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(54) Titre : FILM AUTOADHESIF POUR DENTS OU GENCIVES
(54) Title: SELF-ADHESIVE FILM FOR TEETH OR GUMS

(57) Abrégé/Abstract:
The invention relates to mono- or multilayered, film-shaped, pressure-sensitive adhesive preparations for application in the oral region, containing at least one polymethyl vinyl ether-maleic acid anhydride copolymer, polyvinyl acetate and/or at least one copolymer of the polyvinyl acetate with vinyl alcohol esters of fatty acids, as well as at least one cosmetic and/or pharmaceutical active substance, and a process for the manufacture of such preparations.

ABSTRACT

The invention relates to mono- or multilayered, film-shaped, pressure-sensitive adhesive preparations for application in the oral region, containing at least one polymethyl vinyl ether-maleic acid anhydride copolymer, polyvinyl acetate and/or at least one copolymer of the polyvinyl acetate with vinyl alcohol esters of fatty acids, as well as at least one cosmetic and/or pharmaceutical active substance, and a process for the manufacture of such preparations.

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SELF-ADHESIVE FILM FOR TEETH OR GUMS

Field of the Invention

The present invention relates to film-shaped preparations which are pressure-sensitive adhesive to teeth, gums or the oral mucosa and which are suitable for cosmetic or medical treatment of the teeth, especially the tooth necks, and of the gums. In addition, the present invention relates to a process for the manufacture of such film-shaped preparations.

Background of the Invention

Products for cleaning one's mouth and for active substance delivery having the form of pastes, creams or mouth rinses have long since been known and have been available on the market. These products include tooth pastes and creams which have a cleaning effect, protect against caries, are desensitizing, or have a bleaching effect. Also known are creams, gels and ointments that are applied in the oral region for treating local illnesses and disorders such as anti-inflammatory remedies, analgesic remedies and/or tonics.

For some years, film-shaped, flat-shaped or strip-shaped oral application forms, too, have been commercially available and are used for cosmetic or therapeutic purposes. These application forms include, for example, the Listerine Pocket-Paks® by Pfizer or the "Teeth Whitestrips" by Procter & Gamble. Such application forms are as a rule based on films made up of water-soluble polymers which on use disintegrate rather quickly and are therefore not suitable for a longer-lasting treatment.

In addition, products are known that consist of several layers, such as those disclosed in US 6,582,708, which, however, include only one flexible layer and which, due to their overall thickness of up to 3 mm, are disturbing and unpleasant in the mouth.

The recipes and methods used in the manufacture of the known film-shaped application forms, for the most part, start from water or from water-containing alcoholic polymer solutions. A disadvantage here is that there are limitations to preparing a completely dissolved formulation of lipophile, poorly water-soluble active substances or of active substances that are sensitive to water.

The object of the present invention was thus to provide a mono- or multi-layered, water-soluble or at least partially water-swellable, film-shaped material which has good adhesion to teeth,

gums or the oral mucosa, which is suitable as active substance carrier, and which does not already disintegrate within a few seconds. More particularly, the object is to provide a film-shaped material of the afore-mentioned type which enables administration of water-insoluble or water-sensitive active substances.

Summary of the Invention

This object is achieved by providing a mono- or multilayered, pressure-sensitive-adhesive, film-shaped preparation which contains at least one polymethyl vinyl ether-maleic acid anhydride copolymer, polyvinyl acetate and/or at least one copolymer of the vinyl acetate with vinyl alcohol esters of fatty acids, as well as at least one cosmetic and/or pharmaceutically active substance. Preferably, the content of polymethyl vinyl ether-maleic acid anhydride copolymer in the film-shaped, pressure sensitive adhesive preparations is 5 to 35%-wt.

In one aspect, the invention provides a mono- or multilayer, film-shaped, pressure-sensitive-adhesive preparation for application in the oral region, comprising a layer which contains at least: a polymethyl vinyl ether-maleic acid anhydride copolymer; and at least one polymer selected from the group consisting of polyvinyl acetate, copolymers of vinyl acetate with vinyl alcohol esters of fatty acids; and at least one active substance selected from the group consisting of cosmetic and pharmaceutical active substances.

In another aspect, the invention provides a process for the manufacture of the preparation characterised by mixing of, at least, a polymethyl vinyl ether-maleic acid anhydride copolymer; and at least one polymer selected from the group consisting of polyvinyl acetate, copolymers of vinyl acetate with vinyl alcohol esters of fatty acids; and at least one active substance selected from the group consisting of cosmetic and pharmaceutical active substances, in a solvent mixture that contains one or more organic solvents as its main component; coating a substrate with the compound thus obtained; and removing the solvent mixture by drying.

The content of polyvinyl acetate and/or of the copolymer(s) of the vinyl acetate with vinyl alcohol esters of fatty acids in the film-shaped, pressure-sensitive-adhesive preparations preferably amounts to 4 to 35%-wt.

The film-shaped, pressure-sensitive adhesive preparations in addition have a content of at least one cosmetic and/or pharmaceutical active substance which is determined by the nature of the

illness or by the cosmetic needs. The active substance is preferably a poorly water-soluble active substance or a water-sensitive active substance.

Description of the Invention

The term "poorly water-soluble active substances" is understood to mean such active substances as have a solubility in water of less than 1 g/l. These include, for example, griseofulvin, estradiol and vitamin D_3.

The water-sensitive active substances include those active substances, the aqueous solution of which looses more than 0.1% of its active substance content within 24 hours at room temperature due to decomposition of the active substance. The water-sensitive active substances include, for example, acetylsalicylic acid and iodine.

In a particularly preferred embodiment, the film-shaped, pressure-sensitive adhesive preparation in addition contains carboxymethyl cellulose and/or one of its salts. The content of carboxymethyl cellulose or of one of its salts in the preparation amounts to 5 to 35%-wt.

To manufacture the film-shaped preparations, which are pressure-sensitive adhesive on teeth, gums or the oral mucosa, the various, water-soluble and/or water-swellable polymers are mixed with at least one active substance in solutions containing organic solvents as main component. This mixture is used to coat a substrate, and the coated substrate is dried, optionally by application of heat.

The advantages of the invention arise especially where mixtures of polymethyl vinyl ether-maleic acid anhydride copolymers with polyvinyl acetate or the copolymers of the vinyl acetate with vinyl alcohol esters of fatty acids, are used.

The content of polymethyl vinyl ether-maleic acid anhydride copolymer is preferably 5 to 35%-wt., and the content of polyvinyl acetate and/or the copolymer(s) of the vinyl acetate with vinyl alcohol esters of fatty acids is preferably 4 to 35%-wt., in each case relative to the solids content.

The polymethyl vinyl ether-maleic acid anhydride copolymers sold under the name of "Gantrez®" by the firm of ISP, and the polyvinyl acetates or copolymers of the vinyl acetate with vinyl alco-

hol esters of fatty acids, designated as "VINNAPAS®", of the firm of Wacker Polymer Systems, Burghausen, have proved to be particularly suitable in accordance with the present invention.

Any solvents which dissolve the polymethyl vinyl ether-maleic acid anhydride copolymers and polyvinyl acetate or copolymers of the vinyl acetate with vinyl alcohol esters of fatty acids may be used as the organic solvents which, in the method according to the invention, are contained in the solution as the main component thereof. Of these organic solvents, those are used with preference which also mix with water since by adding small amounts of water, e.g. of 1 to 5%-wt., the dissolving power for the polymers and the active substance/active substances can be adapted to the given requirements. Particular preference is given to those organic solvents which permit addition of the active substance dissolved in ethanol or in an ethanol-water mixture. The especially preferred organic solvent is selected from the group comprising methyl ethyl ketone, ethyl acetate, ethanol, acetone and mixtures thereof.

The consistency and/or tackiness of the resultant film-shaped preparations can be adapted to the demands placed on the product by altering the mixing ratio of ethanol and methyl ethyl ketone. Solvent mixtures containing an ethanol portion of 5 to 20%-wt., relative to the total solvent, have proved advantageous.

To manufacture a preferred embodiment enabling a particularly successful adhesion of the film-shaped preparations on the teeth, gums and/or oral mucosa, carboxymethyl cellulose and/or at least one of its salts is added to the polymer mixture.

Preferably, 5 to 35%-wt. of carboxymethyl cellulose or at least one of its salts, relative to the solids content, is added to the polymer mixture.

To manufacture the preparation according to the invention, at least one polymethyl vinyl ether-maleic acid anhydride copolymer and polyvinyl acetate and/or at least one copolymer of the vinyl acetate with vinyl alcohol esters of fatty acids, together with at least one active substance and, optionally, carboxymethyl cellulose and/or at least one of its salts, are mixed in a solution containing one or several organic solvents as its main component. The resultant compound is applied in liquid form to a support and freed from the solvent mixture, so that a film having a

layer thickness of 4 to 2000 µm, preferably 40 to 500 µm, and particularly preferably 60 to 250 µm, is obtained.

Multilayer, pressure-sensitive-adhesive film-shaped preparations, with which it is possible to achieve, for example, an improved adhesion of the preparation to teeth, can be prepared, for example, by hot lamination, by coating already existent layers with further solvent-containing compounds, as described hereinabove in connection with the manufacture of a monolayer film, or by other processes known to those skilled in the art.

Pieces having a size appropriate to the respective given purposes are then punched out from the film or laminate.

The process according to the present invention results in film-shaped preparations which adhere to teeth, gums or the oral mucosa, which do not already disintegrate within a few seconds, and by means of which water-insoluble and even water-sensitive active substances can be administered. These preparations may advantageously be utilised for medical or cosmetic treatments.

Example

5g of a 33.3% solution (%-wt.) of a vinyl acetate-based polymer in methyl ethyl ketone and 3 g of a 15% solution (%-wt.) of polymethyl vinyl ether-maleic acid anhydride (= copolymer of methyl vinyl ether and maleic acid anhydride) in ethyl acetate were added together and homogenised. This resulted in a solution which was spread at various coating thicknesses and, subsequently, dried. This yielded flexible films which adhered both to the oral mucosa and to the teeth.

CLAIMS

1. A mono- or multilayer, film-shaped, pressure-sensitive-adhesive preparation for application in the oral region, comprising a layer which contains at least:

a) - polymethyl vinyl ether-maleic acid anhydride copolymer; and

- at least one polymer selected from the group consisting of polyvinyl acetate and copolymers of vinyl acetate with vinyl alcohol esters of fatty acids; and

b) - at least one active substance selected from the group consisting of cosmetic and pharmaceutical active substances.

2. The preparation according to claim 1, characterised in that the content of polymethyl vinyl ether-maleic acid anhydride copolymer is 5 to 35%-wt.

3. The preparation according to claim 1 or 2, characterised in that the content of said at least one polymer which is selected from the group consisting of polyvinyl acetate and copolymers of vinyl acetate with vinyl alcohol esters of fatty acids is 4 to 35%-wt.

4. The preparation according to any one of claims 1 to 3, characterised in that the active substance is poorly soluble in water or is sensitive to water.

5. The preparation according to any one of claims 1 to 4, characterised in that it further comprises carboxymethyl cellulose, its salts or a mixture thereof.

6. The preparation according to claim 5, characterised in that the content of carboxymethyl cellulose, its salts or a mixture thereof is 5 to 35%-wt.

7. The preparation according to any one of claims 1 to 6, characterised in that the preparation has a layer thickness of 4 to 2000 µm.

8. A process for coating a substrate with the preparation defined in claim 1, characterised by:

- mixing of, at least,

a) - a polymethyl vinyl ether-maleic acid anhydride copolymer; and
- at least one polymer selected from the group consisting of polyvinyl acetate and copolymers of vinyl acetate with vinyl alcohol esters of fatty acids; and

b) - at least one active substance selected from the group consisting of cosmetic and pharmaceutical active substances,
in a solvent mixture that contains one or more organic solvents as its main component;

- coating a substrate with the mixture thus obtained; and
- removing the solvent mixture by drying.

9. The process according to claim 8, characterised in that the content of the polymethyl vinyl ether-maleic acid anhydride copolymer is 5 to 35%-wt., relative to the solids content of the preparation.

10. The process according to claim 8 or 9, characterised in that the content of said at least one polymer which is selected from the group consisting of polyvinyl acetate and copolymers of vinyl acetate with vinyl alcohol esters of fatty acids is 4 to 35 %-wt., relative to the solids content of the preparation.

11. The process according to claim 8, characterised in that the solvent mixture further contains 1 to 5%-wt. of water relative to the total weight of the solvent.

12. The process according to any one of claims 8 to 11, characterised in that the active substance is poorly soluble in water or is sensitive to water.

13. The process according to any one of claims 8 to 12, characterised in that the solvent mixture is selected from the group consisting of methyl ethyl ketone, ethyl acetate, ethanol, acetone and mixtures thereof.

14. The process according to claim 13, characterised in that the solvent mixture is a mixture of ethanol and methyl ethyl ketone.

15. The process according to claim 14, characterised in that the solvent mixture has a content of ethanol of 5 to 20%-wt relative to the total weight of the solvent.

16. The process according to any one of claims 8 to 15, characterised in that it further comprises at least one substance added to the mixture before it is spread onto the substrate, wherein said at least one substance is carboxymethyl cellulose, its salts or a mixture thereof.

17. The process according to claim 16, characterised in that the content of said at least one substance is 5 to 35%-wt., relative to the solids content of the preparation.

18. The process according to any one of claims 8 to 17, characterised in that after drying of the coating, one or more further layers are applied to the already present layer(s) by hot lamination or by coating the existent layer(s) with one or more coatings of the mixture prepared as defined in claim 8, thus obtaining a multilayer preparation.

19. The process according to any one of claims 8 to 18, characterised by application of the mixture onto the substrate, so that, after drying, a layer thickness of 4 to 2000 µm is obtained.

20. Use of a preparation as defined in any one of claims 1 to 7 for cosmetic or pharmaceutical treatments of the teeth or gums.