, use, exhibition or other means
- 'PI' document published prior to the international filing date but later than the priority date claimed

'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

'I' document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

'V' document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents such combination being obvious to a person skilled in the art

'S' document member of the same patent family

Date of the actual completion of the international search
17 November 2009

Date of mailing of the international search report
24/11/2009

Name and mailing address of the ISA/
European Patent Office, P B 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel (+31-70) 340-2040,
Fax (+31-70) 340-3016

Authorized officer
S. von Eggei Kraut-G
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Thomson Scientific, London, GB; AN 2008-J52094
XP002553961
LIZ; LIU C; SUN H: "Feedstuff additive for use in improving milk"
-4 CN 101 218 962 A (NORTHEAST INST OF GEOGRAPHY AN [CN])
16 July 2008 (2008-07-16)
abstract
claim 1 |
**INTERNATIONAL SEARCH REPORT**

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<td>Although claims 18-19 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition</td>
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<td><strong>☐</strong> Claims Nos because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be earned out, specifically</td>
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<td><strong>☐</strong> As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees</td>
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<td><strong>☐</strong> As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid specifically claims Nos</td>
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<td><strong>☐</strong> No required additional search fees were timely paid by the applicant Consequently, this international search report is restricted to the invention first mentioned in the claims, it is covered by claims Nos</td>
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**Remark on Protest**

- **☐** The additional search fees were accompanied by the applicant's protest and where applicable, the payment of a protest fee
- **☐** The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation
- **☐** No protest accompanied the payment of additional search fees

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2005)
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