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COMPOSITION FOR PREVENTING AND TREATING GINGIVAL DISEASES

FIELD OF THE INVENTION

The present invention relates to a composition for preventing and treating gingival diseases. More specifically, it pertains to a composition comprising 5 to 30 parts by weight of Camomile tincture; 5 to 30 parts by weight of Rhatany tincture; 2.5 to 15 parts by weight of Myrrh tincture; 300 to 1500 parts by weight of sodium hydrogencarbonate; 3 to 50 parts by weight of Sage oil; 10 to 70 parts by weight of glycyrrhetinic acid; 0 to 50 parts by weight of tocopherol; 10 to 50 parts by weight of medicated soap and emulsifier; 20 to 100 parts by weight of glycerin; a proper amount of a thickener selected from the group consisting of sodium carboxymethyl cellulose, alginic acid, carrageenan, agar and gelatin; and a proper amount of water.

BACKGROUND OF THE INVENTION

The dental calculus formed on the teeth by the microorganisms is a major cause of gingivitis and pyorrhea alveolaris. Accordingly, control of the dental calculus is very important in treating such gingival diseases. The dental calculus is mostly a complex of microorganisms, polysaccharides secreted by them, and other materials. When the dental calculus is observed under a microscope, evenly arranged colonies of microorganisms are shown. At the initial stage of development of the dental calculus, the major microorganisms found in the surface of the teeth are gram positive bacteria such as *Actinomyces viscosus* and *Actinomyces israelii*, and *Streptococcus mutans*(Socranscky, S. S., *Journal of Periodontology*, *48*, 497-504(1977)). At

the late stage, numerous gram negative bacteria such as *Actinobacillus*, *Actinomycetemcomitans*, *Bacteroides gigivalis* and *Bacteroides intermedius* are related to the periodontal disease(Moor, W. E. C., et al., *Journal of Periodontal Research, 12*, 120-128(1983)).

In the treatment of gingivitis and pyorrhea alveolaris, it is considered as the most important thing that each individual removes the dental calculus regularly through oral hygiene and, thereby, making it possible to treat the infection caused by the microorganisms with antibacterial agents. Many antibacterial agents have been examined for their capability to treat pyorrhea alveolaris, however, little of them can control the dental calculus. The potential drugs include plant extracts, metallic salts, phenol and bisbiguanides(Lander, P. E, et al., *J. Clin. Periodontal., 13*, 74-80(1986)). Among them, the galenical preparations, i.e., the plant extracts, are considered as excellent pharmaceuticals which are capable of minimizing the various adverse effects which may caused by the use of chemical agents, such as dental discoloration, stimulative feeling and problems due to the long term use. Further, it has been reported that symptoms of periodontal diseases, e.g., ulorrhagia and edema, have been significantly improved by using the galenical preparations(Yankell, L. L., *et al., J. Clin. Dent., 1*, A6-A8(1988); and Kitagaki, K., et al., *J. Antibact. Antifung. Agents, 11*, 451-61(1983)).

Further, Renggli, H. H. has reported that a gargle containing Camomile, Sage, Rhatany and Myrrh is effective for the suppression of microorganisms and the change of microorganisms under gingival margin, and exhibits fang-lubricating effect due to the detoxification in the surface of the cement, in the darkfield microscope study(*J. Clin. Dent., 1*, A34(1988)). Moreover, Lee M.S., et al. has reported that, when the clinical observation was conducted and the change in the constitution of dental plaque was observed under a darkfield microscope after having patients suffered from incipient pyorrhea alveolaris use

a prescription for treating periodontal disease containing Camomile, Rhatany and Myrrh(e.g., Parodontax), significant decreases in the dental plaque index, gingiva index and ulorrhagia index were shown in the experimental group(*Journal of Korean Dentist Association, 27*, 385-95(1989)). Therefore, it is expected that the pharmacological effect as a treating agent for periodontal disease can be enhanced significantly by administering the parodontax composition in combination with other antibacterial materials.

The present inventors have endeavored to find a material which can enhance the antibacterial activity of the Parodontax composition and finally have discovered that the antibacterial activity of the Parodontax composition is enhanced significantly by the addition of glycyrrhetinic acid.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a composition for preventing and treating gingival diseases which has enhanced antibacterial activity.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the present invention, there is provided a composition for preventing and treating gingival diseases which comprises Camomile tincture; Rhatany tincture; Myrrh tincture; sodium hydrogencarbonate; Sage oil; medicated soap and emulsifier; glycerin; a thickener selected from the group consisting of sodium carboxymethyl cellulose(Na-CMC), alginic acid, carrageenan, agar and gelatin; water; glycyrrhetinic acid; and, if necessary, one or more component selected from

the group consisting of tocopherol, tocopherol acetate and sodium monofluorophosphate.

The composition of the present invention preferably comprises: 5 to 30 parts by weight of Camomile tincture; 5 to 30 parts by weight of Rhatany tincture; 2.5 to 15 parts by weight of Myrrh tincture; 300 to 1500 parts by weight of sodium hydrogencarbonate; 3 to 50 parts by weight of Sage oil; 10 to 70 parts by weight of glycyrrhetinic acid; 0 to 50 parts by weight of tocopherol; 0 to 50 parts by weight of sodium monofluorophosphate; 10 to 50 parts by weight of medicated soap and emulsifier; 20 to 100 parts by weight of glycerin; a proper amount of a thickener selected from the group consisting of Na-CMC, alginic acid, carrageenan, agar and gelatin; and a proper amount of water.

The following Examples are intended to further illustrate the present invention without limiting its scope.

Example 1: Parodontax composition

Component and content(per 1g of product)

Camomile tincture: 12.5mg

Rhatany tincture: 12.5mg

Myrrh tincture: 6.2mg

sodium hydrogencarbonate: 679.0mg

Sage oil: 10.5mg

medicated soap and emulsifier: 19.8mg

glycerin: 62.6mg

Na-CMC: q.s.

distilled water: q.s.

Example 2: Composition of the present invention

* Code number: BK 200

Component and content(per 1g of product)

Camomile tincture: 12.5 mg

Rhatany tincture: 12.5 mg

Myrrh tincture: 6.2 mg

sodium hydrogencarbonate: 679.0 mg

Sage oil: 16.5 mg

glycyrrhetinic acid: 30 mg

tocopherol acetate: 25 mg

medicated soap and emulsifier: 19.8 mg

glycerin: 62.6mg

Na-CMC: q.s.

distilled water: q.s.

Example 3: Composition of the present invention

* Code number: BK 201

Component and content(per 1g of product)

Camomile tincture: 12.5 mg

Rhatany tincture: 12.5 mg

Myrrh tincture: 6.2 mg

sodium hydrogencarbonate: 679.0 mg

Sage oil: 16.5 mg

glycyrrhetinic acid: 30 mg

medicated soap and emulsifier: 19.8 mg

glycerin: 62.5mg

Na-CMC: q.s.

distilled water: q.s.

Example 4: Composition of the present invention

* Code number: BK 202

Component and content(per 1g of product)

Camomile tincture: 10.0 mg

Rhatany tincture: 10.0 mg

Myrrh tincture: 6.2 mg

glycyrrhetinic acid: 35.0 mg

sodium hydrogencarbonate: 670.0 mg

Sage oil: 20.0 mg

tocopherol acetate: 30 mg

medicated soap and emulsifier: 20.0 mg

glycerin: 60.0 mg

Na-CMC: q.s.

distilled water: q.s.

Example 5: Composition of the present invention

* Code number: BK 203

Component and content(per 1g of product)

Camomile tincture: 15.0 mg

Rhatany tincture: 15.0 mg

Myrrh tincture: 6.2 mg

sodium hydrogencarbonate: 670.0 mg

sodium monofluorophosphate: 7.6 mg

Sage oil: 15.0 mg

glycyrrhetinic acid: 40.0 mg

medicated soap and emulsifier: 20.0 mg

glycerin: 50.0 mg

Na-CMC: q.s.

distilled water: q.s.

Parodontax, BK 200, BK 201, BK 202 and BK 203 of above Examples 1 to 5 were prepared by using vacuum emulsifier(VM-12) in accordance with the conventional method for the preparation of a paste.

Test Example:

1. Materials and Methods

1) Microorganisms and medium

Three species of microorganisms, i.e., *Actinomyces viscosus* ATCC 15987, *Candida albicans* ATCC 10231 and *Streptococcus mutans* ATCC 10449, were used in the test. *Actinomyces viscosus* ATCC 15987 and *Candida albicans* 10231 were cultured on YM medium(glucose 10g/L, yeast extract 3g/L, malt extract 3g/L, bactopeptone 5g/L), and *Streptococcus mutans* ATCC 10449 was cultured on TH medium(Todd Hewitt broth 30g/L, sucrose 50g/L).

Actinomyces viscosus ATCC 15987 and *Candida albicans* 10231 stored on YM medium, and *Streptococcus mutans* ATCC 10449 stored on TH medium were transferred respectively to each of three plates containing 17g/L of bactoagar by streaking.

Actinomyces viscosus ATCC 15987 was cultured at 26℃, and *Candida albicans* ATCC 10231 and *Streptococcus mutans* ATCC 10449 were cultured at

37℃. The microorganisms were cultured for 18 hours in an incubator.

2) Assay for antibacterial activity(M.I.C. assay)

100μg/L each of Parodontax, BK 200 and BK 201 were subjected to the serial double dilutions for 16 times to reach the final concentration of 0.002μg/mL. The microorganisms cultured in the above 1) were diluted with used media to a concentration of 10^7 cells/mL and 50μL each of the microorganism solutions were inoculated to the tubes containing one of the samples which were diluted into a various conc. The microorganisms were cultured with shaking for 18 hours. *Actinomyces viscosus* ATCC 15987 and *Candida albicans* ATCC 10231 were cultured with YM medium and *Streptococcus mutans* ATCC 10449 were cultured with TH medium. The lowest concentration of the composition which can inhibit the growth of the microorganisms was determined as the minimum inhibitory concentration(M.I.C.).

3) Results

The M.I.C. of each composition against *Actinomyces viscosus* are shown in Table 1. As shown in Table 1, BK 200 and BK 201 exhibit good antibacterial activity with inhibiting the growth of the microorganism at a concentration of 12.5μg/ml, while Parodontax exhibits weak antibacterial activity.

Table 1. M.I.C. against *Actinomyces viscosus*

Test composition	M.I.C.(μg/ml)
BK 200	12.5
BK 201	12.5
Parodontax	50.0

Table 2 shows the M.I.C. of each composition against *Candida albicans*. BK 200 and BK 201 inhibit the growth of the microorganism significantly, while Parodontax shows weak inhibitory activity.

Table 2. M.I.C. against *Candida albicans*

Test composition	M.I.C.(ug/ml)
BK200	25.0
BK201	25.0
Parodontax	50.0

Table 3 shows the M.I.C. of each composition against *Streptococcus mutans*, wherein BK 200, BK 201 and Parodontax shows similar antibacterial activities.

Table 3. M.I.C. against *Streptococcus mutans*

Test composition	M.I.C.(μg/ml)
BK200	25.0
BK201	25.0
Parodontax	25.0

4) Discussion

Although the dental calculus can be formed on the surface of the teeth spontaneously, periodontal diseases or carious teeth may be occurred if the amount of dental calculus overs a certain limit while the oral hygiene is not properly conformed. The toothbrushing method carried out by most people is not suitable for maintaining a proper dental calculus condition in order to keep

a healthy oral state. Accordingly, the addition of chemical agents such as an antiplaque or antibacterial agents to the dental products has been proposed in order to decrease the dental diseases caused by dental calculus.

There have been many studies on the control of dental calculus by various antibacterial agents. In order to treat pyorrhea alveolaris caused by foreign pathogens or the opportunistic infection, the antibiotics should be present in the infected site for a long time at a high concentration, as far as possible. It is preferable that such concentration is selected for killing the pathogens, rather than suppressing the growth of the pathogens. Consequently, minimum bactericidal concentration(MBC), which means the concentration of test compound killing more than 99% of the test microorganisms in a given time, and minimum inhibitory concentration(MIC), which means the minimum concentration of test compound suppressing the growth of the microorganisms, are determined. Generally, MIC value is known as a primary indicator for the strong activity controlling dental calculus. However, when comparing the drugs acting on the oral microorganisms, the clinical effectiveness thereof may be exhibited variably, notwithstanding their similar MIC values or action spectra and, accordingly, MIC is not necessary just as an indicator for clinical effectiveness(Gjermo P, et al., *J. Periodont Res., 5*, 102-109(1970); Moran J. and Addy M., *J. Periodontol., 55*, 278-282(1984)). However, MIC assay is a usual experimental method for testing the possibility and potentiality of a drug as a treating agent for pyorrhea alveolaris.

As described in the above, many antibacterial agents have been examined for their capability to treat pyorrhea alveolaris, however, little of them can control the dental calculus. The potential drugs include plant extracts, metallic salts, phenol and bisbiguanides(Lander, P. E, *et al., supra*). Among the bisbiguanides, chlorhexidine is known as a most effective

preparation and it reduces dental calculus and gingivitis in a human body(Dolan M. M., et al., *Arch. Oral Biol., 17*, 147-54(1972)). However, in spite of its strong antibacterial activity, its use is limited by the problems of the damage of cell membrane and the discoloration of dental tissue(Grossman E, *et al., J. Periodont. Res., 21*(16 Suppl.), 33-43(1986); Lang N.P. and Brecx M. C.. *J. Periodont. Res., 21*(16 Suppl.), 74-89(1986)). Further, numerous studies have been conducted to develop an antibacterial material which induces no adverse effect in a long-term use while showing potent antibacterial activity against the dental plaque.

Parodontax is a medicinal product applied to the gingiva for treating the periodontal diseases, and alleviates the periodontoclasia and bleeding. It showed a very effective result in a clinical test. Lee M. S. et al.(*Journal of Korean Dentist Association*, 385-395(1989)) have conducted a clinical test by employing 35 incipient pyorrhea alveolaris patients as subjects. The experimental group was consisting of 25 patients, who were administered with parodontax for 4 weeks by topical painting. The control group was consisting of 10 patients, who were not administered with Parodontax. At the initial practice, and 2 and 4 weeks thereafter, the clinical indices(dental plaque index, gingiva index, ulorrhagia index) of the patients, as well as the depth of periodontal cyst and the morphological distribution of the dental plaque were observed and Lee et al. came to the following conclusion. First, the experimental group has shown significantly reduced dental plaque index, gingiva index and ulorrhagia index at 2 and 4 weeks, respectively, in comparison with the control group. Secondly, the depth of periodontal cyst has been significantly reduced in the experimental group during the experimental period in comparison with that measured in the initial practice. In the morphological distribution of the dental plaque under the gingival margin, the cocci were increased but the motile bacillus and spirillum were

decreased significantly in the experimental group in comparison with those measured in the initial practice.

However, the present inventors have not been satisfied with this result, and have endeavored to develop a product(tentatively named "BK 200") having a higher antibacterial activity than the existing product such as Parodontax. Finally, the present inventors have developed a new composition which contains, in addition to the existing product, glycyrrhetinic acid having a good antibacterial activity and one or more components having a superior antioxidative property which are selected from the group consisting of tocopherol(or tocopherol acetate) and sodium monofluorophosphate. When the MIC of the new composition was tested against *Actinomyces viscosus*, *Candida albicans* and *Streptococcus mutans*, the new composition showed a higher antibacterial activity against *Actinomyces viscosus* and *Candida albicans* by 2 to 3 times than the existing product, and an antibacterial activity against *Streptococcus mutans* which is similar to that of the existing product. Accordingly, the composition of the present invention is expected to be useful for the prevention and treatment of pyorrhea alveolaris.

While the invention has been described with respect to the above specific embodiments, it should be recognized that various modifications and changes may be made to the invention by those skilled in the art which also fall within the scope of the invention as defined by the appended claims.

CLAIMS

1. A composition for preventing and treating the gingival disease which comprises: 5 to 30 parts by weight of Camomile tincture; 5 to 30 parts by weight of Rhatany tincture; 2.5 to 15 parts by weight of Myrrh tincture; 300 to 1500 parts by weight of sodium hydrogencarbonate; 3 to 50 parts by weight of Sage oil; 10 to 70 parts by weight of glycyrrhetinic acid; 0 to 50 parts by weight of tocopherol; 10 to 50 parts by weight of medicated soap and emulsifier; 20 to 100 parts by weight of glycerin; a proper amount of a thickener selected from the group consisting of sodium carboxymethyl cellulose, alginic acid, carrageenan, agar and gelatin; and a proper amount of water.

2. A composition for preventing and treating the gingival disease which comprises: 5 to 30 parts by weight of Camomile tincture; 5 to 30 parts by weight of Rhatany tincture; 2.5 to 15 parts by weight of Myrrh tincture; 300 to 1500 parts by weight of sodium hydrogencarbonate; 3 to 50 parts by weight of Sage oil; 2.5 to 20 parts by weight of sodium monofluorophosphate; 10 to 70 parts by weight of glycyrrhetinic acid; 0 to 50 parts by weight of tocopherol; 10 to 50 parts by weight of medicated soap and emulsifier; 20 to 100 parts by weight of glycerin; a proper amount of a thickener selected from the group consisting of sodium carboxymethyl cellulose, alginic acid, carrageenan, agar and gelatin; and a proper amount of water.

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