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DETERGENT COMPOSITIONS

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No Drawing. Continuation-in-part of abandoned application Ser. No. 808,336, Mar. 18, 1969. This application Sept. 11, 1970, Ser. No. 71,410
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U.S. Cl. 252—107 2 Claims

ABSTRACT OF THE DISCLOSURE

An antibacterial detergent composition, e.g. a toilet bar contains a synergistic mixture of 4,2',4'-trichloro-2-hydroxydiphenylether, 3,4,4'-trichlorocarbanilide and 4,4'-dichloro-3-trifluoromethylcarbonilide.

This application is a continuation-in-part application of our application Ser. No. 808,336 filed on Mar. 18, 1969 now abandoned.

BACKGROUND

Field of the invention

This invention relates to anti-bacterial detergent formulations.

For an anti-bacterial compound to be acceptable for use in a detergent bar it must fulfill certain requirements. The anti-bacterial compound should at the concentrations at which it is used, be compatible with the detergent, not discolour the bar on storage, not cause rancidity, be substantive to skin, not cause sensitization or irritation and have sufficiently high anti-bacterial activity. In vitro and in vivo tests are used to test the anti-bacterial effectiveness of compounds as anti-bacterial compounds for use in detergent bars; techniques commonly used are described by B. M. Gibbs and L. W. Stuttard in J. Appl. Bact., 1967, 30(1). Tests normally include a "finger imprint" test to judge the anti-bacterial activity and substantivity to the skin of the anti-bacterial compound and a hand-washing test under user conditions.

Prior art

The mixture of anti-bacterial compounds, 0.67% 3,4',5-tribromosalicylanilide, 0.67% 4,4' - dichloro-3-trifluoromethyl-carbanilide and 0.67% 3,4,4'-trichlorocarbanilide, has been strongly recommended for use in detergent bars. Results have been reported by various authors, for example, Kooistra, Bannan and Carter, J. Soc. Cosmetic Chemists, 1966 17, 343–353; and Leonard, Arch. Derm., 1967, 95, 520–523.

SUMMARY OF THE INVENTION

It has now been discovered that mixtures of the anti-bacterial compounds, 4,2',4'-trichloro-2-hydroxydiphenyl-ether, 3,4,4'-trichlorocarbanilide and 4,4'-dichloro-3-trifluoromethylcarbanilide, have at least as good properties and in some respects better properties for use in a detergent bar. The applicants have further discovered that this mixture shows anti-bacterial activity when included in a liquid detergent formulation. The term "liquid" herein defines liquid, gel or paste-like compositions. Mixtures containing, by weight, at least 10% of each of the three compounds have been found to show synergistic anti-bacterial properties. The weight ratio of any one compound in the synergistic mixture to the other two compounds should preferably be between 1:4 and 3:1.

The invention provides an anti-bacterial detergent bar or liquid formulation containing a synergistic mixture of 4,2',4' - trichloro-2-hydroxydiphenylether, 3,4,4'-trichlorocarbanilide and 4,4'-dichloro-3-trifluoromethylcarbanilide.

The liquid compositions are particularly useful for industrial and other large scale use, as for example in hospitals, when they may be dispensed from special dispensers for convenient and economic use.

As described and claimed in co-pending application Ser. No. 721,610 filed Apr. 16, 1968, a soap bar that contains 4,2',4'-trichloro-2-hydroxydiphenylether should preferably contain at least 1% of C_{8-22} fatty acid. Otherwise it is advisable to use a powerful colorant to obscure any discolouration that occurs on storage.

The total amount of the mixture in the formulation should preferably be from 0.5 to 5% by weight of the formulation, more preferably from 0.75 to 2.5%.

The liquid detergent compositions may incorporate synthetic detergent active compounds or soaps and in either case the compositions usually comprise a major proportion of water. The synthetic detergent compounds used are generally anionic or nonionic compounds. Examples of anionic compounds are alkyl benzene sulphonates, alkane sulphonates, alkyl sulphates and alkyl ether sulphonates; whilst the nonionic compounds are usually condensation reaction products of alkyl phenols with alkyelne oxides, particularly ethylene oxides.

Preferred liquid detergent compositions are the liquid soap products of the type described and claimed in the complete specification of our United Kingdom patent application No. 56,253/67 of Dec. 11, 1967. Such compositions comprise:

(a) from about 10 to about 30% by weight of total fatty matter of which about 0.1 to about 10% by weight is free fatty acids, the remainder being in the form of soaps of which at least about 50% by weight are potassium soaps,
(b) from about 0.1 to about 7.5% by weight of an opacifying agent,
(c) from about 0.1 to 5% by weight of an alkyl cellulose, and
(d) the balance being predominantly water.

In addition to the essential ingredients mentioned above, the liquid composition may incorporate minor amounts of optional additives including, for example, thickeners, opacifiers, hydrotropes, solvents, lather boosters, preservatives, colourants and perfumes.

A preferred detergent bar according to the invention is a soap bar.

Examples 1 to 4 describe soap bars of the invention and Examples 5 to 7 describe liquid formulations.

EXAMPLE 1

Soap bars were prepared containing various mixtures of anti-bacterial compounds.

The bars were prepared from ribbons of soap derived from a fat charge consisting of 84% tallow and 16% coconut soap. To the ribbons were added perfume, opacifier and 2% of coconut fatty acid. After these had been mixed, the anti-bacterial compounds were added and the ribbons were milled twice. The ribbons were then crimped and plodded under vacuum. Bars were formed by extrusion and stamping.

The Finger Imprint Test used was a modification of the test of L. J. Vinson et al.; J. Pharm. Sci., 1961, 50, (10), 827, "In Vitro Tests for Measuring Anti-bacterial Activity of Toilet Soap and Detergent Bars," instead of simulated washing of the hands with soap solutions containing anti-bacterial, subjects washed their hands with test soap bars containing the anti-bacterial mixtures. Also, the scale for evaluation of the high level of anti-bacterial contained in the mixtures was effectively expanded by use of a larger volume of media and inoculum than that described by Vinson, and in addition plates were prepared as described by Vinson, but in which *E.*

coli was substituted for *Stap. aureus*. The following results were obtained.

Bar: Anti-bacterial compounds (percent by weight)				Finger imprint rating against	
A	B	C	D	*S. aureus*	*E. coli*
0.67	0.67	0.67		1.7	0
	0.2	1	0.5	3.0	3.8
	0.3	1	0.5	3.7	4.0
	0.5	1	0.5	3.9	3.8
	0.3	1.2	0.5	3.0	3.7

NOTE.—A is 3,4',5-tribromosalicylanilide; B is 4,2',4'-trichloro-2-hydroxydiphenylether; C is 3,4,4'-trichlorocarbanilide; D is 4,4'-dichloro-3-trifluoromethylcarbanilide.

This example demonstrates the suprising effectiveness of the synergistic mixtures of the invention against *S. aureus* and *E. coli*. Effectiveness against *E. coli* enables bars according to the invention to be used not only in personal working but also in general hygiene, for instance in hospital both as a surgical aid and also in maintaining antibacterial conditions in more general situations.

Hand-washing tests were done using bars containing various mixtures of anti-bacterial compounds A, B, C and D. The following results were obtained:

Bar: Anti-bacterial compounds (percent by weight)				Percent reduction in skin flora	
A	B	C	D	Best estimate	Confidence limits
0.67	0.67	0.67		94.2	83.8-97.9
	0.2	1	0.5	82.1	47.2-93.9
	0.3	1	0.5	89.2	70.2-96.1
	0.5	1	0.5	94.3	83.3-98.1
	0.3	1.2	0.5	94.8	83.9-98.3

The example demonstrates that synergistic mixtures of the invention are at least as good as a ternary mixture that has been regarded as remarkably good.

The handwashing test was performed as follows:

Thirty-six subjects, who had previously been using control soap (free of anti-bacterial compound) for at least a week, were used to evaluate each test soap. They were instructed to use the soap for all personal washing and asked to avoid contact with other anti-bacterial substances for a period of one week. On the 6th and 7th days their resident bacterial flora were sampled in the laboratory by a serial wash technique. Each subject made four consecutive washes with the test soap, the first three up to the elbows, whereas in the fourth, the hands and wrists only were included. Fifteen seconds' soaping, 60 seconds' lathering and 15 seconds' rinsing were used in each case. This fourth wash was done in a bowl containing 2 litres of sterile water. The bacteria in 10. 1.0 and 0.1 ml. aliquots of water were counted on yeastrel-glucose agar. After incubation at 37° C. for 48 hours the number of colonies was counted. The log counts were used in analyses of variance. The resultant mean log counts were then compared with the mean log count obtained when subjects had used control soap for the same period.

For each test soap the difference between the means of the result for that treatment and for the control soap were determined by statistical analysis so that best

estimates of percentage reductions of levels of bacteria together with confidence limits (P=0.95; that is 95% certainty that real value lies within the limits) were determined.

It should be noted that repetition of the test, use of a larger number of subjects or extension of the test period would narrow the confidence limits.

EXAMPLE 3

Hand-washing tests, as in Example 2, were done using bars containing various mixtures of anti-bacterial compounds A, B, C and D. The bars were prepared as in Example 1. The following results were obtained:

Bar					Percent reduction in skin flora		Rating against—	
	Anti-bacterial compounds (Percent by weight)							
Total	A	B	C	D	Best estimate	Confidence limits	*S. aureus*	*E. coli*
1.8		0.3	1.2	0.3	95.8	91.6-97.9	2.7	3.8
2	0.67		0.67	0.67	91.6	83.6-95.7	1.8	0
1.8		0.3	1.0	0.5	92.1	84.9-95.9	3.3	4.0

The example demonstrates again the surprisingly good anti-bacterial properties of synergistic mixtures according to the invention. Thus 1.8% of mixtures according to the invention give at least as good Hand-washing results and better Finger Imprint results than 2% of a mixture of A, C and D.

EXAMPLE 4

Hand-washing tests, as in Example 2, were done using bars containing various mixtures of anti-bacterial compounds A, B, C and D. The bars were prepared as in Example 1. The following results were obtained.

Bar					Percent reduction in skin flora	
	Anit-bacterial compounds (percent by weight)					
Total	A	B	C	D	Best estimate	Confidence limits
2	0.67		0.67	0.67	95.8	91.8-97.8
2		1	1		81.6	83.6-95.7
2		1		1	94.3	88.8-97.1
2			1	1	90.2	80.7-94.9
2	0.67	0.67	0.67		94.5	89.3-97.2

This example demonstrates the synergistic nature of the surprising anti-bacterial properties of mixtures according to the invention.

EXAMPLE 5

1.8% by weight, based on the total composition, of a ternary mixture comprising 0.3% of 4,2',4'-trichloro-2-hydroxy diphenyl ether, 1.2% of 3,4,4'-trichloro-carbanilide and 0.3% of 4,4'-dichloro-3-trifluoro-methyl carbanilide was thoroughly mixed into an opaque liquid soap composition having the following formulation:

Ingredient:	Percentage
Total fatty matter	20.0
Free fatty acids	0.2
Potassium and sodium soaps (calc. as fatty matter)	17.3
Calcium soaps (calc. as fatty matter)	2.5
Glycerol	2.4
Methyl cellulose (MW about 1000)	0.4
Perfume	0.35
Preservatives	0.045
Colourant	0.0004
Water to 100.0.	

The composition was prepared by saponifying a mixture of triglicerides, derived from tallow and palm kernel oil (4:1), with a 25% aqueous solution of potassium and

sodium hydroxides (5:1) at 90° C. Calcium chloride solution (25% aqueous) was sprayed onto the reactants during saponification. Water was added as necessary to maintain the total fatty matter at about 25 to 30%. After saponification, fatty acids derived from tallow and palm kernel oil (4:1) were added. Methyl cellulose was added gradually until the mixture reached the desired viscosity, and the mixture then cooled to 40° C. The other materials were added to give a pearlescent product with a viscosity of 250 cps. at 25° C.

The anti-bacterial properties of this composition were determined in comparison with a commercially available anti-bacterial liquid composition containing 3% of the conventional germicidal ingredient hexachlorophene, by a procedure in which 17 persons used one or other of the liquid compositions for hand washing on four occasions for three days, using conventional non-bacterial toilet bars for other hand washing as required, and then on the fourth and fifth days the liquid compositions were used twice in the mornings and in the afternoons samples of hand flora were taken. The results were as follow:

Composition:	Reduction in hand flora (percent)
As example with ternary germicide mixture	99.8
Commercial product	85.8

EXAMPLE 2

A composition was prepared as in Example 1 with the exception that the liquid soap composition was replaced by a clear composition of following formulation:

Ingredient:	Percentage
Nonyl phenol-8 EO	16.0
Soap	3.5
Isopropanol	4.0
Sodium pyrophosphate	0.5
Perfume	0.3
Water	75.7
	100.0

Ingredient:	Percentage
Isopropanol	4.0
Sodium pyrophosphate	0.5
Perfume	0.3
Water	75.7
	100.0

The anti-bacterial properties of the resultant composition were determined by the Finger Imprint Test described in Example 1 of this specification with the difference that the tests were of course completed using the liquid composition instead of the soap bars.

The Finger Imprint Ratings of the liquid composition were as follows:

Against G+ve bacteria	2.9
Against G—ve bacteria	2.4

By way of comparison the liquid composition without the germicide was totally ineffective against either type of bacteria.

EXAMPLE 7

A composition was prepared as in Example 5 with the exception that the opaque liquid soap composition was replaced by a gel having the following formulation:

Ingredient:	Percentage
Coconut fatty acids	15.0
Diethanolamine	15.0
Acrylic resin (thickener)	0.4
Isopropanol	3.3
Sodium hydroxyethyl cellulose	1.2
Preservatives, colourants, perfume	1.0
Water to 100.0.	

The gel with added germicides was tested by the Finger Imprint Test and gave the following ratings:

Against G+ve bacteria	2.8
Against G—ve bacteria	3.5

What is claimed is:

1. A fatty acid soap toilet bar having good antibacterial properties against *S. aureus* containing by weight of the bar, from 0.5 to 5.0% of a synergistic mixture of approximately equal proportions of each, based on the weight of said mixture, of three anti-bacterial compounds, said compounds being

4,2',4'-trichloro-2-hydroxydiphenylether,
3,4,4'-trichlorocarbanilide and
4,4'-dichloro-3-trifluoromethyl carbanilide.

2. A detergent formulation having good antibacterial properties against *S. aureus* comprising,

(a) from about 10 to about 30% by weight of total fatty matter of which about 0.1 to about 10% by weight is free fatty acids, the remainder being in the form of soaps of which at least about 50% by weight are potassium soaps,

(b) from about 0.1 to about 7:5% by weight of an opacifying agent,

(c) from about 0.1 to about 5% by weight of an alkyl cellulose,

(d) from 0.5 to 5.0% by weight of approximately equal proportions of each, based on the weight of said mixture, of three antibacterial compounds, said compounds being

4,2',4'-trichloro-2-hydroxydiphenylether,
3,4,4'-trichlorocarbanilide and
4,4'-dichloro-3-trifluoromethylcarbanilide, and

(e) the balance being predominantly water.

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