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Kooistra

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[54] **SYNERGISTIC ANTIBACTERIAL COMBINATION**

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[51] **Int. Cl.** **A01n 9/00**

[58] **Field of Search** 424/263, 340, 245; 252/106; 117/138.5

[56] **References Cited**

UNITED STATES PATENTS

3,235,455 2/1966 Judge et al. 424/322

OTHER PUBLICATIONS

Chemical Abstracts, Vol. 63 (1965) p. 11431b

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[57] **ABSTRACT**

Antibacterial compositions containing a combination of the zinc salt of 1-hydroxy-2-pyridinethione and 2,4,4′-trichloro-2′-hydroxydiphenyl ether, in a ratio of from about 9:1 to about 1:9 respectively, said combination possessing a synergistic activity permitting use at low concentrations.

1 Claim, No Drawings

SYNERGISTIC ANTIBACTERIAL COMBINATION

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to antibacterial compositions which possess synergistic activity through the use of a combination of antibacterial agents. More specifically, the present invention relates to a combination of the zinc salt of 1-hydroxy-2-pyridinethione (ZPT) and 2,4,4'-trichloro-2'-hydroxydiphenyl ether (TCDPE)

During recent years, there has been considerable research in the field of antibacterials to develop new broad-spectrum antibacterial agents which are effective when used in products for use on the skin and on various textile products. It has been estimated that over 40 percent of the toilet soap bar sales are products containing some form of an antibacterial system with projections for sales substantially greater. Further, an increasing number of laundry products are being marketed containing various antibacterial agents.

Numerous compounds have been suggested in the past for use in soaps, detergents and various cosmetic preparations. Early compounds investigated for use in soaps and other cleansing products were phenols and phenolic fatty acid esters. A bit more recently, mercuric compounds were widely used. Most recently, a number of new compounds have been suggested for use in soaps, detergents and cosmetic preparations. These include the halogenated salicylanilides and carbanilides, and the halogenated bisphenols. Perhaps the most popular of these is a halogenated bisphenol known as G-11, more commonly known as hexachlorophene.

It is well known, however, by those skilled in the art that several of the above-mentioned compounds have some serious limitations in their use. For example, phenols and phenol esters, although effective in an aqueous solution, were found to be ineffective in the presence of soap or detergent compositions. Other antibacterial agents heretofore mentioned, although being effective, were seriously limited in their application because their scope of effectiveness was severely limited to a very narrow range of organisms.

The best known antibacterial agent G-11 (hexachlorophene), is disadvantageous in that halogenated bisphenols are light-sensitive and when incorporated into a soap or detergent bar, will discolor the bar upon prolonged exposure to sunlight. Further, when incorporated into soap or detergent bars at sufficiently high levels to obtain good antibacterial effectiveness, i.e., up to 2 percent or more, the discoloration is so pronounced as to necessitate the bar being dyed a similar color to match the discoloration.

In some instances, the problem of high levels of concentration of the antibacterial compounds has been alleviated by the discovery that certain binary and ternary combinations of certain antibacterial agents exhibit synergism when admixed and incorporated into various soap, detergent and cosmetic products. Such synergism makes possible a higher level of antibacterial effectiveness than that possible from either antibacterial agent when used alone. The net result is that this enables a manufacturer to use a lesser amount of antibacterial agents while retaining a high degree of effectiveness. It should be noted that such anti-bacterial agents and

combinations are in great need and demand, especially those that exhibit effectiveness against both Gm + and Gm − organisms, and can be used on the skin as well as on various textile products.

2. The Prior Art

The use of the zinc salt of 1-hydroxy-2-pyridinethione as an antibacterial agent for use in various soap, detergent and cosmetic preparations is well known to the art and is disclosed in U.S. Pat. Nos. 3,412,033 issued on Nov. 19, 1968 to Karsten et al., 3,281,366 issued on Oct. 25, 1966 to Judge et al., and 3,235,455 issued on Feb. 15, 1966 to Judge et al.

It has also been found by others that 2,4,4'-trichloro-2'-hydroxydiphenyl ether possesses antibacterial properties and that such properties can be imparted to various soap, detergent and cosmetic preparations. Further, the synergistic properties of 2,4,4'-trichloro-2'-hydroxydiphenyl ether when combined with certain specific antibacterial agents have also been disclosed. Such disclosures can be found in an article by Furice and Schenkel in Vol. 44 No. 1 in Soap & Chemical Specialties, Jan. 1968 on pages 47–50, 116, 118, 120 and 122. Other prior art disclosing the use of 2,4,4'-trichloro-2'-hydroxydiphenyl ether as an antibacterial agent and exhibiting synergistic properties are U.S. Pat. No. 3,445,398 issued on May 20, 1969 to Jungerman et al., British Patent 1,038,185 published on Aug. 10, 1966, and a South African application number 66/5968 published on May 29, 1968. However, no prior art is known which describes the specific combination of this invention, nor specifically suggests that synergism would result. Further, nothing in the prior art specifically discloses that the combination of this invention would be effective and suitable for use in soaps, detergent compositions and cosmetic preparations.

It is, therefore, an object of this invention to provide a synergistic antibacterial composition which possesses a high level of antibacterial effectiveness.

It is further an object of the present invention to provide antibacterial compositions which are effective against both Gram-positive and Gram-negative organisms.

It is still a further object of the present invention to provide antibacterial compositions which are effective when incorporated in soap, detergent and cosmetic compositions.

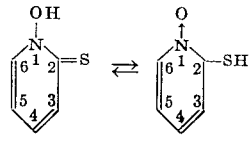
Other objects and advantages and a fuller understanding of this invention will be made apparent from the description and examples hereinafter.

SUMMARY OF THE INVENTION

These objects are achieved by the present invention which is directed towards a synergistic combination of the zinc salt of 1-hydroxy-2-pyridinethione and 2,4,4'-trichloro-2'-hydroxydiphenyl ether in a ratio of from about 9:1 to about 1:9 respectively. The term "synergistic combinations" as used herein refers to the cooperative action of discrete agencies such that the total effect is greater than the sum of the two effects taken independently. The synergistic combinations of the present invention have special and essential ratios of their components as hereinafter specifically defined.

PREFERRED EMBODIMENTS OF THE INVENTION

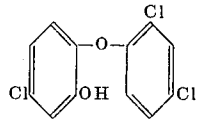
The pyridinethione compound used in this invention has the structural formula in the tautomeric form of:



1-hydroxy-2-pyridinethione 2-pyridinethiol 1-oxide or
2-mercaptopyridine 1-oxide

The metal salt disclosed herein represents substitution of the corresponding metal for the hydrogen of one of the tautomeric forms. The preferred pyridinethione compound utilized in this invention is the zinc salt of 1-hydroxy-2-pyridinethione.

The other antibacterial compound of this invention is 2,4,4'-trichloro-2'-hydroxydiphenyl ether having the structural formula:



The precise method by which any of these compounds can be prepared constitutes no part of this invention. The compounds are all available commercially.

More specifically, it has been surprisingly found that a combination of the zinc salt of 1-hydroxy-2-pyridinethione (ZPT) and 2,4,4'-trichloro-2'-hydroxydiphenyl ether (TCDPE) in a range of ratios of from about 9:1 to about 1:9, preferably from about 3:1 to about 1:1, most preferably 1:1, of ZPT to TCDPE, respectively, results in a combination possessing synergistic antibacterial properties.

It has also been found that the above-disclosed combination of antibacterial agents possesses synergistic antibacterial properties whereby a lasting antibacterial effect is obtained particularly in soap and non-soap synthetic detergent compositions, and other products where an antibacterial action is desired. Such compositions containing the synergistic combination of the present invention in amounts of from about 0.2 percent to about 3 percent, preferably about 1 percent, are particularly effective.

The term "soap" as used herein is meant to designate alkali metal soaps such as the sodium and potassium salts of the higher fatty acids of naturally occurring plant or animal esters, e.g., palm oil, coconut oil, babassu oil, soybean oil, castor oil, tallow, whale and fish oils, grease and lard and mixtures thereof. Sodium and potassium soaps can be made by direct saponification of the fats and oils or by the neutralization of the fatty acids which are prepared in a separate manufacturing process. Examples of suitable soaps are the sodium, potassium, ammonium and alkylolammonium salts of higher fatty acids (C_{10} –C_{20}). Particularly useful are the sodium and potassium salts of the mixtures of fatty acids derived from coconut oil and tallow, i.e., sodium or potassium tallow and coconut soap.

Anionic synthetic detergents which can be used with the antibacterial combinations of the present invention can be broadly defined as the water-soluble salts, including the alkali metal, ammonium and substituted ammonium salts, of organic sulfuric reaction products having in their molecular structure an alkyl radical 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 synthetic detergents which can be used with the compositions of the present invention are the following: an alkali metal (e.g., sodium and potassium) ammonium and substituted ammonium (e.g., lower alkyl ammonium) salts; alkyl sulfates, especially those obtained by sulfating the higher alcohols produced by reducing the glycerides of tallow or coconut oil; random paraffin oxide; in which the alkyl from about 8 to about 22 carbon atoms, prepared by treating random paraffin hydrocarbons in sulfur dioxide and chlorine in the presence of light followed by treating with a base; branched or linear alkyl benzene sulfonates, in which the alkyl group contains from about 8 to about 18 carbon atoms, preferably from about 10 to about 14 carbon atoms, especially those of the types described in U.S. Pat. Nos. 2,220,099, and 2,477,383; sodium alkyl glyceryl ether sulfonates, especially those ethers of the higher alcohols derived from tallow and coconut oil; coconut oil fatty acid monoglyceride sulfates and sulfonates; sulfuric acid esters of the reaction product of one mole of a higher fatty alcohol (e.g., tallow or coconut alcohols) and from about 1 to about 6, preferably about 3 moles of ethylene oxide, alkyl phenol ethylene oxide ethylene oxide ether sulfates with about 4 units of ethylene oxide per molecule and in which the alkyl radicals contain about nine carbon atoms; the reaction product of fatty acids esterified with isethionic acid and neutralized with sodium hydroxide where, for example, the fatty acids are derived from coconut oil; fatty acid amides of the methyl taurine in which the fatty acids, for example, are derived from coconut oil; sulfonated olefins of U.S. Pat. No. 3,332,880; and others known in the art, a number being specifically set forth in U.S. Pat. Nos. 2,486,921, 2,486,922 and 2,396,278.

The nonionic synthetic detergents which can be used with the antibacterial combinations of the present invention may be broadly defined as compounds produced by the condensation of alkylene oxide groups (hydrophilic in nature) with an organic hydrophobic compound which may be aliphatic or alkyl-aromatic in nature. The length of the hydrophilic or polyoxyalkylene radical which is condensed with any particular hydrophobic group can be readily adjusted to yield a water-soluble compound having the desired degree of balance between hydrophilic and hydrophobic elements.

For example, a well-known class of nonionic synthetic detergents is made available on the market under the trade name of "Pluronic." These compounds are formed by condensing ethylene oxide with a hydrophobic base formed by the condensation of propylene oxide with propylene glycol. The hydrophobic portion of the molecule which, of course, exhibits water insolubility has a molecular weight of from about 1,500 to about 1,800. The addition of polyoxyethylene radicals to this hydrophobic portion tends to increase

the water solubility of the molecule as a whole and the liquid character of the products is retained up to the point where polyoxyethylene content is about 50 percent of the total weight of the condensation product.

Other suitable nonionic synthetic detergents include:

1. The polyethylene oxide condensates of alkyl phenols, e.g., the condensation products of alkyl phenols having an alkyl group containing from about six to 12 carbon atoms in either a straight chain or branched chain configuration, with ethylene oxide, the said ethylene oxide being present in amounts equal to 10 to 60 moles of ethylene oxide per mole of alkyl phenol. The alkyl substituent in such compounds may be derived from polymerized propylene, diisobutylene, octane, or nonane, for example. 2. Those derived from the condensation of ethylene oxide with the product resulting from the reaction of propylene oxide and ethylene diamine — products which may be varied in composition depending upon the balance between the hydrophobic and hydrophilic elements which is desired. For example, compounds containing from about 40 percent to about 80 percent polyoxyethylene by weight and having a molecular weight of from about 5,000 to about 11,000 resulting from the reaction of ethylene oxide groups with a hydrophobic base constituted of the reaction product of ethylene diamine and excess propylene oxide, said base having a molecular weight of the order of 2,500 to 3,000, are satisfactory.

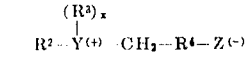
3. The condensation product of aliphatic alcohols having from 8 to 18 carbon atoms, in either straight chain or branched chain configuration, with ethylene oxide, e.g., a coconut alcohol ethylene oxide condensate having from 10 to 30 moles of ethylene oxide per mole of coconut alcohol, the coconut alcohol fraction having from 10 to 14 carbon atoms.

4. Long chain tertiary amine oxides corresponding to the following general formula, $R_1R_2R_3N \rightarrow 0$, wherein R_1 contains an alkyl, alkenyl or monohydroxy alkyl radical of from about 8 to about 18 carbon atoms from 0 to about 10 ethylene oxide moieties, and from 0 to 1 glyceryl moiety, and R_2 and R_3 contain from one to about three carbon atoms and from 0 to about 1 hydroxy group, e.g., methyl, ethyl, propyl, hydroxy ethyl, or hydroxy propyl radicals. The arrow in the formula is a conventional representation of a semi-polar bond. Examples of amine oxides suitable for use in this invention include dimethyldodecylamine oxide, oleyldi(2-hydroxyethyl)amine oxide, dimethyloctylamine oxide, dimethyldecylamine oxide, dimethyltetradecylamine oxide, 3,6,9-trioxaheptadecyldiethylamine oxide, di(2-hydroxyethyl)-tetradecylamine oxide, 2-dodecoxyethyldimethylamine oxide, 3-dodecoxy-2-hydroxypropyldi(3-hydroxypropyl)amine oxide, dimethylhexadecylamine oxide.

5. Long chain tertiary phosphine oxides corresponding to the following general formula $RR'R''P \rightarrow 0$, wherein R contains an alkyl, alkenyl or monohydroxyalkyl radical ranging from eight to 18 carbon atoms in chain length, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety and R′ and R″ are each alkyl or monohydroxy-alkyl groups containing from one to three carbon atoms. The arrow in the formula is a conventional representation of a semipolar bond. Examples of suitable phosphine oxides are:
dodecyldimethylphosphine oxide,
tetradecyldimethylphosphine oxide,
tetradecylmethylethylphosphine oxide,
3,6,9-trioxaoctadecyldimethylphosphine oxide,
cetyldimethylphosphine oxide,
3-dodecoxy-2-hydroxypropyldi(2-hydroxyethyl)phosphine oxide,
stearyldimethylphosphine oxide,
cetylethylpropylphosphine oxide,
oleyldiethylphosphine oxide,
dodecyldiethylphosphine oxide,
tetradecyldiethylphosphine oxide,
dodecyldipropylphosphine oxide,
dodecyldi(hydroxymethyl)phosphine oxide,
dodecyldi(2-hydroxyethyl)phosphine oxide,
tetradecylmethyl-2-hydroxylpropylphosphine oxide,
oleyldimethylphosphine oxide,
2-hydroxydodecyldimethylphosphine oxide.

6. Long chain dialkyl sulfoxides containing one short chain alkyl or hydroxy alkyl radical of one to about three carbon atoms (usually methyl) and one long hydrophobic chain which contains alkyl, alkenyl, hydroxy alkyl, or keto alkyl radicals containing from about eight to about 20 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety. Examples include:
octadecyl methyl sulfoxide, 2-ketotridecyl methyl sulfoxide,
3,6,9-trioxaoctadecyl 2-hydroxyethyl sulfoxide,
dodecyl methyl sulfoxide,
oleyl 3-hydroxy propyl sulfoxide,
tetradecyl methyl sulfoxide,
3-methoxytridecyl methyl sulfoxide
3-hydroxytridecyl methyl sulfoxide,
3-hydroxy-4-dodecoxybutyl methyl sulfoxide.

The zwitterionic synthetic detergents useful with the antibacterial agents of the present invention can be broadly described as derivatives of aliphatic quaternary ammonium, phosphonium, and sulfonium compounds, in which the aliphatic radicals can be straight chain or branched, and wherein one of the aliphatic substituents contains from about 8 to 18 carbon atoms and one contains an anionic water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. A general formula for these compounds is:



wherein R^2 contains an alkyl, alkenyl, or hydroxy alkyl radical of from about eight to about 18 carbon atoms, from 0 to about 10 ethylene oxide moieties and from 0 to 1 glyceryl moiety; Y is selected from the group consisting of nitrogen, phosphorous, and sulfur atoms; R^3 is an alkyl or monohydroxy-alkyl group containing one to about three carbon atoms; x is 1 when Y is a sulfur atom and 2 when y is a nitrogen or phosphorous atom, R^4 is an alkylene or hydroxyalkylene of from 1 to about 4 carbon atoms and Z is a radical selected from the group consisting of carboxylate, sulfonate, sulfate, phosphonate, and phosphate groups.

EXAMPLES INCLUDE:

4-[N,N-di(2-hydroxyethyl)-N-octadecylammonio]-butane-1-carboxylate;
5-[S-3-hydroxypropyl-S-hexadecylsulfonio]-3-hydroxypentane-1-sulfate;

3-[P,P-diethyl-P-3,6,9,-trioxatetracoxylphosphonio]-2-hydroxy-propane-1-phosphate;
3-[N,N-dipropyl-N-3-dodecoxy-2-hydroxypropylammonio]-propane-1-phosphonate;
3-(N,N-dimethyl-N-hexadecylammonio)propane-1-sulfonate;
3-(N,N-dimethyl-N-hexadecylammonio)-2-hydroxypropane-1-sulfonate;
4-[N,N-di(2-hydroxyethyl)-N-(2-hydroxydodecyl)ammonio]-butane-1-carboxylate;
3-[S-ethyl-S-(3-dodecoxy-2-hydroxypropyl)sulfonio]-propane-1-phosphate;
3-[P,P-dimethyl-P-dodecylphosphonio]-propane-1-phosphonate; and
5-[N,N-di(3-hydroxypropyl)-N-hexadecylammonio]2-hydroxy-pentane-1-sulfate.

The amphoteric synthetic detergents useful in the present invention can be broadly described as derivatives of aliphatic secondary and tertiary amines in which the aliphatic radical can be straight chain or branched and wherein one of the aliphatic substituents contains from about 8 to about 18 carbon atoms and one contains an anionic water solubilizing group, e.g., carboxy, sulfonate, sulfate, phosphate, or phosphonate. Examples of compounds falling within this definition are sodium 3-dodecylaminopropionate, sodium 3-dodecylaminopropane sulfonate, dodecyl-β-alanine, N-alkyl-taurines such as the one prepared by reacting dodecylamine with sodium isethionate according to the teaching of U.S. Pat. No. 2,658,072, N-higher alkyl aspartic acids such as those produced according to the teaching of U.S. Pat. No. 2,438,091, and the products sold under the trade name "Miranol" and described in U.S. Pat. No. 2,528,378.

Detergent formulations containing the antibacterial compositions of the present invention can also contain from about 0 percent to about 90 percent, preferably from about 10 percent to about 90 percent of water-soluble alkaline detergency builder salts, either of the organic or inorganic types. Examples of such builder salts can be found in U.S. Pat. No. 3,336,233, issued Aug. 15, 1967, column 9, lines 29–66, which is incorporated herein by reference.

The detergent formulations can also contain any of the usual adjuvants, diluents, and additives, for example, perfumes, anti-tarnishing agents, anti-redeposition agents, dyes, fluorescers, suds builders, suds depressors and the like without detracting from the advantageous properties of the antibacterial compositions of the present invention.

Examples of diluents which may be incorporated into a synthetic detergent bar in amounts of up to about 80 percent of the bar include soaps, especially heavy metal insoluble soaps, (metallic salts of higher fatty acids); starches such as cornstarch; and clays such as china clay or fuller's earth. Other diluents include inorganic salts such as sodium and potassium chlorides and sulfates. Such diluents add bulk to the bar and improve its cosmetic properties without impairing its detergent or cohesive properties.

The antibacterial efficacies of the synergistic combinations of the present invention were established and are demonstrated by the following tests:

1. Tube Dilution Test;
2. Skin Retention Test.

These tests and the results obtained therefrom are described in detail in Examples I and II below.

EXAMPLE I

Tube Dilution Test

This test is designed to determine the Minimal Inhibitory Concentration (MIC). The MIC, or Bacteriostatic Breakpoint is the minimum concentration which just prevents growth of the organism throughout incubation.

A 1,000 ppm stock solution of each of the antibacterial agents was prepared in dimethyl formamide (DMFA). These were combined in a series of concentration ratios as listed in Table I. Appropriate dilutions were made in DMFA so that when 0.1 ml was added to trypticase soy broth (TSB) medium, a series of concentrations (ppm) for each of the above ratios, was realized in a total of 10 ml of tube contents. Each TSB tube in the series was prepared in quadruplicate and four TSB controls were included. All solutions were thoroughly mixed throughout this procedure. Cultures of *Staphylococcus aureus* ATCC No. 6538 and *Escherichia coli* ATCC No. 11229 incubated 18 hours at 37°C. in TSB were diluted 1:100 in 0.1 percent peptone water containing a few glass beads to break up aggregates of cells. 0.01 ml of the 1:100 dilution of an organism was added to all duplicate TSB tubes; thus each concentration for each ratio was tested in duplicate against each organism. All the inoculated tubes were then incubated for 24 hours at 37°C. The weakest concentration which completely prevented growth of the organism in both of the duplicate tubes was the MIC, also known as the bacteriostatic breakpoint. The existance of synergism in each ratio was determined by using the methods of Zwart Voorspuij and Nass as reported in the *Arch. Intern. Pharmacodynamie* 109: pages 211–228, (1957). The following table summarizes the ratios of 1-hydroxy-2-pyridinethione and 2,4,4'-**trichloro-2'-hydroxydiphenyl ether tested, the minimal inhibitory concentrations in parts per million (ppm), of said mixtures, and the ratio sum and activity index for such mixtures. Where the ratio sum is greater than** 1, there is antagonism, and where the ratio sum is less than 1, there is synergism, assuming a straight line relationship for activity vs. concentration. The results clearly demonstrate synergism for the two antibacterial agents of the present invention.

TABLE I

(Tube Dilution MIC Test Results)

Concentration Ratios		Staphylococcus aureus (Gram +)		
ZPT[1]	TCDPE[2]	MIC(ppm)	Ratio[3] Sum	Activity Index[3] (Log of Ratio Sum)
0	100	0.025	1.00	0.0
10	90 *	0.025	0.901	−0.045
20	80 *	0.025	0.802	−0.096
30	70 *	0.025	0.703	−0.153
40	60 *	0.025	0.605	−0.218
50	50 *	0.025	0.506	−0.296
60	40 *	0.025	0.407	−0.390
70	30	0.1	1.232	0.091
80	20 *	0.05	0.418	−0.379
90	10 *	0.2	0.882	−0.055
100	0	2.2	1.00	0.0

[1]zinc salt of 1-hydroxy-2-pyridinethione
[2]2,4,4'trichloro-2'-hydroxydiphenyl ether
[3]See Zwart Voorspuij and Nass reference (see chart below)

Effects

	Ratio Sum	Activity Index
Additive	1	0
Antagonism	>1	>0
Synergism	<1	<0

*Denotes synergism

Concentration Ratios		Escherichai coli (Gram −)		
ZPT[1]	TCDPE[2]	MIC(ppm)	Ratio[3] Sum	Activity Index[3] (Log of Ratio Sum)
0	100	0.3	1.00	0.0
10	90	0.4	1.211	0.083
20	80 *	0.3	0.817	−0.088
30	70 *	0.3	0.726	−0.139
40	60 *	0.4	0.805	−0.094
50	50 *	0.4	0.724	−0.140
60	40 *	0.5	0.753	−0.123
70	30 *	0.6	0.720	−0.143
80	20 *	1.0	0.895	−0.048
90	10	1.8	1.06	0.025
100		3.5	1.00	0.0

[1]zinc salt of 1-hydroxy-2-pyridinethione
[2]2,4,4'trichloro-2'-hydroxydiphenyl ether
3See Zwart Voorspuij and Nass reference (see chart below)

Effects	Ratio Sum	Activity Index
Additive	1	0
Antagonism	>1	>0
Synergism	<1	<0

*Denotes synergism

From the above table, it can readily be seen that synergism is exhibited against both a Gram-positive as well as a Gram-negative organism. Synergism is indicated by an asterisk. Although the 70:30 ratio concentration against *Staphylococcus aureus* did not shown synergism, it should be noted that synergism was demonstrated at this ratio against *Escherichia coli*, which is much more difficult to inhibit than *Staphylococcus aureus*.

EXAMPLE II

Skin Retention Test

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 was cut into small discs (mm in diameter and 0.4 mm thick). These were washed in a standard concentration of soap product containing the antibacterial compound or compounds to be tested for a standard time (10 minutes) and temperature (50°C.). Varying concentrations of the two antibacterials of the present invention were prepared from 10,000 ppm dimethylformamide (DMFA) stock solutions and added to 5 percent Camay solutions. After washing, the discs were rinsed three times with distilled water to remove all traces of soap, and allowed to dry. The dry discs of callus were then imbedded in molten agar previously seeded with the test organism, in this case *Staphylococcus aureus* and *Escherichia coli*. The agar plates plus callus discs were then stored in a refrigerator overnight to permit diffusion of the antibacterial agent from the callus into the surrounding medium. The next day, the plates were placed in the incubator at 37°C. and the organisms were allowed to grow for about 24 hours. The clear zone of inhibited growth of the test organism surrounding the discs is an indication of the antibacterial activity imparted to the callus discs in the washing process.

The following table summarizes the results of the above-described tests. The results clearly shows synergism of the antibacterial agents of the present invention.

TABLE II

Skin Retention Test Results*			
Sanitizer Concentrations in 5% Camay		*Staphylococcus aureus*	*Escherichia coli*
TCDPE**	ZPT***		
	0.5%	0	0
	0.25%	0	0
	0.1%	0	0
0.5%		27.5	10.0
0.25%		24.0	6.5
0.1%		15.0	0
0.5%	0.5%	28.0+	11.0+
0.25%	0.5%	23.0	8.0+
0.1%	0.5%	17.0+	0
0.5%	0.25%	27.5	10.0
0.25%	0.25%	26.0+	7.5+
0.1	0.25%	19.5+	0
0.5%	0.1%	28.0+	10.0
0.25%	0.1%	25.0+	7.9+
0.1%	0.1%	19.0+	0
0.0 - Control	0.0	0	0

*Expressed as total inhibition zone size in mm including skin disc; zero values mean no zone of inhibition.
**2,4,4'-trichloro-2'-hydroxydiphenyl ether
***zinc salt of 1-hydroxy-2-pryidinethione
+Denotes synergism

From the above table, it can be seen that ZPT in soap at a level of from about 0.1 percent to about 0.5 percent has essentially no antibacterial activity as measured by this particular test. It can also be seen that TCDPE in soap at a level of from about 0.1 percent to about 0.5 percent has some antibacterial activity primarily against *Staphylococcus aureus*. It can also be seen that when the two antibacterial agents were combined in ratios of from about 1:5 to about 5:1 and concentrations of from about 0.2 percent to about 1 percent that antibacterial effectiveness was greater than that of the antibacterial agents used alone. It can further be seen that the combination of the present invention results in antibacterial activity greater than that which would be expected on a purely additive basis, thus clearly demonstrating synergism.

EXAMPLE III

A milled toilet detergent bar is prepared in accordance with methods known and used in the art and having the following composition:

	Percent
Sodium alkyl glyceryl ether sulfonate (alkyl group derived from the middle cut[1] of alcohols obtained by catalytic reduction of coconut oil)	8.0
Potassium alkyl sulfate (alkyl group derived from the middle cut[1] of alcohols obtained by catalytic reduction of coconut oil)	20.0
Magnesium soap of 80:20 tallow: coconut fatty acids	17.0
Inorganic salts (sodium and potassium chlorides and sulfates)	32.0
2,4,4'-trichloro-2'-hydroxydiphenyl ether	0.5
zinc salt of 1-hydroxy-2-pyridinethione	0.5
Water and minors	balance to

[1]Middle-cut coconut alcohols having a chain length distribution substantially as follows: 2% C_{10}, 66% C_{12}, 23% C_{14} and 9% C_{16}.

This bar cleans well and exhibits good odor reducing properties evidencing antibacterial effectiveness. It reduces the number of bacteria on the skin and does not discolor significantly.

EXAMPLE IV

A granular built synthetic detergent composition having the following formulation can be prepared and the antibacterial compositions of the present invention can be incorporated therein.

	Percent
Sodium dodecylbenzene sulfonate	17.5
Sodium tripolyphosphate	50.0
Sodium sulfate	14.0
Sodium silicate (SiO_2:Na_2O=2:1)	7.0
ZPT[1]	2.25
TCDPE[2]	0.75
Water and minors	balance to 100

1. Zinc salt of 1-hydroxy-2-pyridinethione
2. 2,4,4'-trichloro-2'-hydroxydiphenyl ether

This composition, in addition to performing well in its cleaning capacity, imparts considerable antibacterial activity to fabrics cleansed in its solution.

Substantially equivalent results are obtained, i.e., good cleaning and good odor reducing properties when the sodium dodecylbenzene sulfonate of Example IV is replaced, on an equal weight basis, by the following:
sodium tallowalkyl sulfate;
potassium coconutalkyl glyceryl ether sulfonate;
sodium salt of randomly sulfonated paraffin containing an average of 15.2 carbon atoms;
ammonium tridecyl sulfate;
condensation product of octyl phenol with 15 moles of ethylene oxide per mole of octyl phenol;
dimethyldodecylamine oxide;
dodecyldimethylphosphine oxide;
tetradecyle methyl sulfoxide; 3-(N,N-dimethyl-N-hexadecylammonio)propane-1-sulfonate; 3-dodecylaminopropronate; and
dodecyl-β-alanine.

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

What is claimed is:

1. An antibacterial composition comprising a bactericidally effective amount of a mixture of the zinc salt of 1-hydroxy-2-pyridinethione and 2,4,4'-trichloro-2'-hydroxydiphenyl ether in a ratio of said zinc salt of 1-hydroxy-2-pyridinethione to said 2,4,4'-trichloro-2'-hydroxydiphenyl ether of about 1:1.

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