

603203

COMMONWEALTH of AUSTRALIA

PATENTS ACT 1952

APPLICATION FOR A STANDARD PATENT 13 APR 1988

LODGED AT SUB-OFFICE

Melbourne

± We ALCIDE CORPORATION
of One Willard Road, Norwalk Connecticut 06851
United States of America

hereby apply for the grant of a Standard Patent for an invention entitled:

"DISINFECTING COMPOSITIONS AND METHODS THEREFOR"

which is described in the accompanying ~~provisional~~ complete specification.

Details of basic application(s):—

<u>Number</u>	<u>Convention Country</u>	<u>Date</u>
038,016	United States of America	14th April, 1987

APPLICATION ACCEPTED AND AMENDMENTS

ALLOWED 15 - 8 - 90

The address for service is care of DAVIES & COLLISON, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

Dated this 13th day of April 19 88

To: THE COMMISSIONER OF PATENTS

H. M. Rimington
.....
(a member of the firm of DAVIES & COLLISON for and on behalf of the Applicant).

Davies & Collison, Melbourne and Canberra.

COMMONWEALTH OF AUSTRALIA

PATENTS ACT 1952

DECLARATION IN SUPPORT OF CONVENTION OR
NON-CONVENTION APPLICATION FOR A PATENT

Insert title of invention.

In support of the Application made for a patent for an invention
entitled: "Disinfecting Compositions and Methods Therefor"

Insert full name(s) and address(es)
of Declarant(s) being the appli-
cant(s) or person(s) authorized to
sign on behalf of an applicant
company.

i
-We of Franklin P. Darmory
of Alcide Corporation
of One Willard Road
Norwalk, Connecticut 06851
United States of America

Cross out whichever of paragraphs
1(a) or 1(b) does not apply.

1(a) relates to application made
by individual(s).

1(b) relates to application made
by company; insert name of
applicant company.

do solemnly and sincerely declare as follows :-

1. (a) ~~I am the applicant~~
~~We are~~

or (b) I am authorized by

ALCIDE CORPORATION

Cross out whichever of paragraphs
2(a) or 2(b) does not apply.

2(a) relates to application made
by inventor(s)

2(b) relates to application made
by company(s) or person(s) who
are not inventor(s); insert full
name(s) and address(es) of inven-
tors.

the applicant..... for the patent to make this declaration on its behalf.
~~their~~

2. (a) ~~I am the actual inventor~~
~~We are~~

or (b)

Robert D. Kross, 2506 Florin Court, Bellmore,
New York 11710; Carol A. Zamojcin, 136 Hawthorne
Avenue, Floral Park, New York 11011
both of United States of America

State manner in which appli-
cant(s) derive title from inven-
tor(s)

~~is~~ the actual inventor..... of the invention and the facts upon which the applicant.....
~~are~~ is
~~are~~ entitled to make the application are as follows :-

Worldwide rights were assigned to applicant
corporation by assignment dated April 2, 1987
from the actual inventors in respect of the
invention.

Cross out paragraphs 3 and 4
for non-convention applications.
For convention applications
insert basic country(s) followed
by date(s) and basic applicant(s).

3. The basic application..... as defined by Section 141 of the Act ~~was~~ made
~~was~~ in United States of America on the 14th of April, 1987
by inventors Kross and Zamojcin
in on the
by
in on the
by

4. The basic application..... referred to in paragraph 3 of this Declaration ~~was~~
the first application..... made in a Convention country in respect of the invention the ~~subject~~
of the application.

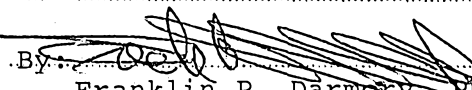
Insert place and date of signature.

Declared at Norwalk this 17th day of March, 1988

Signature of Declarant(s) (no
attestation required).

ALCIDE CORPORATION

Note: Initial all alterations.

By: 
Franklin P. Darmory, Ph.D.

DAVIES & COLLISON, MELBOURNE and CANBERRA.

Executive Vice President & COO

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(19) AUSTRALIAN PATENT OFFICE (10) Acceptance No. 603203

(54) Title
DISINFECTING COMPOSITIONS AND METHODS THEREFOR

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(57) Typically, the invention provides a viscous topical gel composition for the improved treatment of skin infection and irritation on humans and other animals. The viscous, disinfectant, topical gel composition may allow the formation of a long-lasting solid shield on cow teats for the prevention and treatment of mastitis. Alternatively the present invention may provide improved oral hygiene compositions, useful in reducing dental plaque, which are pleasant tasting yet effective to reduce dental plaque and control gingivitis and periodontitis.

CLAIM

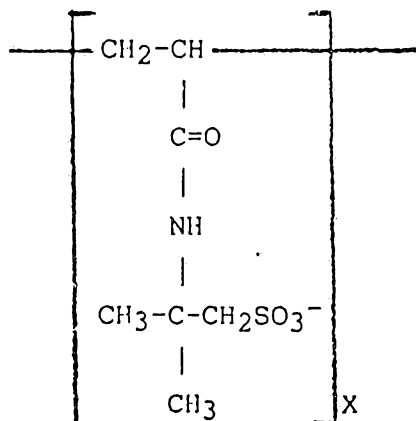
1. A composition for disinfecting substrates and forming a protective barrier comprising a combination of a first gel and a second gel, said first and second gels admixed and adapted to be applied so as to adhere onto said substrate, said first gel comprising an aqueous solution containing suitable amounts of a protic acid, and said second gel comprising an amount of metal chlorite such that, when the gels are combined, the chlorite ion concentration in the form of chlorous acid is no more than 15% by weight of the total amount of

(11) AU-B-14554/88

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(10) 603203

chlorite ion concentration and wherein said second gel also contains a polysulfonic acid salt wherein the anion of said salt has the formula:



wherein X has a value such that the molecular weight of the anionic portion of the polymer is from 1,000,000 to 5,000,000.

COMMONWEALTH OF AUSTRALIA

PATENT ACT 1952

COMPLETE SPECIFICATION

(ORIGINAL)

FOR OFFICE USE

603203

CLASS

INT. CLASS

Application Number:
Lodged:

Complete Specification Lodged:
Accepted:
Published:

Priority:

Related Art:

This document contains the
amendments made under
Section 49 and is correct for
printing.

NAME OF APPLICANT: ALCIDE CORPORATION

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1 Little Collins Street, Melbourne, 3000.

COMPLETE SPECIFICATION FOR THE INVENTION ENTITLED:

"DISINFECTING COMPOSITIONS AND METHODS THEREFOR"

The following statement is a full description of this invention,
including the best method of performing it known to us :-

Technical Field

This invention relates generally to compositions for disinfecting substrates as well as to processes for preparing and using such compositions. Further, this invention relates to disinfecting compositions useful as oral hygiene compositions such as a mouthwash, toothpaste, lozenge, chewing gum, or the like.

Background of the Invention

The term "disinfectant" is used in this specification to broadly include any substance or composition that disinfects, sanitizes, deodorizes, sterilizes, or kills germs.

The use of chlorine compounds in various types of disinfectant compositions is well known. Chlorine compounds suggested for use in this regard include, for example, sodium hypochlorite, used in World War I was a wound irrigant, and chlorinated phenols, such as m-chlorophenol. These compounds have increased bactericidal activity and reduced toxicity, in some instances, when compared to non-chlorinated phenols. Thus, m-chlorophenol has a phenol coefficient of 5.8 (*S. aureus*) to 7.4 (*B. typhosus*). Other chlorine compounds having some form of disinfectant utility include, for example, chlorine gas itself, chlorine dioxide, chloramine T, calcium hypochlorite (a standard swimming pool disinfectant), chloropicrin (a larvicide), chloroform (a fumigant), chlorodane (an insecticide), and chloromycetin (an antibiotic).

Chlorine dioxide in particular has been found to be an especially effective disinfectant. This compound is quite versatile and has long been used as a bleaching agent, such as in the oxidizing of the natural colorant



present in cotton, wood pulp and other cellulosic fibrous material. In such uses, chlorine dioxide, though performing an oxidizing function, is nevertheless noninjurious with respect to the fibrous material.

5 Particularly useful disinfecting compositions which employ chlorine-containing compounds are disclosed in U.S. Patent Nos. 4,330,531 and 4,585,482. These compositions comprise chlorite salts, such as sodium chlorite, in
10 combination with weak organic acids, such as lactic acid, to provide particularly effective disinfectant compositions. These compositions are useful in topically treating skin diseases such as acne and in toothpastes.

 One particularly prevalent disease is mastitis in dairy herds. Mastitis is a highly infectious disease which
15 affects the bovine udder. The losses in dairy production resulting from this disease are staggering. For example, in the United States alone, these losses are estimated to be in the hundreds of millions of dollars. Mastitis not only reduces the production of higher yielding animals, but
20 also shortens their productive life.

 It is well known that mastitis is transmitted from animal to animal. It has also been established that the only route of transmission of the disease is through the teat orifice. Conditions which are help primarily
25 responsible for the high incidence of mastitis include poor udder hygiene and physical damage to the teats. Dairy men and veterinarians have long sought a conditioning and protective composition which is economical and also provides facility of use. A composition which would
30 improve the normal condition of the udder and teats and would also aid in preventing or effectively reducing the incidence of mastitis would serve to substantially increase both the production and productive life of a dairy herd.

 Infectious mastitis is caused by microorganisms.
35 Prior art treatments, such as the use of sulfanilimide, have been only partially effective in controlling the disease because such treatments are useful against only one



type of microorganism which causes mastitis but are not useful against other types. Since the infection is usually of a mixed character, it follows that the effectiveness of drugs such as sulfanilimide is limited for all practical purposes.

It has also been suggested to use penicillin for the treatment of mastitis. The use of this compound is not desirable, however, in view of the high cost and extraordinary conditions necessary for the preservation and use of penicillin.

It has been proposed in U.S. Patent No. 3,222,252 to treat mastitis with a preparation which comprises a blend of edible, semidrying oils and drying oils together with a fatty acid ester, skin emollient, film-forming agent. It is said that the presence of a drying oil in the preparation is essential to provide the desired film-forming property. But for the most part, these film-forming-based treatments of mastitis have been unsuccessful. The use of iodine and peroxide in conjunction with latex emulsion films has led to other problems, including milk contamination and skin irritation.

While chlorine-liberating compounds have germicidal and deodorant properties, their characteristic taste and odor make them unpleasant for use in oral hygiene compositions such as mouthwashes. Other oral hygiene compositions, some commercially available, while pleasant tasting, are ineffective to reduce dental plaque as well as control gingivitis and periodontitis.

The search has continued for new and improved oral hygiene compositions which are both pleasant tasting and effective in reducing dental plaque as well as control gingivitis and periodontitis. This invention was made as a result of that search.

The use of compositions comprising metal chlorite and a weak organic acid, such as lactic acid, is disclosed in U.S. Patent No. 4,330,531. A chlorine dioxide releasing compound offers to substantially alleviate the problems



associated with the prevention of mastitis. For this application, the use of a gelling agent to generate a viscous topical gel is essential. The viscosity is needed for proper adhesion to the skin surface for an extended length of time.

Past attempts to create a useful viscous topical gel containing chlorine dioxide releasing compounds have been less than completely successful. Of the gelling agents tried, none combined the properties needed for substantial effectiveness. Carbohydrate-based gels lose their viscosity at higher pH's as the alkaline chlorites break down the long polymer chains. Inorganic thickeners, such as bentonite clays, participate in the reaction between the acid and chlorite, and tend to form stringy, unsuitable gels.

The search has continued for a viscous topical gel composition capable of embodying alkaline chlorites for the treatment and prevention of skin disease, infection and irritation on humans and other animals. This invention was made as a result of that search.

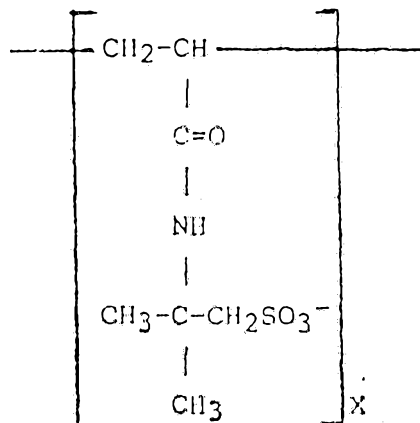
Objects and Summary of the Invention

Accordingly, it is a general object of the present invention to avoid or substantially alleviate the above-identified problems of the prior art.

In accordance with a first aspect of the invention there is provided a composition for disinfecting substrates and forming a protective barrier comprising a combination of a first gel and a second gel, said first and second gels admixed and adapted to be applied so as to adhere onto said substrate, said first gel comprising an aqueous solution containing suitable amounts of a protic acid, and said second gel comprising an amount of metal chlorite such that, when the gels are combined, the chlorite ion concentration in the form of chlorous acid is no more than 15% by weight of the total



amount of chlorite ion concentration and wherein said second gel also contains a polysulfonic acid salt wherein the anion of said salt has the formula:



wherein X has a value such that the molecular weight of the anionic portion of the polymer is from 1,000,000 to 5,000,000.

A second aspect of the invention provides a method of preparing the disinfecting composition defined above, by admixing the first and second gels.

A still further aspect of the invention provides a method for the treatment of skin diseases the method comprising the admixture of the two gels to form the composition, which composition is applied to the affected area of skin.

Typically, the invention provides a viscous topical gel composition for the improved treatment of skin infection and irritation on humans and other animals. The viscous, disinfectant, topical gel composition may allow the formation of a long-lasting solid shield on cow teats for the prevention and treatment of mastitis. Alternatively the present invention may provide improved oral hygiene compositions, useful in reducing dental plaque, which are pleasant tasting yet effective to reduce dental plaque and control gingivitis and periodontitis.



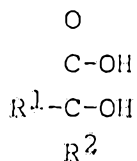
The disinfecting compositions of this invention are believed to disinfect by means of a chlorous acid generating composition. For oral use, the composition preferably comprises a flavoring agent, suitable amount of a carboxylic acid, and a suitable amount of a metal chlorite. The chlorite ion concentration in the form of chlorous acid is no more than about 15 percent by weight of the total amount of chlorite ion concentration.

The oral hygiene formulations of this invention typically contain low concentrations of chlorous acid generating compounds which are extremely effective as oral disinfectants. These compositions may provide effective mouthwashes, toothpastes, and other oral disinfecting compositions without the strong characteristic unpleasant taste of chlorine.

The composition of this invention is formed by combining one gel which comprises a dilute aqueous solution of metal chlorite with another gel which comprises a dilute aqueous solution containing a protic preferably a weak organic acid. The gel containing the metal chlorite also contains the polysulfonic acid salt. The concentrations of chlorite and acid are relative low.

This composition provides a metastable chlorous acid composition formed from small amounts of chlorite and acid. This composition is capable of generating chlorine dioxide over a long period of time at continuing levels of effectiveness. As chlorine dioxide forms, more of the chlorite converts to chlorous acid by interacting with hydrogen ions further generated by ionization of the organic acid.

Weak organic acids which may be used in the present invention include citric, malic, tartaric, glycolic, mandelic and other structurally similar acids as described in Formula I hereinbelow:

FORMULA I

5

R¹ and R² may be the same or different and may be selected from the group consisting of hydrogen, methyl, -CH₂COOH, -CH₂OH, -CHOHCOOH, and -CH₂C₆H₅. The pK
 10 of the organic acid is from about 2.8 to about 4.2, preferably from about 3.0 to about 4.0.

Compositions of a metal chlorite and the weak organic acids of Formula I are disclosed in PCT/US85/00470 = WO 85/04107. The entire disclosure of
 15 that application is hereby incorporated by reference.

The gel containing the protic acid may also contain a gelling agent or thickener which is well known to those skilled in this art. Any gelling agent or thickener which is nontoxic and nonreactive with the other ingredients of
 20 the composition may be used, such as cellulose gels, typically methyl cellulose, or preferably, hydroxy ethyl cellulose. Furthermore, that gel may also contain a preservative, such as benzyl alcohol or sodium benzoate. Other additives, such as buffers to adjust the pH of the
 25 composition to become more compatible with the skin, may be used.

The amount of thickener in the protic acid-containing gel may be generally from about 0.5% to about 5%, typically from 0.8% to about 4%, and preferably from
 30 about 1% to about 3% of the gel, by weight, of the total composition. The amount of preservative in the gel may be generally from about 0.01% to about 0.05%, typically from about 0.01% to about 0.04%, and preferably from about 0.02% to about 0.03%, by weight, of the total composition.

35 The chlorine dioxide liberating compound or metal chlorite and the protic acid are present in separate gels, and the amount of the preservative is present in only that

gel containing the protic acid. Approximately equal amounts of the separate gels ^{will generally} ~~should~~ be used.

The gel containing metal chlorite is thickened with a polysulfonic acid salt. The amount of polysulfonic acid salt added will depend on the desired use of the resulting composition. For a topical cream, toothpaste, or topical gel for the treatment of facial acne, the amount of thickener in the metal chlorite-containing gel may be generally from about 5% to about 15%, typically from about 5% to about 10%, and preferably from about 6% to about 8%, by weight, polysulfonic acid salt based upon the total composition. For a composition particularly suited to be used as a teat dip for treating cow udders, the amount of thickener in the metal chlorite-containing gel may be generally from about 0.5% to about 5%, typically from about 1% to about 4%, and preferably from about 2% to about 3%, by weight, solid polysulfonic acid salt based upon the total composition.

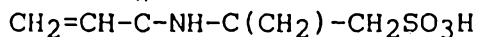
These polysulfonic acid salts are polymers of 2-acrylamido-2-methylpropane sulfonate. The preparation of such polymers is described in U.S. Patent No. 4,128,631, Canadian Patent No. 864,433, and German OLS No. 2,153,292, laid open May 4, 1972, all of which are herein incorporated by reference.

The pH of the gel containing the polysulfonic acid is generally greater than about 8, typically from about 9 to about 12, and preferably from about 10 to about 11.5.

The polymers useful in the present invention are prepared from:

0

"



or a salt thereof. The polymerization reaction may be accomplished by solution, emulsion, or suspension polymerization processes. The medium for the polymerization is conveniently water, an alcohol, or a mixture thereof. The



choice of medium is best dictated by the requirements of the final composition to be formulated.

The polymerization reaction is temperature-, pH- and catalyst-sensitive. In addition, it is desirable to
5 exclude oxygen from the reaction vessel used to form the polymer, as that material inhibits the polymerization process. The catalysts which are included to enhance the rate of polymerization are materials such as ammonium bisulfite, ferrous sulfate, hydrogen peroxide, sodium
10 metabisulfite, or other redox catalysts.

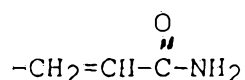
The polymer may be varied in molecular weight by controlling the amount of the catalyst, the pH, or the rate of addition of the monomer to the reaction vessel. The polymerization may be facilitated by converting the monomer
15 from its acid form to a salt which is water-soluble.

The salts of the polymer preferably contain as cations, sodium, potassium ammonium, monethanolamine, diethanolamine, triethanolamine, and 2-amino-2-methyl-1-propanol as well as mixtures thereof. The foregoing list
20 is merely exemplary of water-soluble salts which may be used. Also within the scope of the present invention are water-insoluble salts wherein the final composition is not adversely affected by precipitation of the polymer. Such products in which water-insoluble salts of the polymer may
25 be utilized are toothpastes, or substantially nonaqueous products such as topical creams.

As was previously mentioned, the molecular weight of the polymer may be controlled by the pH, the rate of addition of the monomer, or the judicious use of the cata-
30 lyst. It has been found desirable to utilize the afore-described polymers having a molecular weight of from about 1,000,000 to about 5,000,000, more preferably from about 2,500,000 to about 4,500,000, to improve the viscosity and film-forming characteristics of the composition. That is,
35 extremely high molecular weight polymers of the type described may result in a pituitive or stringy consistency of the end product. It has therefore been found desirable

to limit the pituitiveness by selecting the preferred molecular weight range. To this end, any common chain transfer agent, such as mercaptosuccinic acid, may be used to limit the molecular weight of the polymer.

5 It is noted that the terminal groups on the polymer have little bearing on the desired properties of the final composition and are thus not specified. The terminal groups are most often hydrogens, but may also be hydroxyl, sulfate, sulfonate, or:



All alcohols, particularly the monhydric alcohols, may be used as ingredients with the polymer.

15 Alcohols (C₁-C₂₄) which are nonirritating to the skin, such as methanol, ethanol, isopropanol, propyl, lauryl, myristyl, cetyl, and stearyl, as well as mixtures thereof, are preferred. Polyols such as glycerine, or ethylene glycol or propylene glycol may be utilized advantageously
20 with the polymer. The choice of the alcohol to be utilized with the particular polymer of the composition of the present invention will ordinarily be dictated by product aesthetics and the physical form of the composition. For instance, when liquid compositions are desired, the lower
25 alcohols are preferably utilized, while cream compositions within the scope of the present invention will normally require the higher alcohols. Where the compositions of the present invention contain ingredients other than the polymer or the alcohol in substantial amounts, the choice
30 of the particular alcohol becomes less important.

A desirable variable of the present invention is the incorporation of water with the polymer. A resultant increase in viscosity of the water is noted with no adverse effects on the stability of the product; that is, water is
35 a highly suitable carrier which may be used as a vehicle for contacting the polymer and the substrate. The particular weight ratios at which the desirable increase in

viscosity occurs for mixtures of the polymer and water are respectively from about 1:10,000 to about 1:100. Preferably this ratio is in the range of from about 1:1000 to about 1:500. Within the aforementioned range, highly viscous compositions are obtained with low solids content. Such compositions are desirable in that they allow compositions such as topical creams or gels, acne gels, or teat dips to be formulated in a thickened state, providing greater ease of application.

10 The gel containing the protic acid and the gel containing the metal chlorite are mixed either before application to the affected substrate or preferably in situ. After the gels are mixed, the pH of the final composition is generally less than about 7, typically from about 2 to about 5, and preferably from about 2.5 to about 4.

In the present invention, the composition is ordinarily used at a level of about 0.001 gram per square centimeter to about 0.1 gram per square centimeter of the affected substrate.

20 preferably The oral hygiene compositions of this invention 1 comprise a flavoring agent suitable for use in an oral hygiene composition, a suitable amount of a carboxylic acid, and a suitable amount of a metal chlorite. The concentrations of chlorite and acid are relatively low and are such that the amount of chlorite in the form of chlorous acid is no more than about 15 percent by weight of the total chlorite ion concentration in solution. Typically the amount of the chlorite in the form of chlorous acid is nor more than about 10 percent by weight of the total chlorite ion concentration in solution.

25 The percent by weight of chlorite and chlorous acid may be calculated from the ionization constant of chlorous acid and the amount of hydrogen ion in solution produced by the partial ionization of the carboxylic acid. Thus the hydrogen ion concentration, $[H^+]$, in a solution of the carboxylic acid, HA, of known molar concentration and



whose ionization constant is K_A , may be calculated from the following relationship:

$$K_A = \frac{[H^+][A^-]}{[HA]}$$

This same relationship may be applied to calculate the relative chlorite and chlorous acid concentrations where the ionization constant for chlorous acid is 1.1×10^{-2} . That is:

$$1.1 \times 10^{-2} = \frac{[H^+][ClO_2]}{[HClO_2]}$$

where the hydrogen ion concentration, $[H^+]$, is the quantity already determined by ionization of the known amount of the carboxylic acid, HA. This calculation is well-known to those skilled in this art.

The oral hygiene compositions of this invention provide a metastable chlorous acid composition formed from relatively small amounts of chlorite and acid. This composition is capable of generating chlorine dioxide over a long period of time at continuing levels of effectiveness. As chlorine dioxide forms, more of the chlorite converts to chlorous acid by interacting with hydrogen ions further generated by ionization of the carboxylic acid.

The oral hygiene compositions of this invention are therefore different from many prior art chlorine dioxide generating compositions which consist of relatively high concentrations of chlorite and acid. Prior art chlorine dioxide-containing compositions were not used as mouthwashes or toothpastes and result in the rapid conversion of chlorous acid to chlorine dioxide. The rate of chlorine dioxide formation depends on the sum of the square of chlorous acid concentration and the product of chlorous acid and chlorite concentrations according to the equation:

$$\frac{d[\text{ClO}_2]}{dt} = k_1[\text{HClO}_2]^2 + [\text{HClO}_2][\text{ClO}_2]$$

- 5 See Gordon, "The Chemistry of Chlorine Dioxide," Prog. Inorg. Chem. 15:201 (1972).

Thus the rate at which chlorine dioxide forms depends exponentially on the amount of chlorite ion which is converted to chlorous acid and the amount of chlorite
10 ion present.

In certain embodiments of the invention, the chlorous acid generating composition comprises an aqueous solution containing generally from about 0.01 to about 1, typically from about 0.02 to about 0.5, and preferably from
15 about 0.03 to about 0.3 percent by weight of metal chlorite and a suitable amount of an organic acid having a pK of from about 2.8 to about 4.2. The pH of this composition is generally less than about 7, typically from about 2.2 to about 7.0.

20 In yet another embodiment of this invention, even lower concentrations of chlorite and acid may be used in the composition. These compositions comprise an aqueous solution containing generally up to about 0.4, and typically from about 0.0001 to about 0.03 percent by weight
25 of metal chlorite, and a suitable amount of acid having a pK of from about 2.8 to about 4.2. The pH of the composition is generally less than about 7, typically from about 2.2 to about 7.0.

In certain embodiments of the invention, the
30 carboxylic acid is an alpha-hydroxy carboxylic acid. In preferred embodiments, the alpha-hydroxy carboxylic acid has the structure of Formula I herein.

Optionally the compositions of the invention may contain either a suitable amount of a compound containing
35 vicinal hydroxy groups or an amount of a water-soluble chloride in a significant molar excess to the chlorite, or both. These optional ingredients may facilitate the

formation of chlorine dioxide from chlorous acid and are thus useful in rapidly disinfecting compositions where an increased rate of chlorine dioxide formation is desired while maintaining a low concentration of chlorite and acid.

5 The metal chlorite useful in the present composition may more generally be described as a chlorine dioxide liberating compound. By "chlorine dioxide liberating compound" is meant any compound which, when appropriately treated, effects the production of chlorine
10 dioxide as a result of a change in the valence state of the chlorine atom from +3 to +4. While any chlorine dioxide liberating compound may be used, water-soluble chlorites are preferred because they are readily available and inexpensive. Typical water-soluble chlorites include metal
15 chlorites, such as alkali metal chlorites and alkaline earth metal chlorites. Sodium chlorite and potassium chlorite are preferred. Sodium chlorite is particularly preferred.

 The flavoring agents useful in the compositions
20 of this invention include any flavoring agent or mixture of flavoring agents acceptable in oral hygiene compositions. Such flavoring agents are well-known to those skilled in this art and include l-carvone (mint flavor), peppermint oil, aspartame, saccharin, wintergreen oil, cinnamon oil,
25 clove oil, menthol, thymol, eucalyptol, oil of sassafras, oil of anise, dextrose and levulose, and other flavoring agents well-known to those skilled in this art.

 The term "oral hygiene compositions" is meant to include any composition which is used in the mouth in order
30 to promote oral hygiene. These compositions may be in the form of a mouthwash, toothpaste, chewing gum, lozenge, or the like.

 These compositions may be in the form of aqueous solutions, as in a mouthwash composition, gels, as in
35 toothpaste or dentrifice compositions, solids, as in lozenges, or combined with fillers, as in chewing gum composition.

The compositions of this invention may contain other additives such as chelating agents (e.g., Na_4EDTA), or preservatives (e.g., sodium benzoate). The identity and amount of the other additives will depend upon the type of oral hygiene composition and its end use. Such additives are well-known to those skilled in the art. Suitable penetrants, astringents, deodorants, and other therapeutic or preventive compounds may be added. Dentrifices or toothpaste compositions according to the invention may also contain humectants, binders sudsing agents, abrasive polishing materials, and thickening agents.

The amount of chlorine dioxide liberating compound that may be used in this composition may be generally from about 0.01% to about 1%, typically from about 0.02% to about 0.05%, and preferably from about 0.03% to about 0.3% by weight of the total composition (including the application medium).

At chlorite ion levels higher than about 0.5%, the concentration of chlorous acid formed upon admixture of a carboxylic acid may be in excess of that required for the formation of a metastable chlorous acid solution. These higher concentrations of chlorous acid would cause the formation of chlorine dioxide, through the degradation of chlorous acid at too rapid a rate.

Any acid of low toxicity may be used in the compositions of the invention so long as the chlorite ion concentration limits described above and the degree of conversion to chlorous acid are met. Preferably carboxylic acids are used. Preferred carboxylic acids include citric, malic, tartaric, glycolic, mandelic or other structurally similar acids as described in Formula I hereinabove.

The pK of these carboxylic acids may be generally from about 2.8 to about 4.2, and preferably from about 3.0 to about 4.0.

The amount of carboxylic acid used in these compositions should be sufficient to lower the pH of the composition to less than about 7, typically from about 2.5

to about 6, and preferably from about 3.0 to about 5.0. Furthermore, this amount may be generally from about 0.01% to about 3%, typically from about 0.5% to about 2%, and preferably from about 0.1% to about 1% by weight of the total composition (including the application medium).

The amount of flavoring agent useful in this invention may vary widely but is generally from about 0.01 to about 5, typically from about 0.02 to about 2, and preferably from about 0.05 to about 1 percent by weight based upon the total weight of the composition.

A suitable amount of a vicinal dihydroxy or polyhydroxy compound may also be added to the compositions of the present invention. The use of such compositions enables one to produce compositions according to the invention which are more rapidly effective in higher pH ranges. The use of these vicinal dihydroxy or polyhydroxy compounds also allows for the use of compositions according to the invention which contain a much lower acid concentration than that which is needed if the vicinal polyhydroxy compound comprising at least two vicinal hydroxy groups is absent.

Vicinal polyhydroxy compounds which contain at least two vicinal hydroxy groups are well-known to those skilled in this art and include dextrose and other sugars, glycerin, sorbitol, and inositols. In other embodiments, sugars with vicinal hydroxy groups in the cis configuration such as galactose, mannose, and ribose may be used.

The use of such vicinal polyhydroxy compounds, particularly those with cis-vicinal hydroxy groups, in conjunction with the chlorine dioxide liberating compound and carboxylic acid results in a synergistic composition. The vicinal dihydroxy or polyhydroxy compound catalyzes the formation of chlorine dioxide from chlorous acid. For example, the rate of formation of the active chlorine dioxide entity using a composition comprising sodium chlorite and mandelic acid is substantially enhanced by the addition of a relatively insubstantial amount of a vicinal

polyhydroxy compound. Thus, the use of as little as 0.1% ribose in the composition substantially enhances the rate of formation of the active entity vis-a-vis a composition containing only sodium chlorite and one of the organic acids discussed hereinabove.

Stated otherwise, a composition containing the vicinal polyhydroxy compound may be prepared having substantially the same initial germ-killing efficacy in a specified time period as a composition which does not contain the vicinal polyhydroxy compound even though the composition containing the polyhydroxy compound contains substantially much less organic acid and sodium chlorite. However, such activation of the system results in a more rapid depletion of the chlorite ion in the composition, so that the germ-killing activity at a later time period would be less. The vicinal polyhydroxy compounds may also serve another purpose in the composition in that it may act as a sweetener or enhance the solubility of the flavoring agents.

The amount of vicinal polyhydroxy compound containing at least two vicinal hydroxy groups may vary widely, but in the present invention there is employed generally less than about 20%, typically from about 0.1% to about 10%, and preferably from about 0.2% to about 5% by weight of the total composition.

Alternatively, or in addition, the composition may contain a large excess of chloride ion in the form of an alkali or an alkaline earth metal salt. The excess may be from about a 10 to about a 100-fold excess by weight of chloride ion of total chlorite ion concentration. Large excesses of chloride ion in acid solutions (below a pH of about 7) cause the chlorite ion to decompose in an accelerated manner, via the formation of chlorous acid to form chlorine dioxide. In a preferred embodiment of the invention where rapid disinfection is required, the composition contains both a high excess of chloride ion and

a sufficient amount of vicinal polyhydroxy compound comprising at least two vicinal hydroxy groups.

The chlorine dioxide liberating compound is generally kept separate from the organic acid prior to use
5 in order to avoid premature reaction of the ingredients. The flavoring agent may be combined with either the organic acid or the chlorine dioxide liberating compound, or both, prior to their admixture.

The oral hygiene compositions of this invention
10 result in improved bactericidal, fungicidal, virucidal and taste properties over presently available commercial oral hygiene compositions and aid in dental plaque reduction.

The present invention is illustrated by the following examples. Unless otherwise noted, all parts
15 and percentages in the examples as well as the specification and claims are by weight. Examples IV to VIII do not fall within the claimed invention but suggest various analogous preparations and modes of action assisting in the appreciation and performance of the
20 claimed invention.



EXAMPLE I

This example illustrates the preparation of a toothpaste composition according to the present invention.

There is prepared a two-part disinfectant toothpaste composition according to the invention having a first base paste or gel and a second activator paste or gel.

The formulations of the two toothpaste parts on a percent weight to weight basis are as follows:

10

TOOTHPASTEBASE

% W/W

15

Poly(sulfonic Acid) [16% aqueous solids]	45.0
Sodium hydroxide, 1N	40.0
Bentonite	2.0
Sodium lauryl sulfate	1.0
Titanium dioxide	1.0
Silica, amorphous	0.5
Sodium chlorite	1.0
Water	q.s

20

ACTIVATOR

25

Glycerin	10.0
Magnesium aluminum silicate	5.0
Hydroxyethylcellulose	2.0
Malic acid	1.5
Flavor, wintergreen	0.4
FD&C Blue #1 (0.5% solution)	0.06
Sodium benzoate	0.05
Sodium saccharine	0.05
Water	q.s

30

The pH of the composition resulting from the mixture of substantially equal portions of the base and activator gels of the above formulation is about 4.15.

35

The base gel and the activator gel are preferably stored separately prior to use, e.g., in a double-compartment tube. The two gels are mixed, preferably just prior to use, in substantially equal amounts and the mixture is used in the normal manner as a toothpaste. Alternatively, substantially equal portions of the gels are placed in the

mouth and mixed by the brushing action while the subject brushes his or her teeth.

EXAMPLE II

5 This example illustrates the use of the present invention as a teat dip for application to cow udders.

A first gel is prepared by mixing the following ingredients:

10	Rheothik 80-11 poly(sulfonic acid)	
	[16% aqueous solids]	16.00%
	NaOH, 1N	16.00%
	Naconnol 90F (sodium dodecylbenzene sulfonate)	1.80%
	Sodium chlorite	0.64%
	Na ₄ EDTA	0.19%
	Hi-Sil T-600 (silica)	2.50%
15	Water	q.s.

A second gel is prepared by mixing the following ingredients:

20	Lactic acid	2.64%
	Natrosol 250MR	1.00%
	Isopropyl alcohol	2.00%
	Sodium benzoate	0.04%
	Poloxamer 188	0.40%
	FD&C Yellow #5	0.30%
	Water	q.s.

25 The two solutions are blended, preferably just prior to application. The resulting gel is applied to the cow teat, forming a solid shield around the teat. The film thus formed, following drying, provides a long-lasting and
30 continuously acting disinfectant in direct contact with the skin surface.

EXAMPLE III

35 This example illustrates the preparation of a topical gel useful for the treatment of infection-based facial acne.

A first gel is prepared by mixing the following ingredients:

	Rheothik 80-11 poly(sulfonic acid)	
	[16% aqueous solids]	45.00%
	NaOH, 1N	38.00%
	Naconnol 90F	1.80%
5	Na ₄ EDTA	0.19%
	NaClO ₂	2.50%
	Deionized water	q.s.

A second gel is prepared by mixing the following ingredients:

10	Salicylic acid	2.00%
	Isopropyl alcohol	30.00%
	Sodium benzoate	0.04%
	Natrosol 250MR	2.10%
	Pluronic F-68	0.40%
15	Deionized water	65.46%

The first and second solutions are mixed, preferably just prior to use. The resulting gel is applied to the affected region of the skin. A film forms, creating a long-lasting cover that provides a continuous supply of disinfectant to the covered area of skin for a prolonged period of time.

EXAMPLE IV

This example illustrates the properties of compositions employing hydroxyethyl cellulose as a gelling agent for sodium chlorite in the preparation of a final composition comprising sodium chlorite and lactic acid.

Example I is repeated, but hydroxyethyl cellulose is used at the 2% level in place of the polysulfonic acid salt and excluding the sodium hydroxide. This gel is not storage stable for a commercially acceptable period of time. The cellulose gelling agent depolymerizes and loses viscosity.

EXAMPLE V

This example illustrates the preparation of a mouthwash according to the present invention.

A first solution is prepared by dissolving 0.4 grams of technical grade sodium chlorite, 0.17 grams of powdered $\text{Na}_4\text{EDTA} \cdot 4\text{H}_2\text{O}$, 0.5 grams of l-carvone (mint flavor), and the appropriate amount of a compatible food grade yellow dye in 500 milliliters of aqueous solution. A second solution is prepared by dissolving 1.375 grams of anhydrous citric acid and the appropriate amount of FD&C Blue #1 in a batch of 500 milliliters of a 10 percent by weight aqueous solution of glycerin.

The two solutions are mixed, preferably just prior to use, in substantially equal amounts and the mixture is used in the normal manner as a mouthwash.

EXAMPLE VI

This example also illustrates the preparation of a mouthwash according to the present invention.

A first aqueous solution of 0.25% sodium chlorite and 0.10% NaOH in deionized water is prepared.

A second aqueous activator solution is prepared of 0.75% malic acid, 10.00% glycerine USP, 0.05% sodium benzoate, 0.50% Equal (aspartame diluted with dextrose and corn syrup solids), 0.03% FD&C Blue #1 (0.3% solution), and 0.40% Wintergreen Flavor (BBA), in deionized water.

The two solutions are mixed, preferably just prior to use in substantially equal amounts, and the mixture is used in the normal manner as a mouthwash.

EXAMPLE VII

This example illustrates the ability of a composition of the present invention to reduce dental plaque and control gingivitis and periodontitis.

Mouthwash compositions according to the invention were used in a five day triple-crossover plaque reduction test. In this test, 18 human subjects were divided into three groups of six subjects each. The teeth of each subject were scraped free of plaque immediately prior to the commencement of each five day period.

Each group was subjected to three five day periods of treatment with the following formulations: (a) placebo, (b) low potency mouthwash formulation, and (c) high potency mouthwash formulation. The sequence of the treatments per group were selected in a random fashion. During the five day period the subjects rinsed with the formulation twice daily, i.e., in the morning and afternoon. The subjects did not brush their teeth or perform any other oral hygiene procedures. The same treatment procedure was followed for all three of the formulations. Plaque scores after each five day period were determined by a modified Quigley-Hein index.

The placebo was formulated so that it had substantially the same perceived acidity as the other two formulations. The placebo formulation comprised an aqueous solution of 0.27% citric acid, 0.08% sodium chloride, 0.5% l-carvone, 0.09% FD&C Green #3 (5000 ppm solution), 0.03% FD&C Yellow #5 (5000 ppm solution), and 5.0% glycerin.

The compositions were formulated in two parts, A and B. Equal volumes of the two parts were mixed immediately before rinsing. The percent compositions of parts A and B of the high potency and low potency formulations were as follows:

25

30

35

	<u>INGREDIENT</u>	<u>HIGH POTENCY</u>	<u>LOW POTENCY</u>
	<u>Part A</u>		
5	Sodium chlorite (79%)	0.32	0.08
	l-Carvone	0.10	0.10
	FD&C Green #3		
	(5000 ppm solution)	0.18	0.18
	1 N Sodium hydroxide	q.s.	q.s.
10	<u>Part B</u>		
	Malic acid	0.75	0.275
	Sodium benzoate	0.05	0.05
15	Glycerin	10.00	10.00
	FD&C Yellow #5		
	(5000 ppm solution)	q.s.	q.s.

20 The average plaque scores of the subjects listed below show that the mouthwash compositions of this invention were effective in substantially reducing dental plaque.

	<u>Score (average)</u>	<u>% Reduction</u>
25		
	Placebo	3.82
	Low potency	3.35
	High potency	2.47

30 EXAMPLE VIII

An evaluation was made of the microbiocidal effectiveness of the High Potency mouthwash (0.32% Sodium chlorite - Part A; 0.75% Malic acid - Part B) in Example VII, versus that of 0.2% chlorhexidine digluconate. The 0.2% Chlorhexidine digluconate solution is the recommended reference standard by which other oral hygiene germicides should be measured. The procedure employed was based on

the method in the FDA OTC Oral Health Care Monograph (Federal Register, Vol. 47, No. 101, May 25, 1982, pages 22890-22900). The test organisms were:

5 Candida albicans ATCC 18804 (American Type Culture Collection, Rockville, Md.)

Actinobacillus actinomycetemcomitans Forsyth Clinic Isolate #Y4

Streptococcus mutans ATCC 25175

10 The microorganisms were grown in Brain Heart Infusion, and subcultured for two successive days at 37°C. Two ml of a 50:50 mix of each test organism in sterile fetal calf serum was added to 8 ml of the mouthwash formulation, and triplicate aliquots of the inoculated test
15 formulation were removed at 30 and 60 second for subculture. C. albicans was grown and subcultured aerobically; all other organisms, anaerobically. The High Potency test solutions were neutralized first in fluid thioglycolate medium, and further neutralized in the plate count agar.
20 The chlorhexidine digluconate control solutions were only neutralized in the enumeration agar. Results obtained were as follows:

25	Test Formulation	Organism	Average Microbial Log Reduction*	
			30 Sec. Exp.	60 Sec. Exp.
30	High Potency	<u>C. albicans</u>	3.2	3.0
		<u>Actinobacillus</u>	7.5	7.5
		<u>Strep. mutans</u>	3.5	4.3
35	Chlorhexidine digluconate, 0.2%	<u>C. albicans</u>	3.2	3.3
		<u>Actinobacillus</u>	6.6	6.3
		<u>Strep. mutans</u>	3.0	3.0

*Average of three results.

The High Potency Formulation shows a microbiocidal efficacy equal to or greater than of chlorhexidine digluconate at the 0.2% level.

5 These microbiocidal data strongly indicate that these formulations will not only be helpful in reducing dental plaque formation, but also would inhibit the onset and severity of gingivitis and other associated oral disorders such as periodontitis which could lead to
10 eventual tooth loss.

~~The principles, preferred embodiments, and modes~~
of operation of the invention have been described in the foregoing specification. However, the invention herein
15 which is intended to be protected, is not to be construed as limited to the particular forms disclosed, since these are to be regarded as illustrative rather than restrictive. Variations and changes may be made by those skilled in the
art without departing from the spirit of the invention.

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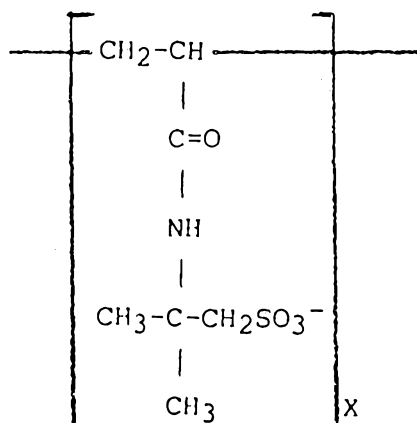
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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A composition for disinfecting substrates and forming a protective barrier comprising a combination of a first gel and a second gel, said first and second gels admixed and adapted to be applied so as to adhere onto said substrate, said first gel comprising an aqueous solution containing suitable amounts of a protic acid, and said second gel comprising an amount of metal chlorite such that, when the gels are combined, the chlorite ion concentration in the form of chlorous acid is no more than 15% by weight of the total amount of chlorite ion concentration and wherein said second gel also contains a polysulfonic acid salt wherein the anion of said salt has the formula:



wherein X has a value such that the molecular weight of the anionic portion of the polymer is from 1,000,000 to 5,000,000.

2. The composition of claim 1 wherein said second gel comprises from 5% to 15% of solid polysulfonic acid salt by weight of the total composition.

3. The composition of claim 1 wherein said second gel comprises from 0.5% to 5% of solid polysulfonic acid salt



by weight of the total composition.

4. The composition of any preceding claim wherein said protic acid has a pK of from 2.8 to 4.2.

5. The composition of any preceding claim wherein said protic acid is salicylic acid.

6. The composition of any preceding claim wherein said composition contains sufficient amounts of fillers and binders to form a topical cream.

7. The composition of any preceding claim wherein said composition comprises sufficient amounts and kinds of fillers and binders to form a toothpaste.

8. The composition of any preceding claim wherein said first gel comprises hydroxyethyl cellulose.

9. The composition of any preceding claim wherein the molecular weight of the anionic portion of said polymer is from 2,500,000 to 4,500,000.

10. The composition of any preceding claim wherein the cation of the polymer is selected from the group consisting of sodium, potassium, ammonium, monoethanolamine, diethanolamine, triethanolamine, and 2-amino-2-methyl-1-propanol and mixtures thereof.

11. A method of preparing a composition for disinfecting a substrate and forming a protective barrier the method comprising admixing a first gel as defined in any one of claims 1, 4, 5 or 8 with a second gel as defined in any one of claims 1, 2, 3, 9 or 10 to form a composition as defined in any preceding claim.

12. A method for treating skin diseases comprising



admixing a first gel as defined in any one of claims 1, 4, 5 or 8 and a second gel as defined in any one of claims 1, 2, 3, 9 or 10 to form a composition as defined in any one of claims 1 to 10 and applying an effective amount of said composition to the affected area of skin.

13. A composition according to claim 1, or a method for the use thereof, substantially as hereinbefore described with reference to the Examples.

DATED this 1st day of August 1990.

ALCIDE CORPORATION
By Its Patent Attorneys
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