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TOPICAL EPITHELIAL ANESTHETIC

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This invention relates in general to topical epithelial anesthetics, and in particular to compositions adapted to serve as anesthetics for epithelial tissue comprising both dry skin and mucous membranes.

It has been found that epithelial anesthetics for application to the skin must, in many cases, come into contact with mucous membranes as in the eye, nose, mouth, and the like, and must be applicable to epithelia which are broken as a result of scratches, cuts, burns and the like. Accordingly, any epithelial anesthetic which has a high anesthetic activity only for dry unbroken epithelia is lacking in an essential requisite, since a low degree of activity on mucous membranes or broken epithelial tissue results in less than complete and satisfactory anesthesia.

Therefore, it is a general object of the present invention to provide an anesthetic for topical application to both unbroken and broken epithelial tissue.

It is a specific object of the invention to provide an anesthetic composition which is characterized by a high anesthetic activity simultaneously on both dry epithelial tissue and mucous membranes.

Other objects of the invention will in part be obvious and will in part appear hereinafter.

According to the present invention there is provided a composition comprising an alkyl amino benzoate which is relatively soluble in water, but not substantially soluble in oil, an alkyl amino benzoate containing not less than five carbon atoms in the alkyl group and having a substantial solubility in oil, and a vehicle for said compounds comprising a solvent for at least one of said compounds, preferably of the oil-soluble alkyl amino benzoate. I have found that the alkyl amino benzoates which contain less than 5 carbon atoms in the alkyl group are sufficiently soluble in water to be highly active anesthetics for mucous membranes or broken epithelial tissue but that these compounds have little or no anesthetic activity on dry unbroken epithelial tissue which are not penetrated by water. On the other hand, I have found that the alkyl amino benzoates which contain 5 or more carbon atoms in the alkyl group have a high solubility in oil and exhibit a unique and unexpected high anesthetic activity on dry unbroken epithelia but exhibit little anesthetic activity on mucous membranes. For example, pentyl para-amino benzoate is about 100% more soluble in oil than the butyl ester, 400% more soluble in oil than the propyl ester and 1000% more soluble in oil than the ethyl ester. Therefore, when the composition of the present invention is applied to epithelia comprising unbroken or broken tissues and mucous membranes, a novel uniform and complete anesthesia is ob-

tained which it is not possible to obtain by the use of any of the alkyl amino benzoates alone.

For the water-soluble alkyl amino benzoates there may be employed any ester of amino benzoic acid with an alcohol having less than 5 carbon atoms in the alkyl radical, such, for example, as the methyl amino benzoates, ethyl amino benzoates, propyl amino benzoates and butyl amino benzoates, all of which dissolve in water in sufficient amount to give a high anesthesia on mucous membranes. Of these compounds, I prefer to use those which have the amino group in the para position with respect to the alkyl group, but the invention includes the use of the alkyl ortho amino benzoates. Solvents for those alkyl amino benzoates include water, and mixtures of water and water-miscible organic solvents such as the lower aliphatic alcohols, esters, ketones and the like.

For the oil-soluble alkyl amino benzoates I may employ any alkyl amino benzoate having 5 or more carbon atoms in the alkyl group, such, for example, as the pentyl amino benzoates, hexyl amino benzoates, heptyl amino benzoates, and the like, all of which compounds are characterized by having a solubility in animal, mineral and vegetable oils sufficient to give a high anesthetic activity. I prefer to use the para compounds but the invention includes the ortho compounds as well.

The alkyl amino benzoates may be prepared in the following manner: nitro benzoyl chloride is condensed with an alcohol. The resulting nitro ester is reduced with iron in the presence of catalysis such as platinum black or platinum oxide.

Suitable solvents for alkyl amino benzoates containing 5 or more carbon atoms in the alkyl group are lipoid substances in genera, such as animal, mineral and vegetable oils such, for example, as olive oil, poppy oil, cocoanut oil, mineral oil and the like; higher fatty acids such, for example, as stearic acid, oleic acid, palmitic acid and the like; fat or animal or vegetable origin such, for example, as lanolin, lard, stearin and the like; and waxes of animal, mineral or vegetable origin, such, for example, as beeswax, spermaceti, ozokerite, paraffin, carnauba wax, candelilla wax and the like.

To make tacky compositions one should employ the vegetable oils and the solid fats. To make non-tacky compositions one may use the mineral oils, waxes and greases.

To the composition of the invention there is preferably added a suitable wetting agent, such, for example, as sulfonated fatty acids, benzyl alcohol, benzoyl benzoate. These substances, by lowering the surface tension of the lipoid, promote wetting of the skin and facilitate penetration of the lipoid through the epithelial tissue.

There may also be added to the composition suitable coloring agents, such as pigments or dyestuffs, so as to indicate the area treated or to change the color of the skin or to absorb certain wave lengths of the spectrum, especially when the composition is used in the treatment of epithelial erythema resulting from exposure to the sun. Perfumes or masking odors may be added to the composition also if desired.

The several ingredients of the novel composition of the invention may be associated in any suitable manner, for example by dissolving them in a suitable solvent mixture, or by emulsifying the water-soluble alkyl amino benzoate in a solution of the oil-soluble alkyl amino benzoate, or by emulsifying the oil-soluble alkyl amino benzoate in an aqueous solution of the water-soluble alkyl amino benzoate. The water-in-oil type emulsion may be thickened by the use of some solid or semi-solid lipoid substances such as fats, waxes and the like, while the oil-in-water type emulsion may be thickened by the use of water-swelling colloids such as gum tragacanth, methyl cellulose, starch, casein, gelatine and the like. The composition may be formed into a cream, paste or salve, if desired. In the now preferred embodiment of the composition, the ingredients are associated in the form of a paste. By way of illustration, but not by way of limiting the invention, the following examples will be given of the general range of ingredients in the composition:

	Examples		
	I	II	III
Water-soluble alkyl amino benzoate, e. g., ethyl para amino benzoate.....	1.0	0.5	0.5
Water.....	15.0	10.0	-----
Oil-soluble alkyl amino benzoate, e. g., pentyl para-amino benzoate.....	1.5	0.5	2.0
Lipoid substance, e. g.:			
Corn oil.....	25.0	-----	35.0
Lanolin.....	-----	45.0	-----
Olive oil.....	-----	-----	60.0
Petroleum jelly.....	25.0	40.0	-----
Beeswax.....	25.0	-----	-----
Wetting agent, e. g., benzyl alcohol.....	4.5	4.0	2.5
	100.0	100.0	100.0

In general, a complete and satisfactory anesthesia may be obtained on broken epithelia by the use of a minor proportion of the water-soluble alkyl amino benzoate and a major proportion (relative thereto) of the oil-soluble alkyl amino benzoate. If the composition is to be used chiefly or solely on mucous membranes, the proportion of the water-soluble alkyl amino benzoate is increased correspondingly in relation to that of the oil-soluble alkyl amino benzoate.

The composition of the invention has a wide variety of uses as an epithelial anesthetic, for example in the desensitizing of tissue for the treatment of eczema, rashes, chapping and burns, also for performing minor operations such as removing hair, cuticle and the like from the skin and in conditions similar to "pruritis ani." One of the most important applications of the present composition is in the treatment of large areas of the skin to relieve pain resulting from sunburn. In sunburn the burned area usually comprises unbroken epithelia with some broken areas and mucous membranes so that the oil-soluble alkyl amino benzoate in the composition desensitizes the unbroken areas and the water-soluble alkyl amino benzoate anesthetizes the broken areas and mucous membranes. Other important applications of the composition of the invention will be apparent to those skilled in the art.

I claim:

An epithelial anesthetic consisting of an oil-in-water emulsion comprising a relatively water-soluble alkyl amino benzoate having less than 5 carbon atoms in the alkyl group dissolved in the aqueous phase, an oil-soluble alkyl amino benzoate having not less than 5 carbon atoms in the side chain and dissolved in the oil phase, the solution of the water-soluble alkyl amino benzoate in the water functioning to desensitize mucous membranes, the solution of the oil-soluble alkyl amino benzoate in the oil serving to desensitize unbroken epithelia, the two phases of the emulsion cofunctioning to give a complete desensitization of the skin area comprising broken and unbroken epithelia.

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