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(54) **Title**: MEDICINE FOR DENTAL DISEASES PROPHYLAXIS

(57) **Abstract**: Technical result of the invention is achieved by practical use of effective formulation containing accessible components based on biologically active agents of natural origin, which has a comprehensive effect on dental tissues and can be recommended for periodontium prophylaxis and treatment as well as caries and non-carious affections prophylaxis. The main purpose of this invention was to elaborate high-efficiency formulation for prophylaxis of dental diseases of teeth and soft tissues of oral cavity in which synergist medications could heighten effect of each other attaining high therapeutic effect and results mentioned above. Medicine for dental diseases prophylaxis contains orally acceptable active and inert components. As active components there are used about 0.3% to 2.2% by weight of lipid concentrate of kelp, 0.5 % to 5.0 % by weight of kelp salt, 0.5% to 4.0 % by weight of dry extract of liquorice root, 0.01% to 0.25% by weight of one or more essential oils to enhance organoleptic properties, and 0.1% to 3.5 % by weight of anticaries mineral adjunct.

Medicine for dental diseases prophylaxis

Field of application

The invention relates to therapeutic and prophylactic formulations for oral care utilized in stomatology, particularly to medicine for dental diseases prophylaxis wherein biologically active agents of natural origin are used.

Background of invention

There is known medicine to prevent and treat oral diseases, including gingivitis, in the form of mouth rinse, tooth paste containing extract of Rosmarimus and anticeptic triclosan in order to enhance antibacterial effect (US 2006/0134025 A1, IPC A61K 8/97 (2006.01), 2006).

There is known therapeutic tooth paste containing plantain extract oil and pine leaf extract oil as well as mexidol and calcium citrate (RU 2310436 C2, IPC A61K 8/97 (2006.01), 2006). This formulation is used to prevent and treat caries, gingivitis, periodontal disease, stomatitis and is aimed to inhibit dental tartar build-up or to reduce dental tartar already built up.

The closest analogue out of the known formulations is tooth paste sold under "Parodontax" brand. It consists of baking soda and a blend of natural ingredients, flavor, sodium fluoride. As natural ingredients it contains a blend of alcohol extracts and oils of echinacea, myrrh, chamomile, rhatany, sage (US 2002/0031481 A1, IPC 7 A61K 7/16, 2002).

The known formulation has considerable concentration of baking soda as abrasive, more than 40% by weight that creates hypertonic medium and may result in gingival sponginess and recession. Therefore this tooth paste cannot be viewed as a means for permanent everyday dental and gingival prophylactic care. Moreover the known formulation does not provide necessary hard teeth tissues mineralization.

Substance of invention

Technical result of the invention is achieved by practical use of effective formulation containing accessible components based on biologically active agents of natural origin, which has a comprehensive effect on dental tissues and can be recommended for periodontium prophylaxis and treatment as well as caries and

non-carious affections prophylaxis. The main purpose of this invention was to elaborate high-efficiency formulation for prophylaxis of dental diseases of teeth and soft tissues of oral cavity in which synergist medications could heighten effect of each other attaining high therapeutic effect and results mentioned above.

Technical result is enhanced by medicine for dental diseases prophylaxis containing orally acceptable active and inert components.

Active components: about 0.3% to 2.2% by weight of lipid concentrate of kelp, 0.5% to 5.0 % by weight of kelp salt, 0.5% to 4.0 % by weight of dry extract of liquorice root, 0.01% to 0.25 % by weight of one or more essential oils to enhance organoleptic properties, and 0.1% to 3.5 % by weight of anticaries mineral adjunct. Inert components content is up to 100% by weight.

In a preferred embodiment, the medicine contains about 0.5% to 1.8% by weight of lipid concentrate of kelp, 0.8% to 4.2 % by weight of kelp salt, 0.8% to 3.6 % by weight of dry extract of liquorice root, 0.03% to 0.22 % by weight of one or more essential oils.

It is preferable when essential oils are used to improve organoleptic properties, hereinafter there are listed essential oils chosen out of the group including anise, thyme, lemon, mandarin, grapefruit, orange, bergamot, nerol, sage, tea tree, manuka, eucalyptus, fir, pine, juniper.

Literal sources indicate to great value of biologically active agents contained in various species of kelp. There is shown particular perspective to extract lipid fractions out of laminaria of northern and far eastern seas. (Study and use of therapeutic and prophylactic medicine based on natural biologically active agents / edited by V.G. Bespalov and V.B. Nekrasova. – Spb.: Eskulap, 2000. – pp.175-176).

Lipid fractions are extracted in the following way regardless of seaweed species specificity: biologically active agents are ethanol extracted or highly volatile diluent extracted out of dry seaweed, then lipid concentrate and aqueous extract are skimmed. Essential biologically active components of lipid concentrate: chlorophyll derivatives, carotinoids (beta-carotine), mannitol, polysaccharides, fatty acids, including essential acids (polyunsaturated acids C18

and C20 omega-3 and omega-6 are most prevalent fatty acids), organically associated phosphor and iodine, sulphur amino acids.

It is common knowledge that seaweed accumulates actively many elements and concentrates various macro-and microelements. While kelp processing there are derived inorganic salts. Biological properties of these compounds are determined by such elements as calcium, iodine, potassium, magnesium, manganese, molybdenium, copper, cobalt, ferrum, germanium, selenium, zink, etc.

As a whole natural biologically active agents obtained through complex kelp processing, included in the formulation for dental diseases prophylaxis intensify metabolic processes, improve trophism and blood circulation in periodontal tissues that reduces alveolar bones atrophy, contributes to nonspecific resistance increase.

Liquorice root extract has been used for thousands of years as a medicine. Medical opportunities are determined by chemical formulation. Liquorice root contains about 6% to 23% of triterpene saponoside glycyrrhizin, blended potassium-calcium-magnesium salt of glycyrrhizinic acid, derivatives of glycyrrhizinic acid, such as glabric acid, 18-glycyrrhetic, 18,19 – dihydroglycyrrhetic, 11-deoxyglycyrrhetic acids, liquiritic acid; up to 4% of flavonoids: liquiritin, isoliquiritin, licurazid, neoliquiritin, glabroside, uraloside, liquiritoside, glabrol, quercetin, kaempferol, apigenin,; mono- and disaccharides (up to 20%); starch (up to 34%); pectins (4-6%); resins(4%); phenolcarbonic acids and their derivatives (3-6%); salicylic, acetic, salicylic and ferulic acids; coumarins: herniarin, liqcoumarine, tanning agents (up to 14%); alkaloids; essential; organic acids such as tartaric, citric, malic, fumaric acids; steroids such as beta-sitosterol, estriol; macroelements such as potassium, calcium, magnesium, ferrum; microelements such as manganese, copper, zinc, barium, vanadium, selenium, nickel, strontium. To date out of liquorice there are derived and described 80 triterpenoids, over 300 individual phenolic compounds, dozens of polysaccharides, amino acids and the like. (Phytotherapy with elements of clinical pharmacology/ Edited by V.G.Koukes. M.:Meditcina, 1999. – pp.66-67).

Flavonoids glabridin and glabren, licochalcon, licoricidin, isolicoflavon B showed antimicrobial activity in vitro in respect to Helicobacter pylori. These flavonoids are also active in relation to clarithromycins and amoxycillins resistant strains of Helicobacter pylori (Fukai T., Marumo A., Kaitou K., et al. Anti-Helicobacter pylori flavonoids from licorice extract. Life Sci. 2002 Aug 9;71(12):1449-63.).

A number of flavonoids derived from liquorice (glabridin, licochalcon) demonstrated antimicrobial activity against methycillin resistant strains of Staphylococcus aureus with minimum inhibitory concentrations of 3.13 to 12.5 μg/ml. Flavonois glabren, isolicoflavon, isolicoflavonol showed activity in relation to these strains in concentration of 1.56 to 25.0 μg/l. (Fukai T., Marumo A., Kaitou K., et al. Antimicrobial activity of licorice flavonoids against methicillin-resistant Staphylococcus aureus. Fitoterapia. - 2002 Oct;73(6):536-9).

Dissolution in vitro test for powder enamel in acid acetate buffer and saliva where glucose was added, has shown that adding of 0.1 M of ammonium glycyrrhisate (out of liquorice extract) results in 30% dissolution decrease whereas under 18-hour incubation solubility reduces by 60% compared with solutions without ammonium glycyrrhisate. This effect can be explained by glycyrrhizic acid ability to inhibit glycolysis and demonstrate buffer properties, i.e. glycyrrhizic acid is presumably endowed with potential caries static properties. (W.M. Edgar Reduction in Enamel Dissolution by Liquorice and Glycyrrhizinic Acid. J.Dent Res 57(1): 59-64 January 1978).

Liquorice root extract is used not only in the form of medicine but also for preparing halva and licorice sweets in food industry which makes it attractive as a means for oral hygiene.

Role of microelements present in liquorice root extract as well as in kelp salt, is relevant. Physiological effect and microelement participation in biochemical metabolic reactions in teeth tissues are discovered to a certain extent on the basis of the data concerning metabolism principles in hard teeth tissues mineralization including teeth and bone. Mineralization is influenced by biological activators. One of these activators is phosphatases which abound in dental germs. It is possible that microelements effect is shown through

phosphatases activation. Definite microelements are supposed to take part in mineralization nucleolus formation resulting from collagen attachment and formation of metalloprotein active complexes. Microelements may have immediate influence on mature teeth by compounding to nonspecific protein contained in dental lymph, that leads to formation of biologically active agents (N.A.Kodola Microelements in dental caries prophylaxis. Kiev, "Zdorovie", 1979, pp.22-23).

Lipid concentrate of kelp has offending scent that is negatively commented by some consumers. In this respect, it has been proposed to introduce one or several ether oils into tooth pastes formulation in order to mask offending scent. There have been chosen following ether oils: anise, thyme, lemon, mandarin, grapefruit, bergamot, nerol, sage, tea tree, manuka, eucalyptus, fir, pine, juniper. Liquorice extract also has a positive effect on tooth paste flavor. Ether oils coupled with liquorice extract perform a number of antimicrobial functions.

Concept of remineralization is part of ideology of the formulation invented. Remineralizing system is a combination of ingredients saturating enamel of healthy teeth with minerals and initial cariogenic damage centres.

For attaining remineralizing effect the formulation contains anticaries mineral additive.

In a preferred embodiment, anticaries mineral adjunct content is 0.2-3.3% by weight.

It is preferable to use calcium glycerophosphate and magnesium inorganic and organic salt as anticaries mineral adjuncts.

As inorganic or organic magnesium salts there may be used salts incorporating magnesium chloride, magnesium sulfate, magnesium nitrate, magnesium citrate, magnesium lactate, magnesium glycerophosphate, magnesium acetate, magnesium ascorbyl phosphate.

This adjunct is conditioned by teeth need for these elements in cases of caries and non-carious affections. Calcium and phosphor are basic building elements of teeth enamel and take part in metabolic processes through the whole human life.

Non-carious teeth affections are often connected with calcium metabolic imbalance and are caused by adverse influence of endogeneous character like thyroid, pancreal, germ glands abnormalities, gastrointestinal tract diseases etc.; by unfavourable external influence such as ionizing radiation, daily long (more that 6 hours) computer work; by hazard influence such as acid fumes, metal dust and their combinations; a range of negative ecological effects, which result in substantial reduction of mineral components in dental tissues and then in affection in the form of caries, erosion defects.

Thereby local application of therapeutic and prophylactic formulations containing phosphor-calcium additives makes it possible not only to prevent but to a certain degree makes up for the loss in case of disease.

Calcium glycerophosphate is a source of active phosphorus and calcium supply to teeth and periodontium tissues and facilitates process of mineralization, improves anticaries effect of formulation, intensifies anabolic processes in tissues.

Magnesium (of inorganic or organic salts) is a structural component of teeth. Magnesium is incorporated in complex formulation as microelement, which is a cofactor for phosphatases ensuring incorporation of phosphates into hard teeth tissues. Under the influence of phosphates there takes place hydrolysis of glycerophosphate and its bioavailability increases correspondingly.

Since the risk of teeth demineralization is substantially lower in absence of solid dental deposit it is probable that formulation does not involve fluorides. Fluoride content in mouth care formulation is relevant if soft dental deposit produces organic acids during breakdown of easy-fermented carbohydrates. However, local fluoride action cannot be traced on teeth enamel maturation (for people aging over 20) even under this condition. It is shown in loss of its efficiency in caries prophylaxis.

At the same time it is admitted in proposed formulation that as anticaries mineral additive there are used sodium monofluorphosphate, potassium monofluorphosphate, calcium monofluorphosphate or magnesium monofluorphosphate in amount of 0.6-1.8 wt %.

It is preferable to prepare medicine for dental disease prophylaxis in the form of tooth paste.

In this case it involves several inert components, wt.%:

abrasive – 10-38,

humectant – 11-50,

gelling agent – 0.5-7,

at least one surfactant – 0.5-3,

at least one flavor – 0.5-2,

at least one preservative – 0.01-0.5.

While preparing a paste, as abrasive, there can be used one or several substances selected out of the group including dicalcium phosphate dihydrate, anhydrious dicalcium phosphate, calcium carbonate, silica, aluminium oxide, aluminium hydroxide, polymethacrylate.

As humectant of a tooth paste there can be used one or several agents selected out of the group including sorbitol, glycerine, polyethylene glycol, propylene glycol.

As gelling agent of a tooth paste there can be used one or several agents selected out of the group including hydroxyethyl cellulose,xanthan gum, guar gum, carbossimethyl callulose, potassium alginate, sodium alginate, thickening silica.

In the process of preparing medicine for dental diseases prophylaxis, there may be used such surfactants as sodium lauryl sulfate, alkylamidobetaine, polysorbate-20, sodium lauryl sarcosinate.

As flavor there may be used one or several substances of the following group comprising ether oils of peppermint oil, spearmint oil, clove, skinleaf and ginger oils, as well as menthol, carvone, anethol, eucalyptol, methyl salicylate; sweeteners such as sodium saccharinate, potassium aspartame, potassium acesulfame, stevioside, xylitol, potassium and sodium glycyrrhizate.

As preservative there can be used one or several substances selected out of the group including methylparaben, propylparaben, and their sodium salts, phenoxyethanol, benzoic acid, sodium benzoate, potassium sorbate.

Realization of invention

Medicine for dental diseases prophylaxis has been described above with reference to illustrative examples.

Qualitative and quantitave tooth paste formulation is represented in Table 1.

Table 1

	Example 1	Example 2	Example 3	Example 4	Example 5
	Concentration, wt. %				
Glycerine	22	16	10	8	5
Sorbitol	-	10	16	22	30
Dicalcium phosphate dihydrate	11	23	38	-	-
Calcium carbonate	5	10	-	35	38
Thickening silica	6	4	3,5	2,8	-
Xanthan gum	0,9	1,1	1,2	1,2	0,8
Kelp salt	1	2	2,5	3,2	4
Lipid concentrate of kelp	0,6	0,8	1,8	1	0,7
Dry liquorice root extract	0,8	1,2	2,5	2,8	3,4
Sodium monofluorphosphate	-	-	-	1,1	0,8
Calcium glycerophosphate	1,2	1	0,8	0,6	0,1
Magnesium glycerophosphate	-	-	-	0,1	0,05
Magnesium chloride	0,1	0,2	0,5	-	-
Sodium lauryl sulfate	1,4	1,2	0,8	-	-
Alkylamidobetaine	-	1,0	1,5	1,3	0,6
Sodium benzoate	0,4	0,3	0,2	0,12	0,08
Lemon oil	0,04	0,12	0,08	0,05	-
Thyme oil	-	-	0,08	0,12	0,2
Stevioside	0,1	0,15	0,2	0,3	0,2
Flavor	0,6	0,8	0,9	1,2	1,5
Water	Up to 100 %	Up to 100 %	Up to 100 %	Up to 100 %	Up to 100 %

Tooth pastes are prepared in the following way.

Weigh required glycerine quantity, then add xanthan gum. Mix till formation of homogeneous mass.

Weigh required quantity of water in a measuring bin, feed it into a mixer, with further adding of stevioside, sodium benzoate, sorbitol, kelp salt, sodium monofluorphosphate (as shown in examples 4,5), magnesium chloride (as shown in examples 1,2,3). Mix to formation of transparent solution.

Xanthan gum suspension in glycerine is charged into the solution obtained, and mixing continues to formation of homogeneous mass. Vacuumize the formulation and mix for 10 minutes to full deaeration of the mixture.

Then add calcium glycerophosphate or magnesium glycerophosphate (as demonstrated in examples 4,5), mixing continues for 15-20 minutes.

Then add thickening silica (as shown in examples 1,2,3,4), calcium carbonate (as shown in examples 1,2,4,5), dicalcium phosphate dihydrate (as in examples 1,2,3), mixing under vacuum continues for 40-50 minutes.

Homogenize tooth-paste with homogenizing pump for 10-20 minutes. Charge the mixer with flavor, ether oil or ether oils blend (as in examples 3,4) and lipid concentrate of kelp. Mix to formation of homogeneous mass for 20-30 minutes.

Feed dry liquorice root extract, sodium lauryl sulfate (as shown in examples 1,2,3), alkylamidobetaine (as in examples 2,3,4,5) and mix for 20-30 minutes till formation of homogeneous mass. The tooth paste prepared is placed into polymer container for filling.

Qualitative and quantitave gel formulation is illustrated in Table 2.

Gels are prepared in the following way.

Weigh required quantity of propylene glycol, add hydroxyethyl cellulose. Mix to formation of homogeneous mass.

Weigh required quality of water in a measuring bin, feed the water into a mixer, add potassium glycyrrhizate, sodium methylparaben, kelp salt, potassium monofluorphosphate (as in examples 4,5), magnesium lactate. Mix to formation of transparent solution.

Charge hydroxyethyl cellulose suspension in glycerine into the solution obtained and mix till formation of homogeneous mass. Mix the formulation under vacuum for 10 minutes to deaeration of the mixture.

Add calcium glycerophosphate with further mixing for 15-20 minutes.

Then add thickening silica (as in examples 1,2,3), mix for 40-50 minutes under vacuum.

Table 2

	Example 1	Example 2	Example 3	Example 4	Example 5
	Concentarion, wt. %				
Propylene glycol	11	15	20	25	12
Thickening silica	4,5	4	3	-	-
Hydroxyethyl cellulose	0,8	1,2	2,5	3	3,5
Kelp salt	0,5	1,2	2,5	4	1,5
Lipid concentrate of kelp	2	1,5	1,2	0,8	0,3
Dry liquorice root extract	1	2,5	3	3,8	0,8
Potassium monofluorphosphate	-	-	-	0,6	0,8
Calcium glycerophosphate	1,5	0,5	0,25	0,15	0,12
Magnesium lactate	0,9	1,5	0,6	0,1	0,08
Sodium lauryl sarcosinate	2	1,6	1	0,8	0,6
Sodim methylparaben	0,02	0,05	0,1	0,12	0,25
Bergamot oil	-	0,03	0,08	0,1	0,15
Tea tree oil	0,03	0,05	0,1	0,12	-
Potassium glycyrrhizate	1	0,6	0,2	0,1	0,05
Flavor	0,05	0,1	0,12	0,2	0,4
Water	Up to 100 %	Up to 100 %	Up to 100 %	Up to 100 %	Up to 100 %

Then homogenize gel with homogenizing pump for 10-20 minutes. Charge flavor, ether oil or blend of ether oils (as in examples 2,3,4) as well as lipid concentrate of kelp into the mixer. Mix to formation of homogeneous mass for 20-30 minutes.

Feed dry liquorice root extract, sodium lauryl sarcosinate and mix to formation of homogeneous mass for 20-30 minutes. The gel prepared is placed into polymer containers for filling.

Qualitative and quantitave formulation of mouth rinses are shown in Table 3.

Mouth rinses are prepared in the following way:

Weigh water required, heat it up to 80 °C, add glycerine, sorbitol (as in examples 3,4,5), xylitol, benzoic acid, magnesium glycerophosphate (examples 1,2), magnesium sulfate (examples 2,3,4,5), calcium glycerophosphate, magnesium monofluorphosphate (examples 1,2,3) and kelp salt. Mix to formation of transparent solution and cool down to the temperature of 40 °C. In the process of mixing add dry liquorice root extract into the solution.

Table 3

	Example 1	Example 2	Example 3	Example 4	Example 5
	concentration, wt. %				
Glycerine	11	15	10	8	5
Sorbitol	-	-	2	3	5
Kelp salt	0,5	0,6	0,8	1,2	2,5
Lipid concentrate of kelp	0,3	0,5	1	1,6	1,2
Dry liquorice root extract	2	1,2	0,8	0,6	0,5
Magnesium monofluorphosphate	0,6	0,7	1	-	-
Calcium glycerophosphate	0,1	0,15	0,2	0,25	0,3
Magnesium sulfate	-	0,1	0,12	0,2	0,15
Magnesium glycerophosphate	0,1	0,05	-	-	-
Polysorbate-20	0,6	0,8	1,2	2,2	1,8
Benzoic acid	0,12	0,06	0,03	0,02	0,01
Thyme oil	0,01	0,05	0,08	0,1	0,16
Grapefriut oil	0,05	0,02	-	-	-
Xylitol	1,8	1,5	1	0,5	0,3
Flavor	0,2	0,5	0,8	0,6	0,3
Water	Up to 100 %	Up to 100 %	Up to 100 %	Up to 100 %	Up to 100 %

In a separate container prepare solution of ether oils, flavor and lipid concentrate of kelp in polysorbate-20. Heat the obtained solution up to 40 °C while mixing.

In the process of mixing add the ingredients solution in polysorbate-20 to the water solution. Mix for 20-30 minutes under the temperature of 40 °C, then cool down to the temperature of 20-25 °C and filter.

The mouth rinse prepared is placed into polymer containers.

Efficacy evaluation

Efficacy of medicine for dental diseases prophylaxis has been tested on a group of volunteers in order to evaluate anti-inflammatory action. There has been used medicine in the form of tooth paste prepared in correspondence with Example 3 of Table 1. As a comparison there was used "Parodontax" tooth paste prepared in accordance with the analogue mentioned above.

Two groups of 15 and 16 people have taken part in clinical studies. There were chosen volunteers with the age varying from 15 to 45 diagnosed with chronic catarrhal gingivitis and chronic periodontitis of mild severity. The experiment took 14 days. Anti-inflammatory effect was evaluated by PMA index (C.Parma, 1964) Index evaluation has been made before and after investigation, i.e. in 14 days.

Clinical data are demonstrated in Table 4.

Table 4

	PMA,%	
	"Parodontax" tooth paste	Tooth paste according to Ex.3
Before investigation	16,35 ± 2,22	20,61± 2,60
In 14 days of application	5,18 ± 0,66	6,28 ± 1,15

Thus application of tooth paste according to example 3 from Table 1 has shown 69.5% reduction. "Parodontax" application has shown 68.3% reduction. In other words gingivitis index in formulation prepared in accordance with the invention has shown more clear-cut reduction.

Thereby it has been elaborated high-efficiency and available therapeutic and prophylactic medicine which has considerable influence on oral cavity tissues.

This medicine can be recommended for treatment and prophylaxis of periodontium diseases as well as for caries and non-carious affections prophylaxis. The invention can be prepared in the form of tooth paste as well as in the form of gel or liquid (mouth rinse, mouthwash) which are also under legal protection which covers all cases of realization of medicine for dental diseases prophylaxis.

Claims

1. Medicine for dental diseases prophylaxis containing orally acceptable active and inert components characterized by comprising about 0.3% to 2.2% by weight of lipid concentrate of kelp, 0.5% to 5.0 % by weight of kelp salt, 0.5% to 4.0% by weight of dry liquorice root extract, 0.01% to 0.25% by weight of one or more essential oils to improve organoleptic properties and 0.1% to 3.5% by weight of anti-caries mineral adjunct, up to 100% by weight of inert components.

2. Medicine according to claim 1, comprising about 0.5% to 1.8% by weight of lipid concentrate of kelp.

3. Medicine according to claim 1, comprising about 0.8% to 4.2% by weight of kelp salt.

4. Medicine according to claim 1, comprising about 0.8% to 3.6% by weight of dry liquorice root extract.

5. Medicine according to claim 1, comprising about 0.03% to 0.22% by weight of one or more essential oils.

6. Medicine according to claim 1, comprising essential oils selected out of the group containing anise, thyme, lemon, mandarin, grapefruit, orange, bergamot, nerol, sage, tea tree, manuka, eucalyptus, fir, pine, juniper.

7. Medicine according to claim 1, comprising about 0.2% to 3.3% by weight of anticaries mineral adjuncts.

8. Medicine according to claim 1, comprising calcium glycerophosphate and inorganic or organic salt as anti-caries mineral adjuncts.

9. Medicine according to claim 8, comprising salts selected out of the group of magnesium chloride, magnesium sulfate, magnesium nitrate, magnesium citrate, magnesium lactate, magnesium glycerophosphate, magnesium acetate, magnesium ascorbyl phosphate as inorganic and organic magnesium salts.

10. Medicine according to claim 8, comprising anticaries mineral adjunct that contains optionally one or several agents selected out of the group of sodium monofluorphosphate, potassium monofluorphosphate, calcium

monofluorphosphate, 0.6% to 1.8% by weight of magnesium monofluorphosphate.

11. Medicine according to claim 1 comprising, in the form of tooth paste, the following inert components, wt. %;

abrasive – 10-38,

humectant – 11-50,

gelling agent– 0.5-7,

at least one surfactant – 0.5-3,

at least one flavor – 0.5-2,

at least one preservative – 0.01-0.5.

12. Medicine according to claim 11, wherein the abrasive is selected out of the group containing dicalcium phosphate dihydrate, anhydrious dicalcium phosphate, calcium carbonate , silica, aluminium oxide, aluminium hydroxide, polymethacrylate.

13. Medicine according to claim 11, wherein the humectant is selected out of the group containing sorbitol, glycerine, polyethylene glycol, propylene glycol.

14. Medicine according to claim 11, wherein the gelling agent is selected out of the group containing hydroxyethyl cellulose, xanthan gum, guar gum, carboxymethyl cellulose, potassium alginate, sodium alginate, thickening silica.

15. Medicine according to claim 11, wherein the surfactant is selected out of the group containing sodium lauryl sulfate, alkylamidobetaine, polysorbate-20, sodium lauryl sarcosinate.

16. Medicine according to claim 11, wherein the flavor is selected out of the group containing ether oils of peppermint, spearmint, clove, skinleaf and ginger, as well as menthol, carvone, anethol, eucalyptol, methyl salicylate, sweeteners like sodium saccharinate, potassium aspartame, potassium acesulfame, stevioside, xylitol, potassium and sodium glycyrrhisate.

17. Medicine according to claim 11, wherein the preservative is selected out of the group containing methylparaben, propylparaben, and their sodium salts, phenoxyethanol, benzoic acid, sodium benzoate, potassium sorbate.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/RU 2010/000130

A. CLASSIFICATION OF SUBJECT MATTER

A61K 36/03 *(2006.01)*
A61K 36/484 *(2006.01)*
A61K 33/06 *(2006.01)*
A61K 8/97 *(2006.01)*
A61P 1/02 *(2006.01)*
A61Q 11/00 *(2006.01)*

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 36/03, 36/484, 33/06, A61P 1/02, A61K 8/97, A61Q 11/00

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 practicable, search terms used)
EAPATIS, Esp@cenet, PAJ, USPTO, RUPTO, Medline, Rossiyskaya meditsina

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	RU 2204990 C1 (OOO NPO "PHITOPHARM") 27.05.2003, description, p. 2, claims	1-17
Y	RU 2006223 C1 (NAUCHNO-PROIZVODSTVENNAYA I VNEDRENCHESKAYA PHIRMA "YUNITEKS") 30.01.1994, description, p. 3, claims	1-17
Y	SU 1782600 A1 (ODESSKIY NAUCHNO-ISSLEDOVATEL'SKIY INSTITUT STOMATOLOGII) 23.12.1992, claims	1-17
Y	EA 011125 B1 (OBSHCHESTVO S OGRANICHENNOY OTVETSTVENNOST'YU "WDS") 30.12.2008, claim 1, 4-8, 14-19	1-17
A	EDGAR W.M., "Reduction in Enamel Dissolution by Liquorice and Glycyrrhizinic Acid", Journal of Dental Research. 1978, vol. 57, No. 1, pp. 59-64	1-17

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is nit considered to be of particular relevance
"E" earlier application or patent 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
"P" 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
"X" 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
"Y" 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
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
18 July 2010 (18.07.2010)	19 August 2010 (19.08.2010)

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/RU 2010/000130

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	RU 2309763 C2 (GU DAL'NEVOSTOCHNIY NAUCHNIY TSENTR PHIZIOLOGII I PATOLOGII DYKHANIYA SIBIRSKOGO OTDELENIYA ROSSIYSKOY AKADEMII MEDITSINSKIKH NAUK) 10.11.2007, claims	1-17
A	GB 1113318 A (ANDRE BOUCLET) 15.05.1968	1-17
A	JP 09-048715 A (LION CORP) 18.02.1997, abstract	1-17