

Description

The present invention relates to a dentifrice having an excellent antibacterial action agent Actinomyces viscosus and effectively preventing the development of calculus and periodontitis.

Calculus is a hard deposit, having a high inorganic content, formed on the surfaces of teeth, and is believed to be a major cause of the development of gingivitis and periodontitis. Accordingly, an inhibition of the formation of calculus effectively prevents and cures the development of periodontal diseases. The rapid deposition of calculus can be prevented to a certain extent by brushing the teeth of frequent intervals. However, brushing alone is not sufficient for removing substantially all of the calculus deposited on the teeth.

The formation of calculus is considered to be caused by the deposition of amorphous or microcrystalline calcium phosphate on membranous portions of bacteria or the substances between bacteria in the plaque, which gradually become dense and change to hydroxyapatite. It is known that the main bacteria forming organic matrixes in old plaque or plaques in gingival sulcus, in which the above-mentioned calcification occurs are filamentous bacteria or rod-shaped bacteria belonging to Actinomyces, Leptotrichia, Bacteroides, and Fusobacterium. Accordingly, an inhibition of a growth of these bacteria will effectively suppress the formation of calculus, and thus prevent the development of periodontal diseases.

The inhibition of the formation of plaque, and the removal of the plaque, are most important for calculus prevention, and to this end, physical methods such as brushing have been used. As mentioned above, brushing alone is not sufficient to prevent and remove calculus and, therefore, chemical methods using antibacterials such as chlorohexidine, benzalkonium chloride, and cetylpyridinium chloride have been used. However, these antibacterials cannot be formulated at a higher amount, from the viewpoint of safety.

Furthermore, it is informed that polyphosphates have inhibited the caries in animal tests (e.g., Journal of Dental Research, Vol. 43, p 1123 - 1136) and also poses antibacterial actions against Streptococcus mutans and Diphtheroids (e.g., Arch. Oral Biol. Vol. 27, p 809 - 816, 1982 and Infection and Immunity, Vol. 1, p 604 - 606, 1970). Furthermore, Arch. Oral Biol., Vol. 15, p 893 - 896 (1970) discloses the effectiveness of a water-soluble phosphate against the formation of calculus. In addition to the above, JP-A-52-108029 (Kokai) proposes the prevention of the formation of calculus by a combination of polyphosphates and polyvalent cations, and JP-A-59-42311 proposes an oral composition formulated with pyrophosphate of anticalculus.

Thus, it is known in the art that the use of polyphosphates in oral compositions is effective for the inhibition. DE-A-3,526,654 discloses an oral composition containing sodium pyrophosphate and an aromatic material which could be anethol. It also discloses an oral composition containing anethol and insoluble sodium metaphosphate (this latter material may be used as a polishing agent in dentifrices). However the combination of the specified polyphosphates and anethol of the present invention is not disclosed, nor is reference made to the unexpected results of an excellent antibacterial effect and the ability effectively to prevent the development of calculus and periodontal diseases as exhibited by compositions according to the present invention.

GB patent No. 2,102,289 discloses a dentifrice comprising polyphosphates and peppermint oil. Although this reference discloses a combination of peppermint oil and sodium trimetaphosphate, the above-mentioned advantageous effects of the present invention are not described or suggested in this citation. This reference is directed to the improvement of the anticariogenic effect by the use of a combination of two or more fluorine compounds. The advantageous effects obtained from the combination of the phosphate and anethol are not taught in the citation.

EP-A-0,002,184 discloses an oral composition comprising polyphosphates and peppermint oil. Nevertheless the synergic effects obtained from the use of the phosphate and anethol are neither disclosed nor taught in this citation.

EP-A-0,097,476 discloses a toothpaste comprising $K_4P_2O_7$ and/or $Na_4P_2O_7$ and "flavour" (e.g., peppermint oil and spearmint oil) but the above-mentioned synergic effects obtained from the use of the phosphate and anethol are neither disclosed nor taught in this citation.

FR-A-2,130,275 and DE-A-2,445,676 also neither disclose nor teach the above-mentioned synergic effects obtained from the use of a phosphate in combination with anethol.

Thus, the effects obtained from the use of polyphosphates per se are not sufficient and, therefore, there is a strong demand for the development of dentifrice having an excellent calculus preventive effect or an effective antibacterial action against filamentous bacteria.

Accordingly, the present invention seeks to eliminate the above-mentioned disadvantages of the prior art and to provide a dentifrice having an excellent antibacterial effect and capable of effectively preventing the development of calculus and periodontal diseases.

In accordance with the present invention, there is provided a dentifrice comprising (i) 0.1% to 10% by weight, based on the total amount of the dentifrice, of at least one polyphosphate selected from either linear polyphosphates of the formula (I):



wherein M represents Na or K and $3 \leq n$, excluding insoluble sodium metaphosphate, or cyclic polyphosphates having the formula (II):



wherein M' represents Na or K and $m = 3, 4$ or 6 and (ii) 0.01% to 2% by weight, based on the total amount of the dentifrice, of anethol in an aqueous medium.

The present inventors have found that, when anethol is used in combination with the polyphosphates, especially those having the above-mentioned formula (I) or (II), these components synergistically function to provide a remarkable antibacterial effect against *Actinomyces viscosus* which forms plaques susceptible to calcification. Thus, the growth of *Actinomyces viscosus* is inhibited and the development of calculus and periodontal diseases is effectively prevented.

The dentifrice according to the present invention includes, as a component (i) for inhibiting the growth of *Actinomyces viscosus* and for suppressing the formation of calculus, a polyphosphate having the above-mentioned formulae (I) and (II). Examples of the linear polyphosphates having the formula (I) are those having an n of 3 in the formula (I), such as sodium tripolyphosphate and potassium tripolyphosphate, those having an n of 4 in the formula (I), such as sodium tetrapolyphosphate and potassium tetrapolyphosphate, and those having a high polymerization degree such as sodium metaphosphate and potassium metaphosphate. Examples of the cyclic polyphosphates having the formula (II) are those having an m of 3 in formula (II), such as sodium trimetaphosphate and potassium trimetaphosphate, those having an m of 4 in the formula II, such as sodium tetrametaphosphate and potassium tetrametaphosphate, and those having an m of 6 in the formula (II), such as sodium hexametaphosphate and potassium hexametaphosphate. These polyphosphates may be used alone or in any mixture thereof. Of these polyphosphates, the linear polyphosphates of the formula (I), are especially used because of their better antibacterial properties.

The polyphosphate of the present dentifrice is formulated in an amount of 0.1% to 10% by weight, preferably 0.5% to 5% by weight, based on the total amount of the present dentifrice. When the amount of the polyphosphate is less than 0.1% by weight, the desired synergic effect thereof with anethol is decreased. Conversely, when the amount of the polyphosphate is more than 10% by weight, the taste of the present dentifrice becomes unpleasant.

As mentioned above, according to the present invention, anethol is used in combination with the above-mentioned polyphosphates. The anethol usable in the present invention may include those isolated from essential oil or synthesized anethol. Furthermore, essential oils containing anethol such as Anise oil, Fennel oil, and Star anise oil, may be directly used, without isolating anethol therefrom. The isolated or synthesized anethol may be used in combination with the above-mentioned essential oils, per se.

Anethol formulated in the present dentifrice is in an amount of 0.01% to 2% by weight, preferably 0.05% to 1% by weight, based on the total weight of the dentifrice. When the amount of anethol is less than 0.01% by weight, the synergic effect thereof with the polyphosphate is not felt, and the growth of *Actinomyces viscosus* is not inhibited. Conversely, when the amount of anethol is to be formulated into the present dentifrice is more than 2% by weight, the practical value as a dentifrice is diminished.

The dentifrice according to the present invention may contain, in addition to the anethol, other essential oils such as spearmint oil (e.g., native type, scotch type) and various flavoring materials such as carvone and eugenol.

The dentifrice according to the present invention may optionally contain, in addition to the above-mentioned essential constituents, any conventional ingredients depending upon, for example, the kinds of the dentifrice and the use thereof.

For example, abrasives such as calcium phosphate (dibasic), calcium carbonate, calcium pyrophosphate, insoluble sodium metaphosphate, aluminum oxide, aluminum hydroxide, silica, silicates and resins; binders such as sodium carboxymethyl cellulose, hydroxyethyl cellulose, alginate, carageenan, gum arabic, polyvinyl alcohol, and colloidal silica; humectants such as polyethylene glycol, sorbitol, glycerol, and propylene glycol; surfactants such as sodium lauryl sulfate, sodium dodecylbenzene sulfonate, sodium hydrogenated coconut fatty acid monoglyceride monosulfate, sodium laurylsulfo acetate, sodium lauroyl sarcosinate, N-acyl glutamate, lauryl diethanolamide, and sucrose fatty acid ester; sweeteners such as

saccharin sodium, stebiocide, neohesperidyl dihydrochalcon, glycyrrhizin, perillartine, and p-methoxy cinnamic aldehyde; preservatives; coloring agents; effective components such as chlorohexidines, dextranase, mutanase, sorbin acid, alexidine, hinokitiol, cetyl pyridinium chloride, alkylglycines, alkyldiaminoethyl glycine salts, allantoin, ϵ -aminocaproic acid, tranexamic acid, azulene, vitamin E, water-soluble monobasic or dibasic phosphates, quaternary ammonium compounds and sodium chloride may be formulated into the present dentifrice. Still other components such as sodium fluoride, sodium monofluorophosphate, and stannous fluoride may be formulated into the present dentifrice.

The dentifrice according to the present invention may be prepared in any conventional manner by, for example, mixing the above-mentioned essential and optional ingredients with water.

According to the present invention, the dentifrice having synergic antibacterial effects against *Actinomyces viscosus* and having excellent preventive effects on the development of calculus and periodontal diseases can be provided by formulating the specified polyphosphate and anethol into the dentifrice.

EXAMPLES

The present invention will now be further illustrated by the following Experiments and Examples, wherein "%" means "% by weight" unless otherwise specified.

Experiment 1

Culture media containing, as a polyphosphate, 0.04% sodium tripolyphosphate ($\text{Na}_5\text{P}_3\text{O}_{10}$), sodium tetrapolyphosphate ($\text{Na}_6\text{P}_4\text{O}_{13}$), and sodium metaphosphate ($\text{Na}_{n+2}\text{P}_n\text{O}_{3n+1}$, $n = 40$ and 128), and a culture medium containing 0.03% of anethol, culture media containing the above-mentioned polyphosphates and 0.03% of anethol were prepared. Subcultured *Actinomyces viscosus* 19246 was inoculated into these media and incubated at a temperature of 37°C for 2 days under an anaerobic condition (i.e., 80% N_2 , 10% H_2 , 10% CO_2). The volume of the inoculated bacterial solution was one hundred of the media. The degree of the bacterial growth was monitored by measuring the optical density at 550 nm.

The results are shown in Table 1.

Table 1

Polyphosphate	Addition of Anethol	
	No	Yes
None	0.85	0.74
Sodium tripolyphosphate	0.60	0.12
Sodium trimetaphosphate	0.78	0.46
Sodium tetrapolyphosphate	0.63	0.06
Sodium metaphosphate ($n = 40$)	0.52	0.08
Sodium metaphosphate ($n = 128$)	0.56	0.11

As is clear from the results shown in Table 1, the growth of *Actinomyces viscosus* is inhibited by the synergic action of the polyphosphates in combination with anethol. Thus, it is revealed that the use of the polyphosphate in combination with anethol provides an excellent antibacterial action against the *Actinomyces viscosus*. Furthermore, when sodium tripolyphosphate or linear polyphosphates having a polymerization degree greater than that of tripolyphosphate are used in combination with anethol, more improved synergic effects are provided and thus a particularly effective antibacterial action can be obtained.

Example 1: Toothpaste	
Ingredient	%
Silicic anhydride	25.0
60% Sorbitol	20.0
Thickening silica	2.0
Propylene glycol	4.0
Sodium carboxymethyl cellulose	1.5
Sodium tripolyphosphate	1.5
Anethol	0.2
Peppermint oil	1.0
Sodium fluoride	0.21
Sodium lauryl sulfate	1.2
Saccharin sodium	0.1
Water	balance
	100.0%

Example 2 : Toothpaste	
Ingredient	%
Aluminum hydroxide	30.0
85% Glycerol	20.0
Polyethylene glycol 400	5.0
Sodium carboxymethyl cellulose	1.2
Sodium metaphosphate (n = 36)	5.0
Spearmint oil	1.0
Anethol	0.1
Dextranase	0.18
α -Olefin sulfonate	1.0
Saccharin sodium	0.1
Water	balance
	100.0%

Example 3: Toothpaste	
Ingredient	%
Silicic acid	20.0
Titanium dioxide	2.0
60% Sorbitol	25.0
Propylene glycol	4.0
Sodium carboxymethyl cellulose	1.2
Sodium metaphosphate (n = 59)	4.0
Japanese mint oil	0.7
Anethol	0.3
Eugenol	0.1
Chlorhexidine gluconate	0.025
Sodium lauryl sulfate	1.2
Saccharin sodium	0.1
Water	balance
	100.0 %

Example 4: Toothpaste

Ingredient	%
Calcium phosphate (dibasic)-dihydrate	40.0
85% Glycerol	25.0
Thickening silica	2.0
Propylene glycol	4.0
Sodium carboxymethyl cellulose	1.2
Sodium polyphosphate (n = 3.2)	1.0
Potassium polyphosphate (n = 3.1)	2.0
1-Menthol	0.5
Anethol	0.3
ϵ -Aminocaproic acid	0.01
Dihydroxy aluminum allantoin	0.01
Saccharin sodium	0.1
Sodium lauryl sulfate	1.2
Water	balance
	100.0%

Example 5: Toothpaste

Ingredient	%
Silicic anhydride	25.0
60% Sorbitol	25.0
Thickening silica	2.0
Polyethylene glycol 400	4.0
Sodium carboxymethyl cellulose	1.2
Sodium tetrapolyphosphate	3.0
Peppermint oil	0.8
Anise oil	0.1
Sodium fluoride	0.21
Chlorhexidine hydrochloride	0.01
Sodium lauryl sulfate	1.2
Saccharin sodium	0.1
Water	balance
	100.0%

Example 6 : Toothpaste	
Ingredient	%
Silicic anhydride	23.0
85% Glycerol	20.0
Thickening silica	2.0
Polyethylene glycol 400	4.0
Sodium carboxymethyl cellulose	1.2
Sodium metaphosphate (n = 14)	3.0
l-Menthol	0.5
Peppermint oil	0.5
Anethol	0.2
Sodium monofluorophosphate	0.76
Sodium lauryl sulfate	1.2
Saccharin sodium	0.1
Water	balance
	100.0%

Claims

1. A dentifrice comprising (i) 0.1% to 10% by weight, based on the total amount of the dentifrice, of at least one polyphosphate selected from either linear polyphosphates of the formula (I):



wherein M represents Na or K and $3 \leq n$, excluding insoluble sodium metaphosphate, or cyclic polyphosphates having the formula (II):



wherein M' represents Na or K and $m = 3, 4$ or 6 and (ii) 0.01% to 2% by weight, based on the total amount of the dentifrice, of anethol in an aqueous medium.

2. A dentifrice as claimed in claim 1, wherein the linear polyphosphate (I) is used as the component (i).
3. A dentifrice as claimed in Claim 1, wherein the cyclic polyphosphate (II) is used as the component (i).

Patentansprüche

1. Zahnputzmittel mit, bezogen auf sein Gesamtgewicht,
(i) 0,1 bis 10 Gew.% mindestens eines Polyphosphats in Form
linearer Polyphosphate der Formel (I):



worin M für Na oder K steht und $3 \leq n$ (mit Ausnahme von unlöslichem Natriummetaphosphat) oder cyclischer Polyphosphate der Formel (II)



worin M' für Na oder K steht und $m = 3, 4$ oder 6 und

(ii) 0,01 bis 2 Gew.% Anethol
in einem wäßrigen Medium.

2. Zahnputzmittel nach Anspruch 1, wobei als Komponente (i) das lineare Polyphosphat (I) verwendet wird.

Example 6 : Toothpaste	
Ingredient	%
Silicic anhydride	23.0
85% Glycerol	20.0
Thickening silica	2.0
Polyethylene glycol 400	4.0
Sodium carboxymethyl cellulose	1.2
Sodium metaphosphate (n = 14)	3.0
l-Menthol	0.5
Peppermint oil	0.5
Anethol	0.2
Sodium monofluorophosphate	0.76
Sodium lauryl sulfate	1.2
Saccharin sodium	0.1
Water	balance
	100.0%

Claims

1. A dentifrice comprising (i) 0.1% to 10% by weight, based on the total amount of the dentifrice, of at least one polyphosphate selected from either linear polyphosphates of the formula (I):



wherein M represents Na or K and $3 \leq n$, excluding insoluble sodium metaphosphate, or cyclic polyphosphates having the formula (II):



wherein M' represents Na or K and $m = 3, 4$ or 6 and (ii) 0.01% to 2% by weight, based on the total amount of the dentifrice, of anethol in an aqueous medium.

2. A dentifrice as claimed in claim 1, wherein the linear polyphosphate (I) is used as the component (i).
3. A dentifrice as claimed in Claim 1, wherein the cyclic polyphosphate (II) is used as the component (i).

Patentansprüche

1. Zahnputzmittel mit, bezogen auf sein Gesamtgewicht,
(i) 0,1 bis 10 Gew.% mindestens eines Polyphosphats in Form
linearer Polyphosphate der Formel (I):



worin M für Na oder K steht und $3 \leq n$ (mit Ausnahme von unlöslichem Natriummetaphosphat) oder cyclischer Polyphosphate der Formel (II)



worin M' für Na oder K steht und $m = 3, 4$ oder 6 und
(ii) 0,01 bis 2 Gew.% Anethol
in einem wäßrigen Medium.

2. Zahnputzmittel nach Anspruch 1, wobei als Komponente (i) das lineare Polyphosphat (I) verwendet wird.



3. Zahnputzmittel nach Anspruch 1, wobei als Komponente (i) das cyclische Polyphosphat (II) verwendet wird.

Revendications

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1. Dentifrice comprenant (i) 0,1% à 10% en poids, basé sur la quantité totale du dentifrice, d'au moins un polyphosphate choisi parmi les polyphosphates linéaires de la formule (I)



dans laquelle M représente Na ou K et $3 < n$, à l'exclusion du métaphosphate de sodium insoluble, ou les polyphosphates cycliques ayant la formule (II)



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dans laquelle M' représente Na ou K et $m = 3, 4$ ou 6 et

(ii) 0,01% à 2% en poids, basé sur la quantité totale du dentifrice, d'anéthol en milieu aqueux.

2. Dentifrice selon la revendication 1 dans lequel le polyphosphate linéaire (i) est utilisé en tant que composant (i).
3. Dentifrice selon la revendication 1 dans lequel le polyphosphate cyclique (II) est utilisé en tant que composant (i).

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