AQUEOUS SOLUTIONS OF HIGHER FATTY ALCOHOLS AND HIGHER FATTY ALCOHOL ESTERS AND A METHOD FOR PREPARING THE SAME

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The present invention relates to aqueous solutions of higher fatty alcohols and higher fatty alcohol esters, and a method for preparing the same, and more particularly to aqueous solutions of the aforesaid materials which are substantially crystal clear and may be used as such in pharmaceutical and cosmetic preparations, and to a method of making such crystal clear solutions.

It has long proved desirable to have the higher fatty alcohols and their esters available in crystal clear aqueous solutions. These materials which are normally insoluble in water have wide applications in a variety of pharmaceutical and cosmetic preparations.

While the use of solubilizing agents has been suggested, the same have proved to be utterly impractical because of the very high concentration of solubilizing agent to alcohol that has been required.

This invention has as an object the provision of aqueous crystal clear solutions of normally water-insoluble fatty alcohols, such as the fatty alcohols having from twelve to twenty carbon atoms, and their esters including their methyl, ethyl, propyl, isopropyl, butyl, isobutyl, amyl, and isoamyl esters.

This invention has as another object the provision of a method for forming the aforesaid crystal clear aqueous solutions.

This invention has as still another object the provision of aqueous crystal clear solutions of normally water-soluble fatty alcohols and esters of the aforesaid types containing a relatively low concentration of solubilizing agent.

This invention has as still another object the provision of a method for forming the aforesaid crystal clear aqueous solutions in which the concentration of solubilizing agent is minimized.

Other objects will appear hereinafter.

I have found that crystal clear aqueous solutions of the higher fatty alcohols, namely the alcohols having from twelve to twenty carbon atoms, and the esters of such fatty alcohols and in particular the esters of such fatty alcohols derived from aliphatic acids of such alcohols and from alcohols having from one to five carbon atoms may be dissolved in water to form a crystal clear aqueous solution provided that Tween 60, a polyoxyethylene sorbitan monostearate emulsifying agent manufactured by the Atlas Powder Company of Wilmington, Delaware, is present in the aqueous solution in a weight ratio in respect to the alcohol or ester of at least three parts by weight of Tween 60 to one part by weight of the alcohol or ester. I have found that the higher fatty alcohols or their esters which are normally liquid require a relatively lower weight ratio of Tween 60 to alcohol or ester than do the alcohols or esters which are normally solids. For example, I have determined that lauryl alcohol which is a liquid may be solubilized to form a crystal clear aqueous solution with amounts of Tween 60 of as low as four to one, namely four parts by weight Tween 60 per part by weight of lauryl alcohol. On the other hand in order to form crystal clear aqueous solutions of cetyl alcohol a higher ratio of Tween 60 must be used, namely something of the order of ten or eleven parts by weight of Tween 60 per part by weight of cetyl alcohol. However, by adding liquid sorbitol in minor concentrations the weight requirements for Tween 60 in respect to the alcohol may be markedly reduced. The solubility of the solid alcohols and esters may also be increased by using such materials in admixture with normally liquid higher alcohols or the esters of the higher alcohols. For example, a lower weight ratio of Tween 60 to alcohol is obtained when a mixture of cetyl alcohol and lauryl alcohol is solubilized in accordance with the method of my invention than would be expected from the arithmetic sum of the relative amounts of Tween 60 that would be required were these materials solubilized separately. I have performed extensive researches with highly purified lanolin oils and find that these materials also exert a high solubilizing action on the solid higher alcohols and their esters.

The method of the present invention comprises forming a mixture of the alcohol and/or ester with the Tween 60 in a weight ratio which should be at least three to one, namely three parts by weight of the Tween 60 to one part by weight of the alcohol and/or ester, and then adding water to the mixture in a thin stream at room temperature under conditions of high agitation. I have found that normally the use of temperatures above room temperature is not advisable as it tends to render the resultant solutions cloudy. Nevertheless, with isopropyl myristate solutions it is necessary to raise the temperature of such solutions after the formation thereof and their agitation to a boiling temperature in order to effect crystal clear solutions. Normally, under no circumstances should the aqueous solution be raised to a temperature in excess of 150°F. to 160°F. and normally the crystal clear solutions should not be raised to a temperature above 120°F. to 130°F. at any time during their formation or subsequent to their formation.

I have found that it is necessary in the method of my invention to effect high agitation. Moreover, such agitation should be continued for protracted time periods, such as at least from five to thirty minutes inclusive of the time of addition of water to the mixture of Tween 60 and the alcohol and/or ester. Due to the necessity for extended and severe agitation, I have found that it is desirable to add a trace amount of an anti-foaming agent to my compositions, such as any of the wide variety of silicone anti-foaming agents which are commercially available.

I have found that crystal clear aqueous solutions may be prepared from any of the higher fatty alcohols, and in particular the fatty alcohols having from twelve to twenty carbon atoms. Thus, aqueous solutions may be prepared from lauryl alcohol, myristyl alcohol, palmityl alcohol, oleyl alcohol, stearyl alcohol, cetyl alcohol, etc. I have found also that the esters of the aforesaid alcohols, and in particular the esters derived from the acids of such alcohols and alcohols having from one to five carbon atoms may be used to form crystal clear aqueous solutions in accordance with the present invention.

Examples of such esters include methyl laurate, ethyl laurate, propyl laurate, isopropyl laurate, butyl laurate, isobutyl laurate, amyl laurate, isoamyl laurate, methyl stearate, ethyl stearate, propyl stearate, isopropyl stearate, butyl stearate, isobutyl stearate, amyl stearate, isoamyl stearate, methyl oleate, ethyl oleate, propyl oleate, isopropyl oleate, butyl oleate, isobutyl oleate, amyl oleate, isoamyl oleate, methyl myristate, ethyl myristate, propyl myristate, isopropyl myristate, butyl myristate, isobutyl myristate, amyl myristate, isoamyl myristate, etc.

As heretofore indicated, it is easier to dissolve the fatty alcohols or the aforesaid esters of the fatty alcohols in water in accordance with the present invention when the fatty alcohol or ester is itself a liquid. However, there is a definite synergistic solubilizing action when a plurality of fatty alcohols and/or esters are solubilized together when the mixture includes liquid
alcohols or esters. Thus, I have noted a definite tendency for the liquid alcohols or liquid esters to aid in the solubilizing of the solid alcohols or esters.

I have found that Tween 60 manufactured by the Atlas Powder Company of Wilmington, Delaware, is a specific for the compositions and method of the present invention. Tween 60 may be designated as (polyoxyethylene)₉₈ sorbitan monostearate. It is a yellow oily liquid having a specific gravity of 1.1, a flash point of about 545°F, and a fire point of about 635°F. It has an acid number of from 3.0 to 2.0, a saponification number of from 54 to 55, and a hydroxyl number of from 81 to 96. Generally, it contains from 2.5 to 3.0 weight percent of water.

I have determined that Tween 60 is unique in respect to the compositions of the present invention. Thus, the closely related Tween 61 sold by Atlas Powder Company of Wilmington, Delaware, which may be designated as (polyoxyethylene)₉₉ sorbitan monooleate was found to be unsatisfactory for the purposes of the present invention. Tween 61 is a tan waxy solid having a specific gravity of 1.06, a flash point of 460°F, and a fire point of 520°F. This material has an acid number of from 48 to 52, a saponification number of from 98 to 113, and a hydroxyl number of from 170 to 200.

A wide variety of related emulsifying agents sold by Atlas Powder Company of Wilmington, Delaware, have been tested by me and have been found to be unsatisfactory for the purposes of the present invention. These agents have included Tween 20 which is a polyoxyethylene sorbitan monolaurate, Tween 40 which is a polyoxyethylene sorbitan monopalmitate, Tween 21 which is a polyoxyethylene sorbitan monostearate, Tween 55 which is a polyoxyethylene sorbitan tristearate, Tween 80 which is a polyoxyethylene sorbitan monoleate, Tween 81 which is a polyoxyethylene sorbitan monooleate, Myris 52 which is a polyoxyethylene stearate, Arlacel 60 which is sorbitan monooleate, G-1441 which is a polyoxyethylene sorbitol laurold derivative, G-2162 which is a polyoxyethylene oxypropylene stearate, and the alkyl phenyl ether of polyethylene glycol.

The chemical characteristics and physical specifications of materials referred to above are set forth in the publication of the Atlas Powder Company of Wilmington, Delaware, entitled: General Characteristics of Atlas Surfactants, which was copyrighted in 1977. Crystal clear aqueous solutions of the aforesaid fatty alcohols and/or esters of the fatty alcohols may be prepared in concentrations up to about 8 to 10 weight percent of the alcohol or ester.

I have discovered that minor amounts of aqueous sorbitol solutions play a profound role in reducing the requirements of Tween 60. Thus, while the aqueous sorbitol solutions have no effect on solubilizing fatty alcohols by themselves, there is a synergistic action between these materials and Tween 60 which markedly reduces the requirements for Tween 60 in a crystal clear solution. The concentration of the aqueous sorbitol solution may be very low, and I have determined that sorbitol is markedly effective in reducing the requirements of Tween 60 when present in as low as one-twentieth of the combined weight of the Tween 60 and the alcohol and/or ester. Thus, for a given alcohol or ester the presence of such minor amount of aqueous sorbitol may have the requirements of Tween 60 to produce a clear solution.

The efficacy of sorbitol in terms of its synergistic action is achieved at a relatively low threshold. Thus, testing has demonstrated that when the threshold concentration of the aqueous solution of sorbitol is reached, increasing the concentration of the sorbitol by a factor of many hundred percent barely modifies its action on the Tween 60 for solubilization. Thus, where a sufficient amount of sorbitol to effect solubilization of a given Tween 60 and alcohol and/or ester mixture is determined, as by a minor amount of preliminary testing, further increase of the sorbitol will be of but little value. Generally, the threshold concentration of the sorbitol is reached within the range of about 4 weight percent to 20 weight percent based on the mixture of Tween 60 and alcohol and/or ester.

The following examples are set forth merely by way of illustration and not by way of limitation:

**Example I**

Five grams of oleyl alcohol were mixed with 45 grams of Tween 60. The aforesaid mixture was then placed in a Waring high shear Blender. Two hundred grams of distilled water containing a drop of Dow Corning Anti-Foam B silicone anti-foaming agent obtained from the Dow Corning Corporation, 600 Fifth Avenue, New York, New York, were added to the mixture of Tween 60 and oleyl alcohol as a thin stream under vigorous agitation conditions at room temperature. The agitation was continued after the addition of the water and silicone anti-foaming agent had been completed for a period of ten minutes with the total time of agitation being about fifteen minutes. A crystal clear solution was obtained. Heating of this crystal clear solution to its boiling temperature and subsequent cooling to room temperature produced a cloudy dispersion.

**Example II**

The procedure set forth in Example I was repeated except that in place of the 5 grams of oleyl alcohol there was substituted 5 grams of lauryl alcohol. A crystal clear solution was obtained. Heating this crystal clear solution to its boiling temperature and then cooling it to room temperature produced a cloudy dispersion.

**Example III**

The procedure set forth in Example I was repeated except that in place of the 5 grams of oleyl alcohol there was substituted 5 grams of ethyl laurate. A crystal clear solution was obtained. Heating this crystal clear solution to its boiling temperature and then cooling it to room temperature produced a cloudy dispersion.

**Example IV**

The procedure set forth in Example III was repeated except that in place of 45 grams of Tween 60 there was substituted 35 grams of Tween 60 and in place of the 200 grams of distilled water there was substituted 210 grams of distilled water. This produced a crystal clear solution. Heating this crystal clear solution to its boiling temperature and then cooling to room temperature produced a cloudy dispersion.

**Example V**

The procedure set forth in Example III was repeated except that the amount of Tween 60 was 25 grams and the amount of distilled water was 220 grams. The resultant mixture constituted a cloudy dispersion. Heating the aforesaid cloudy dispersion to its boiling temperature and then cooling to its room temperature failed to clarify the dispersion.

**Example VI**

The procedure set forth in Example III was repeated except that in place of 45 grams of Tween 60 there was substituted 30 grams of Tween 60 and in place of the 200 grams of water there was substituted 215 grams of water. This produced a crystal clear solution. Heating of the aforesaid crystal clear solution to its boiling temperature and then cooling to room temperature produced a cloudy dispersion.

**Example VII**

The procedure set forth in Example II was repeated
except that in place of 45 grams of Tween 60 there was substituted 35 grams of Tween 60 and in place of the 200 grams of water there was substituted 210 grams of water. This produced a crystal clear solution. Heating of the aforesaid crystal clear solution to its boiling temperature and then cooling to room temperature produced a cloudy dispersion.

**Example VIII**

The procedure set forth in Example II was repeated except that in place of the 45 grams of Tween 60 there was substituted 30 grams of Tween 60 and in place of the 200 grams of distilled water there was substituted 215 grams of distilled water. This produced a crystal clear solution. Heating of this crystal clear solution to its boiling temperature and then cooling to room temperature produced a cloudy dispersion.

**Example IX**

The procedure set forth in Example I was repeated except that in place of the 45 grams of Tween 60 there was substituted isopropyl myristate. This produced a cloudy dispersion. Heating of the resultant cloudy dispersion to its boiling temperature and then cooling to room temperature produced a crystal clear solution.

**Example X**

The procedure set forth in Example IX was repeated except that in place of the 45 grams of Tween 60 there was substituted 35 grams of Tween 60 and in place of the 200 grams of distilled water there was substituted 210 grams of distilled water. The identical results set forth in Example IX were obtained.

**Example XI**

The procedure set forth in Example IX was repeated except that in place of the 45 grams of Tween 60 there was substituted 30 grams of Tween 60 and in place of the 200 grams of distilled water there was substituted 215 grams of distilled water. The identical results set forth in Example IX were obtained.

**Example XII**

The procedure set forth in Example I was repeated except that in place of the 3 grams of oleyl alcohol there was substituted 5 grams of cetyl alcohol. The aforesaid procedure produced a cloudy dispersion as I have found that cetyl alcohol requires relatively high ratios of Tween 60 to cetyl alcohol to effect solubilization. Heating of the aforesaid cloudy dispersion to its boiling temperature and then cooling to its room temperature failed to clarify the mixture.

**Example XIV**

The solubilizing effect of one alcohol or ester upon another is apparent in this example wherein the procedure of Example I was followed using a mixture of 35 grams of Tween 60, one and one-quarter grams of cetyl alcohol, and three and three-quarter grams of isopropyl myristate, with 210 grams of distilled water containing one drop of anti-foaming agent being added. This produced a very slightly cloudy dispersion. Raising the Tween 60 concentration to 40 grams produces a clear solution. Heating of the slightly cloudy dispersion produced by this example to its boiling temperature and then cooling to its room temperature produced a cloudy mixture.

**Example XV**

The profound effect of Arlex, an aqueous solution comprising 83 weight percent of sorbitol and related polyhydric materials, sold by the Atlas Powder Company, of Wilmington 99, Delaware, was demonstrated in this example.

Sixty grams of Tween 60, 15 grams of isopropyl myristate and 3 grams of Arlex were heated together to 158° F. This produced a translucent fluid. This fluid was then diluted to a 2 weight percent concentration with distilled water, and the resultant mixture heated to a boil. Upon cooling to room temperature a clear solution was obtained, which was rechecked after two weeks and found to remain unchanged.

**Example XVI**

The procedure set forth in Example XV was repeated, except that 75 grams of Tween 60 were used in place of the 60 grams. This produced a crystal clear solution, namely a solution far more clear than that of Example XV, which was however a clear solution.

**Example XVII**

The profound synergistic solubilizing effect of having a plurality of alcohols and esters present may be demonstrated by the subject example:

Using the procedure of the preceding example it was determined that approximately 8 parts by weight of Tween 60 to 1 part by weight of isopropyl myristate were required to produce a crystal clear 2 weight percent aqueous solution.

Nevertheless, a crystal clear solution was obtained using the following composition with the materials being present in grams: 60 grams of Tween 60, 15 grams of lanolin oil, 7.5 grams of isopropyl myristate, 2.5 grams of cetyl alcohol, 1.2 grams of hexachlorophene, and 1.0 gram of Arlex.

Similarly, a crystal clear solution was obtained from the mixture comprising 60 grams of Tween 60, 7.5 grams of lanolin oil, 7.5 grams of oil of mink, 7.5 grams of isopropyl myristate, 2.5 grams of cetyl alcohol, and 1.2 grams of hexachlorophene.

The results set forth above have been repeated with a wide variety of mixtures of the aforesaid alcohols and esters. Thus, using the method of the present invention crystal clear solutions may be prepared from mixtures of cetyl alcohol and oleyl alcohol and mixtures of cetyl alcohol, oleyl alcohol and ethyl laurate, and mixtures of myristyl alcohol, isoamyl oleate and laurel alcohol, and mixtures comprising four and more alcohols and/or esters as, for example, mixtures comprising cetyl alcohol and laurel alcohol and ethyl stearate and ethyl laurate. By the use of mixtures comprising solid alcohols and liquid and/or solid alcohols and/or esters it is possible to produce crystal clear solutions of such solid alcohols at concentrations of Tween 60 below those necessitated to render a crystal clear solution when the alcohol is used by itself.

The crystal clear solutions of the present invention have a wide applicability in pharmaceuticals and cosmetics. The concentration of Tween 60 therein is far below that of any presently known solubilizing agent. Thus, the present invention enables the desirable properties of the fatty alcohols and/or the esters of the fatty alcohols to be conferred upon pharmaceutical and cosmetic preparations comprising crystal clear aqueous solutions. It is to be understood that crystal clear aqueous solutions comprising the subject invention and other additives which are neither fatty alcohols nor esters of fatty alcohols are to be deemed as included within the following claims.

The present invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof and, accordingly, reference should be made to the appended claims, rather than to the foregoing specification as indicating the scope of the invention.

**Example XX**

The profound effect of Arlex, an aqueous solution com-
I claim:

1. A crystal clear aqueous solution consisting essentially of a mixture of water, (polyoxyethylene)$_{20}$ sorbitan monostearate, and at least one compound selected from the group consisting of alcohols having 12 through 20 carbon atoms in an alkyl chain and the 1 through 5 carbon atom alkyl chain esters of acids derived from such alcohols, with such (polyoxyethylene)$_{20}$ sorbitan monostearate being present in said mixture in a weight ratio of at least 5 to 1 in respect to said compound.

2. A crystal clear aqueous solution in accordance with claim 1 in which a trace amount of a silicone anti-foaming agent is present in the solution.

3. A crystal clear aqueous solution in accordance with claim 1 in which the compound is oleyl alcohol.

4. A crystal clear aqueous solution in accordance with claim 1 in which the compound is lauryl alcohol.

5. A crystal clear aqueous solution in accordance with claim 1 in which the compound is ethyl laurate.

6. A crystal clear aqueous solution in accordance with claim 1 in which the compound is isopropyl myristate.

7. A crystal clear aqueous solution in accordance with claim 1 in which a plurality of compounds are present, one of said compounds being an alcohol, and another of said compounds being an ester, with the (polyoxyethylene)$_{20}$ sorbitan monostearate being present in the mixture in a weight ratio of at least 3 to 1 in respect to the total combined weights of such compounds.

8. A crystal clear aqueous solution in accordance with claim 1 and further containing sorbitol.

9. A solution in accordance with claim 1 consisting essentially of a plurality of different compounds selected from the group consisting of alcohols having from 12 through 20 carbon atoms in an alkyl chain and the 1 through 5 carbon atom alkyl chain esters of acids derived from such alcohols, with the (polyoxyethylene)$_{20}$ sorbitan monostearate being present in said mixture in a weight ratio of at least 3 to 1 in respect to the combined weights of said compounds.

10. A crystal clear aqueous solution in accordance with claim 9 in which at least one of the compounds is a liquid.

11. A method for forming a crystal clear aqueous solution which consists essentially of the step of adding water to a mixture of (polyoxyethylene)$_{20}$ sorbitan monostearate and at least one compound selected from the group consisting of alcohols having from 12 through 20 carbon atoms in an alkyl chain and the 1 through 5 carbon atom alkyl chain esters of acids derived from such alcohols, with such (polyoxyethylene)$_{20}$ sorbitan monostearate being present in said mixture in a weight ratio of at least 3 to 1 in respect to said compound.

12. A method in accordance with claim 11 in which a trace amount of a silicone anti-foaming agent is present with the water at the time of the addition.

13. A method in accordance with claim 11 in which the addition is carried out at a temperature below 160°F.

14. A method in accordance with claim 11 in which sorbitol is present in the mixture to which water is added.

15. A method in accordance with claim 11 in which the (polyoxyethylene)$_{20}$ sorbitan monostearate and the compound selected from the group consisting of the alcohols and esters are mixed under conditions of vigorous agitation prior to being blended with water.

16. A method in accordance with claim 11 in which the mixture to which the water is added consists essentially of a plurality of compounds and in which the (polyoxyethylene)$_{20}$ sorbitan monostearate is present in the mixture in a weight ratio of at least 3 to 1 in respect to the combined total weight of said compounds.

17. A method in accordance with claim 11 in which at least one of the compounds is a liquid.

18. A method for forming a crystal clear aqueous solution of isopropyl myristate which consists essentially of the steps of adding water to a mixture of (polyoxyethylene)$_{20}$ sorbitan monostearate and isopropyl myristate, with such (polyoxyethylene)$_{20}$ sorbitan monostearate being present in said mixture in a weight ratio of at least 3 to 1 in respect to said isopropyl myristate at a temperature of below 160°F., raising the combined aqueous mixture to its boiling temperature, and then cooling the combined aqueous mixture.

References Cited in the file of this patent

UNITED STATES PATENTS
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