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EFFERVESCENT COMPOSITIONS CONTAINING A SURFACE ACTIVE AGENT

Nathaniel M. Elias, New York, N. Y.

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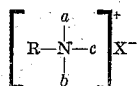
20 Claims. (Cl. 167—58)

This invention relates to nontoxic pharmaceutical compositions which effervesce on contact with moisture which are useful per se as a topical remedy, or as a vehicle for other pharmaceutically active ingredients.

It is well known that solid di- and tri-basic acids such as tartaric, succinic, citric, etc., as well as the acid salts of these acids such as the sodium or potassium acid tartrate, the sodium and potassium acid citrates, the sodium and potassium acid succinates, etc., when mixed with materials which give off carbon dioxide on contacting acids, such as sodium bicarbonate, sodium carbonate, etc., produce effervescence on contact with moisture. However, the foam produced by such compositions consists of coarse bubbles which rapidly disappear. I have found that by adding to such mixtures surface active materials in suitable amounts, much more stable foams with smaller bubbles are formed, so that any physiologic effects can be transmitted to the regions exposed to the foam more effectively and for a longer period of time. Any of the surface active agents or mixtures of compatible ones which are nontoxic may be employed for this purpose. These may be anionic, cationic, nonionic or mixtures of anionic and nonionic or cationic and nonionic surface active agents.

Numerous surface active agents have been described in "Surface Active Agents" by Schwartz & Berry (Interscience Publishers, 1949) and numerous others have been described since the publication of this book. Any of these which are nontoxic are suitable for use in the effervescent composition of my invention.

However, I have found particularly useful the alkali sulfate esters of the alkyl and aralkyl alcohols such as sodium lauryl sulfate, sodium heptadecyl sulfate and the sodium sulfate salt of alkyl phenoxy polyalkoxy alcohols, the polyglycol mono esters of fatty acids having from 8 to 18 carbons, as for example, the ricinoleic acid or lauric acid ester of polyglycol and the polyglycol mono ethers of organic hydroxy compounds having from 8 to 18 carbons, as for example, p-diisobutyl or p-tri-isopropyl phenoxy polyalkoxy ethanol or the lauryl ether of polyalkoxy-ethanol. The alkoxy chain in these compounds may vary from about 6 to 100 alkoxy groups and may be either ethoxy or propoxy groups. Finally, the quaternary nitrogen compounds of the formula



where *a*, *b* and *c* represent relatively small hydrocarbon radicals, or are fused to form a ring structure and *X*⁻ represents an anion such as Cl⁻, Br⁻, SO₄H⁻ etc. and R represents a hydrocarbon group having from 8 to 18 carbons. Examples of these are cocoanut alkyl dimethylbenzyl ammonium chloride, cetyltrimethyl ammonium chloride, dodecyl dimethylallyl ammonium chloride, etc.

Mixtures of cationic and nonionic or anionic and nonionic surface active materials may be used, but not mix-

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tures of cationic and anionic materials, since these tend to neutralize one another. I prefer to use such proportions of acid and carbonate or bicarbonate that a pH of from 2.0 to 10.0 results when the composition is dissolved in water. However, for most purposes a pH between 3.0 and 7.0 is satisfactory.

I have found it desirable to utilize surface active materials of known composition rather than those obtainable from natural sources such as root extracts, etc., since the latter are generally toxic and the products vary from batch to batch in their surface active effectiveness. Of the three general types of surface active materials I have found that I can use high proportions of the nonionic surface active materials in the compositions. Proportions as high as 25% of some of these may be used. Usually, however, 2% to 3% of nonionic surface active material is sufficient to give the desired stable small bubble formation. In the case of anionic surface active agents I have found it desirable to use proportions not over 2% in the composition. In the case of cationic surface active agents I prefer to use concentrations not over 0.2%.

Certain of such compositions have useful physiological effects, for example, many of the anionic surface active materials such as, for example, sodium lauryl sulfate, contribute bactericidal and trichomonadical properties to the composition and the same is true of the cationic surface active materials. In the case of the nonionic surface active materials, many of them have spermicidal effectiveness. However, additional materials may be added to the composition to obtain more and other specific beneficial physiologic effects, since the present compositions act as a convenient vehicle for distributing medication.

Among the various therapeutic agents that may be added to such compositions are, for example, phenolic compounds, antibiotics, sulfa compounds for bactericidal or bacteristatic effects, procaine hydrochloride, butethamine formate or hydrochloride and other anesthetizing substances for anesthetic effects, etc.

Various inert materials may be used in tablets employing the composition of the present invention such as lubricants and excipients and binding material. These may include starch, talc, sucrose, glucose, dextrose, lactose, vegetable gums such as acacia, karaya, arabic, cellulose powder or various cellulose derivatives, polyglycols, and similar materials. However, the essential portion of the composition as a vehicle for medication is the combination of the acid and preferably the carbonate or bicarbonate and the surface active material. Various additional therapeutic substances may then be incorporated for their specific effects.

The following are further illustrative of the present invention, however, this invention is not restricted thereto.

Example I

35 parts tartaric acid
35 parts sodium bicarbonate
3 parts p-triisopropylphenoxy polyethoxyethanol having approximately 9 to 11 ethoxy groups
27 parts sucrose

These ingredients are mixed to form a powder which may then be formed into tablets. When these tablets are dissolved in water a copious dense foam is formed, whereas in the absence of the p-triisopropylphenoxy polyethoxyethanol a much coarser and more evanescent foam develops. This formula is suitable as a vehicle for medication. In addition it has high spermicidal power and is useful as a spermicide. 0.2% of propylparahydroxybenzoate or 0.1% of oxyquinoline sulfate may be added as a bacteriostatic agent when it is used as a spermicide.

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Example 2

If 75 parts of the powder as formed in Example 1 is mixed with 25 parts of sulfacetamide and formed into 1 gram tablets, there is obtained an antibacterial composition which may be given per os and, after disintegration by the moisture present, the sulfacetamide is rapidly absorbed from the gastrointestinal tract. It is effective especially against gram positive cocci but has some effect against gram negative bacilli.

Example 3

If the sulfacetamide in Example 2 is replaced by p-nitrosulfathiazole, the product may again be given per os and is suitable as an adjunct in the local treatment of nonspecific ulcerative colitis and proctitis.

Example 4

If the sulfacetamide in Example 2 is replaced by aureomycin hydrochloride a tablet is obtained which is effective in various vaginal or anal viral and bacterial infections.

Example 5

If the sulfacetamide in Example 2 is replaced by bacitracin a tablet is obtained having a bactericidal effect against a wide variety of gram positive organisms including, among others, the spirochetes of syphilis and also against certain gram-negative organisms including gonococci. The tablet is also highly spermicidal.

Example 6

Crystalline potassium penicillin is used to replace the sulfacetamide of Example 2. A tablet is obtained which is effective against both spirochetes and gonococci, and is also highly spermicidal.

Example 7

Procaine hydrochloride is used to replace the sulfacetamide of Example 2. A tablet is obtained which gives local and superficial anesthesia in topical application in the vaginal and anal orifices.

Example 8

25 parts of tartaric acid and 10 parts of sodium acid tartrate may be substituted for the 35 parts of tartaric acid in Example 1 and will provide a good vehicle for medication as well as an excellent spermicide.

Example 9

2 parts of sodium lauryl sulfate and 1 part of starch may be substituted for 3 parts of the p-triisopropylphenoxypolyethoxyethanol in Example 1 and will provide a good vehicle for medication. It will also act as an excellent trichomonadicide.

Example 10

3 parts of p-diisobutylphenoxypolyethoxyethanol having approximately 9 to 11 ethoxy groups may be substituted for 3 parts of the p-triisopropylphenoxypolyethoxyethanol in Example 1 and will provide a good vehicle for medication as well as an excellent spermicidal composition.

Example 11

In Example 1, 0.2 part of cetyl dimethylbenzylammonium chloride and 2.8 parts of sucrose may be substituted for 3 parts of the tri-isopropylphenoxypolyethoxyethanol to form a highly bactericidal composition also suitable as a vehicle for medication.

Example 12

To 75 parts of any of formulae of Examples 8, 9, 10 or 11 may be added 25 parts of any of the substituents shown in Examples 2, 3, 4, 5, 6, and 7 to produce products satisfactory for the uses indicated in these latter examples.

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Example 13

In Example 1, 0.1 part of cetyl dimethylbenzylammonium chloride may be substituted for 0.1 part of the tri-isopropylphenoxypolyethoxyethanol to give a bactericidal and spermicidal composition which is also suitable as a vehicle for medication.

Example 14

In Example 1, 1 part of sodium lauryl sulfate may be substituted for 1 part of p-triisopropylphenoxypolyethoxyethanol to give a product which is both spermicidal and trichomonadicide, and which may also be used as a vehicle for medication.

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 and restricted solely by the scope of the appended claims.

I claim:

1. A non-toxic pharmaceutical composition which effervesces on contact with moisture which comprises a solid non-toxic polybasic acidic material having at least one acidic hydrogen atom, an alkali metal salt of carbonic acid, and a surface active agent, said polybasic acid material and said alkali metal salt constituting together a major portion of said composition, said polybasic acid material being present in sufficient amounts to convert a major portion of said alkali metal salt to carbon dioxide on contact with moisture, whereby a strong effervescent effect results, said polybasic acid material and said alkali metal salt also being present in said composition in such amounts that a pH from 2.0 to 10.0 results when the composition is dissolved in water.

2. A non-toxic pharmaceutical composition which effervesces on contact with moisture comprising a solid non-toxic acid material having at least one acidic hydrogen atom, a second material which reacts with said acid material on contact with moisture to form a non-toxic gas, and a surface active agent, said acid material and said second material constituting together a major portion of said composition, said acid material being present in sufficient amounts to convert a major portion of said second material to said non-toxic gas on contact with moisture whereby a strong effervescent effect results, said acid material and said second material being present in said composition in such amounts that a pH from 2.0 to 10.0 results when the composition is dissolved in water.

3. A non-toxic pharmaceutical effervescent tablet which effervesces on contact with moisture which comprises a solid non-toxic polybasic organic acid material having at least one acidic hydrogen atom, an alkali metal salt of carbonic acid, and a surface active agent, said polybasic acid material and said alkali metal salt together constituting a major portion of said tablet, said polybasic acid being present in sufficient amounts to convert a major portion of said alkali metal salt into carbon dioxide on contact with moisture whereby a strong effervescent effect results, said polybasic acid material and said alkali metal salt also being present in said composition in such amounts that a pH from 2.0 to 10.0 results when the composition is dissolved in water.

4. A composition according to claim 3 wherein the surface active agent is an anionic surface active agent.

5. A composition according to claim 3 wherein the surface active agent is a cationic surface active agent.

6. A composition of matter according to claim 3 wherein the surface active agent is a nonionic surface active agent.

7. A composition according to claim 3 wherein the surface active agent is a mixture of an anionic and non-ionic surface active agents.

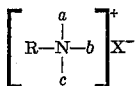
8. A composition according to claim 3 wherein the

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surface active agent is a mixture of a cationic and non-ionic surface active agents.

9. A composition according to claim 4 wherein the anionic surface active agent is selected from the class consisting of alkali sulfate esters of alkali and aralkyl alcohols.

10. A composition according to claim 5 wherein the cationic surface active agent is a quaternary nitrogen compound of formula



wherein *a*, *b*, *c* are relatively low molecular weight hydrocarbon radicals, *R* is a hydrocarbon radical having from 8 to 18 carbon atoms and *X*⁻ is anion selected from the class consisting of Cl⁻, Br⁻, SO₄H⁻ and wherein *a* and *b*; *a* and *c*; *b* and *c*; and *a*, *b* and *c* may be cyclized to form a ring structure.

11. A composition according to claim 6 wherein the nonionic surface active agent is selected from the group consisting of mono ethers of polyglycols with organic hydroxy compounds having from 8 to 18 carbon atoms wherein the polyglycol residue has from 6 to 100 alkoxy groups in the chain, and mono esters of said polyglycols with fatty acids having from 8 to 18 carbon atoms.

12. A non-toxic pharmaceutical tablet which effervesces on contact with moisture which comprises a solid non-toxic polybasic acidic material having at least one acidic hydrogen atom, an alkali metal salt of carbonic acid, and a nonionic surface active agent, said acidic material and said salt of carbonic acid being present in such amounts so that when the composition is dissolved in water the pH of the solution has a value of about 2.0 to 10.0, and said surface active agent being present in an amount not exceeding 25% by weight of the composition wherein said polybasic acid material and said alkali metal salt constitute together a major portion of said composition, said polybasic acid material being present in sufficient amounts to convert a major portion of said alkali metal salt to carbon dioxide on contact with moisture, whereby a strong effervescent effect results.

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13. A composition according to claim 12 wherein the acidic material and salt of carbonic acid are present in such amounts so that when the composition is dissolved in water the pH of the solution has a value of about 3.0 to 7.0 and said surface active agent is present in the amount of about 0.1% to 3% by weight of the composition.

14. An effervescent tablet suitable for use as a spermicide having a composition according to claim 12 wherein the nonionic surface active agent is selected from the class consisting of *p*-diisobutylphenoxypolyethoxyethanols and *p*-triisopropylphenoxypolyethoxyethanols.

15. An effervescent tablet having the composition described in claim 2 and containing in addition a sulfa drug.

16. An effervescent tablet having the composition described in claim 2 and containing in addition an antibiotic material.

17. An effervescent tablet having the composition described in claim 2 and containing in addition an antibacterial and antiviral agent.

18. An effervescent tablet according to claim 14 containing in addition a material selected from the class consisting of penicillin and bacitracin and suitable as a combined prophylactic material to protect against the gonococcus and the spirochete and as a spermicide.

19. An effervescent tablet having the composition described in claim 2 and containing in addition a local anesthetic.

20. An effervescent tablet effective as a spermicide and a trichomonadicide having the composition described in claim 2 wherein the surface active agents is a mixture of sodium lauryl sulfate and *p*-triisopropylphenoxypolyethoxyethanol.

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