UNDECYLENE ACID ALKYLAMIDE DERIVATIVES FOR CONTROLLING BACTERIA, FUNGI, AND DANDRUFF

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No Drawing. Filed July 31, 1962, Ser. No. 213,598

8 Claims. (Cl. 167—22)

It has been previously disclosed that certain alkylamides derived from undecylenic acid are valuable bactericidal and fungicidal agents. It has now been found that it is possible to prepare derivatives of such alkylamides which have a greater field of usefulness. Said compounds previously disclosed were generally only soluble in water if prepared by association with free alkylalumine in the form of a complex. Otherwise, they were usually sparingly soluble or insoluble in water.

It has now been found that the compounds according to the present invention are normally appreciably soluble in water without need for the presence of free alkylalumine and, therefore, can be used not only in alkaline solution, but in neutral or even acid solution.

The compounds of this invention show marked bactericidal and/or fungicidal effect against many, though not all, microorganisms. The preferred examples described hereinafter are particularly effective against fungi, such as Trichophyton mentagrophytes, which is believed to cause the condition known as athlete's foot. Said preferred examples have also been found valuable in hair preparations for controlling and treating dandruff. It is sometimes assumed that dandruff is caused by a microorganism Pityrosporum ovale and it may well be that the effectiveness of said preferred compounds is due to their activity against this organism.

It is a further feature of the new compounds and derivatives of this invention that, apart from being water-soluble, they appear to some extent to exhaust from their solution onto the hair or skin. This substantivity may well account in part for the good results obtained by treating dandruff by shampoos containing the new compounds of the invention. These compounds or derivatives, although they may occasionally be used by themselves, will normally be employed after incorporation in a composition which comprises the active compound of this invention in association with an acceptable vehicle. The term “vehicle” is used herein to denote the wide variety of carriers, extenders, or diluents, which may find service in compositions containing compounds or derivatives of this invention, and is qualified by the term “acceptable” only in that it excludes any possibility that the nature of the composition, considered in relation to the route by which it is intended to be administered, or the use to which it is to be put, could be harmful rather than beneficial. The choice of a suitable mode of presentation for any desired administration or application is completely within the competence of persons skilled in the art of preparation of pharmaceutical, toilet, cosmetic, or related or similar compositions.

Where the composition is to be applied to the skin, the carrier may be a solid powder, such as talc; an aqueous solvent base is used where a lotion is required and a non-aqueous solvent base, where a tincture is required. The compounds of this invention may also be applied to the skin in a composition taking the form of a cream, when the active compound will be in association with materials of the class comprising oils, fats, and waxes and water and generally an emulsifying agent.

The compounds of this invention are especially suitable for use together with soaps and with synthetic detergents, e.g., in the formulation of shampoos and skin-cleaning compositions. However, the same compounds can also be employed in washing preparations not necessarily intended to clean the skin but for general cleaning purposes.

The compounds embodying the present invention may also be incorporated in other compositions. Examples of further carriers are: plasticized solid bases comprising pastes, suppositories, lipstick, and soap tablets and cakes. The compounds may also be used in hair oils, brilliants, hair creams and hair tonic preparations. If the compositions comprise only oil, fat and wax, the compound must normally first be dissolved in water or other suitable solvent and this dissolved or emulsified in the main carrier.

The compounds of this invention may also be incorporated in aerosol compositions by normally dissolving them in an organic solvent containing a suitable propellant such as a fluorinated hydrocarbon, or butane. The derivate of the alkylamides of undecylenic acid suitable for use according to this invention correspond to the following general formula:

\[ \text{R} \left( \text{C}_6\text{H}_{13}, \text{C}_6\text{H}_{11}\text{O}_2\right) \cdot \text{COC}_{12}\text{H}_{25}\text{COOY} \]

\[ \text{R} \]

\[ \text{R} \left( \text{C}_6\text{H}_{13}, \text{C}_6\text{H}_{11}\text{O}_2\right) \cdot \text{OCH}_2\text{CH}_2\text{COOY} \]

\[ \text{R} \]

\[ \text{C}_6\text{H}_{13}\text{O}_2 \left( \text{C}_6\text{H}_{13}, \text{C}_6\text{H}_{11}\text{O}_2\right) \cdot \text{OCH}_2\text{CH}_2\text{COOY} \]

\[ \text{R} \]

In the above formulas R is a radical selected from the group comprising hydrogen, alkyl, hydroxyl-substituted alkyl and polyglycol ether, and may contain 1–4 carbon atoms when it is alkyl and hydroxyl-substituted alkyl, but may contain 1–30 carbon atoms when it is polyglycol ether; where y is selected from the group consisting of zero and an integer 1–30; m is an integer of the value 1–4; n is an integer of the value 1–3; where R’ and R” are selected from the group consisting of hydrogen and the radicals —SO_2X and —O SO_2X and X is selected from the group consisting of hydroquin, alkaln metal, ammonium, organic amine and substituted organic amine; and where Y is selected from the group consisting of hydrogen, alkaln metal, ammonium, organic amine and substituted organic amine. The compound as defined may frequently be made by reacting a suitable alkylalumine with the anhydride of a dibasic acid. In cases where the sulphate is desired, this may be obtained by reacting the derivative from maleic anhydride with a sulphite. It will be appreciated that during manufacture mixtures of isomers and some side reaction products may be obtained, but impure commercial preparations will normally be suitable for the invention. Furthermore, mixtures of compounds which are individually suitable, may be used.

The preferred examples are products obtained by neutralizing with soda or an alkylolamine, the compounds obtained by reacting undecylenic acid monoesters with monoisoamamidole, with phthalic, maleic or succinic anhydride and the compounds made by reacting these alkylamides with maleic anhydride, and treating the result with sodium sulfite or bisulphite. Also suitable are the similar products obtained using in place of the stated alkylamides the products obtained by reacting these with 1–6 molecules of ethylene oxide.

The present invention also relates to a process for inhibiting the growth of and destroying microorganisms and for the relief and treatment of diseases caused by microorganisms by using the compounds of the invention as defined, either by themselves or incorporated in a suitable composition.

The following examples illustrate some specific em-
bodiments of and best modes for carrying out the invention, to which the invention is not limited. The parts and % mentioned herein are by weight if not otherwise mentioned.

Example 1

A product is obtained by reacting succinic anhydride undecylenic acid monoethanolamide for about 30 minutes at 70° C. The materials are reacted in equimolecular proportions. The resulting product is neutralized with caustic soda in the presence of water. A composition is then prepared, comprising 2 parts of the material just described in one hundred parts of a vehicle containing thirty parts of ethyl alcohol, the balance being water. The resulting composition or tincture can be used as a hair tonic for treating dandruff.

Example 2

A product is prepared as in the above Example 1, using maleic anhydride in the place of succinic anhydride. The resulting compound is not neutralized but is reacted in aqueous solution at about 85° C. with sodium sulfate. An equimolecular proportion of sodium sulfate is employed and the amount of water adjusted, so that the resulting solution has a final total solid content of about 33%. The compound thus prepared in aqueous solution is added in the appropriate amount to a solution of triethanolamine lauryl sulfate and lauric acid diethanolamide, so that the final composition contains 15 parts of the lauryl sulfate, 2 parts of the diethanolamide and 2 parts of the undecylenic derivative (on a 100% basis) just prepared. The resulting composition can be used as a shampoo to treat dandruff conditions.

Example 3

10 parts of olive oil are mixed at about 70° C. with 10 parts of propylene glycol monostearate and 5 parts stearic acid, and the whole poured with stirring into a mixture containing 2 parts of triethanolamine, 5 parts of propylene glycol and 2 parts of the undecylenic acid derivative (on a 100% basis) as prepared in the above Example 2 and 66 parts of water. The latter ingredients are all at a temperature of 40° C. Stirring is continued while the whole mix is cooled to 30° C. The resulting cream may be applied to the skin to treat fungicidal conditions.

It will be appreciated from the above that this invention is not limited to the embodiments, conditions, steps, etc. specifically described herein and can be carried out with various modifications within the scope of the invention as defined in the appended claims. Thus, in the compounds of the invention, the symbols R, X, Y, etc., may stand for the various radicals, substituents, groups or reactants, or their mixtures, as described in the application. The various products embodying the invention can be prepared by processes and under conditions which are substantially analogous to those more specifically described in the above Examples 1-3. The solvent used as a carrier may be an aqueous or non-aqueous solvent or a mixture and may contain a synthetic detergent in solution or suspension. The products of the invention may be used in combination with soap and/or synthetic detergents. They may also be used for sterilization of articles or surfaces or the like, infected by microorganisms.

I claim:

1. A process for inhibiting the growth of and destroying harmful bacteria and fungi which comprises contacting said bacteria and fungi with an effective amount of a compound selected from the group consisting of the free acids and alkalai metal, ammonium and alkylammonium salts of a member selected from the group consisting of the reaction product of equimolecular proportions of:

(a) phthalic anhydride with a member of the group consisting of undecylenic acid monostearate and undecylenic acid monoethanolamide;

(b) maleic anhydride with a member of the group consisting of undecylenic acid monoethanolamide and undecylenic acid monoiso-propanolamide;

(c) succinic anhydride with a member of the group consisting of undecylenic acid monoethanolamide and undecylenic acid monoiso-propanolamide; and

(d) the sodium sulfite reaction product of (b).

2. A process for treating dandruff which comprises applying to the scalp an effective amount of a compound as defined in claim 1.

3. A process according to claim 1, wherein the compound is the sodium salt of the reaction product of equimolecular proportions of succinic anhydride with undecylenic acid monoethanolamide.

4. A process according to claim 1 wherein the compound is the reaction product of equimolecular proportions of sodium sulfite with the reaction product of equimolecular proportions of maleic anhydride with undecylenic acid monoethanolamide.

5. A composition for inhibiting the growth of and destroying harmful bacteria and fungi comprising:

(i) An effective amount of a compound selected from the group consisting of the free acids and alkalai metal, ammonium and alkylammonium salts of a member selected from the group consisting of the reaction product of equimolecular proportions of:

(a) phthalic anhydride with a member of the group consisting of undecylenic acid monoethanolamide and undecylenic acid monoiso-propanolamide;

(b) maleic anhydride with a member of the group consisting of undecylenic acid monoethanolamide and undecylenic acid monoiso-propanolamide;

(c) succinic anhydride with a member of the group consisting of undecylenic acid monoethanolamide and undecylenic acid monoiso-propanolamide and

(d) the sodium sulfite reaction product of (b); and

(ii) A suitable topical carrier.

6. A composition for treating dandruff comprising two parts by weight of the sodium salt of the reaction product of equimolecular proportions of succinic anhydride with undecylenic acid monoethanolamide in one hundred parts by weight of a vehicle containing thirty parts of ethyl alcohol, the balance being water.

7. A composition for treating dandruff comprising two parts by weight of the reaction product of equimolecular proportions of sodium sulfite with the reaction product of equimolecular proportions of maleic anhydride with undecylenic acid monoethanolamide, fifteen parts by weight of triethanolamine lauryl sulfate and fifty parts by weight of lauric acid diethanolamide and the balance water on a one hundred percent by weight basis.

8. A composition for inhibiting the growth of fungi comprising two parts of the reaction product of equimolecular proportions of sodium sulfite with the reaction product of maleic anhydride with undecylenic acid monoethanolamide, ten parts of olive oil, 10 parts of propylene glycol monostearate, 5 parts of stearic acid, 2 parts triethanolamine, 5 parts propylene glycol and 66 parts of water, all parts being by weight.

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UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,385,755

May 28, 1968

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It is certified that error appears in the above identified patent and that said Letters Patent are hereby corrected as shown below:

Column 2, lines 60 and 61, "alkylalamides" should read -- alkylolamides --. Column 3, line 6, after "succinic anhydride" insert -- with --.

Signed and sealed this 7th day of October 1969.

(SEAL)

Attest:

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