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(54) **Acrylic Plaster**

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(72) **Inventor:** SASAKI, Hiroaki
Nitto Electric Industry Co., Ltd.
1-1-2 Shimohodumi,
Ibaraki-shi

(72) **Inventor:** HORIUCHI, Tetsuo
Nitto Electric Industry Co., Ltd.
1-1-2 Shimohodumi, Ibaraki-shi

(72) **Inventor:** SAWAGUCHI, Mareyoshi
Nitto Electric Industry Co., Ltd.
1-1-2 Shimohodumi, Ibaraki-shi

(71) **Applicant:** Nitto Electric Industry Co., Ltd.
1-1-2 Shimohodumi, Ibaraki-shi

(74) **Agent:** Patent Attorney, TAKASHIMA, Hajime

SPECIFICATION

1. Title of the Invention

Acrylic Plaster

2. Claims

(1) An acrylic adhesive plaster characterized by blending at least one tocopherol selected from tocopherols with a plaster comprising an acrylic adhesive substance.

(2) The plaster recited in claim (1), wherein a drug is further blended therewith.

(3) The plaster recited in claim (1), wherein the drug has at least one of a phenolic hydroxyl group and an amino group.

3. Detailed Description of the Invention

The present invention relates to an improvement of a plaster comprising an acrylic adhesive substance.

Conventionally, drugs administered to the epidermis were drugs that were intended to act locally on the epidermis or tissues therebelow, such as bactericides, disinfectants and skin stimulants. Recently, however, attempts have been made to administer drugs having systemic effects via the epidermis, and there have been proposals of, or attempts at, epidermal administration of various drugs.

Epidermal drug administration is, for example, performed in the form of an adhesive patch preparation, in which a drug is blended with a plaster comprising an adhesive substance; but if a preparation in which a drug is blended with a plaster comprising an acrylic adhesive substance is stored for a long period of time, there is a tendency for the therapeutic effect of said preparation to be greatly reduced due to breakdown and dissipation of the drug and the like.

Here, it is possible to prevent the dissipation and photodecomposition of the drug by way of sealing and light shielding with aluminum laminate packaging or the like, but with drugs blended with a plaster comprising an adhesive substance as described above, and especially phenolic hydroxyl group-containing compounds, amine compounds and the like, breakdown of the drug will still proceed, even with aluminum laminate packaging, and there are more than a few drugs that cannot withstand usage involving storage for two to three years. In particular, there is a marked content loss over time with compounds having a phenolic hydroxyl group or an amino group, such as salicylic acid derivatives such as methyl salicylate and monoglycol salicylate, which are anti-inflammatory analgesic agents, skin stimulants such as capsaicin, nonyl vanillylamide

and chili extract, and ethanolamine based antihistamines such as diphenhydramine.

As a countermeasure, BHA, BHT, gallic acid esters and the like are added to such preparations, but sufficient stabilizing effects are not produced, and usage thereof is being progressively restricted in view of safety matters, such as carcinogenicity.

Accordingly, there is a demand for the development of a plaster comprising an acrylic adhesive substance or an adhesive patch preparation, with which, if a drug is blended therein, breakdown of said drug will not progress.

Under such circumstances, the present inventors undertook various investigations and discovered that, if a tocopherol is blended in a plaster comprising an acrylic adhesive substance, if a drug is blended in said plaster, the drug will be stably present without breaking down.

The present invention was completed on the basis of such new knowledge, and relates to an acrylic adhesive plaster resulting from blending a tocopherol with a plaster for adhesive patch preparation comprising an acrylic adhesive substance, and to a plaster obtained by blending a drug therewith, namely an adhesive patch preparation.

There are no particular limits on the acrylic adhesive substance so long as it is a material which has been conventionally used or proposed as a plaster for acrylic adhesive patch preparations, and examples thereof include acrylic compositions such as copolymers of one or two or more (meth)acrylic acid esters, such as n-butyl (meth)acrylate, hexyl (meth)acrylate, 2-ethylbutyl (meth)acrylate, isooctyl (meth)acrylate, 2-methoxyethyl (meth)acrylate, 2-ethylhexyl (meth)acrylate, decyl (meth)acrylate, dodecyl (meth)acrylate, and tridecyl (meth)acrylate, and a functional monomer that can be copolymerized with said ester, such as (meth)acrylic acid, itaconic acid, maleic acid, maleic anhydride , hydroxyethyl acrylate, hydroxypropyl acrylate, acrylamide, dimethyl acrylamide, methylaminoethyl methacrylate and methoxyethyl (meth)acrylate, and/or a vinyl monomer such as acrylonitrile, vinyl acetate or vinyl propionate.

The plaster comprising an acrylic adhesive substance may be further blended with, as a third component, a tackifier such as terpene based resins and petroleum based resins, an adhesion or holding power modifier such as liquid paraffin, animal and plant oils (for example, olive oil, soybean oil, beef tallow, or lard) , polybutene, lower isoprenes and waxes, a filler such as titanium oxide, zinc oxide, aluminum metasilicate, calcium sulfate, calcium phosphate, water, an emulsifier (for example, sorbitan monooleate or sodium lauryl sulfonate), an emulsification enhancer (for example, magnesium stearate or aluminum stearate) or the like.

In the present invention, the term, tocopherols, [refers to] the general concept indicating α-tocopherol, β-tocopherol, γ-tocopherol, δ-tocopherol, and derivatives thereof, where the derivative is preferably an organic acid derivative, and in particular an organic acid ester.

These tocopherols may be any of an α-isomer, an l-isomer, or a dl-isomer, and a mixture of two or more thereof may also be used. Specific examples of tocopherols include dl-α-tocopherol, dl-β-tocopherol, d-γ-tocopherol, d-γ-tocopherol [*sic*], d-δ-tocopherol, and acetic acid esters and succinic acid esters thereof.

The amount of tocopherol blended is on the order of 0.005 to 5 wt%, and preferably on the order of 0.05 to 1 wt% relative to the acrylic adhesive.

The plaster of the present invention may be further blended with an oxyacid such as citric acid, malic acid or maleic acid, or a polyphosphoric acid or the like.

The plaster of the present invention can be made into an adhesive patch preparation by blending it with a drug that can be used on the epidermis. Then, the adhesive patch preparation using the plaster according to the present invention has an [advantageous] effect wherein the drug blended therewith is kept stable without breaking down.

There are no particular limits on the drug which is blended in the plaster of the present invention,

so long as this is a drug that can be formed into an adhesive patch preparation and administered, and examples include percutaneous absorption drugs (where this may be a drug which is percutaneously absorbed with the aid of a percutaneous absorption enhancer or the like, and may be either a local drug or a systemic drug), drugs for treatment of skin disease, skin stimulating drugs, drugs for treatment of indefinite complaints, and the like. In particular, there was a marked loss in content of phenolic hydroxyl group-containing compounds, amine based compounds and the like in conventional plasters comprising an acrylic adhesive substance, and thus the plaster of the present invention is particularly significant when making such drugs into preparations. Examples of phenolic hydroxyl group-containing compounds include salicylic acid derivatives (monoglycol salicylate, methyl salicylate and the like), capsaicin and the like; furthermore, amine based compounds include ethanolamine based antihistamine drugs such as diphenhydramine, ethylene diamine based antihistamine drugs such as chlorpheniramine, and lidocaine and the like. Examples of other medicinal components include cool-sensation skin stimulating drugs such as l-menthol, dl-camphor, thymol and d-borneol, nonsteroidal anti-inflammatory drugs such as indomethacin and diclofenac sodium, steroidal anti-inflammatory drugs such as dexamethasone and betamethasone, bactericides such as chlorhexidine diglyconate and acrinol, warm-sensation skin stimulating drugs such as chili extract, nonyl vanillylamide, capsaicin, ginger extract, tincture of cantharides and cantharidin, and raw drugs such as lithospermum root and Japanese angelica root, and the like.

Note that, in preparing the adhesive patch preparation of the present invention, needless to say, a drug may be first added to the adhesive substance, followed by adding a tocopherol.

Furthermore, the adhesive patch preparation of the present invention is normally used by way of spreading it onto a support such as cloth or plastic film.

Hereafter, the present invention is described in more specific terms by way of setting forth working examples and experimental examples, but the present invention is not limited to these.

Example 1

adhesive	10 g
d-δ-tocopherol	0. 05 g
monoglycol salicylate	0. 2 g
diphenhydramine	0. 2 g
ethyl aminobenzoate	0. 2 g
citric acid	0.005 g

A 2-ethylhexyl acrylate/2-methoxyethyl acrylate/vinyl acetate copolymer was used as the adhesive, and after preparation with ethyl acetate as a solvent so that the concentration of the above substances was 25 %, the preparation was applied to a polyester film at a thickness of 0. 2 mm and dried at 80°C to produce a drug blend plaster.

Example 2

A drug blend plaster was produced in the same manner as in Working Example 1, except for eliminating citric acid from the formulation in Working Example 1.

Comparative Example 1

A drug blend plaster was produced in the same manner as in Working Example 1, except for eliminating d-δ-tocopherol and citric acid from the formulation in Working Example 1.

Experimental Example

The drug blend plasters produced in Working Examples 1 and 2 and Comparative Example 1 were each sealed in aluminum laminate polyethylene film and stored at 40°C for 3 months, the drug breakdown rates were found, and the results were set forth in Table 1.

Table 1 : Dug breakdown rates (%)

Drug	Drug breakdown rates (%)		
	Working Example 1	Working Example 2	Working Example 3
monoglycol salicylate	3.2	3.9	16.2
diphenhydramine	5.6	7.9	20.1
ethyl aminobenzoate	2.8	2.6	8.9

Patent Translations Inc.
1700 Seventh Avenue, Suite 2100 mail@PatentTranslations.com
Seattle, WA 98101 http://www.PatentTranslations.com
Fax: 1-800-844-5695 (or 206-299-3692) Tel: 1-800-844-0494 (or 206-357-8508)

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Martin Cross
President, Patent Translations Inc.
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