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SPERMICIDAL ALKYLPHENOXY-POLYETHOXY-ETHANOL EMULSION

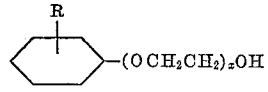
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5 Claims. (Cl. 167—58)

This invention relates to novel compositions of matter and more particularly to novel compositions which are intended for topical use. In one of its more specific aspects the invention is directed to novel compositions of matter useful chiefly for application to the mucous surfaces of the vaginal cavity where they act as spermicidal media.

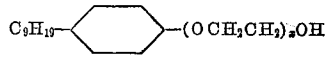
Prior to this invention, a number of different spermicidal compositions have been proposed, such as the spermicidal compositions disclosed in the U.S. patents of Frank V. Sander, No. 2,330,846, issued on October 4, 1943, and No. 2,541,103, issued on February 13, 1951. The spermicidal compositions of these patents comprise essentially an aqueous vehicle in the nature of a gel having therein an unsaturated fatty acid of ten or more carbon atoms, e.g., ricinoleic, oleic and linoleic acids, and a surface tension depressant, e.g., unsaturated fatty acids and alcohols and the salts and esters thereof as well as a water-soluble alkylphenoxyethanol having the following general formula:



R being an alkyl radical, preferably in the position para to the oxygen atom, and x being one or greater than one. The alkylphenoxyethanol could also be in the form of a mixture, x in the preferred form, having a value of from 9.25 to 10.25, and the average molecular weight being 959 to 639.

It has been reported that it is desirable for spermicidal compositions to be buffered at an acid pH since most of the spermicidal compositions, and particularly those relying upon surface active agents and higher unsaturated fatty acids for their spermicidal power, are rendered more effective and more highly spermicidal when buffered at a pH of 4 to 6 with an acid buffer system. Although spermicidal compositions buffered at a pH within the above range have been widely used, it has been found that they result in undesirably high incidence of irritation of the vaginal mucosa. Because of the undesirable irritation produced by the above type of spermicidal compositions which are buffered with an acid buffer system, it has been long felt desirable to provide a spermicidal composition which is highly effective at the pH of the cervical mucus which is normally from about 7 to 7.5 as well as at the pH of seminal fluid which is about 7.7. In other words, it has been felt desirable to provide a spermicidal formulation which has high effectivity at pH ranging from slightly acid to slightly basic in order that there be a minimum of irritation of the vaginal mucosa.

We have now discovered that a spermicidal composition which is highly spermicidal at a pH of from about 6.8 to about 8.6 may be provided by incorporatnig in an oil-in-water emulsion base, a water-soluble alkylphenoxyethanol having the following formula:



in which x has a value of from six to ten inclusive and in which the alkyl group may be straight or branched-chain in configuration, the former being preferred. If x has a value below six and above ten, the spermicidal power of the formulation in an aqueous vehicle containing the said alkylphenoxypolyethoxyethanol is substantially reduced. The formulations of our invention do not require the presence of a higher unsaturated fatty acid to have superior spermicidal power.

The aqueous vehicle is an oil-in-water emulsion. The naturally occurring fatty acids, such as stearic and palmitic acids, as well as fats, such as glycerol mono-, di- and tri-stearates and palmitates may be employed in the vehicles in the nature of oil-in-water emulsions. The acids and glyceryl esters may be used alone or in combination with oils and higher alcohols such as natural oils, which includes peanut oil, sesame oil and the like, and fatty alcohols, which includes cetyl, stearyl and palmityl alcohols and the like. It is preferred that a humectant, such as glycerin, propylene glycol, sorbital and the like, also be present in the formulation.

In general, the oil-in-water emulsion may be prepared by melting the fatty constituents together, such as the acids, fats, fatty alcohols and natural oils; and bringing the temperature to about 60° to 85° C. and then adding the melted constituents slowly and with good stirring to a solution of the remaining constituents in the water, which solution is also at a temperature of 60 to 85° C. After addition is complete, the formulation is stirred for at least one hour or until it has cooled to room temperature.

The amount of the alkylphenoxypolyethoxyethanol present in the various vehicles is preferably about five but may be within the range of from three to seven percent by weight.

Our invention, accordingly, comprises compositions of matter possessing the characteristics, properties, and the relation of constituents which will be exemplified in the compositions herein after described and the scope of the invention will be indicated in the claims.

For a fuller understanding of the invention reference should be made to the following examples which are given as specific illustrations. It should be understood, however, that the invention is not limited to the specific details set forth in the illustrations.

In the formulations of the following examples, all parts are given by weight:

Example I

Stearic acid	15.00
Cetyl alcohol	1.00
Potassium hydroxide	0.75
Glycerin	10.00
Para-normal-nonylphenoxypolyethoxyethanol having six ethoxy groups	5.00
Distilled water	68.25

Example II

Glyceryl monostearate	15.00
Peanut oil	5.00
Glycerin	5.00
Para-normal-nonylphenoxypolyethoxyethanol having seven ethoxy groups	5.00
Distilled water	60.00

The formulation of Example I is prepared by heating a mixture of the stearic acid and cetyl alcohol to 85° C. and adding this slowly with stirring to a solution of the remaining ingredients in the water, which is also at a temperature of 85° C. Stirring is continued until the formulation has cooled to room temperature.

The formulation of Example II is prepared by heating a mixture of the glyceryl monostearate and peanut oil to a temperature of 85° C. and adding this slowly with

stirring to a solution of the remaining ingredients in the water, which is also at a temperature of 85° C. Stirring is continued until the formulation has cooled to room temperature.

The specific spermicidal compositions of Examples I and II were tested to determine their spermicidal power according to the following procedure:

The spermicidal compositions of Examples I and II were each diluted with physiological saline solution to give concentrations of one part formulation to 150 parts saline, the saline solution containing nine grams of sodium chloride per liter of water. The dilutions of formulations in saline were shaken vigorously in order to form a uniform mixture. One cc. of each of the saline dilutions of the formulations was added to a separate test tube containing 0.2 cc. of fresh human semen. The contents were thoroughly and quickly mixed and examined microscopically in each instance to determine the motility of the spermatozoa. The time required for mixing, placing of the sample on a suitable slide and its subsequent microscopic examination required a maximum of twenty seconds. In all instances, the spermatozoa were completely immotile when first examined under the microscope. The human semen used in making the tests was obtained by pooling individual specimens from three donors and the semen specimens were collected, pooled, cooled and used within a few hours to insure that the spermatozoa had full motility at the time the tests were made. The pH of the dilutions of the formulations of Examples I and II in saline mixed with human semen were 6.8 and 7.4, respectively.

The formulations of Examples I and II are most effective at a pH of from near neutral to slightly basic. Portions of a dilution of the formulation of Example I which contained one part of the formulation to 100 parts of physiological saline solution were buffered with an acid buffer system at a pH of 4.2, 6.0, 7.4 and 8.6. The various buffered dilutions were tested for spermicidal activity in the same manner as above. The buffered dilution-semen mixtures had, for the dilutions buffered at a pH of 4.2, 6.0, 7.4 and 8.6, a pH of 5.48, 6.5, 7.22 and 8.36 respectively. One minute and fifteen seconds were required for spermatozoa to become completely immotile when mixed with the dilution buffered at a pH of 4.2; three minutes were required for spermatozoa to become completely immotile when mixed with the dilution buffered at a pH of 6.0; less than twenty seconds were required for spermatozoa to become completely immotile when mixed with the dilution buffered at a pH of 7.4; and 40 seconds were required for spermatozoa to become completely immotile when mixed with a dilution buffered at a pH of 8.6.

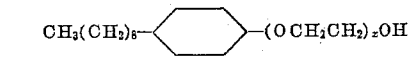
A formulation was prepared corresponding to that of Example I, except that para-tertiary octylphenoxypolyethoxyethanol having an average number of ethoxy groups of approximately 9.75 was substituted for the para-normal-nonylphenoxypolyethoxyethanol having six ethoxy groups. This formulation had a pH of 5.5 and was tested for spermicidal activity in the same manner as above. The highest dilutions of this formulation found capable of immotilizing spermatozoa in twenty seconds contained one part formulation and 150 parts physiological saline solution when buffered at a pH of 4.2, one part of formulation and 100 parts of physiological saline solution when buffered at a pH of 6.0, one part of formulation and 100 parts of physiological saline when buffered at a pH of 7.4, and one part of formulation and 80 parts of physiological saline when buffered at a pH of 8.6. This formulation was found to be irritating to vaginal mucosa and the incidence of irritation was of such an order as to render its use in the vagina undesirable. The formulations of Examples I and II were found to be without any irritating effects on the vaginal mucosa.

A formulation was prepared corresponding to that of Example I, except the para-normal-nonylphenoxypolyethoxyethanol having six ethoxy groups was replaced with water. This formulation had a pH of 6.8 and was tested for spermicidal activity in the same manner as above. A dilution containing one part of the formulation and five parts of physiological saline solution was incapable of immotilizing spermatozoa in three hours.

Since certain changes may be made in the above compositions of matter and different embodiments of the invention could be made without departing from its scope, it is intended that all matter shall be interpreted as illustrative and not in a limiting sense.

What is claimed is:

1. A spermicidal composition consisting of an alkylphenoxypolyethoxyethanol of the following general formula:



in which x has a value of six to ten inclusive incorporated in an oil-in-water emulsion vehicle.

2. A composition according to claim 1 in which the principal constituent of the oil-in-water emulsion vehicle is stearic acid.

3. A spermicidal composition according to claim 1 in which the alkylphenoxypolyethoxyethanol is predominantly para-normal-nonyl-phenoxyoctaethoxyethanol.

4. A spermicidal composition consisting of para-normal-nonylphenoxyoctaethoxyethanol incorporated in an oil-in-water emulsion vehicle.

5. A spermicidal composition consisting of para-normal-nonylphenoxyoctaethoxyethanol incorporated in an oil-in-water emulsion vehicle in which the principal constituent is stearic acid.

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