Concentrated Foam-Producing Spermicides

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20 Claims. (Cl. 167—58)

This application is a continuation-in-part of my co-pending application, S.N. 308,289, filed September 6, 1952, now abandoned.

The present invention relates to compositions adapted chiefly for use as topical remedies in contact with the mucous membranes in the vaginal cavity and to a method of preparing such a composition. The topical remedies of this invention comprise concentrated spermicidal compositions which are designed for use with moistened sponges or sponge-like masses such as tampons, rubber sponges, marine sponges, cellulose sponges, sponges made of cellular plastic material, etc., and which produce foam while in use.

One of the chief drawbacks to the use of spermicides has been their cost. One object of the present invention is to provide a highly concentrated spermicidal material which may be diluted with water just before use, which can be applied without the use of complex and expensive apparatus, and which is not irritating to the membranes in use. The use of such highly concentrated spermicidal material cuts down packaging, handling and shipping costs.

I have found that the use of a sponge or sponge-like mass, moistened with sufficient water to dilute the non-irritating concentrated spermicide, will give a satisfactory means for reducing the cost of application, provided (1) sufficient spermicidal power is inherent in the concentrated spermicide, (2) sufficient foam is produced by the spermicide to distribute it thoroughly throughout the vaginal canal, and (3) the composition mixes quickly with seminal fluid. The foam-producing property is highly important as a means of distribution of the spermicidal liquid. The moist sponge acts as a vehicle for distribution of the spermicidal liquid and as a reservoir for foam production.

I have also found that concentrated solutions of high spermicidal and foam-producing power may be obtained which are not irritating. This may be done with certain water-soluble non-ionic and foam-forming agents whose pH can be regulated to any point required and solutions of which are compatible with various salts and acids. This is found to be possible with high spermicidal power are sufficiently foam-forming only in the absence of insoluble ingredients and belong to the class represented by the generic formula

\[
\text{OH} \quad \text{OCH}_3 \quad \text{CHOCH}_3 \quad \text{OCH}_3 \quad \text{OH}
\]

In this formula \( R \) represents an alkyl group and \( R_1 \) represents a member of the class consisting of alkyl groups and hydrogen. Preferably one alkyl group is in the para position to the oxygen atom and \( x \) may be any number greater than 4, e.g., from 5 to 12. A mixture of water soluble polyethylene glycol monoothers of alkyl phenols may be used and in the preferred practices \( x \) has an average value between 8 and 12. In the preferred specific embodiment of my invention \( x \) is approximately 9.75, \( R \) is either the trisopropyl group or the tetramethyl group and is in the para position and \( R_1 \) is hydrogen. Generally \( R \) may have from 1 to 23 carbon atoms and \( R_1 \) may have from 0 to 23 carbon atoms except that the sum of the carbon atoms in \( R \) and \( R_1 \) should not be less than 4 or more than 23.

An important advantage of using these materials is the fact that solutions containing them are neutral and may be adjusted to any pH value, and that they do not react with weak acids or alkalies or with buffer salts or neutral salts.

The quantity of active spermicide described above in Formula 1 which may be employed in the present composition will vary considerably. In a preferred practice of this invention it will constitute from 15 to 75% by weight of the total composition.

I have found that certain neutral salts such as sodium or potassium chloride or sulfate or other similar salts are valuable additions to these compositions in that they increase enormously the speed of miscibility of the non-ionic foam-forming spermicidal materials with seminal fluid so that quick spermicidal action is assured. These neutral salts desirably constitute 5% to about 20% by weight of the spermicidal composition.

By using the materials of this invention, I have found it easy to possible to make solutions, 30 grams of which are ample for 60 or more applications, free of resulting irritation in use with a moistened sponge. Even higher concentrations are practicable.

The method of application is simple also in that a glass, plastic, wooden or similar rod may be moistened with the solution and then rubbed on the moistened sponge. This may be repeated three or four times, the material being applied on all sides. For example, \( \rac{1}{2} \) cc. may be so transferred very quickly and easily. As an example of the sponge mass which may be used, a sheet of rubber sponge about \( \frac{3}{4} \) " thick by 2" square would be suitable. It will act as a reservoir for 3—5 cc. of water. After the transfer of the spermicidal and foam-forming concentrate to it, it is slightly compressed and released several times to mix the solution into the water in the sponge. It thus distributes the concentrated liquid throughout the water stored in the sponge before insertion. It is of course also possible to apply the concentrated liquid to the sponge in other ways, such as by the use of an eye dropper, dropping tube, scoop or brush. It is generally convenient to have the means of applying the liquid to the sponge attached to the closure of the container and extending into said container.

Tests have shown that the moisture in the sponge, as used, may range between \( \frac{1}{2} \) cc. and 3 cc. so that when a solution containing 15% of the active spermicidal agent is applied to the sponge in an amount of \( \frac{1}{2} \) cc., the resulting concentration which is used topically may range from 7½% to 2.14%. If a 20% solution is applied to the wet sponge under these conditions in the amount of \( \frac{1}{2} \) cc., the resulting solution which is used topically may range from 10% to 2.86%.

I am aware that some of the polyglycol monoothers of alkyl phenols have been used in spermicidal jellies and suppositories. However, they have been used almost always in the presence of insoluble materials such as ricinoleic acid, glyceryl monolaurate, vegetable and other gums, etc., or in the presence of strong spermicidal materials such as phenyl mercuric acetate, etc., to enhance the effectiveness of these other spermicides. There has been no disclosure that they are spermicidal in themselves nor that they can be used in high concentrations without causing irritation. In addition, the presence of insoluble materials
inhibits foam formation so that the teaching of these previous disclosures would be insufficient for the development of the present invention since foam formation is essential to its proper functioning. I have now found it possible to obtain with these materials both high spermicidal power and high foam-forming power simultaneously without the use of heavy metal or other spermicides.

In addition, by using a neutral salt such as sodium chloride in conjunction with these materials, I have found a great increase in the speed of mixing of the spermicides with semen, thus resulting in a substantial increase in effectiveness.

Glycerine, propylene glycol or other polyhydroyx compounds or ures may be added to any of the formulae in the examples given below to prevent freezing in cold weather.

Since no gums are present in any of the formulae nor any substances which may cause mold formation, no mold inhibiting material is necessary for this purpose. However, such substances as methyl, ethyl, propyl or butyl parahydroxy benzoate, oxyquinoline sulfate, phenols, alkyl phenols, chlorinated phenols, chlorinated thymols, the alkali alkyl sulfate, etc., may be used for their bacteriostatic and fungistatic effect.

Water soluble acids with or without buffer salts may be used to regulate the pH value. The pH value of the compositions of the present invention may range between 1 and 8.5 although a pH of about 4.5 (the normal pH of the vaginal membranes) is preferred. The limitations on the pH are placed in this range simply because in this range the chances of irritation are less than at higher or lower pH values and a pH in this range is less favorable for invasion by undesirable organisms.

The acids which may be used include among others lactic, boric, acetic, tartaric, etc., and the buffer salts include sodium or potassium salts of these acids as well as of phosphoric acid and others.

The following are typical examples of concentrated foam-producing spermicidal compositions suitable for effective use with a wet sponge mass or tampon.

**Example 1**

<table>
<thead>
<tr>
<th>Parts by wt.</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>p-Trisopropyl phenyl monoether of nona ethylene glycol</td>
<td>15</td>
</tr>
<tr>
<td>Lactic acid</td>
<td>1.5</td>
</tr>
<tr>
<td>Sodium lactate</td>
<td>1.5</td>
</tr>
<tr>
<td>Water sufficient to make a total of 100.00 parts by weight.</td>
<td></td>
</tr>
</tbody>
</table>

**Example 2**

A concentrated foam-producing spermicidal composition having the same formula as Example 1 but in which the p-trisopropyl phenyl monoether of nona ethylene glycol is replaced with a mixture consisting of the p-trisopropyl phenyl monoether of nona ethylene glycol and the p-trisopropyl phenyl monoether of dodecanethylene glycol.

**Example 3**

A concentrated foam-producing spermicidal composition having the same formula as Example 1 but in which the p-trisopropyl phenyl monoether of nona ethylene glycol is replaced with p-tetraethyl phenyl monoether of dodecanethylene glycol.

**Example 4**

A concentrated foam-producing spermicidal composition having the same formula as Example 1 except that the proportion of sodium chloride is increased from 5% to 10%.

**Example 5**

A concentrated foam-producing spermicidal composition having the same formula as Example 1 in which the lactic acid is replaced by 1.5 parts of boric acid.

**Example 6**

A concentrated foam-producing spermicidal composition having the same formula as Example 1 in which the lactic acid is replaced by 1.5 parts of boric acid and the sodium lactate is replaced by 1.5 parts of sodium borate.

**Example 7**

When 1/2 cc. of any of the compositions described in the above examples is applied to a sponge containing 5 cc. of water, the resulting solution comes well within the spermicidal requirements recommended by the Council of Pharmacy of the A.M.A., using the Brown & Gamble technique.

The compositions included in this invention may be shipped as described in the aforesaid examples or may be shipped in even more concentrated form to remote countries or localities and there they may be diluted and packed in containers of local origin. The following are examples of such higher concentrates.

**SHIPPING CONCENTRATES**

**Example 8**

| p-Trisopropyl phenyl monoether of nona ethylene glycol | 30 |
| Lactic acid | 3.0 |
| Sodium lactate | 3.0 |
| Sodium chloride | 10.0 |
| Water sufficient to make a total of 100.0. |  |

Example 8 is twice the concentration of Example 1. On arriving at its destination, it may be diluted with an equal quantity of water, giving the formula of Example 1.

**Example 9**

| p-Trisopropyl phenyl monoether of nona ethylene glycol | 60 |
| Lactic acid | 6.0 |
| Sodium lactate | 6.0 |
| Sodium chloride | 5.0 |
| Water sufficient to make 100.0. |  |

Example 9 requires the addition of 30 parts of sodium chloride solution containing 15 parts of salt to obtain a composition identical with that in Example 1.

**Example 10**

| p-Trisopropyl phenyl monoether of nona ethylene glycol | 75 |
| Lactic acid | 5.0 |
| Sodium chloride | 20 |

On diluting this with 400 parts of water there would be obtained a product suitable for use containing: p-Trisopropyl phenyl monoether of nona ethylene glycol | 15 |
| Lactic acid | 1 |
| Sodium chloride | 4 |

It is obvious that by using such concentrates for shipping purposes freight, container and other shipping costs are greatly reduced.

**Example 11**

| p-Trisopropyl phenyl monoether of nona ethylene glycol | 20 |
| Lactic acid | 3.0 |
| Sodium chloride | 6.0 |
| Water sufficient to make 100. |  |
Example 12

p-Trisopropyl phenyl monoether of nona ethylene glycol

Boric acid
Propyl p-hydroxybenzoate
Sodium chloride

Water sufficient to make 100.

The germicidal composition of the present invention may be prepared for application to a sponge-like mass by mixing a concentrated water solution of a non-ionic, foam-producing, surface active agent of the class represented by the formula

\[
\text{R} - \text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{OH}
\]

in which \( R \) represents an alkyl group and \( R_1 \) represents a member of the class consisting of alkyl groups and hydrogen, with a neutral salt and a buffer system.

A variety of laboratory and clinical tests were carried out to verify the effectiveness and the safety of the compositions of the present invention. These are outlined below.

The following composition was prepared (composition of Example 1) and tested for its germicidal activity using the Brown & Gamble technique:

<table>
<thead>
<tr>
<th>Parts by wt.</th>
<th>p-Trisopropyl phenyl monoether of nona ethylene glycol</th>
<th>Lactic acid</th>
<th>Sodium lactate</th>
<th>Sodium chloride</th>
<th>Water sufficient to make a total of 100 parts by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
<td>1.5</td>
<td>1.5</td>
<td>5</td>
<td>35</td>
</tr>
</tbody>
</table>

The Brown & Gamble technique consists of mixing one part of the germicidal material with four parts of physiological saline solution. The resulting mixture is then mixed on a slide with an equal volume of human semen and the time for complete immobilization is observed.

One-half cc. of the above composition was mixed with 5 cc. of water in a sponge, after which 1 part of the resulting solution was taken from the sponge and diluted with 5 parts of physiological saline solution. One part of this final solution was then mixed with an equal volume of human semen on a slide, and the time for complete immobilization was observed.

Complete immobilization of the sperm resulted in less than five minutes.

The effectiveness of said solution comes well within the germicidal requirements recommended by the Council of Pharmacy of the American Medical Association using the Brown & Gamble technique. This requirement is that immobilization occur in thirty minutes or less.

The clinical safety of the compositions of the present invention were tested by the Margaret Sanger Research Bureau. The spermicide tested had the following composition:

<table>
<thead>
<tr>
<th>Parts by wt.</th>
<th>p-Trisopropyl phenyl monoether of nona ethylene glycol</th>
<th>Boric acid</th>
<th>Propyl p-hydroxybenzoate</th>
<th>Sodium chloride</th>
<th>Water sufficient to make 100 parts by weight</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
<td>3</td>
<td>2</td>
<td>10</td>
<td>20</td>
</tr>
</tbody>
</table>

The purpose of the test was to determine the effect upon the genital mucosa of the recommended dosage of the foam liquid when used for 21 consecutive days. Application of the liquid to a moistened cellulose plastic sponge was made by wiping the rod attached to the closure of the bottle containing the liquid twice on each side of the moistened sponge and working it into a foam. Twelve women participated in the study. An initial examination was performed and all findings were recorded. Particular attention was paid to the condition of the vulva, vaginal and cervical mucosa. The women were instructed to insert the foam filled sponge nightly for a period of 21 days. A string was attached to the sponge for easy removal. The patient was instructed to make a careful note of any evidence of irritation. Vaginal examinations were made twice weekly as well as after the test period was completed and all objective findings were recorded.

There was no complaint of irritation in 11 patients. One complained of slight itching.

There were no objective signs of irritation in any of the 12 subjects.

To further test the clinical safety and effectiveness of the present composition the following clinical experiments were carried out at the St. Elizabeth Health Department in Black River, Jamaica, B.W.I. The germicidal composition used in these experiments are identified as "Durafoam Liquid" and consists of a water solution containing

<table>
<thead>
<tr>
<th>Percent</th>
<th>p-Trisopropyl phenyl monoether of nona ethylene glycol</th>
<th>Boric acid</th>
<th>Sodium chloride</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20</td>
<td>3</td>
<td>6</td>
</tr>
</tbody>
</table>

In said clinical experiment "Durafoam Liquid" was distributed to patients with instructions as to its use. It was dispensed with a small sponge and the patients were instructed that said sponge is to be moistened on both sides with ½ cc. of said "Durafoam Liquid" before insertion and use. The "Durafoam Liquid" was distributed to patients in a small dropper bottle to make measurement easy and the patients were instructed to bring the bottles back to be refilled. The patients were instructed to return when they required additional material. The public health nurses of St. Elizabeth Health Department were used in this experiment for distribution of the "Durafoam Liquid" and to follow up patients who were using it.

Set forth below in Table I is a report of the above described clinical experiment covering a period of 18 months.

<table>
<thead>
<tr>
<th></th>
<th>Total patients given &quot;Durafoam Liquid&quot; with sponge</th>
<th>Total patients discontinued use of &quot;Durafoam Liquid&quot;</th>
<th>Total patients using &quot;Durafoam Liquid&quot; with sponge at end of period</th>
<th>Total number of months of test</th>
<th>Average period of use</th>
<th>Total number of pregnancies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>640</td>
<td>69</td>
<td>571</td>
<td>18</td>
<td>9</td>
<td>18</td>
</tr>
</tbody>
</table>

Multiplying the figure 571 by 9 and dividing by 12 gives 428 woman years use with 18 pregnancies. This is 4.2 pregnancies per 100 woman years. The normal rate in this population is between 70 and 80 per 100 woman years. The "Durafoam Liquid" therefore reduces the pregnancy rate very substantially. Of the 69 patients who discontinued the use of the method 18 became pregnant. Of these 18, 12 admitted irregular use and 4 stated that their husbands objected to the presence of the sponge. Fifty-one discontinued either because they were planning a pregnancy or were indifferent and did not want to be bothered with using the method.

The results of these tests indicate that the present germicidal composition with sponge is a very effective method for reducing the pregnancy rate and is well adapted for use in rural areas where education is at a low level. It is also quite evident that the alkyd phenoxyethanol is highly and effectively germicidal in use and especially so in the presence of a salt.

While the invention has been described with particular reference to specific embodiments, it is to be understood that it is not limited thereto, but is to be construed broadly...
2,948,979

2. A composition according to claim 1 wherein R₈ is hydrogen, and R₉ is para to the group

-OCH₂CH₂(OH)₃CH₂OH

and has from 8 to 12 carbon atoms in the chain, and x has an average value of from about 6 to about 12.

3. A composition according to claim 2 wherein said composition as applied topically contains from about 2% to 10% of said alkylphenoxypolyethoxyethanol.

4. A composition according to claim 1 wherein the alkylphenoxypolyethoxyethanol is a mixture of p-alkylphenoxypolyethoxyethanols wherein R₈ is hydrogen, R₉ is para to the group

-OCH₂CH₂(OH)₃CH₂OH

and R has from 8 to 12 carbon atoms in the chain and x has an average value of from about 6 to about 12.

5. A composition according to claim 1 wherein said chief spermicidal ingredient is p-triisopropyl phenyl monomethoxy of nonaethylene glycol.

6. A spermicidal composition according to claim 1 wherein the vehicle contains urea.

7. A spermicidal composition according to claim 1 wherein said vehicle contains boric acid.

8. A spermicidal composition consisting essentially of a buffered pharmaceutical vehicle and containing as its chief spermicidal active ingredient a compound of the general formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₉ is not less than 4 or greater than 23, said composition having a pH in the range from about 1 to about 8.5 inclusive.

13. A spermicidal composition according to claim 8 wherein the spermicidally active ingredient is present in an amount of 60% by weight of the spermicidal composition.

14. A spermicidal composition consisting essentially of a hydrous pharmaceutical vehicle containing as its chief spermicidally active ingredient a compound of the general formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₉ is not less than 4 or greater than 23, said spermicidally active ingredient being present in sufficient amounts to act as a spermicidal agent, said composition having a pH in the range from about 1 to about 8.5 inclusive.

15. A spermicidal composition consisting essentially of a buffered pharmaceutical vehicle and containing, as applied topically, from 2% to 10% of a compound of the general formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₉ is not less than 4 or greater than 23 as its chief spermicidal agent, said composition having a pH in the range from about 1 to about 8.5 inclusive.

16. An article useful as a spermicide comprising a sponge-like mass moistened with a buffered liquid spermicidal concentrate containing a neutral salt and as the chief spermically active ingredient a compound of the general formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₉ is not less than 4 or greater than 23, said concentrate, on dilution with the water in the moist sponge, having a pH in the range from about 1 to about 8.5 inclusive.

17. A spermicidal method which comprises applying to a wet, sponge-like mass a liquid spermicidal concentrate containing a neutral salt and as the chief spermicidally active ingredient a compound of the general formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an amount of 60% by weight of the spermicidal composition.

What is claimed is:

1. A spermicidal composition consisting essentially of a buffered pharmaceutical vehicle and as chief spermicidal ingredient an alkylphenoxypolyethoxyethanol of the formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₉ is not less than 4 or greater than 23, said composition having a pH in the range from about 1 to about 8.5 inclusive.

2. A composition according to claim 1 wherein R₈ is hydrogen, and R₉ is para to the group

-OCH₂CH₂(OH)₃CH₂OH

and has from 8 to 12 carbon atoms in the chain, and x has an average value of from about 6 to about 12.

3. A composition according to claim 2 wherein said composition as applied topically contains from about 2% to 10% of said alkylphenoxypolyethoxyethanol.

4. A composition according to claim 1 wherein the alkylphenoxypolyethoxyethanol is a mixture of p-alkylphenoxypolyethoxyethanols wherein R₈ is hydrogen, R₉ is para to the group

-OCH₂CH₂(OH)₃CH₂OH

and R has from 8 to 12 carbon atoms in the chain and x has an average value of from about 6 to about 12.

5. A composition according to claim 1 wherein said chief spermicidal ingredient is p-triisopropyl phenyl monomethoxy of nonaethylene glycol.

6. A spermicidal composition according to claim 1 wherein the vehicle contains urea.

7. A spermicidal composition according to claim 1 wherein said vehicle contains boric acid.

8. A spermicidal composition consisting essentially of a buffered pharmaceutical vehicle and containing as its chief spermicidal active ingredient a compound of the general formula

-R₉-OCH₂CH₂(OH)₃CH₂OH

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₉ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₉ is not less than 4 or greater than 23, said spermicidally active ingredient being present in sufficient amounts to act as a spermicidal agent, said composition having a pH in the range from about 1 to about 8.5 inclusive.

9. A composition according to claim 8 wherein the spermicidally active ingredient is present in the range of about 15 to 75% by weight of the spermicidal composition.

10. A composition according to claim 8 wherein the spermicidically active ingredient is present in an amount of 15% by weight of the spermicidal composition.

11. A spermicidal composition according to claim 8 wherein the spermicidically active ingredient is present in an amount of 30% by weight of the spermicidal composition.

12. A spermicidal composition according to claim 8 wherein the spermicidically active ingredient is present in an amount of 60% by weight of the spermicidal composition.
average value of from about 5 to 12, and wherein the sum of the carbon atoms in R and R₁ is not less than 4 or greater than 23, and applying the resulting spermicidally treated sponge-like mass into the vaginal cavity in contact with the mucous membranes to serve as a topical remedy.

18. A spermicidal method which comprises introducing into the vaginal cavity a spermicidal composition consisting essentially of a pharmaceutical carrier and as chief spermicidal ingredient an alkylphenoxypolyethoxyethanol of the formula

\[
\text{OCH}_2\text{CH(OCH}_2\text{CH)}_n\text{OH}
\]

wherein R represents an alkyl group having from 1 to 23 carbon atoms in the chain and R₁ represents a member selected from the class consisting of alkyl groups having from 1 to 23 carbon atoms in the chain and hydrogen, and x has an average value of from about 5 to about 12, and wherein the sum of the carbon atoms in R and R₁ is not less than 4 or greater than 23.

19. A method according to claim 18 wherein R₁ is hydrogen and R is para to the group

\[-\text{OCH}_2\text{CH}_3\text{(OCH}_2\text{CH)}_x\]

and has from 8 to 12 carbon atoms in the chain, and x has an average value of from about 6 to about 12.

20. A method according to claim 19 wherein said composition as applied topically contains from about 2% to 10% of said alkylphenoxypolyethoxyethanol.

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