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Carlson et al.

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[54] **STABLE AQUEOUS ANTI-DANDRUFF
SHAMPOO CONTAINING CAPTAN**

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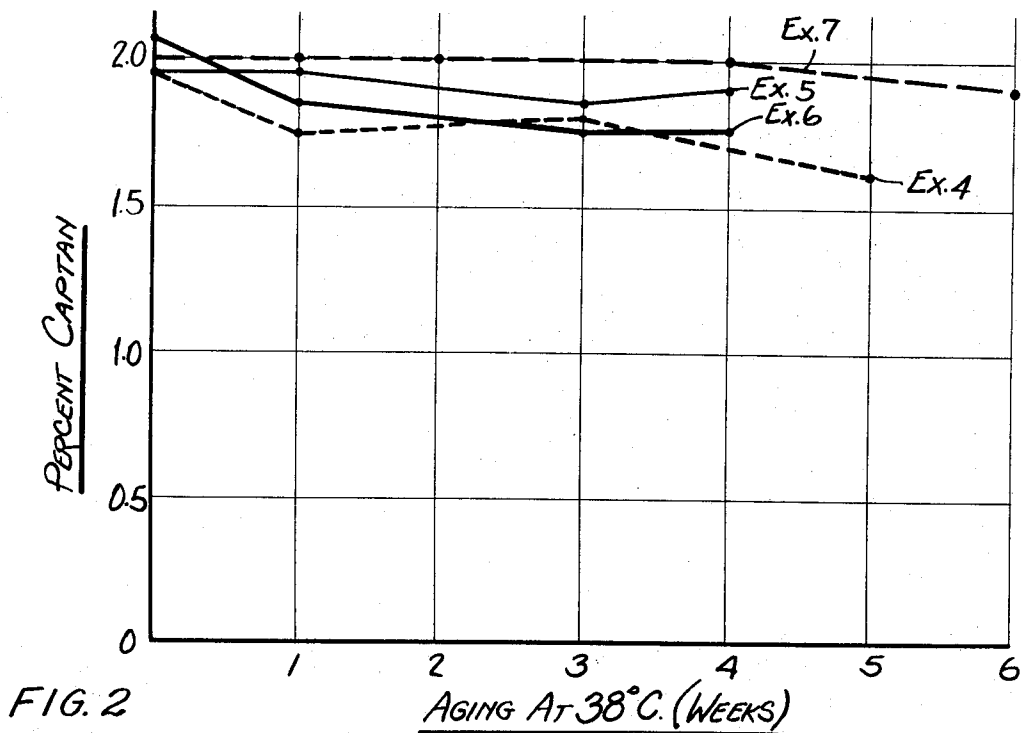
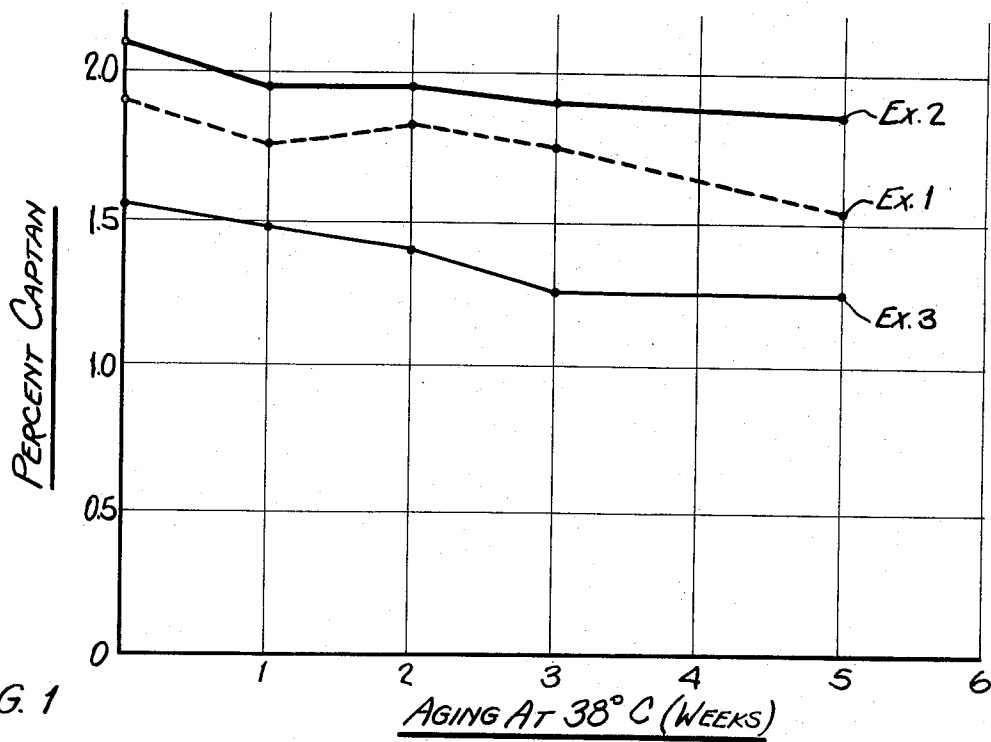
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[57]

ABSTRACT

N-Trichloromethylthio-4-cyclohexene-1,2-dicarboximide (captan) may be incorporated in an aqueous shampoo formulation having an acceptable shelf life if the pH of the formulation is in the range of from about 3.0 to about 7.0 and the detergent is at least one of an organic sulfate or sulfonate detergent or a non-ionic detergent free from amino nitrogen.

4 Claims, 2 Drawing Figures



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STABLE AQUEOUS ANTI-DANDRUFF SHAMPOO CONTAINING CAPTAN

This application is a continuation-in-part of application, Ser. No. 570,053 filed Aug. 3, 1966, now abandoned.

The present invention relates to shampoo compositions comprising N-trichloromethylthio-4-cyclohexene-1,2-dicarboximide as an active agent, and more particularly to such compositions in which the said active agent is substantially stable.

The compound N-trichloromethylthio-4-cyclohexene-1,2-dicarboximide, which is also known by the generic name captan, is well known in the art as a fungicide. Soon after the invention of captan, researchers found that it possessed exceptional bactericidal and fungicidal properties. In view of the continuing interest in developing anti-dandruff preparations, captan was tested by various researchers to determine its properties in this respect. (See Ball, *A New Treatment for Seborrheic Dermatitis*, A.M.A. Arch. Dermatol., 71, 696-8 (1955); Tarnoff, *Dermato-Applications of Sulphur-bearing Organic Bactericide-Fungicides*, American Perfumer, 77, 35-38 (1962); and Lubowe, *Anti-Seborrheic Agents*, Drug and Cosmetic Industry, 81, 602-3, 674, 676 (1957).)

Although the work described in the literature indicates that captan has outstanding potential as an anti-dandruff agent, aqueous shampoo formulations containing captan have not attained widespread use. This is because it was generally found that captan was unstable and rapidly decomposed in aqueous shampoo formulations, and consequently the bactericidal and fungicidal effect of such formulations had exceedingly short shelf life.

In view of the foregoing, it is an object of this invention to provide an aqueous shampoo composition containing captan in which the captan is relatively stable.

It is a further object of this invention to provide an aqueous anti-dandruff shampoo composition which contains captan and has a good shelf life.

Further objects and features of the invention will become apparent upon reading the description which follows in conjunction with the appended drawings.

In the drawings:

FIGS. 1 and 2 are graphs showing the stability of captan in various aqueous shampoo formulations as a function of time.

Briefly stated, the aqueous compositions of this invention comprise water, captan, and at least one surface active agent of certain selected classes of known detergents which provides effective detergent action at a pH of less than about 7.0, and water. All of the shampoo formulations of this invention have a pH in the approximate range of from 3.0 to 7.0. The preferred range is from 4.5 to 6.5 because it more closely approximates the range of pH of human skin. The preferred formulations contain certain anionic detergents, certain nonionic detergents, or a combination thereof.

Hair shampoo compositions according to this invention may contain an anionic detergent as the sole detergent, but in general more effective results are obtained in compositions containing both an anionic and a nonionic detergent. An anionic detergent agent is highly desirable because the anionics usually give the highest foaming, exceeding that which can be obtained with a nonionic detergent. On the other hand, the nonionic detergents give good foam stability and hair "feel", and except for those containing amino nitrogen, are generally more compatible with captan. Consequently, in order to take advantage of the beneficial properties of both anionic and nonionic detergents, it has been found that shampoo formulations of the invention desirably include a combination of both types.

As used herein, the word "detergent" is employed in the conventional sense as meaning a cleansing substance. It is to be noted that detergent compounds, i.e., cleansing compounds, are well known to the art as are the conditions under which they exhibit detergent activity. Accordingly, the present invention does not depend upon which of the known surface active compounds are detergents and which are not. Thus, although illustrative examples of useful detergents are given

below, such illustration should not be construed as making the disclosed compositions, as such, critical to the invention. What is important is the discovery that, of the well-known surface active agents which have sufficient detergent action to be useful in aqueous shampoo formulations, only certain ones can be used without adverse effect on captan. That is, certain surface active compounds which have detergent properties and are frequently used in aqueous shampoos have been found to contribute to the instability of captan, and the present invention is based upon the discovery of a class of detergents having use in aqueous shampoos which does not promote the decomposition of captan. Specifically, it has been discovered that organic sulfate and organic sulfonate anionic detergents and nonionic detergents free of amino nitrogen do not cause captan to decompose in aqueous shampoo formulations, whereas organic carboxylate anionic detergents, and nonionic detergents including amino nitrogen do contribute to the decomposition of captan.

Particularly preferred classes of known anionic detergents for use in accordance with this invention are anionic detergents within the classes of long chain aliphatic alcohol sulfates and sulfonates, N-fatty acylamides of aminosulfonic acids, fatty acyl esters of hydroxysulfonic acids, alkylaryl sulfonates, and sulfonates of certain nonionic detergents as discussed below. Nonionic detergents which are preferred for use in accordance with this invention include ethylene oxide adducts of long chain aliphatic alcohols and alkylphenols as well as the ethylene oxide-propylene oxide condensates known as the "Pluronic."

Typically, detergents of the long chain aliphatic alcohol sulfate and sulfonate type have alkyl groups of from about 12 to about 26 carbons, with sodium lauryl sulfate serving to illustrate this class of detergents.

Fatty acyl amides of amino-sulfonic acids typically include amides of aliphatic acids of from about 12 to about 18 carbons and an aminosulfonic acid such as taurine. The acyl group can be pure, i.e., be derived from a single acid, or it can be a mixture of acyl groups, such as that obtained from coconut oil, hereinafter referred to as cocoyl. In addition to the acyl group, the amino radical may be substituted by a lower alkyl, e.g., methyl, group. A typical example of a detergent within this class is sodium N-cocoyl-N-methyltaurate, which is commercially available under the trade mark Igepon TC-42.

The fatty acyl esters of hydroxysulfonic acids, like the amides just discussed, typically include acyl radicals of from about 12 to about 18 carbons. The hydroxysulfonic acid moiety is typified by isethionic acid. This class of detergents is illustrated by sodium cocoylisethionate, which is available commercially under the trade mark Igepon AC-78.

Alkylaryl sulfonate detergents are found within the class of surface active compounds having at least eight carbons, e.g., eight to 22 carbons and preferably 10-16 carbons, in the alkyl group thereof. A typical example of such a detergent is sodium dodecylbenzene sulfonate.

The last of the preferred anionic detergents are found in the class of surface active agents composed of sulfonates of ethylene oxide adducts of alkylphenols as disclosed below. A typical example of a useful detergent within this class is the alkyl aryl polyether sulfonate marketed under the trade mark Triton X-202.

Nonionic detergents which are of particular utility include ethylene oxide adducts of long chain aliphatic alcohols and alkylphenols wherein the number of ethylene oxide groups is balanced with respect to the hydrophobic long chain aliphatic or alkylphenol moiety to give good detergent and surface active qualities. Typically, long chain aliphatic groups contain from about 12 to about 26 carbons, and the alkylphenols have alkyl groups of at least about eight carbons, e.g., from eight to about 20 carbons, with octyl and nonyl being preferred. The number of ethylene oxide units can vary, but typically is at least about three, and may be in the range of from about six to about 100. Illustrative examples of these nonionic detergents include alkylphenoxy polyoxyethylene ethanols such as Makon 10 and Makon NP-10.

Another desirable class of nonionic detergents is that sold under the trade mark Pluronics and disclosed in U.S. Pat. No. 2,674,619. These detergents are ethylene oxide-propylene oxide condensates composed of a polyoxypropylene hydrophobic portion having a molecular weight of from about 950 to about 3,250, and having from about 10 to about 80 percent of the product composed of polyoxyethylene hydrophilic units. A useful Pluronic detergent is Pluronic 68, which has a polyoxypropylene unit having a molecular weight of about 1,750 and about 80 percent polyoxyethylene.

The presence of amino nitrogen in nonionic detergents has been found to be highly deleterious to the stability of captan. The presence of such compounds is therefore avoided in the compositions of this invention. The term "amino nitrogen" is used generically to denote trivalent nitrogen and encompasses amines, amides, and substituted amines and amides. The use of alkanolamide compounds such as lauric diethanolamide in compositions of this invention is avoided because of the tendency of such compounds to cause rapid breakdown of captan.

Amphoteric detergents, such as alkali metal salts of N-cocobeta-amino-propionate, should also be avoided because of their tendency to cause decomposition of captan.

Nonionic detergents in general do not possess the superior foaming properties which are typical of anionic detergents, and for this reason it is desirable to use the nonionics in combination with anionic types. Where high sudsing properties are not required, the nonionic detergents useful in the present invention can be employed satisfactorily even in the absence of an anionic detergent.

Certain surface active materials not possessing cleansing properties are commonly compounded into shampoo formulations as emulsifiers for fatty or oily emollients, as thickening agents, and for other special purposes. Among them are acetylated monoglyceride, acetylated lanolin, and glyceryl monostearate, all of which are nonionic. Tests have shown that these materials are not deleterious to captan in the concentrations in which they are normally used.

Compositions of this invention may be prepared in any desired consistency, liquid, paste, or solid, by means well known to the art. In general, the proportion of total detergent may vary from about as low as 10 percent up to about 90 percent of the total weight of the aqueous shampoo compositions, with the products varying from fluid to paste-like products as the proportion of detergent is increased. The considerations which dictate the proportion of total detergent in the compositions form no part of this invention and are well known in the art.

Captan is effective in the aqueous hair shampoo formulations of this invention in amounts ranging from about 0.1 percent to about 5 percent, by weight of the total formulation. Larger amounts can be incorporated if desired without adverse effect. On the other hand, no additional advantages are obtained by using amounts greater than 5 percent. Excellent results are obtained in compositions containing about 0.25 percent to about 3 percent by weight of captan, which constitutes the preferred range for this material.

This invention will now be described further with reference to specific embodiments thereof as illustrated in the examples which follow.

Seven formulations according to this invention are shown in Examples 1 to 7 below. In each example, the captan was added as the final ingredient after the formulation was buffered to the desired pH. All formulations had the consistency of a paste. The formulations are indicated in percentage of active ingredients by weight, whether or not the ingredients were water-diluted compositions.

EXAMPLE 1

Components	% by Wt.
Dodecylbenzene sodium sulfonate (Ultrawet K, anionic)	39.7

Ethylene oxide-propylene oxide-propylene glycol condensate containing a polyoxypropylene hydrophobic base having a typical molecular weight of 1750 and 80% polyoxyethylene in the total molecule ("Pluronic F-68", nonionic)

5	Acetylated lanolin	8.8
	Glyceryl monostearate	1.8
	Stearic acid	17.6
	Water	3.5
	Captan	26.6
10		2.0

The pH of this formulation was buffered to 5.1 by the addition of citric acid.

EXAMPLE 2

Components		% by Wt.
20	Sodium alkyl aryl polyether sulfonate (Triton X-202, anionic)	16.6
	Dodecylbenzene sodium sulfonate (Ultrawet K, anionic)	18.6
	"Pluronic F-68" (nonionic)	6.9
	Acetylated lanolin	1.4
	Glyceryl monostearate	9.7
25	Stearic acid	4.1
	Water	40.7
	Captan	2.0

30 The pH of this formulation was buffered to 5.2 by the addition of citric acid.

EXAMPLE 3

35	Components	% by Wt.
	Triton X-202 (anionic)	24.5
	Cocoyl sarcosine (anionic)	4.7
	"Pluronic F-68" (nonionic)	4.7
	Acetylated lanolin	1.0
40	Glyceryl monostearate	4.7
	Stearic acid	1.9
	Water	56.5
	Captan	2.0

45 The pH of this formulation was buffered to 5.0 by the addition of citric acid.

EXAMPLE 4

50	Components	% by Wt.
	Triton X-202 (anionic)	12.7
	Dodecylbenzene sodium sulfonate (anionic)	30.4
55	"Pluronic F-68" (nonionic)	8.5
	Acetylated lanolin	1.7
	Glyceryl monostearate	11.8
	Water	32.9
	Captan	2.0

60 The pH of this formulation was buffered to 5.2 by the addition of citric acid.

EXAMPLE 5

	Components	% by Wt.
65		
	Triton X-202 (anionic)	11.3
	Dodecylbenzene sodium sulfonate (anionic)	12.7
	"Pluronic F-68" (nonionic)	4.7
70	Colloidal magnesium aluminum silicate ("Veegum K")	3.0
	Acetylated lanolin	0.9
	Glyceryl monostearate	6.6
	Stearic acid	2.8
	Water	56.0
75	Captan	2.0

The pH of this formulation was buffered to 5.0 by the addition of citric acid.

EXAMPLE 6

Components	% by Wt.
Triton X-202 (anionic)	7.5
Dodecylbenzene sodium sulfonate (anionic)	18.0
"Pluronic F-68" (nonionic)	5.0
"Veegum K"	3.0
Acetylated lanolin	1.0
Glyceryl monostearate	7.0
Water	56.5
Captan	2.0

The pH of this formulation was buffered to 5.3 by the addition of citric acid.

EXAMPLE 7

Components	% by Wt.
Sodium cocoyl isethionate (anionic)	15.0
Sodium N-coconut acid-N-methyltaurate (anionic)	6.0
"Veegum K"	1.0
Acetylated polyoxyethylene derivative of lanolin (Solulan 98)	3.5
Cetyl alcohol	1.8
Glyceryl monostearate	5.9
Water	64.8
Captan	2.0

The pH of this formulation was buffered to 5.5 by the addition of citric acid.

In each of Examples 1 through 7, addition of citric acid was made to achieve a pH in the range of 5.0 to 5.5. As indicated above, the optimum pH range of compositions is from 4.5 to 6.5, and the Examples were performed to center this range. Of course, other acidic buffering systems can be suitably used to attain this desired result.

Each of the above seven shampoo formulations, containing 2 percent by weight of captan, was analyzed by a colorimetric method based on that of A. R. Kittleson, Anal. Chem. Vol. 24, 1,173-5 (1952), then stored at 38° C. and reanalyzed at regular intervals thereafter over a period of 4 to 5 weeks. Four to five weeks of aging at 38° C. corresponds to many months of shelf aging at ambient temperatures.

The analytical results are presented in FIGS. 1 and 2. After an initial decrease in captan content of many of the formulations (that at 0 weeks), a relatively stable high level of captan was maintained after 4 to 5 weeks of accelerated aging at 38° C. This stability is far different from the drop to zero within 1 day to 2 weeks which has been characteristic of the captan preparations heretofore known to the art. While some of the formulations of the Examples are more stable than others with respect to captan, all are seen to retain substantial amounts of captan after accelerated aging.

EXAMPLE 8

The skin substantivity and stability of captan in the shampoo formulation of Example 2 were determined by means of a hide substantivity test. Three untanned calf skin discs were soaked for 5 minutes in an 8 percent aqueous mixture of the freshly prepared composition of Example 2, which was maintained at 37° to 40° C. After soaking for 5 minutes the discs were removed and rinsed through four successive 500 ml. portions of tap water for 1 minute each. The excess water was

removed by squeezing the discs and placing them momentarily on cardboard. The discs were then placed on separate agar plates respectively seeded with the bacteria *Staphylococcus aureus* and *Salmonella choleraesuis*, and the fungus *Trichophyton mentagrophytes*. The two bacterial plates were incubated at 37° ± 0.5° C. for 24 hours, and the fungus plate was incubated at 26° C. for 4 days. The diameter of the clear zone of inhibition of bacterial or fungal growth around each disc was measured in millimeters and the diameter of the disc was subtracted therefrom, providing a difference reported as the zone of inhibition.

The same tests were repeated, using the composition of Example 2 after storage for 7 weeks at 38° C., and also using control shampoos of identical composition except for the omission of captan.

The diameters of the zones of inhibition for each test are given in Table I below:

TABLE I.—HIDE SUBSTANTIVITY, ZONE INHIBITION IN MM.

Test shampoo	<i>Staphylococcus aureus</i>		<i>Salmonella choleraesuis</i>		<i>Trichophyton mentagrophytes</i>	
	Control	Captan	Control	Captan	Control	Captan
Freshly prepared	4.5	9	4	10	0	7
Stored 7 wks. at 38° C.	0	9	4	9	0	6

The results of these tests show that compositions of this invention suffer very little loss in substantive biostatic activity following shelf storage for 7 weeks at 38° C. The zone of inhibition for the control formulations may indicate that one or more ingredients other than captan has some biostatic activity when the composition is freshly prepared, but this biostatic activity against all organisms except *Salmonella choleraesuis* disappeared in the accelerated shelf storage test. However, some biostatic activity is not uncommon among surface active agents. Nevertheless, the tests show very clearly that the captan-containing formulations retained virtually all their bactericidal and fungicidal properties after storage for 7 weeks at 38° C.

In addition to captan, one or more detergents and water, the hair shampoos of this invention may contain additional ingredients which are well known in the art of hair shampoo preparations. An emulsifier such as glyceryl monostearate to give the shampoo "body" and "creaminess" and physical stability is generally incorporated, along with emollients such as lanolin derivatives which soften the hair. Other ingredients, including thickeners, perfumes and various inorganic salts such as sodium chloride, sulfates and phosphates, may be added, providing that the pH of the formulation is maintained within the limits described above.

While this invention has been described with reference to specific embodiments thereof, it will be understood that these embodiments are merely by way of illustration, and that the scope of the invention shall not be limited except by the claims.

In the claims:

1. A stable aqueous anti-dandruff shampoo formulation consisting essentially of water, and about 0.1 percent to about 5 percent by weight of N-trichloromethylthio-4-cyclohexene-1,2-dicarboximide as the anti-dandruff agent, said formulation having a pH in the approximate range of from 4.5 to 6.5, and from about 10 percent to about 90 percent of a detergent, said detergent being selected from the group consisting of an anionic detergent, a nonionic detergent and mixtures thereof, wherein said anionic detergent is selected from the group consisting of an alkali metal long chain aliphatic sulfate having from 12 to 26 carbons, an alkali metal long chain aliphatic sulfonate having from 12 to 26 carbons, an alkali metal salt of an N-fatty acyl acid amide of an aminosulfonic acid whose acyl group contains from 12 to 18 carbons and whose amino group may be substituted by lower alkyl, an alkali metal salt of a fatty acyl acid ester of a hydroxysulfonic acid whose acyl group contains from 12 to 18 carbons, an alkali metal alkylarylsulfonate having eight to 22 carbons in the alkyl group thereof, an alkali metal sulfonate of an ethylene oxide adduct of an alkylphenol having eight to 20 carbons in the alkyl group

thereof and from six to 100 ethylene oxide units, and mixtures thereof; and said nonionic detergent selected from the group consisting of an ethylene oxide adduct of a long chain aliphatic alcohol containing from about 12 to about 26 carbons, or an alkylphenol having eight to 20 carbons in the alkyl group thereof, said adduct containing from six to 100 ethylene oxide units and being free of amino nitrogen, an ethylene oxide-propylene oxide condensate composed of a polyoxypropylene hydrophobic portion having a molecular weight from 950 to 3,250, having from 10 to 80 weight percent ethylene oxide units and being free of amino nitrogen, and mixtures thereof.

2. A stable aqueous anti-dandruff shampoo formulation consisting essentially of water, and about 0.1 percent to about 5 percent by weight of N-trichloromethylthio-4-cyclohexene-1,2-dicarboximide as the anti-dandruff agent, said formulation having a pH in the approximate range of from 4.5 to 6.5, and from about 10 percent to about 90 percent of a detergent, said detergent being selected from the group consisting of an anionic detergent, a nonionic detergent and mixtures thereof, wherein said anionic detergent is selected from the group consisting of an alkali metal alkyl sulfate having from 12 to 26 carbons, an alkali metal alkyl sulfonate having from 12 to 26 carbons, an alkali metal salt of an N-fatty acyl acid amide of taurine whose acyl group contains from 12 to 18 carbons and whose amino group may be substituted by methyl, an alkali metal salt of a fatty acyl acid ester of isethionic acid whose

acyl group contains from 12 to 18 carbons, an alkali metal alkyl benzene sulfonate having eight to 22 carbons in the alkyl group thereof, an alkali metal sulfonate of an ethylene oxide adduct of an alkylphenol having eight to 20 carbons in the alkyl group thereof and from six to 100 ethylene oxide units, and mixtures thereof; and said nonionic detergent is selected from the group consisting of an ethylene oxide adduct of a long chain aliphatic alcohol containing from about 12 to about 26 carbons or an alkylphenol having eight to 20 carbons in the alkyl group thereof, said adduct containing from six to 100 ethylene oxide units and being free of amino nitrogen, an ethylene oxide-propylene oxide condensate composed of a polyoxypropylene hydrophobic portion having a molecular weight from 950 to 3,250, having from 10 to 80 weight percent ethylene oxide units and being free of amino nitrogen, and mixtures thereof.

3. The shampoo composition of claim 2 in which said detergent is a mixture of dodecylbenzene sodium sulfonate and an ethylene oxide-propylene oxide-propylene glycol condensate containing a polyoxypropylene hydrophobic base having a molecular weight of 1,750 and 80 percent polyoxyethylene in the total molecule.

4. The shampoo composition of claim 2 in which said detergent is a mixture of sodium cocoylisethionate and sodium N-coconut acid-N-methyltaurate.

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