SUNSCREEN FORMULATION CONTAINING TRIETHANOLAMINE NEUTRALIZED 2-HYDROXY-4-METHOXY-BENZOPHENONE-5-SULFONIC ACID

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Filed: Jan. 22, 1971
Appl. No.: 108,961

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Attorney—Hill, Sherman, Meroni, Gross & Simpson

ABSTRACT

An active sunscreen ingredient comprised of 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid, neutralized with triethanolamine, and formulated with various compatible vehicles to produce effective sunscreens for human use.

7 Claims, No Drawings
1 SUNSCREEN FORMULATION CONTAINING 
TRIETHANOLAMINE NEUTRALIZED 2-HYDROXY-4-
METHOXY-BENZOPHENONE-5-SULFONIC ACID 

CROSS-REFERENCE TO RELATED APPLICATIONS 

This is a continuation-in-part application of application Ser. No. 698,679 filed Dec. 18, 1967, now abandoned. Attention is also directed to prior application Ser. No. 358,616 filed Apr. 8, 1964, now abandoned. 

BACKGROUND OF THE INVENTION 

1. Field of the Invention 
The present invention relates to ultraviolet absorbers and more particularly to sunscreen formulations for protection of human skin from solar radiation. 

2. Prior Art 
Many sun tanning formulations for human skin are known, however, these do not effectively screen solar radiation from the skin. Chronic exposure to sunlight, even with such sun tanning formulations, has a deleterious effect on at least certain humans. For example, chronic exposure to sunlight appears to significantly influence aging of human skin and/or produce skin cancer. Additionally, sunlight appears to precipitate or at least aggravate lupus erythematosus and concentric skin lesions of pellagra and porphyria to the exposed skin areas. Also, a significant number of commonly used drugs produce photosensitivity in certain humans, which often result in polymorphic light sensitive eruptions. Among the more commonly used agents which produce sensitivity are the sulfa 

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2 DESCRIPTION OF THE PREFERRED EMBODIMENTS 

The invention provides a sunscreen agent that prevents and/or substantially minimizes the photochemical degradation and other adverse effects caused by exposure of human skin to sunlight through the absorption of ultraviolet wave lengths. The sunscreen agents of the invention absorb or screen radiation wave lengths responsible for erythema on human skin, minimizes the aging effects of solar radiation on humans and inhibits freckling or irregular pigmentation from such radiation. The sunscreen agents of the invention are readily incorporated into various types of vehicles for cosmetic materials, such as make-up bases, face powders, after-shave lotions, etc. for use by individuals who freckle, are afflicted with chloasma, or prefer their natural color, as well as by others. The sunscreen agents of the invention also tend to decrease sunlight accelerated aging and sunlight induced carcinogenesis on exposed human skin which has been coated with a formulation of said agents. 

The sunscreen agents of the invention comprise 2-hydroxy-
4-methoxy-benzophenone-5-sulfonic acid neutralized with a neutralization agent having properties of triethanolamine and are formulated into any desired carrier, vehicle, emulsion, cream, lotion, ointment, solution, suspension, gel, aerosol or in any other form suitable for human usage. In its most preferred form, the active sunscreen agent of the invention is 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid neutralized with triethanolamine. The amount of active sunscreen agent of the invention in a given formulation ranges from about 0.1 percent to about 30 percent or more as desired. 

The emulsions, gels, vehicles, etc. utilized in preparing sunscreen formulations containing the active sunscreening agents of the invention contain any one or combinations of: cetyl alcohol, stearyl alcohol, stearic or lauric acids and all other fatty acids and alcohols generally used in cosmetic and like materials emulsions or other formulations intended for human use; various waxes such as beeswax, microcrystalline wax, spermaceri, etc., and all other waxes generally used in cosmetic and like material emulsions or other formulations intended for human use; various petroleum materials, such as petrolatum, liquid petrolatum, mineral oil, silicone oil, etc. and all other oils, fats, and the like materials generally used in cosmetic and like material emulsions or other formulations intended for human use; fatty acid esters, such as isopropyl myristate and similar esters of fatty acids having a composition generally ranging from about C6 to about C20, various silicone derivatives, polyvinyl pyrrolidone methyl or propyl paraben, C1 to C4 glycols, various stearates, and other materials whether similar or otherwise that are generally used or considered suitable for use in cosmetic and like material emulsions or other formulations intended for human use.

Additionally, the vehicle materials, emulsifiers, combination of emulsifiers, and other like material compatible with the active sunscreen ingredients or agents of the invention are also selected from various anionic surfactants, including amine soaps of fatty acids such as characterized by triethanolamine stearate; cationic surfactants, such as characterized by monoethanol ammnonum fluoride; amphoteric surfactants such as characterized by N-fatty β-amino-propionate (RNH—

CH2—CH—COOH); and nonionic surfactants such as characterized by sorbitan derivatives of C12 to C18 fatty acids, polyoxylethylene sorbitan derivatives of C12 to C18 fatty acids, polyoxylethylene esters of C12 to C18 fatty acids, glyceryl stearates, fatty acid polyisopropylene complexes; and ethylen oxide fatty acid lanolin complexes. Other compatible materials, vehicles, carriers, gels and like materials include perfumes, clays, preservative agents, etc. and are all utilizable with the active sunscreen agents of the invention in formulating suitable gels, emulsions, either of the water-in-oil type or the oil-in-water type, aerosols, etc. or other forms suitable for application to humans.
In order to illustrate the invention and compare it with known sun-protective agents, comparative evaluations were made of twenty-four agents by applying such agents to the shaved abdomens of albino rabbits and determining the Minimal erythema dose (M.E.D.). An embodiment of the invention within this comparative group was triethanolamined neutralized 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid. The M.E.D. for an unprotected rabbit (i.e. one without having any protective agent on it) was found to be 25–30 seconds. Of the known protective agents, the longest or best protection provided was 3 to 5 minutes and only four of the preparations studied gave results that were this satisfactory. A 5 percent concentration of PABA (para-aminobenzoic acid) and a 5 percent concentration of triethanolamine neutralized 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in a compatible vehicle, each provided protection for about 20 to 25 minutes. By doubling the concentration of these two agents in similar formulations and applying them to rabbits, the M.E.D. was increased in both instances to approximately 100 minutes. However, PABA and its esters tended to produce epidermal sensitization and to produce cross-sensitization reaction with benzocaine, sulfonamides, and the antiline dyes.

The active sunscreen agents of the invention generally comprise suitably neutralized 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid, and similar benzophenone derivatives having the formula:

![Chemical Structure](image)

wherein A is selected from a neutralizing agent having properties characterized by triethanolamine. The active sunscreen agents of the invention are utilized in a variety of formulations and are present therein in amounts ranging from about 0.1 percent to about 30 percent by weight.

In order to further illustrate, and not limit the sunscreen agents of the invention in various formulations, bases, carriers, emulsifiers and other compatible vehicles, the following examples are set forth.

A 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid is available from Antara Chemical, New York, New York under the registered trademark "UVINUL MS-40" and "UVINUL-40-20 percent Aqueous Solution." UVINUL MS-40 is a free flowing powder at 25°C, light-cream in color and has a molecular weight of 309 and a pH 2 for a 1 percent aqueous solution, with a solubility of about 5 g/100 ml of water at 25°C after 15 minutes of agitation. Of course "UVINUL MS-40-20% Aqueous Solution" is the same material in an aqueous solution at the concentration indicated. In preparing sunscreen formulations utilizing powdered "UVINUL MS-40," the powder is first dissolved in water and then combined with a suitable neutralizing agent and a particular vehicle.

**EXAMPLE I**

A typical embodiment of an oil-in-water emulsion formulation utilizing "UVINUL MS-40-20% Aqueous Solution," (referred to as Benzophenone Derivative) in its neutralized form, as the active ingredient is as follows, with all parts being by weight unless otherwise noted.

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Amounts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophenone Derivative</td>
<td>10%</td>
</tr>
<tr>
<td>Triethanolamine (U.S.P.)</td>
<td>Q.S.*</td>
</tr>
<tr>
<td>Emulsion Vehicle</td>
<td>&quot;ARLACEL 165&quot; (Glycerin Monostearate) 5%</td>
</tr>
<tr>
<td>Cetyl Alcohol</td>
<td>2%</td>
</tr>
<tr>
<td>Isopropyl Palmitate</td>
<td>2%</td>
</tr>
<tr>
<td>Dimethyl Silicon Oil</td>
<td>3%</td>
</tr>
<tr>
<td>Light Liquid Petroleum</td>
<td>2%</td>
</tr>
<tr>
<td>Polyvinyl Pyrrolidone</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

* "ARLACEL 165" is a tradename for a glyceryl monostearate containing emulsifier available from Atlas Chemical Industries, Inc., of Wilmington, Delaware and "Sorbo 70%" is a tradename for a sorbitol containing emulsifier having 70 percent solids also available from Atlas Chemical Industries, Inc. An alternative emulsifier useful in place of "ARLACEL 165" is "Promulgen," a tradename for an emulsifier available from Robinson Wagner Company, Inc., of Mamaroneck, New York.

The above embodiment of a particular formulation can be varied by adjusting the amount of active ingredient so as to vary between about 0.1 percent to about 30 percent and by adjusting and/or omitting certain ingredients of the vehicle. For example, the amount of glycerol monostearate can vary between about 3 percent to 5 percent, the silicone oil, i.e. dimethyl silicone oil, and/or the petrolatum can be replaced by mineral oil and the amount varied between about 1 percent to 15 percent, the amount of sorbitol varied between about 3 percent to 30 percent or partially replaced by a glycol, the amounts of isopropyl palmitate, and polyvinyl pyrrolidone may also be varied and/or replaced with other comparable material and even omitted in further embodiments set forth hereinafter. Of course, minor amounts of perfumes and/or preservative agents are added as desired.

It will be understood that the invention is not limited to the specific propriety items set forth in the examples but includes all emulsifiers, emollients, carriers, vehicles, preservatives, perfumes and other materials generally found in cosmetic materials, sun protective formulations, etc., suitable for use on human skin.

The formulation of the above embodiment of an oil-in-water emulsion is carried out by placing the appropriate amounts of "ARLACEL 165," cetyl alcohol, dimethyl silicone oil and light liquid petrolatum in a suitable steam-jacketed kettle or the like and subjecting the mixture to slow agitation and heating conditions to about 70°C so as to form a first solution. The remaining ingredients of the emulsion vehicle, i.e. all of the remainder ingredients except the active ingredient, are placed in another suitable container and slowly agitated and heated up to about 75°C to form a second solution. The two solutions are then combined with continuous and vigorous agitation by adding the second solution to the first solution. Thereafter the sulfonated 2-hydroxy-4-methoxy-benzophenone derivative is neutralized with a sufficient amount of an amine having properties characterized by triethanolamine and added to the combined solutions at about 35°C with agitation sufficient to achieve a generally homogeneous or uniform mixture. Perfumes or preservative agents such as methyl and/or propyl paraben or the like can readily be included in the formulation in an appropriate amount, if desired.

**EXAMPLE II**

A typical embodiment of a water-in-oil formulation utilizing 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in its neutralized form as the active ingredient is as follows, again all parts being by weight unless otherwise noted.

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Amounts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophenone Derivative</td>
<td>3% to 10%</td>
</tr>
<tr>
<td>Triethanolamine (U.S.P.)</td>
<td>Q.S.*</td>
</tr>
<tr>
<td>Emulsion Vehicle</td>
<td>&quot;ARLACEL 186&quot; (Mono- and dioleic acid esters of fatty acids) 3%</td>
</tr>
<tr>
<td>&quot;SORBO&quot; (70% aqueous solution of d-sorbitol) 27%</td>
<td></td>
</tr>
<tr>
<td>Ceresin Wax</td>
<td>1%</td>
</tr>
<tr>
<td>Beeswax</td>
<td>1%</td>
</tr>
<tr>
<td>Mineral Oil</td>
<td>11%</td>
</tr>
<tr>
<td>Water</td>
<td>to 100%</td>
</tr>
</tbody>
</table>
“ARLACEL 186” and “SORBO” are tradenames of an emulsifier and an emollient respectively, available from the Atlas Chemical Industries, Inc. referred to earlier. The formulation of the above embodiments is carried out by preparing an intermediate gel comprising of adding a small amount of “SORBO” and “ARLACEL 186” and subjecting the mixture of mechanical agitation to form a relatively thick slurry. Thereafter, the remainder of “SORBO” ingredient is added with continuous agitation and then the benzophenone derivative, in its neutralized form, the waxes and the mineral oil are added to the intermediate gel and slowly agitated and heat up to about 70°C. The water is then heated to about 72°C. and added to the gel mixture with continuous agitation. The agitation is continued until the resultant formulation cools to room temperature. In order to provide maximum smoothness and stability, the formulation is subjected to homogenization or milling procedures.

EXAMPLE III

A typical embodiment of a liquid solvent formulation utilizing 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in its neutralized form as the active ingredient is as follows, with all parts being by weight.

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Amounts</th>
<th>Neutralizing Agent</th>
<th>Solvent Vehicle</th>
<th>Specially Denatured Alcohol (SDA-40)**</th>
<th>Alcohol Soluble Silicone Oil</th>
<th>Purified Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophene Derivative</td>
<td>10%</td>
<td>Q.S.*</td>
<td></td>
<td></td>
<td>20%</td>
<td></td>
</tr>
<tr>
<td>Sodium Lauryl Sulfate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3%</td>
<td></td>
</tr>
</tbody>
</table>
| ** A denatured ethyl alcohol approved by the U.S. Government for use in various cosmetics and like formulations.**

The formulation of the above embodiment is carried out by combining the active ingredient with the solvent vehicle under vigorous agitation and gentle heat conditions for a period of time sufficient to produce a relatively clear solution. Perfumes or the like are also added as desired.

EXAMPLE IV

A typical embodiment of a gel (clear or opaque) formulation utilizing 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in its neutralized form as the active ingredient is as follows, with all parts being by weight.

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>Amounts</th>
<th>Gel Vehicle</th>
<th>Specially Denatured Alcohol (SDA-40)**</th>
<th>Alcohol Soluble Silicone</th>
<th>“Carbopol 940” (Synthetic Hydrophilic Colloids in white free flowing powder form)</th>
<th>Water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophene Derivative</td>
<td>10%</td>
<td>Triethanolamine (U.S.P.)</td>
<td></td>
<td>30%</td>
<td>0.5%</td>
<td></td>
</tr>
<tr>
<td>Sodium Lauryl Sulfate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>to 100%</td>
<td></td>
</tr>
</tbody>
</table>

**Ibid.

“Carbopol 940” is a tradename for an emulsifier material comprised of a vinyl polymer with active carboxyl groups available from B. F. Goodrich Company (The Merck Index, 8th Edition, 1968, Page 201). The formulation of the above gel embodiment is carried out by combining the gel vehicle with the benzophenone derivative under agitation and heat conditions sufficient to produce a clear gel solution. Thereafter the triethanolamine is slowly stirred into the solution until a gel forms. The formed gel is suitable for use on human skins.

The benzophenone derivative is carried into an appropriate vehicle by dissolving or suspending it in water, alcohol, glycerine, propylene glycol or any other suitable solvent or combination of solvents generally recognized as safe or compatible to human skin. Further suitable suspension agents, such as organic clays, pectin, synthetic resins, etc. are also utilizable in appropriate proportions in the formulations of the invention, additionally, tragacanth, agar-agar or similarly characterized thickening agents are also suitable for use in the formulations of the invention.

In order to further illustrate the sunscreen agents and formulations of the invention and to illustrate their relative effectiveness on humans and compared them with known sun protective agents, a number of known sun protective agents and the sunscreen formulation essentially identical to that of Example I having various concentrations of active sunscreen ingredients were applied to male and female volunteers. An ultraviolet lamp, Burdick Model QA-450-N, producing ultraviolet radiation ranging from 2,400 to 3,300 angstroms, with the majority of the radiation being between 2,800 to 3,200 angstroms was used. (Sunburn to human skin is generally produced by the electromagnetic spectrum located between 2,900 and 3,170 angstroms, with maximal effects at about 2,970 angstroms.) The M.E.D. (Minimal Erythema Dose) for each volunteer was established on the abdomen and the back with the ultraviolet lamp at a distance of thirty inches. The various formulations studied were applied by hand and rubbed into a skin area in the same manner as an individual does before being exposed to the sun. No excess material was utilized and the amount varied, but was generally only sufficient to permit the volunteers to feel comfortable. In each instance, the applied formulations were allowed to dry before exposure to the ultraviolet and the results were averaged.

<table>
<thead>
<tr>
<th>Sun Protective Material</th>
<th>Average Protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>5% Menthyl anthranilate</td>
<td>less than 5</td>
</tr>
<tr>
<td>Ethoxylmethoxy-cinnamate</td>
<td>less than 5</td>
</tr>
<tr>
<td>Para- amino benzoic acid 15%</td>
<td>30 but less than 60</td>
</tr>
<tr>
<td>in Aquaphor</td>
<td>less than 5</td>
</tr>
<tr>
<td>Red Veterinary Petroleum</td>
<td>30 but less than 40</td>
</tr>
<tr>
<td>2-ethoxy-ethyl-p-methoxy-cinnamate</td>
<td>40 but less than 60</td>
</tr>
<tr>
<td>Yellow Vasoline (U.S.P.)</td>
<td>less than 5</td>
</tr>
<tr>
<td>Digalloyl-triobate</td>
<td>less than 5</td>
</tr>
</tbody>
</table>

**The non-neutralized benzophenone derivative in a lotion base was considered to be irritating and unacceptable for human use.

In summation, the invention provides active sunscreen agents or ingredients compatible with a wide variety of vehicles or carriers in sunscreen formulations wherein the active ingredient is present in amounts ranging from about 0.1 percent to about 30 percent. The preferred active ingredient of the invention is 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid neutralized with triethanolamine, although other suitably neutralized 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid derivatives are also utilizable. It is to be understood that the foregoing relates only to the preferred embodiments of the invention and changes, modifications and variations can be effected without departing from the scope or spirit of the novel concepts of the invention. I claim:

1. A sunscreen formulation in the form of an emulsified lotion suitable for application to human skin comprising an active ingredient consisting essentially of 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in amounts ranging from 0.1 percent to 30 percent of said formulation, said sulfonic acid being neutralized with triethanolamine, and a compatible vehicle comprising a mixture of, by weight, 3 percent to 5 percent glycerol monostearate, 1 percent to 3 percent cetyl al-
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cobol, 1 percent to 3 percent isopropyl palmitate, 1 percent to 15 percent dimethyl silicone oil, 0 percent to 3 percent liquid petrolatum, 0.1 percent to 1 percent polyvinyl pyrrolidone, 3 percent to 30 percent sorbitol and up to 100 percent water.

2. A sunscreen formulation as defined in claim 11 wherein the compatible vehicle includes a preservative amount of preservative material selected from the group consisting of methyl paraben, propyl paraben and mixtures thereof.

3. A sunscreen formulation in the form of an emulsified lotion suitable for application to human skin comprising; an active ingredient consisting essentially of 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid in amounts ranging from 0.1 percent to 30 percent by weight of said formulation, said sulfonic acid being neutralized with triethanolamine, and a compatible vehicle comprising a mixture of, by weight, 3 percent to 5 percent glycerol monostearate, 2 percent cetyl alcohol, 2 percent isopropyl palmitate, 3 percent dimethyl silicone oil, 2 percent light liquid petrolatum, 0.5 percent polyvinyl pyrrolidone, 7 percent sorbitol and up to 100 percent water.

4. A sunscreen formulation in the form of an emulsified lotion suitable for application to human skin comprising; an active ingredient of 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in an amount of 10 percent by weight of said formulation, said sulfonic acid being neutralized with triethanolamine, and a compatible vehicle comprising a mixture of, by weight, 5 percent glycerol monostearate, 2 percent cetyl alcohol, 2 percent isopropyl palmitate, 3 percent dimethyl silicone oil, 2 percent light liquid petrolatum, 0.5 percent polyvinyl pyrrolidone, 7 percent sorbitol and up to 100 percent water.

5. A sunscreen formulation in the form of an emulsified lotion suitable for application to human skin comprising; an active ingredient consisting essentially of 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid in amounts ranging from about 3 percent to 10 percent by weight of said formulation, said sulfonic acid being neutralized with triethanol-amine, and a compatible vehicle comprising a mixture of, by weight, 3 percent glycerol mono- and di-stearate, 19 percent sorbitol, 1 percent cerein wax, 1 percent beeswax, 11 percent mineral oil and up to 100 percent water.

6. A sunscreen formulation in the form of a liquid suitable for application to human skin comprising; an active ingredient of 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in an amount of 10 percent by weight of said formulation, said sulfonic acid being neutralized with triethanolamine, and a compatible vehicle comprising a mixture of, by weight, 20 percent denatured alcohol, 3 percent dimethyl silicone oil and up to 100 percent water.

7. A sunscreen formulation in the form of a liquid suitable for application to human skin comprising; an active ingredient of 2-hydroxy-4-methoxy-benzophenone-5-sulfonic acid in an amount of 10 percent by weight of said formulation, said sulfonic acid being neutralized with triethanolamine, and a compatible vehicle comprising a mixture of, by weight, 30 percent denatured alcohol, 3 percent dimethyl silicone oil, 0.5 percent glycerol monostearate and up to 100 percent water.

* * * * *
UNITED STATES PATENT OFFICE
CERTIFICATE OF CORRECTION

Patent No. 3,670,074 Dated June 13, 1972

Inventor(s): Abraham J. Doner

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

Column 6, line 42, change "location" to --lotion--.
Column 7, line 6, change "11" to --1--.

Signed and sealed this 17th day of September 1974.

(SEAL)
Attest:
McCOY M. GIBSON JR. C. MARSHALL DANN
Attesting Officer Commissioner of Patents