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3,235,455

SYNERGISTIC ANTIBACTERIAL COMPOSITIONS

Leo F. Judge, Colerain Township, Hamilton County, and Daniel J. Kooyman, Wyoming, Ohio, assignors to The Procter & Gamble Company, Cincinnati, Ohio, a corporation of Ohio

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1 Claim. (Cl. 167-58)

This application is a continuation-in-part of copending application Serial No. 172,079, filed February 9, 1962, now abandoned.

This invention relates to antibacterial compositions which contain a mixture of antibacterial agents possessing synergistic activity. More specifically this invention relates to a mixture of 1-hydroxy-2-pyridinethione and salts thereof, and one or more halogenated bisphenols, halogenated carbanilides and halogenated salicylanilides, said mixture exhibiting synergistic antibacterial activity and especially when incorporated into a soap or detergent product formulation or a cosmetic, for example.

Many compounds have been suggested in the past for use as antibacterial agents in soaps, detergents, cleansing creams, and other compositions such as antiperspirants and deodorants. Among the early compounds suggested for use in soaps and other cleansing agents were the phenols and the phenolic fatty acid esters. Later, certain of the mercuric compounds were used. More recently, agents such as certain of the halogenated bisphenols, the most widely known of which is hexachlorophene or G-11, the halogenated salicylanilides and the halogenated carbanilides have been used in soap, detergent compositions, and other products.

It is well known, however, by those skilled in the art that many of the above mentioned compounds have some serious limitations in their use. For example, it was found that phenols and phenol esters, while effective in an aqueous solution, were rendered ineffective in the presence of soap or detergent compositions. Other antibacterial agents of those mentioned are effective only against a relatively narrow range of organisms. It is also well known that the halogenated bisphenols are photo-sensitive and when incorporated into a soap or detergent bar will discolor the bar upon prolonged exposure to sunlight. When incorporated into soap or detergent bars at sufficiently high enough levels to obtain good antibacterial effectiveness, i.e., up to 2% or more, the discoloration of the soap by the bisphenolic compounds becomes so pronounced that the bar must be colored or dyed yellow in order to mask the discoloration.

Some of the compounds suggested by the prior art, although they may be relatively good antibacterial agents, are not truly effective until they are present in the composition at relatively high levels, i.e., up to 2% to 3% by total weight of the detergent product. This, of course, makes the product more expensive to manufacture and as a result it becomes increasingly difficult to manufacture a product which can be priced competitively.

Some of these problems have been alleviated by the discovery that certain binary combinations of antibacterial agents exhibit synergism when admixed and incorporated into soap and detergent formulations and other products. Synergistic combinations of antibacterial agents such as the halogenated bisphenols and halogenated carbanilides, halogenated bisphenols and the halogenated salicylanilides have been disclosed. The synergism provides a higher level of antibacterial effectiveness for an equal amount of antibacterial agent used, or more important, it enables a manufacturer to use a lesser amount of antibacterial agents yet retain a relatively high degree of effectiveness. It is significant to note that effective synergistic combina-

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tions of antibacterial agents are relatively rare and when such combinations are discovered, the synergism is entirely unpredictable. It should be appreciated, therefore, that there is a continual need for still more effective antibacterial agents and combinations of agents having increased substantivity to the skin. Such an agent or mixtures of agents can be incorporated into the soap at lower concentrations than is now practiced, to provide an even greater antibacterial effectiveness of the soap or detergent product under conventional usage conditions.

It is therefore an object of this invention to provide synergistic antibacterial compositions which possess a high level of antibacterial effectiveness.

It is a further object of this invention to provide antibacterial compositions which are effective in a soap, or detergent product medium.

It is a still further object of this invention to provide an antibacterial composition which has increased substantivity to the skin and which is effective over a wide range of organisms.

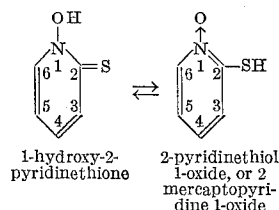
It is a still further object of this invention to provide an antibacterial composition which is economical and which does not have significant discoloration problems or toxicity problems.

Other objects and improvements will become apparent from the following description.

In accordance with this invention, it has been found that mixtures of 1-hydroxy-2-pyridinethione and salts thereof, and a bactericidal agent selected from the group consisting of halogenated bisphenols, halogenated carbanilides and halogenated salicylanilides, and mixtures thereof, form synergistic combinations of antibacterial agents when admixed and incorporated into a soap or detergent product, or other personal preparations at low levels of concentration.

The term "synergistic combinations" as used herein refers to a mixture of two or more discrete agencies which when combined display a degree of antibacterial activity which is greater than the sum of the antibacterial activity of the agents taken independently.

The pyridinethione compound used in this invention has the following structural formula in tautomeric form, the sulfur being attached to the No. 2 position of the pyridine ring:

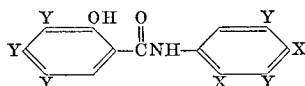


The metal salts disclosed herein represent substitution of the corresponding metal for the hydrogen of one of the tautomeric forms. While the preferred pyridinethione compound utilized in this invention is the zinc salt of 1-hydroxy-2-pyridinethione, other salts capable of being used include salts prepared from iron, lithium, manganese, sodium, potassium, magnesium, ammonium, barium, calcium, strontium, cadmium, aluminum and lead. The disulfide (2,2'-dithiodipyridine 1,1'-dioxide) has also been found to be useful. The disulfide represents the attachments of two 1-hydroxy-2-pyridinethione rings by the elimination of the two hydrogens from the sulfur atoms to give a sulfur to sulfur linkage. Organic salts also show synergism when incorporated into the compositions of this invention. Compounds such as the alkyl amine and imidazole salts of 1-hydroxy 2-pyridinethione are suitable organic salts for use in this invention.

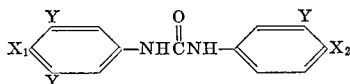
The other antibacterial compounds of this invention

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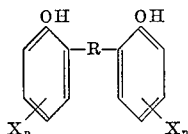
used in admixture with the zinc pyridinethione compound above are selected from the group consisting of (a) a substituted salicylanilide compound having the general formula:



wherein X is a member of the group consisting of hydrogen and halogen, and Y is a member of the group consisting of hydrogen, halogen and trifluoromethyl and (b) a substituted carbanilide compound having the general structural formula:



wherein Y is a member of the group consisting of hydrogen, halogen and trifluoromethyl, X₁ is a member of the group consisting of halogen and ethoxy, X₂ is a member of the group consisting of hydrogen and halogen, and (c) a substituted bisphenol having the general structural formula:



where X is a halogen and n is an integer from 1 to 3, R is selected from the group consisting of an alkylene radical having from 1 to 4 carbon atoms and divalent sulfur, and (d) mixtures of (a), (b), and (c). The compounds in (c) above which R represents an alkylene radical are more fully described in U.S. Letters Patent 2,555,077, granted December 26, 1950. The preferred compounds of the general class of (c) above are those which are symmetrical in structural configuration, such as bis(5-chloro-2-hydroxyphenyl) methane, bis(3,5-dichloro-2-hydroxyphenyl) methane, bis(3,5,6-trichloro-2-hydroxyphenyl) methane, bis(3,5-dichloro-2-hydroxyphenyl) sulfide, bis(3,5,6-trichloro-2-hydroxyphenyl) sulfide, and mixtures thereof.

The following combinations of antibacterial agents are illustrative of synergistic compositions of this invention, but not limited thereto.

Zinc salt of 1-hydroxy-2-pyridinethione + bis(2-hydroxy-3,4,6-trichlorophenyl) methane

Lead salt of 1-hydroxy-2-pyridinethione + bis(2-hydroxy-3,5-dichlorophenyl) sulfide

Zinc salt of 1-hydroxy-2-pyridinethione + 3,3',4'-trichlorocarbanilide

Magnesium salt of 1-hydroxy-2-pyridinethione + 3,4,4'-tribromocarbanilide

Zinc salt of 1-hydroxy-2-pyridinethione + 3,4,3',4'-tetrachlorocarbanilide

Aluminum salt of 1-hydroxy-2-pyridinethione + 3,5,4'-tribromosalicylanilide

Zinc salt of 1-hydroxy-2-pyridinethione + 3,5,4'-tribromosalicylanilide

Zinc salt of 1-hydroxy-2-pyridinethione + 3-trifluoromethyl-4,4'-dichlorocarbanilide

Magnesium salt of 1-hydroxy-2-pyridinethione + bis(2-hydroxy-3,5,6-trichlorophenyl)-methane + 3,5,4'-tribromocarbanilide

Zinc salt of 1-hydroxy-2-pyridinethione + bis(2-hydroxy-3,5,6-trichlorophenyl)-methane + 3,5,4'-tribromosalicylanilide

Calcium salt of 1-hydroxy-2-pyridinethione + bis(2-hydroxy-3,5,6-trichlorophenyl)-methane + 3-bromo-3,4-dichlorocarbanilide + 3-trifluoromethyl-4,4'-dichlorocarbanilide

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Iron salt of 1-hydroxy-2-pyridinethione + bis(2-hydroxy-3,5-dichlorophenyl)-sulfide + 3,5,4'-tribromosalicylanilide + 3-trifluoromethyl-4,4'-dichlorocarbanilide

Zinc salt of 1-hydroxy-2-pyridinethione + 3,5,4'-tribromosalicylanilide + 3,4,4'-trichlorocarbanilide + 3-trifluoromethyl-4,4'-dichlorocarbanilide

It has been found that the above listed combinations and similar variations thereof possess synergistic antibacterial properties whereby a lasting bactericidal effect is obtained when they are used in soap and detergent compositions and other products such as antiperspirants and deodorants. This synergism can be more readily seen by reference to the following examples based on several representatives of the above combinations.

EXAMPLE I

In this example the antibacterial synergism of the present invention is demonstrated by means of a skin retention test. In this test callus taken from the plantar surface of the human foot is cut into small blocks (approximately 2-3 mm. cubes). These are washed in a standard concentration of soap product containing the antibacterial compound or compounds to be tested for a standard time (5 minutes) and temperature (48° C.). (The soap was a mixture of 80% sodium tallow soap and 20% sodium coconut oil soap.) After washing, the blocks are thoroughly rinsed with distilled water to remove all traces of soap, and allowed to dry. The dry blocks of callus are imbedded in molten agar previously seeded with the test organism, in this case a gram positive coccus and a gram positive rod, two common bacterial types found on the surface of the skin; then the agar plates plus callus blocks are stored in a refrigerator overnight to permit diffusion of the antimicrobial agent from the callus into the surrounding medium. The next day, the plates are placed in the incubator at 37° C. and the organisms are allowed to grow for 24-48 hours. The clear zone of inhibited growth of the test organism surrounding the blocks is an indication of the antimicrobial activity imparted to the callus blocks in the washing process.

Skin retention test

[Diameters of the zones of inhibition (mm.) surrounding blocks of callus washed with product]

Product ¹	Type of organism isolated from human skin	
	Gram plus coccus	Gram plus rod
1. Soap plus 0.5% zinc pyridinethione.....	0	0
2. Soap plus 0.333% 3,5,4'-tribromosalicylanilide plus 0.333% 3-trifluoromethyl-4,4'-dichlorocarbanilide plus 0.333% 3,4,4'-trichlorocarbanilide.....	15	13
3. Soap plus 0.333% 3,5,4'-tribromosalicylanilide plus 0.333% 3-trifluoromethyl-4,4'-dichlorocarbanilide plus 0.333% 3,4,4'-trichlorocarbanilide plus 0.50% zinc pyridinethione.....	18	19

¹ The percent of antibacterial agent present in the product is based on the weight of the soap.

From the table it can be seen that the zinc pyridinethione in soap at a 0.5% level (1) in this test has essentially no antibacterial activity but when combined with a mixture of other antibacterial agents the combination (3) shows considerably more activity than the combination of three antibacterial agents used alone in soap (2). One would instead expect the pyridinethione to contribute nothing to the antibacterial activity of the mixture and the zone of inhibition should remain approximately constant. The fact that the level of activity did not remain the same but rather an increased level of activity was obtained indicates a synergistic activity between the zinc pyridinethione and the other compounds.

EXAMPLE II

In this example the synergism of the compounds of the present invention is exhibited by means of a deodorant test. The test is conducted as follows:

10 males in a panel are given bars of ordinary toilet soap, a milled toilet bar (containing a blend of 80% tallow soap and 20% coconut oil soap), at the beginning of the week and are instructed to use this bar for bathing for four days. On the evening of the 4th day, each subject is supervised while he washes under his arms with the toilet soap, following a standard washing procedure. The subjects are then instructed not to wash under their arms until late in the afternoon of the next day, at which time the underarm area of both arms of each subject are independently sniffed by four expert judges and the intensity of the odor under each arm is graded on a standard scale (0 being no body odor and 10 very strong and disagreeable, with the remaining numbers between 1 and 10 representing intermediate values). Each subject is then assigned one test bar containing the antibacterial agents to be tested to use under one arm and a second bar to use under the other arm. These assignments are balanced for normal odor level and handedness, i.e., balanced to insure the test bar is used to wash under an equal number of right arms as left arms. For 6 days the subjects wash under their arms twice daily (a.m. and p.m.) under supervision following a standard washing procedure using the assigned bars.

No washing is done the following morning. Late in the afternoon of the seventh day, approximately 24 hours after the last wash, the odor level under each arm is again graded by four expert judges as previously described. The twice daily supervised washes are then continued for another week and at the end of the second week the odor level is again graded as previously described. The grades are averaged and the relative deodorant effectiveness of the test bars is determined. The above described procedure is repeated for each antibacterial containing bar desired to be tested.

Deodorant effect

Product ¹	Average Odor Level ²	Expected Grade (Additive Basis)
1. Soap alone (Milled Toilet Bar)	5.42	
2. Soap plus 0.2% zinc pyridinethione	4.34	
3. Soap plus 0.333% 3,5,4'-tribromosalicylanilide plus 0.333% 3,4,4'-trichlorocarbani- lilide plus 0.333% 3-trifluoromethyl 4,4-dichlorocarbani- lilide	4.16	
4. Soap plus 0.166% 3,5,4'-tribromosalicylanilide plus 0.166% 3,4,4'-trichlorocarbani- lilide plus 0.166% 3-trifluoromethyl 4,4-dichlorocarbani- lilide plus 0.1% zinc pyridinethione	3.84	4.25

¹ The percent antibacterial agent present in the product is based on the weight of the soap.

² The higher positive number represents the higher odor. LSD (least significant difference) at a 95% confidence level = ± 0.16 in odor grade.

The Expected Grade on an additive basis of 4.25 for product 4 is obtained by taking the average of the odor level grades actually obtained for products 2 and 3. The average of the grades of products 2 and 3 was taken to find the Expected Grade because product 4 contains only half as much zinc pyridinethione as does product 2 and half as much of the ternary mixture of antibacterial agents as does product 3; therefore, the odor level grade of product 4 would be expected to fall halfway between the grades actually obtained for product 2 and product 3. Since the value actually obtained (3.84) for product 4 is significantly less than would be expected (4.25) (the lower positive number representing the greater effectiveness), the example shows that the mixture of zinc pyridinethione and the other antibacterial agents possess synergistic activity when incorporated into a soap or detergent composition.

Similar results can be obtained by using other salts and derivatives of the 1-hydroxy-2-pyridinethione compound.

EXAMPLE III

In this example, the synergism of the mixture of zinc pyridinethione and the other antibacterial agents disclosed herein in a soap composition is shown by means of a hand-washing test. This test is a modification of the well known Cade handwashing test (Arthur R. Cade, Papers on Evaluation of Soaps and Detergents, Special Technical Publication No. 115, published by American Society of Testing Materials, 1952) and can be described as follows:

A panel of 10 subjects are given a test bar (a blend of 80% sodium tallow soap and 20% sodium coconut oil soap) containing the antibacterial agent or mixtures of agents to use at home and are also supplied with a similar bar to use at work. The hands are washed at least three times a day for four days. On the fifth day, the hands are washed five successive times, the last time being in a measured quantity of sterile distilled water. The hands are carefully rinsed in the water in the basin and an aliquot sample of the wash water is then immediately taken for bacterial counts. The sample is filtered through a bacteria filter and the bacteria collected on the special filter are placed in a nutrient medium in sterile petri plates and incubated 48 hours at 37° C. The number of colonies which appear is counted. From the size of the aliquot used, the number of organisms in the fifth basin can be calculated.

The number of organisms removed during washing is proportional to the total number on the skin. Hence, by comparing the number of organisms removed in the fifth wash on the fifth day after use of the test bar with the number removed after use of a blank bar under the same conditions, the degerming effectiveness of the bar can be estimated. It is customary to express the results as "percent reduction in removable bacteria" over the control.

Handwashing tests

Percent reduction in the average number of organisms removed from the hands during the fifth of a series of standard handwashings, after using the product exclusively for one week.

Product ¹	Percent Reduction
1. Soap plus 1% 3,5,4'-tribromosalicylanilide, 1% 3-trifluoromethyl-4,4'-dichlorocarbani- lilide	96.5
2. Soap plus 0.1% zinc pyridinethione	87.4
3. Soap plus 0.5% zinc pyridinethione	92.5
4. Soap plus 0.5% 3,5,4'-tribromosalicylanilide, 0.5% 3-trifluoromethyl-4,4'-dichlorocarbani- lilide, 0.1% zinc pyridinethione	99.4
5. Soap plus 0.5% 3,5,4'-tribromosalicylanilide, 0.5% 3-trifluoromethyl-4,4'-dichlorocarbani- lilide, 0.5% zinc pyridinethione	99.8
6. Soap plus 0.333% 3,5,4'-tribromosalicylanilide, 0.333% 3-trifluoromethyl-4,4'-dichlorocarbani- lilide	97.0
7. Soap plus 0.333% 3,5,4'-tribromosalicylanilide, 0.333% 3-trifluoromethyl-4,4'-dichlorocarbani- lilide, 0.333% 3,4,4'-trichlorocarbani- lilide	99.2
8. Soap plus 0.75% 3,4,4'-trichlorocarbani- lilide, 0.75% bis(2-hydroxy-3,5,6-trichlorophenyl)methane, 0.5% zinc pyridinethione	99.0
9. Soap plus 1.5% 3,4,4'-trichlorocarbani- lilide, 1.5% bis(2-hydroxy-3,5,6-trichlorophenyl)methane	85.2
10. Soap plus 0.75% 3,5,4'-tribromosalicylanilide, 0.75% bis(2-hydroxy-3,5,6-trichlorophenyl)methane, 0.5% zinc pyridinethione	99.9
11. Soap plus 0.5% 3,5,4'-tribromosalicylanilide, 0.5% 3-trifluoromethyl-4,4'-dichlorocarbani- lilide, 0.25% zinc pyridinethione	99.5

¹ The percent antibacterial agent present is based on the weight of the soap.

By examining the above table, it can be seen that products 4, 5 and 11, containing respectively 1.1%, 1.25% and 1.5% by weight of the soap of the antibacterial combinations of this invention exhibit significantly greater activity than product 1 which contains at a total level of 2%, two of the three antibacterial agents used

in products 4, 5 and 11, the only exception being that product 1 does not contain zinc pyridinethione. Similar conclusions can be drawn by comparing products 6 and 7 and products 8 and 9. Products 2 and 3 indicate that zinc pyridinethione when used as the single antibacterial agent in the soap composition has a relatively low level of antibacterial effectiveness, therefore, it would be expected that when admixed with the other antibacterial agents used herein a dilution effect would be observed. That such a dilution effect did not occur, but in fact, a significantly increased level of activity was obtained over that which would be expected on a purely additive basis indicates synergism.

EXAMPLE IV

The examples shown heretofore have exhibited the synergism of the zinc salt of 1-hydroxy-2-pyridinethione in combination with multiple mixtures of other antibacterial agents. This example will show the synergism of the zinc pyridinethione compound and individual antibacterial agents. The testing was one in vitro by means of the "Standard Tube Dilution Tests," which consists essentially of preparing serial dilutions of the antibacterial compositions to be tested in a trypticase soy broth medium, inoculating with the chosen test organism and observing the weakest concentration which prevents growth of the organism after incubation. This concentration (total quantity of antibacterial agent) is called the bacteriostatic breakpoint. In this in vitro test, there were two organisms used, a gram positive coccus and a gram positive bacillus, two common organisms found on the skin. Subsequent to the serial dilution of the antibacterial agent, one drop of the organism is added to the tube containing the antibacterial agent after which the tube is incubated for 24 hours at 37° C., and thereafter the bacteriostatic breakpoint is determined.

In the following table the mixtures of antibacterial agents are in a 1 : 1 ratio and the following letters represent the compounds indicated.

Legend:

ZP—Zinc salt of 1-hydroxy-2-pyridinethione
TCC—3,4,4'-trichlorocarbaniide
TFC—3-trifluoromethyl-4,4'-dichlorocarbaniide
BSA—3,5,4'-tribromosalicylanilide
G-11—Bis(2-hydroxy-3,5,6-trichlorophenyl)-methane

*Bacteriostatic breakpoints**

	Isolate 1			Isolate 2		
	Found	Expected	LSD	Found	Expected	LSD
TCC-----	.08	-----	-----	.2	-----	-----
ZP-----	6.0	-----	-----	6.0	-----	-----
TFC-----	.1	-----	-----	.2	-----	-----
BSA-----	1.0	-----	-----	.5	-----	-----
G-11-----	.2	-----	-----	.2	-----	-----
ZP+TCC---	.1	.16	±.01	.2	.4	±.1
ZP+TFC---	.1	.2	±.01	.3	.4	±.1
ZP+BSA---	.9	2.0	±.1	.5	1.0	±.1
ZP+G-11---	.2	.4	±.1	.2	.4	±.1

Skin isolate #1—gram positive bacilli.

Skin isolate #2—gram positive rod.

*Expressed a p.p.m. total quantity of antibacterial agent required to inhibit growth.

LSD—least significant difference.

An examination of the above table indicates that the combinations of zinc pyridinethione and the other antibacterial agents admixed therewith exhibits significantly greater and surprising antibacterial activity than would be expected if the activity of the mixture were purely additive. Such unexpected results indicate synergism.

Relatively small amounts of the synergistic antibacterial agent mixtures of the present invention are sufficient to render soap bactericidal. The term "soap" as used herein is employed in a broad sense, in that the term refers not only to ordinary sodium or potassium

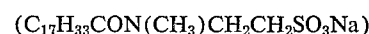
soap made by the saponification of fat or fatty acids as natural anionic detergent agents but it also refers to compositions made of synthetic (ordinarily referred to as non-soap) anionic and nonionic detergent agents in liquid, paste, solid, flake, granular or other similar form. A soap is termed "bactericidal" if it is effective against the staphylococcus aureus organism, whether or not it happens to be effective against any other type of bacteria.

Because of the synergistic activity of the compounds of the present invention, it will be appreciated that smaller amounts than usual with conventional antibacterials can be incorporated into the soap and still achieve good antibacterial effectiveness. Amounts as low as ½ of 1% of the synergistic mixtures described herein with the zinc pyridinethione compound being present at a .1% level, based on the weight of the total soap bar or detergent product, have proved satisfactory; however, it is preferred to use amounts of the mixtures ranging from 1% to 2% by total weight of the bar or detergent product. The upper limit of the amount of agent to be used is determined by practical and economic considerations and is usually about 5%. The ratio of the pyridinethione agent to the total quantity of the other antibacterial compounds of this invention can vary from about 10:1 to about 1:10 with the preferred ratio being about 1:3.

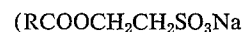
Generally speaking, an increase in concentration of the synergistic mixture increases the bactericidal effectiveness of the soap products. However, it is apparent that the cost of the agent in the soap or shampoo itself mitigates against the use of an excessive amount. Additionally, if too large an amount of agent is incorporated into the soap, the detergent properties of the soap or detergent product may be lessened.

The anionic synthetic detergent agent which can be employed with this invention is generally defined as a water-soluble salt of an organic sulfuric reaction product having in its molecular structure an alkyl group containing from about 8 to about 22 carbon atoms and a radical selected from the group consisting of sulfonic acid and sulfuric acid ester radicals. Important examples of the synthetics of this group which may be benefited through the incorporation therein of the mixtures of this invention, are the sodium or potassium alkyl sulfates, especially those derived by sulfation of higher alcohols produced by reduction of glycerides of tallow or coconut oil; sodium or potassium alkyl benzene sulfonates, especially those of the types described in U.S. Letters Patents 2,220,099, granted November 5, 1940, and 2,477,383, granted July 26, 1949, in which the alkyl group contains from about 9 to about 15 carbon atoms; sodium alkyl glyceryl ether sulfonates, especially those ethers in which the alkyl group is derived from the higher alcohols obtained from tallow and coconut oil; sodium coconut oil fatty acid monoglyceride sulfates and sulfonates, sodium salts of sulfuric acid esters of the reaction product of one mole of a higher fatty alcohol (e.g., tallow or coconut oil alcohols) and about three moles of ethylene oxide, and others known in the art, a number being specifically set forth in Byerly, U.S. Letters Patent 2,486,921, granted November 1, 1949, and Strain, U.S. Letters Patent 2,486,922, granted November 1, 1949.

Additional anionic surface active sulfonates which can be employed in this invention are the sulfonated alkyl acid amides such as Igepon T



the sulfonated esters such as Igepon AP



where R is an alkyl radical containing from 11 to 17 carbon atoms), sodium salt of the bisulfate of a dialkyl dicarboxylate, sodium salt of the sulfonic acid derivative of a dialkyl dicarboxylate, sodium sulfosuccinic esters such as $NaOOCCH_2CH(SO_3Na)CONHC_{18}H_{37}$ and the like.

The nonionic synthetic detergents hereinbefore described as beneficially affected by the synergistic antibacterial mixtures of this invention may be broadly defined as compounds produced by the condensation of alkylene oxide groups with an organic hydrophobic compound which may be aliphatic or alkyl aromatic in nature, e.g., the condensation products of alkyl phenols having a straight or branched chain alkyl group containing from about 6 to 12 carbon atoms, with from about 10 to about 25 moles of ethylene oxide per mole of alkyl phenol. The alkyl substituent in each compound can be conveniently derived from polymerized propylene diisobutylene, octane, or nonane or from any other natural or artificial source which will provide alkyl chains with the requisite number of carbon atoms as specified hereinbefore.

For example, a well known class of nonionics to which significant levels of antibacterial activity will be imparted through the incorporation of minor amounts of the synergistic mixtures of this invention is marketed under the trade name of "Pluronic" by the Wyandotte Chemical Co., of Wyandotte, Michigan. These compounds are formed by condensing ethylene oxide with a hydrophobic base formed by the condensation of propylene oxide with propylene glycol.

Other suitable nonionics may be derived by the condensation of ethylene oxide with the product resulting from the reaction of propylene oxide and ethylene diamine.

A minor amount, totaling about 2%, of a 2:2:1 mixture of 3,5,4'-tribromosalicylanilide, 3-trifluoromethyl-4,4'-dichlorocarbaniide, and the zinc salt of 1-hydroxy-2-pyridinethione, for example, renders a composition containing any of the above detergents or mixtures thereof, antibacterially active against a broad range of microorganisms including some which are gram negative.

The synergistic mixtures of this invention have been found to increase the antibacterial activity of soap compositions in bar and granular form and can be incorporated into the soap composition by any suitable method preferably which yields as a result a uniform distribution of bactericidal agents throughout the whole mass.

Regular use of a "Camay" or "Ivory" type soap bar containing 1.5% of the synergistic mixtures of this invention results in substantial reductions in the bacterial population of the skin and thereby markedly reduces body odor attributable to the bacterial degradation of perspiration.

A sample formula for a milled toilet detergent bar which can be prepared by means known and used in the art is as follows. ("Middle-cut" as used herein refers to that fraction of distilled coconut alcohol which consists predominantly of lauryl and myristyl alcohols.)

20.0% potassium alkyl sulfate (alkyl group derived from the middle cut of alcohols obtained by catalytic reduction of coconut oil)

8.0% sodium alkyl glyceryl ether sulfonate (alkyl group derived from the middle cut of alcohols obtained by catalytic reduction of coconut oil)

33.81% sodium soap of 20:80 coconut:tallow fatty acids

17.07% magnesium soap of 20:80 coconut:tallow fatty acids

5.81% inorganic salts

.75% 3,4,4'-trichlorocarbaniide

.75% 3,5,4'-tribromosalicylanilide

.50% zinc salt of 2-hydroxy-1-pyridinethione

8.0% moisture

Balance miscellaneous

A granular built synthetic anionic detergent composition having the following formulation can be prepared by conventional means and the antibacterial agents of this invention may be incorporated therein.

17.5% sodium alkyl benzene sulfonate (the alkyl radical averaging about 12 carbon atoms and being derived from polypropylene)

49.7% sodium tripolyphosphate

13.3% sodium sulfate

7.0% silicate solids

0.75% 3,5,4'-tribromosalicylanilide

0.75% 3,4,3'-trichlorocarbaniide

0.50% zinc pyridinethione

Balance water and miscellaneous.

Other salts and derivatives of 1-hydroxy-2-pyridinethione can be substituted in the above examples to obtain comparable results.

As shown by the above examples, especially Example III, particularly outstanding synergistic antibacterial effectiveness is exhibited in combinations of (1) ZP and (2) at least two antibacterial agents selected from the group consisting of BSA, G-11, TFC and TCC wherein the proportions by weight of (1) and (2) are in the range of about one part of (1) to from about .666 to about 5 parts of each of the agents selected from this group and these combinations are used with water on the human body from a medium in which the concentration of ZP ranges from about 0.1% to about 0.5% and the total concentration of the agents from this group is not more than about 1.5%.

The invention has been described above in conjunction with various illustrative examples of antibacterial compositions, toilet and laundry detergents. It will be obvious to those skilled in the art, however, that the antibacterial mixtures can also be beneficially employed in such products as shampoos, antiseptic ointments, foot powders, antiperspirants, deodorants, and the like.

What is claimed is:

An antibacterial composition comprising a combination of (1) the zinc salt of 1-hydroxy-2-pyridinethione and (2) at least two antibacterial agents selected from the group consisting of 3,5,4'-tribromosalicylanilide, bis(2-hydroxy-3,5,6-trichlorophenyl)methane, 3-trifluoromethyl-4,4'-dichlorocarbaniide, 4,3,3'-trichlorocarbaniide and 3,4,4'-trichlorocarbaniide, the proportions by weight of (1) and (2) being in the range of about one part of ingredient (1) to from about .666 to about 5 parts of each of the agents selected from said group, the said combination displaying a synergistic antibacterial action when used with water on the human body from a medium in which the concentration of ingredient (1) ranges from about 0.1% to about 0.5% by weight and the total concentration of the agents selected from said group is not more than about 1.5% by weight.

No references cited.

JULIAN S. LEVITT, *Primary Examiner.*