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(54) **Title**: ORAL ADHERING COMPOSITIONS THAT APPLY RHIZOPHORA MANGLE EXTRACT IN THE MOUTH

(57) **Abstract**: This invention is directed to compositions that adhere in the mouth to impede inflammation and promote resolution thereof in tissues of the oral mucosa, including mouth, throat, and esophagus, including gingivitis, periodontitis, laryngitis, esophagitis, mucositis, stomatitis, vestibulitis, aphthous ulcerations, and Behcet's syndrome, whether caused by bacterial or viral infections, trauma, or other cause. The compositions may be oral adhering discs or denture paste or oral gel that release Rhizophora Mangle extract.

Oral adhering compositions that apply Rhizophora Mangle extract in the mouth

BACKGROUND

Mucositis is an inflammation of the mucous membranes, including mouth ulcers or denture sores. Mucositis in the mouth (stomatitis), is one of the most common oral problems occurring after chemotherapy and radiation therapy. Oral mucositis can contribute to oral infections, inability to taste normally and pain arising from the resulting open sores that can develop. Oral mucositis can become so painful that the patient will not eat or drink, contributing to dehydration and malnutrition.

Mucositis typically manifests as an erythematous, burn-like lesion or as random, focal-to-diffuse, ulcerative lesions. Stomatitis refers to an inflammatory reaction affecting the oral mucosa, with or without ulceration, that may be caused or intensified by pharmacological, particularly chemotherapeutic treatments, or by radiotherapy. Stomatitis can range from mild to severe; the patient with severe stomatitis is unable to take anything by mouth.

About 20 percent of people suffer from recurrent stomatitis in the form of aphthous ulcers, also called mouth ulcers, mouth sores, or canker sores. Many women get oral aphthous ulceration at specific times of the menstrual cycle. This is sometimes very severe and can require strong painkillers and sedatives. The most severe form is called Behcet's syndrome.

People who use dentures often suffer from inflammation (denture sores) at points of contact of the dentures with gums. Orthodontic braces and other appliances often cause inflammation at points of contact with mucosa.

SUMMARY OF THE INVENTION

The present invention provides muco-adhering compositions that time release Rhizophora Mangle extract for topical absorption by oral epithelial tissues that are subject to mucositis. The extract may be made with water or alcohol and water. The compositions may be oral adhering discs or muco-adhering denture paste. The disc may have an adhesive on one side suitable for adhering to mucosa or to teeth or gums or it may be adherent on both sides.

Armas et al reported in Current Medical Research and Opinions that the application of a liquid extract of Rhizophora Mangle (red mangrove root), once a day, speeded healing of aphthous ulcers.

The disclosed adhering compositions release an amount of Rhizophora Mangle extract that is effective for prevention or treatment when delivered topically to the oral mucosal tissues. The delivery is typically at least once each day, or as continuously as practical day and night. It was

known in the prior art to deliver these molecules by liquid. It was not previously known to topically deliver these molecules to inflamed oral mucosa from an oral adhering disc or a denture adhesive.

In the present invention, the adhering aspect allows a high concentration to be maintained in tissues near the composition while having low concentrations in the rest of the body to minimize side effects and maximize cost-benefit. Because the composition adheres, it may be used while sleeping which is when saliva flow is lowest and the topically delivered Rhizophora Mangle extract molecules can achieve maximum topical application.

In one aspect, the invention is an adhering disc, at least 5 millimeters in each of two planar dimensions, comprising the above described Rhizophora Mangle extract molecules in a quantity effective to reduce or prevent mucositis when used on moist epithelial tissues. The adhering disc may comprise at least 4 milligrams of the Rhizophora Mangle extract molecules. The adhering disc may use carbomer or collagen as an adhesive, and it may be thin in the shape of a patch. On a side of the disc intended to be adherent, the adhesive molecules dominate over molecules that reduce adhesion such that the disc will adhere to a roof of a mouth of a human against force of gravity.

In another aspect, the invention is a muco-adhering paste, such as denture adhesive paste, comprising the above described Rhizophora Mangle extract molecules in a quantity effective to reduce or prevent mucositis when used on moist epithelial tissues. The adhering paste may comprise at least 1% Rhizophora Mangle extract molecules.

In another aspect, the invention is a muco-adhering gelatinous liquid, often called an oral gel, comprising the above described Rhizophora Mangle extract molecules in a quantity effective to reduce or prevent mucositis when used on moist epithelial tissues. The adhering oral gel may comprise at least 1% Rhizophora Mangle extract molecules.

In another aspect, the invention is a method for treating or preventing oral mucositis in a patient by regularly applying to an oral mucosal surface an adhering composition with an effective amount of the Rhizophora Mangle extract molecules. The adhering composition may be administered at least once a day every day for prevention. The mucositis may occur as stomatitis or aphthous ulcers. The mucositis may occur in the oro-pharynx or the esophagus.

The present invention can be more fully explained by reference to the following detailed description and illustrative examples.

DETAILED DESCRIPTION OF THE INVENTION

Rhizophora Mangle extract is prepared from the bark of red mangrove, which is prolific in the Caribbean, by water extraction or by extraction with water and alcohol. The extract is dried and may be spray dried or freeze dried.

Oral adhering discs

In an oral adhering disc, 4 - 300 milligrams of the Rhizophora Mangle extract molecules may be used. The adhering discs may further comprise one or more other active ingredients, such as an analgesic, anti-inflammatory, emollients, local anesthetics, and the like. It is helpful if the mixture released by the disc can adhere to mucosa to provide a protective coating for exposed nerve endings and hold the active molecules in topical application, such as by including collagen or alginate or other adhering hydrocolloid in the disc. Furthermore, the disc ingredients may include moisturizing humectant ingredients such as xylitol or cellulose gum or molecules that promote production of mucous to reduce further irritation.

For release of the Rhizophora Mangle extract molecules in the mouth, the disc may include binder molecules that erode as they become hydrated. In the mouth, the adhering disc may be hard or it may have a feel and texture like gummy candies. It may be made with slowly dissolving hydrocolloids so that that it typically lasts in the mouth for at least twenty minutes to six hours. The adhering disc can be formed in the shape of a disc or tablet or a wafer or any other desired shape.

An adhering disc preferred for release to the mouth generally or the throat includes hydrophilic gums that slow its rate of dissolution and has a layer of adhesive on one side so it may be adhered to a tooth or gingiva, as described in US patent application 11/800381 (37-3) filed May 4, 2007 by the same inventor, which is incorporated by reference. This adhering disc is made in two layers. A first layer of uniform thickness is 60% to 100% acacia gum or carbomer for adhesion, and it may include up to 40% Rhizophora Mangle extract molecules. A second layer is about 20-90% Rhizophora Mangle extract molecules, 5-30% dissolving sugar such as lactose or sorbitol to achieve dissolution, 2-20% carbomer or carboxymethylcellulose to slow dissolution, and 0.4-1.5% calcium or magnesium stearate for tablet pressing lubrication. The preferred size is 9-14 mm across, domed on the second layer to reduce catching by the tongue or teeth, and includes 10-300 mg Rhizophora Mangle extract molecules. The surface of the adhesive layer is preferably dimpled to assist with adhesion to teeth or braces.

The preferred instruction to users with mucositis in the mouth generally or in the throat where discs cannot be adhered to the site is to adhere the disc to the roof of the mouth or to the outside of a molar and allow released ingredients to wash over the mouth.

An alternate shape particularly suitable for mouth ulcers is a thin tapered patch, nearly flat on one side. A detailed description of such an adhering disc and how to make it are disclosed by the same inventor in US patent application serial number 10/287,843 filed November 5, 2002. One such patch formulation is made by combining 5-50 mg Rhizophora Mangle extract molecules per disc with collagen and with other binder ingredients. Collagen, which is the organic molecule that makes up skin and the lining of the mouth (a form of skin), tends to adhere very well to itself, making it glutinous, and therefore adheres very well to the lining of the mouth. An effective and cost effective form of collagen is food grade gelatin which is made from animal skins. The disc is made by depositing a blog of viscous gel or the ingredients mixed with solvent such as water or alcohol, then drying the solvent out of the blob

Adhering discs in the form of single layer dissolving muco-adhesive tablets may be made by pressing powders including mucoadhesive hydrocolloids. One form of such an adhering disc may be made by mixing dry powders consisting of about 40 - 70 percent carbomer (Carbolpol 971 or 974 from Lubrizol) or 50 – 75% gelatin for adhesion and 25 to 50 percent Rhizophora Mangle extract molecules. The tablet may be pressed into the shape of a tablet that is domed on one side. Such a tablet is preferably about 9-14 mm in diameter and 70-150 milligrams in weight.

Other methods for making adhering discs include hot extrusion of a sheet of viscous adherent hydrocolloids such as gelatin plus water mixed with the extract and then cooling and die cutting to make thin discs or hot pressing the sheet with dies that squish the viscous sheet of gel to separate it into individual discs and then cooling. The water is dried out the discs after they are formed.

The preferred instruction to users with aphthous ulcers is to stick an adhering disc on the ulcer or to gums near a tooth or to a tooth, placing it on the tongue side of the teeth if the patient suffers particularly from inflammation on or under the tongue, and otherwise placing it on the cheek side. For prevention use while sleeping, the user is advised to place one adhering disc in each cheek where it can adhere to molars or gums beside molars.

Oral adhering gel

In a dissolving oral adhering water-based gel such as for squeezing onto oral surfaces with the tongue, 2 – 10% Rhizophora Mangle extract molecules is a suitable dose. In gel formulations, the gel is made highly viscous and muco-adherent, such as by using partially evaporated aloe vera sap or including a hydrophilic gum such as polyvinylpyrrolidone, xanthan gum, locust bean gum, konjac gum, guar gum, collagen from any source including food grade gelatin, or carboxymethylcellulose (CMC) such as Ticalose from Tic Gums. In one embodiment, the viscosity of the composition is from about 500 to about 2000 centipoise, adjusted with water, food oil, and/or glycerin. In an embodiment, the primary thickener and adhesive is

polyvinylpyrrolidone which is from about 3 to about 10% by weight of the composition. In another embodiment, the polyvinylpyrrolidone is from about 7 to about 10% by weight of the composition. In yet another embodiment, the viscosity of the composition is from about 2000 to about 1,000,000 centipoise.

The gel may be packaged in a pump bottle that pumps a roughly equal dose with each pump stroke. Because microbes may grow in a water solution, in one embodiment, the bottle contains little water and mostly food oils or glycerin.

The gel may be provided in a flexible packet sealed pouch comprising from about 3 to about 30 milliliters of the gel.

Oral adhering paste

For use on denture sores, a preferred for is a dissolving oral adhering paste, with a viscosity greater than 1,000,000 centipoise and 2% - 50% Rhizophora Mangle extract molecules. 5 – 20% Rhizophora Mangle extract molecules is preferred. Other ingredients are a denture adhesive component, described below, and an edible oil, such as mineral oil. A denture wearer in need thereof applies the composition to the oral cavity and/or the denture prosthesis at a spot where a denture sore tends to form and thereafter secures the denture to the oral cavity. Alternatively, the paste may be used by itself without placing a denture.

Considerable effort has been made over the years to develop improved denture adhesive compositions. Both synthetic and natural polymers and gums have been used alone, in combination, and in combination with various other adhesive materials in an attempt to improve hold and reduce oozing of the adhesive from under the dental plate. For example, alkyl vinyl ether-maleic copolymers and salts thereof are known for providing good hold in denture adhesive compositions. Such disclosures include: U.S. Pat. No. 3,003,988, Germann et al., issued Oct. 10, 1961; U.S. Pat. No. 4,980,391, Kumar et al., issued Dec. 25, 1990; U.S. Pat. No. 5,073,604, Holeva et al., issued Dec. 17, 1991; U.S. Pat. No. 5,525,652, Clarke, issued Jun. 11, 1996; U.S. Pat. No. 5,340,918, Kittrell et al., issued Aug. 23, 1994; U.S. Pat. No. 5,830,933, Synodis et al., issued Nov. 3, 1998; and U.S. Pat. No. 6475498, Rajaiah et al. issued November 5, 2002.

The denture adhesive component is generally at a level of from 20% to 90% by weight of the composition, the balance being oil and Rhizophora Mangle extract molecules. The denture adhesive component may be selected from the group consisting of AVE/MA, salts of AVE/MA, AVE/MA/IB, salts of AVE/MA/IB, and mixtures thereof, or any other effective denture adhesive. The term "AVE/MA" as used herein refers to alkyl vinyl ether-maleic acid or anhydride copolymer. The term "AVE/MA/IB" refers to terpolymers with alkyl vinyl ether, maleic acid or anhydride, and isobutylene. The term "mixed polymer salts" or "mixed salts", as used herein, refers to salts of AVE/MA and/or AVE/MA/IB.

The AVE/MA copolymers have a range of specific viscosities. For example, the specific viscosity is preferably from 1.2 to 14, as preferably measured as a 1% weight/volume solution of the starting anhydride or acid of the copolymer, in methyl ethyl ketone at 25 degrees C. Other methods and solvents can be used to measure the specific viscosity such as a 1% weight/volume solution in DMF (dimethyl formamide) at 25 degrees C and a 1% weight/volume solution in 2-butanone at 25 degrees C.

AVE/MA and salts thereof and AVE/MA/IB and salts thereof, are also described in U.S. Pat. No. 5,073,604 to Holeva et al., issued Nov. 17, 1991; U.S. Pat. No. 5,525,652, issued Jun. 11, 1996, Clarke et al.; U.S. Pat. No. 4,758,630, issued Jul. 19, 1988, Shah et al.; U.S. Pat. No. 5,304, 616, issued Apr. 19, 1994, Rajaiah et al.; U.S. Pat. No. 5,424,058, issued Jun. 13, 1995, Rajaiah; 5,424,058, issued Jun. 13, 1995, Rajaiah et al.; U.S. Pat. No. 4,758,630, issued Jul. 19, 1988, Shah et al.; U.S. Pat. No. 5,830,933, issued Nov. 3, 1998, Synodis et al.; U.S. Pat. No. 2,047,398, issued Jul. 14, 1936, Voss et al.; U.S. Pat. No. 3,003,988, issued Oct. 10, 1961, Germann et al.; U.S. Pat. No. 5,880,172, Rajaiah et al., issued Mar. 9, 1999; U.S. Pat. No. 5,900,470, Prosise et al., issued May 4, 1999; U.S. Pat. No. 5,037,924, Tazi et al., issued Aug. 6, 1991; U.S. Pat. No. 5,082,913, Tazi et al, issued Jan. 21, 1992; U.S. Pat. No. 6,239,191, issued May 29, 2001; all of which are incorporated herein by reference in their entirety.

Suitable AVE/MA copolymers may be prepared by well-known methods of the prior art; see, for example, U.S. Pat. No. 2,782,182, and U.S. Pat. No. 2,047,398, both of which are incorporated by reference herein in their entirety. The terpolymers can be made by the methods discussed in U.S. Pat. No. 5,900,470, Prosise et al., issued May 4, 1999; U.S. Pat. No. 5,037,924, Tazi et al., issued Aug. 6, 1991; and U.S. Pat. No. 5,082,913, Tazi et al., issued Jan. 21, 1992, herein incorporated by reference in their entirety.

The alkyl vinyl ether maleic anhydride copolymers are obtained by co-polymerizing an alkyl vinyl ether monomer, such as methyl vinyl ether, ethyl vinyl ether, divinyl ether, propyl vinyl ether and isobutyl vinyl ether, with maleic anhydride to yield the corresponding alkyl vinyl ether-maleic anhydride copolymer which is readily hydrolyzable to the acid copolymer. Both anhydride and acid forms are also available from commercial suppliers. For example, the ISP Corporation, Wayne, N.J. provides both the polymeric free acid form (I) and the corresponding anhydride form under its "GANTREZ" trademark as the "GANTREZ S Series" and "GANTREZ AN Series", respectively.

Methods of making mixed salts of AVE/MA polymers are further disciosed in U.S. Pat. Nos. 5,073,604, Holeva et al., issued Dec. 17, 1991; 5,872,161, Liang et al., issued Feb. 16, 1999; 5,830,933, Synodis et al., issued Nov. 3, 1998, all of which are herein incorporated by reference in their entirety.

Alternative suitable adhesive components may include a water-soluble hydrophilic colloid or polymer having the property of swelling upon exposure to moisture to form a mucilaginous mass. In one embodiment the other adhesive components are selected from the group consisting of: natural gums, synthetic polymeric gums, synthetic polymers, mucoadhesive polymers, hydrophilic polymers, saccharide derivatives, cellulose derivatives, and mixtures thereof. In another embodiment the other adhesive components are selected from the group consisting of natural gums, synthetic polymeric gums, anhydride, cellulose derivatives, and mixtures thereof. Examples of such materials include karaya gum, acacia gum, guar gum, gelatin, algin, sodium alginate, tragacanth, chitosan, polyethylene glycol, acrylamide polymers, cross-linked polyacrylic acid, polyvinyl alcohol, polyamines, polyquarternary compounds, polybutenes, silicones, ethylene oxide polymers, polyvinylpyrrolidone, cationic polyacrylamide polymers, and mixtures thereof.

In addition, one or more toxicologically-acceptable plasticizers may also be included in the present compositions. The term "toxicologically-acceptable", as used herein, is used to describe materials that are suitable in their toxicity profile for administration to humans and/or lower animals. Plasticizers that may be used in the present compositions include dimethyl phthalate, diethyl phthalate, dioctyl phthalate, glycerin, diethylene glycol, triethylene glycol, sorbitol, tricresyl phosphate, dimethyl sebacate, ethyl glycolate, ethylphthalyl ethyl glycolate, o- and p-toluene ethyl sulfonamide, and mixtures thereof. Plasticizers may be present at a level of from about 1% to about 50%, preferably from about 2% to about 30%, by weight of the compositions.

Treatment methods

The patient, after applying the composition to the oral mucosa, may refrain from eating or drinking for a certain time, ranging from minutes up to hours. Alternatively, the patient, if desired, may eat or drink within minutes after applying the composition.

The method for treating or preventing mucositis inflammation in a patient comprises administering to a patient in need thereof an effective amount of the composition. The composition may be administered as often as practical, at least once daily up to all hours of the day and night, for as long as symptoms persist. In another embodiment, the adhering disc is administered at least once daily for at least seven consecutive days. In addition to its ordinary meaning, the term treatment encompasses inhibition of progression of symptoms or amelioration of symptoms of inflammation and mucositis. These methods may provide an effective therapeutic or preventive treatment for mucositis and stomatitis of various origins and severity and, more generally, of the lesions of the oro-pharynx cavity and oesophagus, particularly those caused by recurrent aphthous ulceration, dental devices, by radiotherapy or chemotherapy, and by surgery.

The precise dose to be employed will depend on the route of administration and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances. In principle, however, for oral applications, at least once but up to six times or more daily, will be sufficient to provide an optimal therapeutic or preventive response. The treatment can be protracted until remission of symptoms, usually for at least 2 days, but preferably 5-10. More prolonged treatments are not contraindicated, considering very low toxicity of the components of the formulations, and daily use as a preventive is effective for many conditions.

EXAMPLES

The following examples are presented by way of illustration and not by way of limitation on the scope of the invention.

EXAMPLE 1

Manufacturing of a thin, single layer deposited and dried oral adhering disc containing Rhizophora Mangle extract molecules, listed by dry-weight:

Rhizophora Mangle extract 20%

Collagen 70%

Konjac and Xanthan gum 7%

Cellulose 3%

This mixture is mixed with water for processing, stirred and heated to 140 – 200° F so as to produce a uniform viscous gel. Drops of the mixture are deposited onto sheets to form blobs at a temperature of about 150° F and then dried at room temperature. The resultant discs are about 60 – 100 mg and contain about 12 - 20 milligrams Rhizophora Mangle extract.

EXAMPLE 2

Manufacturing of a single layer oral adhering disc containing the Rhizophora Mangle extract molecules, listed by weight:

Rhizophora Mangle extract 25%

Collagen (gelatin) 75%

This dry mixture is mixed and pressed at 1 - 4 tons as to produce a 13.5 mm diameter tablet of 100 – 200 milligrams. The resultant adhering discs each contain about 25 - 50 milligrams of Rhizophora Mangle extract molecules.

EXAMPLE 3

Manufacturing of a bi-layer disc, the adhesive layer containing the Rhizophora Mangle extract molecules, listed by weight:

Rhizophora Mangle extract 49%

Carbomer 50%

Magnesium stearate 1%

This dry mixture is mixed and pressed at ½ - 1 ton as to produce a 13.5 mm diameter tablet of 100 – 200 milligrams. The upper punch is lifted and a 1 mm thick layer of sorbitol and carboxymethylcellulose (to slow dissolution) (30 – 100 mg) is pressed on top with 2-4 tons of pressure. The resultant adhering discs each contain about 50 - 100 milligrams of Rhizophora Mangle extract molecules.

EXAMPLE 4

Manufacturing of a bi-layer disc, the non-adhesive layer containing the Rhizophora Mangle extract molecules, listed by weight:

Rhizophora Mangle extract 60%

Lactose or Sobitol 29%

Carbomer or Carboxymethylcellulose 10%

Magnesium stearate 1%

This dry mixture is mixed and pressed at ½ - 1 ton as to produce a 12 - 14 mm diameter tablet of 200 – 500 milligrams. The upper punch, which is flat or nearly flat, is lifted and a 1 mm thick layer of acacia gum adhesive is pressed on top with 2-4 tons of pressure. The resultant adhering discs each contain about 120 - 300 milligrams of Rhizophora Mangle extract molecules that released to the mouth generally and to the throat.

EXAMPLE 5

Denture paste is made by mixing 70 - 90% denture adhesive with 10 - 30% Rhizophora Mangle extract. Mineral oil is added to offset the further thickening effect of the dry powder of Rhizophora Mangle extract to achieve a preferred consistency.

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims.

I claim:

1. An oral adhering disc, at least 5 mm in two dimensions, that, when held in a human mouth, adheres and remains in the mouth as a single item that will not spread to be in a plurality of locations in the mouth at one time, releasing Rhizophora Mangle extract molecules, comprising, by dry weight:

(a) between 1% and 50% molecules of extract of Rhizophora Mangle; and

(b) between 10% and 98% adhesive molecules that adhere to mucosa in a human mouth;

(c) the disc having two sides and, on at least one side, the disc will self-adhere to a roof of a mouth of a human against force of gravity.

2. The adhering disc of claim 1 wherein the Rhizophora Mangle extract is a water extract of bark of Rhizophora Mangle.

3. The adhering disc of claim 2 wherein the Rhizophora Mangle extract is a water plus alcohol extract of bark of Rhizophora Mangle.

4. The adhering disc of claim 1 wherein the adhesive molecules comprise one or more of collagen, gelatin, alginate, starch, pectin, polyvinylpyrolidone, acacia gum, hydroxymethylcellulose, carboxymethylcellulose, polyvinyl acid, polyacrylic acid, and carbomer.

5. The adhering disc of claim 1 made by pressing dry powders in a tablet press.

6. The adhering disc of claim 1 made by depositing a blog of viscous gel mixed with solvent, then drying the solvent out of the blob.

7. The adhering disc of claim 1 made by extruding of a sheet of viscous adherent hydrocolloids mixed with the extract and then cooling and die cutting to make thin discs, or hot pressing the sheet with dies that squish the viscous sheet of gel to separate it into individual discs and then cooling.

8. The adhering disc of claim 1 wherein the adhering disc comprises two layers, a first layer will self-adhere to a roof of a mouth of a human against force of gravity comprised of, by dry weight, at least 10% Rhizophora Mangle extract molecules and at least 50% adhesive molecules

and a second layer that will not self-adhere to a roof of a mouth of a human against force of gravity.

9. The adhering disc of claim 1 wherein the adhering disc comprises two layers, a first non-adherent layer that will not self-adhere to a roof of a mouth of a human against force of gravity comprised of, by dry weight, at least 10% Rhizophora Mangle extract molecules and a second layer comprised of at least 40% adhesive molecules where the second layer will self-adhere to a roof of a mouth of a human against force of gravity.

10. A method for treating or preventing oral mucositis in a patient comprising:

applying to a surface in a mouth of a patient in need thereof an oral adhering disc, at least 5 mm in two dimensions, that, when held in the human mouth, adheres and remains in the mouth as a single item that will not spread to be in a plurality of locations in the mouth at one time, releasing Rhizophora Mangle extract molecules, comprising, by dry weight:

(a) between 1% and 50% molecules of extract of Rhizophora Mangle; and

(b) between 10% and 98% adhesive molecules that adhere to mucosa in a human mouth;

(c) the disc having two sides and, on at least one side, the disc will self-adhere to a roof of a mouth of a human against force of gravity.

11. The method of claim 10 wherein the Rhizophora Mangle extract is a water extract of bark of Rhizophora Mangle.

12. The method of claim 10 wherein the Rhizophora Mangle extract is a water plus alcohol extract of bark of Rhizophora Mangle.

13. The method of claim 10 wherein the mucositis is an aphthous ulcer and the disc is applied directly on the ulcer.

14. The method of claim 10 wherein the mucositis occurs in an oro-pharynx or an esophagus and the disc is applied where saliva will carry Rhizophora Mangle extract molecules from the disc to the mucositis.

15. An oral adhesive denture paste composition comprising, by dry weight, at least 45% denture adhesive paste mixture with a viscosity greater than 1,000,000 centipoise and 2% - 50% Rhizophora Mangle extract molecules.

16. The paste of claim 15 comprising alkyl vinyl ether maleic anhydride copolymers as an adhesive.

17. The paste of claim 15 comprising as an adhesive a water-soluble hydrophilic colloid or polymer having the property of swelling upon exposure to moisture to form a mucilaginous mass selected from the group consisting of: natural gums, synthetic polymeric gums, synthetic polymers, mucoadhesive polymers, hydrophilic polymers, saccharide derivatives, cellulose derivatives, karaya gum, acacia gum, guar gum, gelatin, algin, sodium alginate, tragacanth, chitosan, polyethylene glycol, acrylamide polymers, cross-linked polyacrylic acid, polyvinyl alcohol, polyamines, polyquarternary compounds, polybutenes, silicones, ethylene oxide polymers, polyvinylpyrrolidone, and cationic polyacrylamide polymers.

18. An oral adhering gel with a viscosity between 500 and 1,000,000 centipoise comprising 2% - 50% Rhizophora Mangle extract molecules.

19. The gel of claim 18 comprising polyvinylpyrollidone as an adhesive.

20. The gel of claim 18 comprising as an adhesive aloe vera sap, xanthan gum, locust bean gum, konjac gum, guar gum, collagen, gelatin, carbomer or carboxymethylcellulose.