AEROSOLIZABLE PREPARATION

The present invention relates to an aerosolizable preparation having a distinguished antipruritic effect on itching due to insect biting, athlete's foot, etc.

Skin response to insect biting develops itching or rubor, including two types, i.e. fast response occurring a few minutes to one hour after the biting and a slow response occurring more than 10 hours to one day after the biting.

Itching due to the slow response can be suppressed by application of a preparation such as an ordinary ointment containing a local anesthetic or an antipruritic agent, or the like. On the other hand, itching due to the fast response cannot be suppressed fully by application of the above-mentioned preparation or even by cooling due to evaporation of a volatile solvent such as ethanol, etc. as a preparate ingredient, or due to mere spraying of a propellant.

An object of the present invention is to provide a preparation having a distinguished antipruritic effect on itching due to the fast response by biting or on itching due to the athlete's foot.

As a result of extensive studies, the present inventors found that an aerosolizable preparation comprising a specific surfactant, and specific

proportions of menthol and camphor can have such a distinguished antipruritic effect, and established the present invention.

The present invention provides an aerosolizable preparation, which comprises a concentrate comprising the following ingredients (A) to (C) in a mixed solvent of water and a lower alcohol, and a propellant:

(A) at least one surfactant selected from the group consisting of polyoxyethylene sorbitan fatty acid esters and sorbitan fatty acid esters;

(B) 0.5 to 8% by weight of menthol, on the basis of the concentrate; and

(C) 1 to 0.5 part by weight of camphor per part by weight of the menthol.

Polyoxyethylene sorbitan fatty acid esters and sorbitan fatty acid esters (A) for use as an ingredient in the concentrate of the present aerosolizable preparation as at least one surfactant are in a paste state or a semi-solid state at room temperature before prepared into the concentrate and are preferably single polyoxyethylene (6) sorbitan monostearate or a mixture of polyoxyethylene (20) sorbitan monostearate, polyoxyethylene (20) sorbitan tristearate and sorbitan monostearate.

Surfactant (A) for use as another ingredient in the concentrate of the present aerosolizable preparation is in an amount of 0.5 to 8% by weight,

preferably 0.5 to 4% by weight, on the basis of the concentrate.

The mixed solvent for use in the concentrate of the present aerosolizable preparation is a mixture of water and a lower alcohol preferably in a ratio of the former to the latter by weight of 30:70 to 70:30.

The propellant for use in the present aerosolizable preparation is a liquefied gas, which includes, for example, dimethyl ether, n-butane, isobutane, propane or mixtures thereof. A propellant containing at least 80% by weight of dimethyl ether is preferable. The propellant is used in an amount of 40 to 80% by weight, preferably 50 to 70% by weight, on the basis of the aerosolizable preparation.

The present aerosolizable preparation can further contain ingredients usually contained in the antipruritic and the antifungal agent, such as antipruritics (e.g. Crotamiton, Ichthammol, Mochthammol, Thymol acid, etc.); antifungal agents (e.g. Tolnaftate, Miconazole Nitrate, etc.); antihistamic agents (e.g. Diphenhydramine, Diphenhydramine hydrochloride, Isothipendyl hydrochloride, Chlorpheniramine maleate, etc.); local anesthetics (e.g. Lidocaine, Dibucaine hydrochloride, etc.); disinfectants (e.g. potassium iodide, chlorhexidine gluconate, Acrinol, Benzalkonium chloride, etc.); antiphlogistics (e.g. Allantoin, glycyrrhetic acid, methyl salicylate, etc.); antioxidants (e.g. dibutyl hydroxyl toluene, etc.); solubilizing

agents (e.g. diisopropyl adipate, isopropyl myristate, lactic acid, sodium hydroxide, etc.); perfumes, etc. to such a degree as not to deteriorate the effect of the present aerosolizable preparation.

The present aerosolizable preparation can be prepared by mixing ingredients together except the propellant with heating and stirring to obtain a liquid homogeneous solution or dispersion and then by filling the solution or dispersion into an aerosol container together with the propellant.

According to the present invention, the aerosolizable preparation thus-obtained adheres as a cooling sherbet-like foam when sprayed to the skin surface, and has an excellent antipruritic effect by the specific content ratio of menthol and camphor.

The present invention can provide an aerosolizable preparation capable of fastly and continuously releasing itching due to fast response by insect biting or itching due to athlete's foot.

Fig. 1 is a diagram showing antipruritic effects of the present aerosolizable preparation and a liquid preparation of Comparative Example 4, where the ordinate shows itching scores and the abscissa shows time in minutes.

Fig. 2 is a diagram showing antipruritic effects of the aerosolizable preparation of Comparative Examples, where the ordinate shows itching scores and the abscissa shows time in minutes.

The present invention will be described in detail below, referring to Examples and Comparative Examples.

Example 1

Concentrate

Ingredients

Lidocaine	0.6 g
Diphenhydramine	0.3 g
Menthol	0.6 g
Camphor	0.6 g
Nikkol TS-10 [trademark of polyoxyethylene (20) sorbitan monostearate]	0.9 g
Nikkol TS-30 [Trademark of polyoxyethylene (20) sorbitan tristearate]	0.6 g
Nikkol SS-10 [trademark of sorbitan monostearate]	0.9 g
Ethyl alcohol	10.5 g
Purified water to make total 30 ml	

Propellant

Dimethyl ether	70 ml

The ingredients of the concentrate were mixed together with heating and stirring to obtain a homogeneous solution and filled into an aerosol container together with the propellant to obtain an aerosolizable preparation.

Examples 2 and 3 and Comparative Examples 1 to 3

Aerosolizable preparations were prepared according to formulations given in the following Table 1 in the same manner as in Example 1.

Comparative Example 4

A concentrate was prepared according to the formulation given in the following Table 1 and used as such, as a liquid preparation.

Table 1

Formulation	Comp. Ex. 1	Comp. Ex. 2	Example 2	Example 3	Comp. Ex. 3	Comp. Ex. 4
Menthol	1.2 g	2.4 g	0.6 g	1.2 g	-	0.6 g
Camphor	-	-	0.6 g	0.6 g	2.4 g	0.6 g
Nikkol TS-10	0.9 g	0.9 g	0.9 g	0.9 g	0.9 g	0.9 g
Nikkol TS-30	0.6 g	0.6 g	0.6 g	0.6 g	0.6 g	-
Nikkol SS-10	0.9 g	0.9 g	0.9 g	0.9 g	0.9 g	-
Ethyl alcohol	10.5 g	10.5 g	10.5 g	10.5 g	10.5 g	10.5 g
Purified water to make:	Total 30 ml	Total 30 ml	Total 30 ml	Total 30 ml	Total 30 ml	Total 30 ml
Dimethyl ether (propellant)	70 ml	70 ml	70 ml	70 ml	70 ml	-

Test Example

Testing procedure

(1) Put on a rubber glove having an opening, 5 mm in diameter, on the back side and put the hand with the rubber glove into a cage provided with a mosquito (Aedes albopictus) therein.

(2) Allow the mosquito to bite the back of hand through the opening of the rubber glove.

(3) Withdraw the hand from the cage after the mosquito has sucked blood thoroughly, and take off the rubber glove.

(4) Spray an appropriate amount (duration of 1-3 seconds at a distance of 3 cm) of each sample (aerosolizable preparations prepared in Examples 2 and 3 and Comparative Examples 1 to 3) or apply an appropriate amount of the liquid preparation prepared in Comparative Example 4, when itching exceeds the tolerable limit.

(5) Make self-scoring of itching level at every minutes right after the spraying or application according to scores given in the following Table 2.

Control shows that no treatment has been made at all from the time when itching exceeded the tolerable limit as the starting time.

Table 2

Score	Itching level
0	No itching at all
1	Negligeble itching
2	Appreciable itching
3	Extreme itching

Results

Results are given in Figs. 1 and 2 on the basis of averages of five subjects. As is evident from Figs. 1 and 2, the present aerosolizable preparations of Examples 2 and 3 had itching levels of score 1 or less, that is, the negligeble itching level, and thus had an effective itching-suppressing effect for people.



WHAT IS CLAIMED IS:

1. An aerosolizable preparation, which comprises a concentrate comprising the following ingredients (A) to (C) in a mixed solvent of water and a lower alcohol, and a propellant:

(A) at least one surfactant selected from the group consisting of polyoxyethylene sorbitan fatty acid esters and sorbitan fatty acid esters;

(B) 0.5 to 8% by weight of menthol, on the basis of the concentrate; and

(C) 1 to 0.5 part by weight of camphor per part by weight of the menthol.

2. An aerosolizable preparation according to Claim 1, wherein the propellant contains at least 80% by weight of dimethyl ether.

3. An aerosolizable preparation according to Claim 1, wherein the propellant is in an amount of 50 to 70% by weight on the basis of the aerosolizable preparation.