

SPECIFICATION

METHOD OF TREATING INFECTIOUS DISEASES, METHOD OF
PRESERVING COSMETICS, ANTIBACTERIAL AND
ANTIFUNGAL AGENTS, AND COSMETICS

5

TECHNICAL FIELD

This invention relates to a method of treating infectious diseases caused by bacteria or fungi, to a method of preserving cosmetics, to antibacterial and antifungal agents, and to cosmetics.

10

BACKGROUND ART

Zinc oxide is generally applied to affected sites of the skin in eczema, dermatitis, abrasion, burn or the like as a local astringent, desiccant and protectant and for relief of stimulations and absorption of secretion. This substance is used in various dosage forms, such as powder, solution, oil, lotion, liniment, ointment, paste, plaster and so on. Particularly, the ointment is used most generally.

Referring to the ointment, the Japanese Pharmacopoeia lists Zinc Oxide Ointment. However, this ointment has the drawback that because it does not contain any bactericide or preservative, the skin lesions become more susceptible to the infection of bacteria and fungi when it is repeatedly used over a long time.



Zinc oxide ointments supplemented with ichthammol, acrinol, boric acid or the like are also known.

However, these ointments also have various drawbacks.

Ichthammol, which is incorporated for reducing inflammation or relieving itching, has a peculiar odor and a

brownish black color, so that zinc oxide ointments

containing ichthammol have been delisted from the new

Japanese Pharmacopeia (12th edition). Acrinol, which is

incorporated for purposes of local sterilization or

disinfection, may sometimes induce symptoms of irritation

and has the drawback that it readily undergoes

discoloration upon exposure to light and stains clothes

yellow. Boric acid, which is incorporated for the

purpose of sterilization, has only a weak inhibitory

effect on bacterial growth and, when continuously used

over a long period of time, it is absorbed through the

skin and may cause poisoning, such as nausea and vomiting

or diarrhea. Therefore, the use of this substance is

rigorously controlled.

Furthermore, the above-mentioned various zinc

oxide ointments containing antimicrobial agents are not

sufficiently safe or low in irritation. Thus, they can

hardly be applied to patients sensitive to irritation.

DISCLOSURE OF INVENTION

In view of the above state of the art, we made



intensive investigations in an attempt to develop an antibacterial and antigungal agent having excellent antibacterial and antifungal activities. As a result, we found that when a zinc compound, inclusive of zinc oxide and the like, is used in combination with hinokitiol or a salt thereof, markedly improved antibacterial and antifungal activities are obtained. We also found that, due to these excellent antibacterial and antifungal activities, the combination of a zinc compound and hinokitiol or a salt thereof is very useful particularly for treating infectious diseases caused by bacteria or fungi, for preserving cosmetics, and for other purposes. The present invention has been completed based on the above findings.

Thus, the present invention provides a method of treating a patient with an infectious disease caused by bacteria or fungi which comprises administering to said patient an effective amount of a zinc compound and an effective amount of hinokitiol or a salt thereof.

The invention also provides the use of a combination of a zinc compound and hinokitiol or a salt thereof for producing an agent for treating infectious diseases caused by bacteria or fungi.

The invention further provides a method of preserving a cosmetic which is characterized in that said



cosmetic contains an effective amount of a zinc compound and an effective amount of hinokitiol or a salt thereof.

Furthermore, the invention is concerned with antibacterial and antifungal composition which comprises
5 an effective amount of a zinc compound and an effective amount of hinokitiol or a salt thereof, and with a cosmetic which contains an effective amount of a zinc compound and an effective amount of hinokitiol or a salt thereof.

In the practice of the invention, the zinc
10 compound to be used is not limited to any particular species but includes a wide variety of per se known zinc compounds, such as, for example, zinc oxide, zinc chloride, zinc nitrate, zinc sulfate, zinc phosphate, zinc aluminate, zinc fluoride, zinc iodide, zinc hydro-
15 xide, zinc carbonate, zinc chromate, zinc benzoate, zinc acetate, zinc paraaminobenzoate, zinc paradimethylaminobenzoate, zinc paraphenolsulfonate, zinc paramethoxycinnamate, zinc lactate, zinc-2-mercaptopyridine N-oxide complex, zinc gluconate, zinc
20 picrate, zinc citrate, zinc aspartate, zinc naphthenate, zinc salicylate, zinc phenolsulfonate, zinc sebacate, sodium zinc tripolyphosphate, zinc stearate, zinc caprate, zinc laurate, zinc myristate, zinc palmitate, zinc oleate, zinc polyphosphonate, zinc
25 chondroitinsulfate, zinc undecylenate, zinc ascorbate,



zinc citrate, zinc pyrithione, hinokitiolato zinc, zinc
dipicolinate, zinc-glycerol complex, zinc-bishistidine
complex, zinc-3,4-dihydroxybenzoic acid complex, zinc
nicotinate, zinc-nicotinamide complex, and other zinc
5 complexes and zinc salts. In the practice of the
invention, these zinc compounds may be used either singly
or in combination as a mixture of two or more.

Examples of the salt of hinokitiol to be used
in the practice of the invention are inorganic salts
10 including alkali metal salts such as sodium salt and
potassium salt, alkaline earth metal salts such as
magnesium salt and other metal salts such as copper salt
and zinc salt, and organic salts including alkanolamine
salts such as diethanolamine salt, 2-amino-2-ethyl-1,3-
15 propanediol salt and triethanolamine salt, heterocyclic
amine salts such as morpholine salt, piperazine salt and
piperidine salt, ammonium salt, and basic amino acid
salts such as arginine salt, lysine salt and histidine
salt. The basic amino acids each may be in the D form or
20 in the L form or in the form of a mixture of these. In
the practice of the invention, hinokitiol and salts
thereof may be used either singly or two or more of them
may be used in combination.

The proportions of the zinc compound and
25 hinokitiol or a salt thereof to be incorporated into the



compositions of the invention are not particularly limited provided that the intended effects of the invention can be produced. Generally, however, it is recommended that both are incorporated in a former:latter
5 weight ratio of about 10-99.95:90-0.05, preferably about 50-99.9:50-0.1. Thus, it is recommended to use the zinc compound in an amount of about 10 to 99.95% by weight, preferably about 50 to 99.9% by weight, and to use hinokitiol or a salt thereof in an amount of about 90 to
10 0.05% by weight, preferably about 50 to 0.1% by weight, based on the total amount of the zinc compound and hinokitiol or the salt thereof.

When the compositions of the invention are to be used as medicaments, the zinc compound and hinokitiol
15 or a salt thereof may be used in a manner such that both of them are contained in a single pharmaceutical preparation. It is also possible to formulate them independently into separate preparations and utilize both of the pharmaceutical preparations. Such preparations
20 are produced by using diluents or excipients that are generally used, including fillers, bulking agents or extenders, binders, humectants, disintegrating agents, surfactants, lubricants and so on. For these pharmaceutical preparations, various forms can be
25 selected depending on the purpose of therapy and, as



typical examples thereof, there may be mentioned tablets, pills, powders, solutions, suspensions, emulsions, granules, capsules, suppositories, injections (solutions, suspensions, etc.), oleaginous ointments, emulsion
5 ointments, water-soluble ointments, pastes, plasters, lotions, liniments and other preparations for external use.

When the compositions of the invention are to be used as cosmetics, they can be added as antidandruff
10 agents, bactericides and/or preservatives to the cosmetics for enabling preservation of the cosmetics, for instance. Said cosmetics may be used in various forms including skin care products such as cleansing preparations, creams, milk lotions, makeup creams, oils,
15 packs or the like; makeup cosmetics such as foundations, lipsticks, cheek rouges, eyeliners, mascaras, eye shadows, manicures, face powders or the like; hair care preparations such as hair dressing preparations, hair tonics or the like; bath preparations, whitening
20 preparations, sunscreen preparations, acne treatment preparations, etc. These can be produced by the methods that are conventional in the art.

In producing such cosmetics, various known cosmetic base materials, such as vehicles, binders,
25 lubricants, disintegrating agents, etc., can be used as



necessary and, further, various oleaginous materials, such as oils, fats, waxes, hydrocarbons, fatty acids, higher alcohols, ester oils, metal soaps, etc., pharmacologically active materials, such as animal or plant
5 extracts, vitamins, hormones, amino acids, etc., surfactants, colors, dyes, pigments, perfumes, preservatives, bactericides, humectants, thickening agents, anti-oxidants, metal sequestering agents and other already known various components or additives can be used as
10 necessary in a suitable combination.

In using the compositions of the invention as medicaments, the active ingredient concentrations are not particularly limited provided that the compositions have the desired effects or benefits. Generally, however,
15 they recommendably contain a zinc compound and hinokitiol or a salt thereof in a total amount of about 0.001 to 20% by weight, preferably about 0.01 to 15% by weight.

In cases where the compositions of the invention are to be used as cosmetics, the concentration thereof may vary depending on the form and the like,
20 hence cannot be specified in a general manner or are not particularly limited. Generally, however, the compositions recommendably contain a zinc compound and hinokitiol or a salt thereof in a total amount of about
25 0.0001 to 99.9% by weight, preferably about 0.001 to 30%



by weight. The cosmetics mentioned above may be used after further dilution with water, olive oil or some other suitable solvent.

In shaping into the form of tablets, a variety
5 of materials so far well known as carriers or vehicles in this field of art can be used. Thus, for example, use may be made of excipients such as lactose, sucrose, sodium chloride, glucose, urea, starch, calcium carbo-
nate, kaolin, crystalline cellulose, silicic acid, etc.,
10 binders such as water, ethanol, propanol, simple syrup, glucose solution, starch solution, gelatin solution, carboxymethylcellulose, shellac, methylcellulose, potassium phosphate, polyvinylpyrrolidone, etc., disintegrating agents such as dried starch, sodium
15 alginate, agar powder, laminaran powder, sodium hydrogen carbonate, calcium carbonate, polyoxyethylenesorbitan fatty acid esters, sodium lauryl sulfate, stearic acid monoglyceride, starch, glucose, etc., disintegration preventing agents such as sucrose, stearin, cacao butter,
20 hydrogenated oils, etc., absorption promoting agents such as quaternary ammonium bases, sodium lauryl sulfate, etc., humectants such as glycerin, starch, etc., adsorbents such as starch, lactose, kaolin, bentonite, colloidal silicic acid, etc., lubricants such as purified
25 talc, stearic acid salts, corn starch, waxes,



polyethylene glycol, etc., and so forth. The tablets may further be processed to tablets coated with an ordinary coating film, for example sugar coated tablets, gelatin coated tablets, enteric-film coated tablets, film coated
5 tablets, or double-layered tablets or multilayered tablets.

In shaping into the form of pills, a wide variety of materials so far known as carriers or vehicles in this field of art can be used. Thus, for example, use
10 may be made of excipients such as glucose, lactose, starch, cacao butter, hardened vegetable oils, kaolin, talc, etc., binders such as gum arabic powder, tragacanth powder, gelatin, ethanol, etc., disintegrating agents such as laminaran, agar, etc., and so forth.

15 In shaping into the form of suppositories, a wide variety of materials so far known as carriers or vehicles in the art can be used. Thus, for example, there may be mentioned polyethylene glycol, cacao butter, higher alcohols, higher alcohol esters, gelatin,
20 semisynthetic glycerides, and so on.

In preparing injections, the solutions, emulsions and suspensions are sterilized and are preferably isotonic with blood. For producing these forms, all diluents conventionally used in this field can
25 be employed. Thus, for instance, water, ethyl alcohol,



macrogols, propylene glycol, ethoxylated isostearyl alcohol, polyoxylated isostearyl alcohol, polyoxyethylene sorbitan fatty acid esters and the like can be used. In this case, sodium chloride, glucose or glycerin may be incorporated into the pharmaceutical preparations in an amount sufficient to give isotonic solutions. Conventional solubilizing agents, buffers, soothing agents and the like may also be added.

In preparing ointments, a wide variety of oleaginous bases so far known in this field can be used. As specific examples, there may be mentioned fats and oils such as peanut oil, sesame oil, soybean oil, safflower oil, avocado oil, sunflower oil, corn oil, rapeseed oil, cottonseed oil, castor oil, camellia oil, coconut oil, olive oil, poppy seed oil, cacao oil, beef tallow, lard, wool oil, etc. (lard being particularly preferred), mineral oils such as vaseline, paraffin, silicone oil, squalane, etc. (white vaseline being particularly preferred), higher fatty acid esters, higher aliphatic alcohols and waxes such as isopropyl myristate, n-butyl myristate, isopropyl linoleate, propyl ricinoleate, isopropyl ricinoleate, isobutyl ricinoleate, heptyl ricinoleate, diethyl sebacate, diisopropyl adipate, cetyl alcohol, stearyl alcohol, bleached beeswax, spermaceti, Japan wax, etc, higher fatty acids



such as stearic acid, oleic acid, palmitic acid, etc.,
mono-, di- and triglyceride mixtures derived from
saturated or unsaturated fatty acids containing 12 to 18
carbon atoms (lipophilic glycerin monostearate being
5 particularly preferred), and so on. In the practice of
the invention, these bases may be used either singly or
in combination as a mixture of two or more.

Conventional additives, for example metal
soaps, animal or plant extracts, vitamins, hormones,
10 amino acids or other pharmacologically active substances,
surfactants, coloring matters, dyes, pigments, perfumes,
ultraviolet absorbers, humectants, thickening agents,
antioxidants, metal sequestering agents, pH adjusting
agents, etc., may be incorporated, as necessary, into the
15 compositions of the invention.

The compositions of the invention are produced
by a conventional method.

The method of administration of the above-
mentioned pharmaceutical preparations is not particularly
20 limited but the preparations are administered by a method
suitably selected depending on the dosage form, the age,
sex and other conditions of the patient, the severity of
the disease and other factors. Thus, tablets, pills,
solutions, suspensions, emulsions, granules and capsules,
25 for instance, are administered orally. Injections are



administered, either as such or in admixture with an ordinary parenteral fluid containing glucose, amino acids or the like, by the intravenous route. If desired, they are administered as such via intramuscular, intradermal, 5 subcutaneous or intraperitoneal route. Suppositories are administered rectally. External preparations are applied to the affected parts.

These pharmaceutical preparations of the present invention are recommendably administered in such 10 an amount that the total amount of the active ingredients, i.e., a zinc compound and hinokitiol or a salt thereof is about 1 to 20 mg/kg body weight per human adult per day, and the preparations are administered in a single dose or two or three divided doses.

15 The compositions of the invention have excellent antibacterial and antifungal activities and are particularly useful in the treatment of various infectious diseases caused by various bacteria and/or fungi, for example various skin diseases including 20 dermatitis such as atopic dermatitis, nummular dermatitis, autosensitization dermatitis, diaper dermatitis and stasis dermatitis, eczema such as housewives (hand) eczema and dry eczema, pustular psoriasis, burn, redness resulting from burn, rash, 25 miliaria, sore, abrasion, secondary infection through



scratching, etc.

In addition, the compositions of the invention are very low in skin irritancy and allergy-inducing potential and therefore can be applied not only to
5 babies, infants, children and other patients with skin diseases, for example patients susceptible to skin irritation, but also in the treatment of skin diseases in mammals other than humans (pet animals such as dogs, cats, etc., domestic animals such as cattle, horses,
10 etc., and so on).

The compositions of the invention possess excellent antibacterial and antifungal activities, are safe and very weak in irritancy, and can be suitably used in babies, infants, children and other patients with skin
15 diseases, patients susceptible to irritation and so forth. The compositions of the invention can also be suitably used in patients with atopic dermatitis or contact dermatitis.

EXAMPLES

20 The following production examples and test examples are further illustrative of the present invention. Hereinafter, "%" means "% by weight".

Production Example 1 (Zinc oxide ointment)

	Hinokitiol	0.5 g
25	Lard	300.0 g



Bleached beeswax	60.0 g
Zinc oxide	100.0 g
White petrolatum	q.s.
Total	1000.0 g

- 5 (1) Hinokitiol was weighed, and a portion of lard was added thereto, and the mixture was heated to about 40°C and stirred to give a homogeneous melt. (2) The remaining portion of lard, bleached beeswax and white petrolatum were dissolved on a water bath and stirred to
10 give a mixture at 80°C. (3) Zinc oxide was weighed into a mortar. Thereto was added portionwise the mixture prepared in the above-mentioned step (2) with stirring to give a homogenous mixture, which was then cooled to about 40°C with stirring. (4) Then, the mixture prepared in
15 the above step (1) was added at about 40°C and stirring was continued until solidification to give the desired zinc oxide ointment.

Production Example 2 (Zinc oxide ointment)

	Hinokitiol	0.1 g
20	Olive oil	100.0 g
	Zinc oxide	100.0 g
	Simple ointment (Japanese Pharmacopoeia)	
		q.s.
	Total	1000.0 g

- 25 (1) Hinokitiol was weighed. To this was added



a portion of olive oil. The mixture was heated to about 40°C and stirred to give a homogeneous melt. (2) The remaining portion of olive oil and simple ointment (Japanese Pharmacopoeia) were dissolved on a water bath and then stirred to give a mixture at 80°C. (3) Zinc oxide was weighed into a mortar. Thereto was added portionwise with stirring the mixture prepared in the above step (2) to give a homogenous mixture, which was then cooled to about 40°C with stirring. (4) Then, the mixture prepared in the above step (1) was added at about 40°C, followed by stirring well until solidification to give the desired zinc oxide ointment.

Production Example 3 (Absorptive zinc oxide ointment)

	Lipophilic glycerin monostearate	50.0 g
15	Zinc oxide	50.0 g
	White petrolatum	q.s.
	Hinokitiol sodium salt	0.05 g
	Glycerin	30.0 g
	Purified water	50.0 g
20	Total	1000.0 g

(1) Hinokitiol sodium salt, glycerin and purified water were heated to about 60°C and stirred to give a homogeneous melt. (2) Lipophilic glycerin monostearate and white petrolatum were dissolved on a water bath and then stirred to give a mixture at 60°C. (3)



The mixture prepared in the above step (1) was added portionwise to the mixture prepared in the above step (2) with uniform stirring. The whole mixture was then cooled to about 40°C with stirring. (4) Zinc oxide was weighed into a mortar. Thereto was added portionwise the mixture prepared in the above step (3), followed by thorough stirring until solidification to give the desired zinc oxide ointment.

Production Example 4 (Vanishing cream)

10	Stearic acid	10.0%
	Paraffin wax (135F)	2.0%
	Spermaceti	2.0%
	Cetyl alcohol	2.0%
	Cetyl isooctanoate	5.0%
15	Polyoxyethylenesorbitan	
	(20EO) monolaurate	3.0%
	Zinc acetate	0.015%
	Sodium hydroxide	0.15%
	Concentrated glycerin	5.0%
20	Hinokitiol	0.02%
	Perfume	suitable amount
	Purified water	Balance
	Total	100.0%

(1) Stearic acid, paraffin wax (135F), spermaceti, cetyl alcohol, cetyl isooctanoate and polyoxy-



ethylenesorbitan (20EO) monolaurate were heated to 80-85°C to give a homogeneous melt. (2) Zinc acetate, sodium hydroxide, concentrated glycerin and purified water were heated to 80-85°C and stirred to give a homogeneous mixture. (3) At 80°C, the mixture prepared in the above step (2) was added portionwise to the mixture prepared in the above step (1) and, after uniform emulsification, the whole mixture was cooled to 45°C with stirring. (4) At 45°C, hinokitiol and perfume were added to the mixture prepared in the above step (3), and the mixture was stirred to homogeneity and cooled to room temperature with stirring to give the desired vanishing cream. Said vanishing cream was in the form of a stable emulsion.

15 Production Example 5 (Cleansing cream)

	Bleached beeswax	3.0%
	Liquid paraffin	30.0%
	Cetyl alcohol	2.0%
	Cetyl isooctanoate	10.0%
20	Triethanolamine	0.2%
	Propylene glycol	5.0%
	Zinc acetate	0.1%
	Antioxidant	suitable amount
	Hinokitiol	0.05%
25	Perfume	suitable amount

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Purified water	Balance
Total	100.0%

The above ingredients were admixed for emulsification following the procedure of Example 4 to give a stable emulsion.

Production Example 6 (Milk lotion)

	Stearic acid	3.0%
	Spermaceti	3.0%
	Lipophilic glycerin monostearate	2.0%
10	Bleached beeswax	2.0%
	Saturated fatty acid (C_8-C_{12}) triglyceride	10.0%
	L-Arginine	1.0%
	Sorbitol	3.0%
15	Zinc pyrithione	0.02%
	Hinokitiol	0.02%
	Perfume	0.1%
	Purified water	Balance
	Total	100.0%

The above ingredients were admixed for emulsification following the procedure of Example 4, whereupon a stable emulsion was obtained.

Production Example 7 (Lotion)

	Ethyl alcohol	10.0%
25	Polyoxyethylene (9EO) lauryl ether	2.0%



	Kankoh SO 201	0.001%
	Perfume	suitable amount
	Concentrated glycerin	5.0%
	1,3-Butylene glycol	3.0%
5	Hinokitiolato zinc	0.05%
	Hinokitiol	0.05%
	Color	suitable amount
	Purified water	Balance
	Total	100.0%
10	(1) Polyoxyethylene (9EO) lauryl ether, Kankoh SO 201 and perfume were added to and uniformly dissolved in ethyl alcohol. (2) Concentrated glycerin, 1,3-butylene glycol and hinokitiolato zinc were added to and uniformly dissolved in purified water. (3) At 80°C, the	
15	mixture prepared in the above step (2) was added to the mixture prepared in the above step (1) and, after uniform stirring for solubilization, hinokitiol was added and color was further added for coloration to give a lotion.	
	Production Example 8 (Zinc oxide ointment)	
20	Lard	20.95%
	Bleached beeswax	7.0%
	Lipophilic glycerin monostearate	2.0%
	White petrolatum	60.0%
	Zinc oxide	10.0%
25	Hinokitiol	0.05%

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Total

100.0%

(1) Hinokitiol was weighed. To this was added a portion of lard and the mixture was heated to about 40°C and stirred to give a homogeneous melt. (2) The
5 remaining portion of lard, lipophilic glycerin monostearate, bleached beeswax and white petrolatum were dissolved on a water bath and stirred to give a mixture at 80°C. (3) Zinc oxide was weighed into a mortar. To this was added portionwise the mixture prepared in the
10 above step (2) with uniform stirring. The resulting mixture was cooled to about 40°C with stirring. (4) Then, the mixture prepared in the above step (1) was added at about 40°C. The whole mixture was stirred well until solidification to give the desired zinc oxide
15 ointment.

Test Example 1 (Antibacterial activity test)

The drugs tested were hinokitiol SP (Takasago Perfumery Co., Ltd.; Lot 112108) and zinc oxide (Wako Pure Chemical Industries, Ltd.; Lot 71620). The test
20 bacterial strain used was Staphylococcus epidermidis KPUI (Staphylococcus epidermidis).

Cells of the above test strain precultured on SCD slant medium (18 to 20 hours, 37°C) were suspended in SCD medium and the suspension was diluted and adjusted to 10^6
25 to 10^7 cells/ml and allowed to stand for several tens of



minutes. This cell suspension was added to drug solutions which had been adjusted to predetermined drug concentrations. Then, shaking culture was performed (diluent: SCDLP medium or sterile physiological saline; 5 medium: SCDLP agar medium; incubation temperature: 37°C; incubation period: 24 to 48 hours) and viable cells were counted at timed intervals.

The concentrations of drugs for testing and the method of preparing the drugs were as follows. Thus, a 10 control was prepared by adding 9 ml of the cell suspension to 1 ml of sterile distilled water. Hinokitiol (0.02%) was prepared by diluting an alcohol solution containing hinokitiol at a concentration of 5% with sterile distilled water to give a 0.2% hinokitiol 15 solution and adding 9 ml of the cell suspension to 1 ml of said 0.2% solution. Hinokitiol (0.04%) was prepared by diluting an alcohol solution containing hinokitiol at a concentration of 5% with sterile distilled water to give a 0.4% hinokitiol solution and adding 9 ml of the 20 cell suspension to 1 ml of said 0.4% solution. Zinc oxide (0.1%) was prepared by adding 10 ml of the cell suspension to 0.01 g of zinc oxide (ZnO). Hinokitiol (0.04%) + zinc oxide (0.1%) was prepared by adding 1 ml of the 0.4% hinokitiol solution to 0.01 g of zinc oxide, 25 followed by addition of 9 ml of the cell suspension.



Zinc acetate (0.4%) was prepared by adding 10 ml of the cell suspension to 0.04 g of zinc acetate ($\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 2\text{H}_2\text{O}$). Hinokitiol (0.02%) + zinc acetate (0.4%) was prepared by adding 1 ml of the 0.2% hinokitiol solution to 0.04 g of zinc acetate, followed by addition of 9 ml of the cell suspension.

Viable cells were counted at timed intervals. The results obtained are shown in Fig. 1 and Fig. 2.

From Fig. 1 and Fig. 2, which are graphs showing the change in the number of viable cells counted with time, it is apparent that the use of hinokitiol in combination with zinc oxide or zinc acetate results in markedly increased antibacterial activity.

Test Example 2 (Antibacterial activity test)

The effects of the combined use of hinokitiol and zinc acetate were examined by the checkerboard dilution method.

Hinokitiol SP and zinc acetate (Wako Pure Chemical Industries, Ltd.; Lot LKR 3395) were used as the test drugs. The following six bacterial strains were used as the test microorganisms.

Bacterial strains used:

Staphylococcus (S.) aureus 209 PJC

S. aureus ATCC 6538 (Staphylococcus aureus)

S. epidermidis KPU1 (Staphylococcus epidermidis)



Escherichia coli K-12 (Escherichia coli)

Escherichia coli ATCC 8739 (Escherichia coli)

Bacillus subtilis IAM 1213 (Bacillus subtilis)

Each strain was precultured in Mueller-Hinton

5 medium (incubation temperature: 37°C; incubation period:
18 to 20 hours), and the culture was diluted with
Mueller-Hinton medium to 10^8 cells/ml or 10^6 cells/ml and
the dilutions were used as the test bacterial cell
suspensions.

10 The concentrations of the drug for testing and the
method of preparing the drugs were as follows. Thus, an
alcohol solution containing hinokitiol at a concentration
of 5% was diluted with sterile distilled water to give a
0.4% hinokitiol solution. This solution was serially
15 double-diluted with sterile distilled water to give
solutions containing hinokitiol at concentrations of 2000
 $\mu\text{g/ml}$, 1000 $\mu\text{g/ml}$, 500 $\mu\text{g/ml}$, 250 $\mu\text{g/ml}$, 125 $\mu\text{g/ml}$, 62.5
 $\mu\text{g/ml}$, 31.3 $\mu\text{g/ml}$ and 15.6 $\mu\text{g/ml}$. Separately, an aqueous
solution containing zinc acetate at a concentration of
20 3.2% was serially double-diluted with sterile distilled
water to give aqueous solution containing zinc acetate at
concentrations of 16000 $\mu\text{g/ml}$, 8000 $\mu\text{g/ml}$, 4000 $\mu\text{g/ml}$,
2000 $\mu\text{g/ml}$, 1000 $\mu\text{g/ml}$, 500 $\mu\text{g/ml}$ and 250 $\mu\text{g/ml}$.

When hinokitiol and zinc acetate were to be used
25 combinedly, 0.5 ml each of the above two drug solutions



containing respectively 20 times concentrations used were added, together with 9 ml of the medium, to each petri dish to obtain an agar plate. When hinokitiol and zinc acetate were to be used each individually, 1 ml of a 10-
5 fold concentrated hinokitiol or zinc acetate solution and 9 ml of the medium were added to each petri dish to obtain an agar plate.

Mueller-Hinton plate media containing hinokitiol and/or zinc acetate at various concentrations were
10 prepared by the above method and inoculated with each cell suspension with a cell concentration of 10^8 cells/ml or 10^6 cells/ml and, after incubating at 37°C for 48 hours, judgment was made as to whether cells had grown or not. The results obtained are shown in Table 1 through
15 Table 12. In the following tables, "+" means that growth was observed, "-" means that no growth was observed, and "±" means that very slight growth was observed.

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Table 1

Bacterial strain used: Staphylococcus aureus 209PJC

Inoculum size: 10^8 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	±
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	+	+
	6.25	-	-	-	-	-	-	+	+
	3.13	-	-	-	-	-	+	+	+
	1.56	-	-	-	-	+	+	+	+
	0	-	-	+	+	+	+	+	

Table 2

Bacterial strain used: Staphylococcus aureus 209PJC

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	+
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	-	-	-	-
	0	-	-	+	+	+	+	+	



Table 3

Bacterial strain used: Staphylococcus aureus ATCC 6538

Inoculum size: 10^8 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	+
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	+	+
	6.25	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	+	-	-	-
	0	-	-	+	+	+	+	+	

Table 4

Bacterial strain used: Staphylococcus aureus ATCC 6538

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	±	+
	6.25	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	-	-	-	-
	0	-	-	±	+	+	+	+	



Table 5

Bacterial strain used: Staphylococcus epidermidis KPU 1

Inoculum size: 10^8 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	+
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	+	+
	6.25	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	-	-	-	-
	0	-	-	+	+	+	+	+	

Table 6

Bacterial strain used: Staphylococcus epidermidis KPU 1

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	+
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	-	-	-	-
	0	-	-	+	+	+	+	+	

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Table 7

Bacterial strain used: Escherichia coli K-12

Inoculum size: 10^8 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	-
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	+	+	+	+
	3.13	-	-	-	+	+	+	+	+
	1.56	-	-	+	+	+	+	+	+
	0	-	-	+	+	+	+	+	

Table 8

Bacterial strain used: Escherichia coli K-12

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	+	+	+	+
	3.13	-	-	-	+	+	+	+	+
	1.56	-	-	+	+	+	+	+	+
	0	-	-	+	+	+	+	+	



Table 9

Bacterial strain used: Escherichia coli ATCC 8739

Inoculum size: 10^8 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	+	+	+	+
	3.13	-	-	-	+	+	+	+	+
	1.56	-	-	-	+	+	+	+	+
	0	-	-	+	+	+	+	+	

Table 10

Bacterial strain used: Escherichia coli ATCC 8739

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	+	+	+	+
	3.13	-	-	-	-	+	+	+	+
	1.56	-	-	-	+	+	+	+	+
	0	-	-	-	+	+	+	+	

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Table 11

Bacterial strain used: Bacillus subtilis IAM 1213

Inoculum size: 10^8 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	-	-	+	+
	3.13	-	-	-	-	-	-	-	+
	1.56	-	-	-	-	-	+	+	+
	0	-	-	+	+	+	+	+	

Table 12

Bacterial strain used: Bacillus subtilis IAM 1213

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc acetate							
		1600	800	400	200	100	50	25	0
Hinoki-tiol	200	-	-	-	-	-	-	-	-
	100	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	+
	25	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	-	-	+
	6.25	-	-	-	-	-	-	-	+
	3.13	-	-	-	-	-	-	-	+
	1.56	-	-	-	-	-	-	+	+
	0	-	-	-	+	+	+	+	

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From Tables 1 to 12 shown above, it is apparent that the combined use of hinokitiol and zinc acetate results in markedly improved antibacterial activity.

Test Example 3 (Antibacterial activity test)

5 The effects of the combined use of hinokitiol and zinc chloride were examined after 24 hours of incubation at 37°C in the same manner as in Test Example 2 (except that the medium alone was changed, namely, Tryptic Soy Bouillon medium was used as the preculture medium, dried
10 bouillon medium for dilution, and heart infusion agar medium for plate preparation).

Hinokitiol SP and zinc chloride (Wako Pure Chemical Industries, Ltd.; Lot TWQ 1277) were used as the test drugs, and the following three bacterial strains as the
15 test organisms.

Strains used:

Staphylococcus aureus 209PJC

Bacillus subtilis PCI 219

Micrococcus luteus ATCC 9341

20 The results obtained are shown below in Table 13 through Table 15.

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Table 13

Bacterial strain used: Staphylococcus aureus 209PJC

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc chloride										
		400	200	100	50	25	12.5	6.25	3.13	1.56	0.78	0
Hinoki- tiol	100	-	-	-	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	+	+	+	+
	12.5	-	-	-	-	-	+	+	+	+	+	+
	6.25	-	-	-	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	-	-	-	-	-	-	-
	0.78	-	-	+	+	+	+	+	+	+	+	+
	0.39	-	-	+	+	+	+	+	+	+	+	+
	0.20	-	-	+	+	+	+	+	+	+	+	+
	0	-	-	+	+	+	+	+	+	+	+	+

Table 14

Bacterial strain used: Bacillus subtilis PCI 219

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc chloride										
		400	200	100	50	25	12.5	6.25	3.13	1.56	0.78	0
Hinoki- tiol	100	-	-	-	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	-	-	-	-
	12.5	-	-	-	-	-	-	+	+	+	+	+
	6.25	-	-	-	-	-	-	+	+	+	+	+
	3.13	-	-	-	-	-	-	+	+	+	+	+
	1.56	-	-	-	-	+	+	+	+	+	+	+
	0.78	-	+	+	+	+	+	+	+	+	+	+
	0.39	-	-	+	+	+	+	+	+	+	+	+
	0.20	-	-	+	+	+	+	+	+	+	+	+
	0	-	-	+	+	+	+	+	+	+	+	+

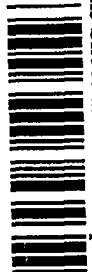
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Table 15

Bacterial strain used: Micrococcus luteus ATCC 9341Inoculum size: 10^6 cells/ml(Unit: $\mu\text{g/ml}$)

		Zinc chloride										
		400	200	100	50	25	12.5	6.25	3.13	1.56	0.78	0
Hinoki- tiol	100	-	-	-	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	-	-	-	+
	12.5	-	-	-	-	-	+	+	+	+	+	+
	6.25	-	-	-	-	+	+	+	+	+	+	+
	3.13	-	-	-	-	+	+	+	+	+	+	+
	1.56	-	-	+	+	+	+	+	+	+	+	+
	0.78	-	+	+	+	+	+	+	+	+	+	+
	0.39	-	+	+	+	+	+	+	+	+	+	+
	0.20	-	+	+	+	+	+	+	+	+	+	+
	0	-	+	+	+	+	+	+	+	+	+	


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Test Example 4 (Antibacterial activity test)

The effects of the combined use of hinokitiol and zinc dipicolinate were investigated after 24 hours of incubation at 37°C in the same manner as in Test Example 2 (except that the medium alone was changed, namely Trypto Soy Bouillon medium was used as the preculture medium, dried bouillon medium for dilution, and heart infusion agar medium for plate preparation).

Hinokitiol SP and zinc dipicolinate were used as the test drugs and the following two bacterial strains as the test organisms.

Strains used:

Staphylococcus epidermidis KPU-1

Bacillus subtilis ATCC 6633

The results obtained are shown below in Table 16 and Table 17.

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Table 16

Bacterial strain used: Staphylococcus epidermides KPU-1

Inoculum size: 10^6 cells/ml

(Unit: $\mu\text{g/ml}$)

		Zinc dipicolinate										
		400	200	100	50	25	12.5	6.25	3.13	1.56	0.78	0
Hinoki- tiol	100	-	-	-	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-	-	+	-
	25	-	-	-	-	-	+	+	+	+	+	+
	12.5	-	-	-	-	-	-	+	+	+	+	+
	6.25	-	-	-	-	-	-	-	-	-	-	-
	3.13	-	-	-	-	-	-	-	-	-	-	-
	1.56	-	-	-	-	-	-	-	-	-	-	-
	0.78	-	-	-	-	-	-	-	-	-	-	-
	0.39	-	-	-	-	-	-	-	-	-	-	-
	0.20	-	+	+	+	+	+	+	+	+	+	+
	0	+	+	+	+	+	+	+	+	+	+	+

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Table 17

Bacterial strain used: Bacillus subtilis ATCC 6633Inoculum size: 10^6 cells/ml(Unit: $\mu\text{g/ml}$)

		Zinc dipicolinate										
		400	200	100	50	25	12.5	6.25	3.13	1.56	0.78	0
Hinoki- tiol	100	-	-	-	-	-	-	-	-	-	-	-
	50	-	-	-	-	-	-	-	-	-	-	-
	25	-	-	-	-	-	-	-	-	+	+	+
	12.5	-	-	-	-	-	+	+	+	+	+	+
	6.25	-	-	-	-	+	+	+	+	+	+	+
	3.13	-	-	-	-	+	+	+	+	+	+	+
	1.56	-	-	+	+	+	+	+	+	+	+	+
	0.78	-	-	-	+	+	+	+	+	+	+	+
	0.39	-	+	+	+	+	+	+	+	+	+	+
	0.20	-	+	+	+	+	+	+	+	+	+	+
	0	-	+	+	+	+	+	+	+	+	+	



CLAIMS

1. A method of treating an infectious disease caused by bacteria or fungi in a patient which comprises administering to said patient a zinc compound and at
5 least one member selected from the group consisting of hinokitiol and salts thereof.

2. A method as claimed in Claim 1, wherein the ratio of said zinc compound (A) and said at least one member (B) selected from the group consisting of
10 hinokitiol and salts thereof is A:B = about 10 to 99.95:90 to 0.05 by weight.

3. A method as claimed in Claim 2, wherein the ratio of said zinc compound (A) and said at least one member (B) selected from the group consisting of
15 hinokitiol and salts thereof is A:B = about 50 to 99.9:50 to 0.1 by weight.

4. A method as claimed in Claim 1, wherein based on the total amount of said zinc compound and said at least one member selected from the group consisting of
20 hinokitiol and salts thereof, said zinc compound is used in an amount of about 10 to 99.95% by weight and said at least one member selected from the group consisting of

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hinokitiol and salts thereof is(are) used in an amount of about 90 to 0.05% by weight.

5. A method as claimed in Claim 4, wherein based on the total amount of said zinc compound and said at
5 least one member selected from the group consisting of hinokitiol and salts thereof, said zinc compound is used in an amount of about 50 to 99.9% by weight, and said at least one member selected from the group consisting of hinokitiol and salts thereof is(are) used in an amount of
10 about 50 to 0.1% by weight.

6. A method as claimed in any one of Claims 1 to 5, wherein said zinc compound is at least one member selected from the group consisting of zinc oxide, zinc chloride, zinc nitrate, zinc sulfate, zinc phosphate,
15 zinc aluminate, zinc fluoride, zinc iodide, zinc hydroxide, zinc carbonate, zinc chromate, zinc benzoate, zinc acetate, zinc paraaminobenzoate, zinc paradimethylaminobenzoate, zinc paraphenolsulfonate, zinc paramethoxycinnamate, zinc lactate, zinc-2-
20 mercaptopyridine N-oxide complex, zinc gluconate, zinc picrate, zinc citrate, zinc aspartate, zinc naphthenate, zinc salicylate, zinc phenolsulfonate, zinc sebacate, sodium zinc tripolyphosphate, zinc stearate, zinc

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caprate, zinc laurate, zinc myristate, zinc palmitate,
zinc oleate, zinc polyphosphonate, zinc
chondroitinsulfate, zinc undecylenate, zinc ascorbate,
zinc citrate, zinc pyrithione, hinokitiolato zinc, zinc
5 dipicolinate, zinc-glycerol complex, zinc-bishistidine
complex, zinc-3,4-dihydroxybenzoic acid complex, zinc
nicotinate and zinc-nicotinamide complex.

7. A method as claimed in Claim 6, wherein said
at least one member selected from the group consisting of
10 hinokitiol and salts thereof is at least one member
selected from the group consisting of hinokitiol and
sodium salt, potassium salt, magnesium salt, copper salt,
zinc salt, diethanolamine salt, 2-amino-2-ethyl-1,3-
propanediol salt, triethanolamine salt, morpholine salt,
15 piperazine salt, piperidine salt, ammonium salt, arginine
salt, lysine salt and histidine salt of hinokitiol.

8. A method as claimed in Claim 1, wherein based
on the total amount of said zinc compound (a) and said at
least one member (b) selected from the group consisting
20 of hinokitiol and salts thereof, said zinc compound (a)
is used in an amount of about 50 to 99.9% by weight and
said at least one member (b) selected from the group
consisting of hinokitiol and salts thereof is(are) used

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in an amount of about 50 to 0.1% by weight, said zinc compound (a) being at least one member selected from the group consisting of zinc oxide, zinc acetate, zinc pyrithione, hinokitiolato zinc, zinc chloride and zinc
5 dipicolinate and said component (b) being at least one member selected from the group consisting of hinokitiol and hinokitiol sodium salt.

9. A method as claimed in Claim 8, wherein based on the total amount of zinc oxide and hinokitiol, zinc
10 oxide is used in an amount of about 50 to 99.9% by weight and hinokitiol is used in an amount of about 50 to 0.1% by weight.

10. A method of preserving a cosmetic which comprises causing said cosmetic to contain a zinc
15 compound and at least one member selected from the group consisting of hinokitiol and salts thereof.

11. A method as claimed in Claim 10, wherein the ratio of said zinc compound (A) and said at least one member (B) selected from the group consisting of
20 hinokitiol and salts thereof is A:B = about 10 to 99.95:90 to 0.05 by weight.

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12. A method as claimed in Claim 11, wherein the ratio of said zinc compound (A) and said at least one member (B) selected from the group consisting of hinokitiol and salts thereof is A:B = about 50 to 99.9:50
5 to 0.1 by weight.

13. A method as claimed in Claim 10, wherein based on the total amount of said zinc compound and said at least one member selected from the group consisting of hinokitiol and salts thereof, said zinc compound is used
10 in an amount of about 10 to 99.95% by weight and said at least one member selected from the group consisting of hinokitiol and salts thereof is(are) used in an amount of about 90 to 0.05% by weight.

14. A method as claimed in Claim 13, wherein based
15 on the total amount of said zinc compound and said at least one member selected from the group consisting of hinokitiol and salts thereof, said zinc compound is used in an amount of about 50 to 99.9% by weight, and said at least one member selected from the group consisting of
20 hinokitiol and salts thereof is(are) used in an amount of about 50 to 0.1% by weight.

15. A method as claimed in any one of Claims 10 to





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14, wherein said zinc compound is at least one member selected from the group consisting of zinc oxide, zinc chloride, zinc nitrate, zinc sulfate, zinc phosphate, zinc aluminate, zinc fluoride, zinc iodide, zinc
5 hydroxide, zinc carbonate, zinc chromate, zinc benzoate, zinc acetate, zinc paraaminobenzoate, zinc paradimethylaminobenzoate, zinc paraphenolsulfonate, zinc paramethoxycinnamate, zinc lactate, zinc-2-mercaptopyridine N-oxide complex, zinc gluconate, zinc
10 picrate, zinc citrate, zinc aspartate, zinc naphthenate, zinc salicylate, zinc phenolsulfonate, zinc sebacate, sodium zinc tripolyphosphate, zinc stearate, zinc caprate, zinc laurate, zinc myristate, zinc palmitate, zinc oleate, zinc polyphosphonate, zinc
15 chondroitinsulfate, zinc undecylenate, zinc ascorbate, zinc citrate, zinc pyrithione, hinokitiolato zinc, zinc dipicolinate, zinc-glycerol complex, zinc-bishistidine complex, zinc-3,4-dihydroxybenzoic acid complex, zinc nicotinate and zinc-nicotinamide complex.

20 16. A method as claimed in Claim 15, wherein said at least one member selected from the group consisting of hinokitiol and salts thereof is at least one member selected from the group consisting of hinokitiol and sodium salt, potassium salt, magnesium salt, copper salt,



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zinc salt, diethanolamine salt, 2-amino-2-ethyl-1,3-propanediol salt, triethanolamine salt, morpholine salt, piperazine salt, piperidine salt, ammonium salt, arginine salt, lysine salt and histidine salt of hinokitiol.

5 17. A method as claimed in Claim 10, wherein based
on the total amount of said zinc compound (a) and said at
least one member selected from the group consisting of
hinokitiol and salts thereof, said zinc compound (a) is
used in an amount of about 50 to 99.9% by weight and said
10 at least one member selected from the group consisting of
hinokitiol and salts thereof is(are) used in an amount of
about 50 to 0.1% by weight, said zinc compound (a) being
at least one member selected from the group consisting of
zinc oxide, zinc acetate, zinc pyrithione, zinc
15 hinokitiolato zinc, zinc chloride and zinc dipicolinate
and said component (b) being at least one member selected
from the group consisting of hinokitiol and hinokitiol
sodium salt.

20 18. A method as claimed in Claim 17, wherein based
on the total amount of zinc oxide and hinokitiol, zinc
oxide is used in an amount of about 50 to 99.9% by weight
and hinokitiol is used in an amount of about 50 to 0.1%
by weight.





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19. An antibacterial and antifungal agent which comprises a zinc compound and at least one member selected from the group consisting of hinokitiol and salts thereof.

5 20. A cosmetic which contains a zinc compound and at least one member selected from the group consisting of hinokitiol and salts thereof.

21. A cosmetic as claimed in Claim 20, wherein said zinc compound and said at least one member selected from the group consisting of hinokitiol and salts thereof are incorporated therein as an antidandruff agent, bactericide and/or preservative.

22. A cosmetic as claimed in Claim 21, wherein the ratio of said zinc compound (A) and said at least one member (B) selected from the group consisting of hinokitiol and salts thereof is A:B = about 10 to 99.95:90 to 0.05 by weight.

23. A cosmetic as claimed in Claim 22, wherein the ratio of said zinc compound (A) and said at least one member (B) selected from the group consisting of hinokitiol and salts thereof is A:B = about 50 to 99.9:50



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to 0.1 by weight.

24. A cosmetic as claimed in Claim 21, wherein based on the total amount of said zinc compound and said at least one member selected from the group consisting of
5 hinokitiol and salts thereof, said zinc compound is used in an amount of about 10 to 99.95% by weight and said at least one member selected from the group consisting of hinokitiol and salts thereof is(are) used in an amount of about 90 to 0.05% by weight.

10 25. A cosmetic as claimed in Claim 24, wherein based on the total amount of said zinc compound and said at least one member selected from the group consisting of hinokitiol and salts thereof, said zinc compound is used in an amount of about 50 to 99.9% by weight, and said at
15 least one member selected from the group consisting of hinokitiol and salts thereof is(are) used in an amount of about 50 to 0.1% by weight.

26. A cosmetic as claimed in any one of Claims 21 to 25, wherein said zinc compound is at least one member
20 selected from the group consisting of zinc oxide, zinc chloride, zinc nitrate, zinc sulfate, zinc phosphate, zinc aluminate, zinc fluoride, zinc iodide, zinc





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- hydroxide, zinc carbonate, zinc chromate, zinc benzoate, zinc acetate, zinc paraaminobenzoate, zinc paradimethylaminobenzoate, zinc paraphenolsulfonate, zinc paramethoxycinnamate, zinc lactate, zinc-2-
- 5 mercaptopyridine N-oxide complex, zinc gluconate, zinc picrate, zinc citrate, zinc aspartate, zinc naphthenate, zinc salicylate, zinc phenolsulfonate, zinc sebacate, sodium zinc tripolyphosphate, zinc stearate, zinc caprate, zinc laurate, zinc myristate, zinc palmitate,
- 10 zinc oleate, zinc polyphosphonate, zinc chondroitinsulfate, zinc undecylenate, zinc ascorbate, zinc citrate, zinc pyrithione, hinokitiolato zinc, zinc dipicolinate, zinc-glycerol complex, zinc-bishistidine complex, zinc-3,4-dihydroxybenzoic acid complex, zinc
- 15 nicotinate and zinc-nicotinamide complex.

27. A cosmetic as claimed in Claim 26, wherein said at least one member selected from the group consisting of hinokitiol and salts thereof is at least one member selected from the group consisting of hinokitiol and
- 20 sodium salt, potassium salt, magnesium salt, copper salt, zinc salt, diethanolamine salt, 2-amino-2-ethyl-1,3-propanediol salt, triethanolamine salt, morpholine salt, piperazine salt, piperidine salt, ammonium salt, arginine salt, lysine salt and histidine salt of hinokitiol.



28. A cosmetic as claimed in Claim 21, wherein based on the total amount of said zinc compound (a) and said at least one member (b) selected from the group consisting of hinokitiol and salts thereof, said zinc compound (a) is used in an amount of about 50 to 99.9% by weight and said at least one member (b) selected from the group consisting of hinokitiol and salts thereof is(are) used in an amount of about 50 to 0.1% by weight, said zinc compound (a) being at least one member selected from the group consisting of zinc oxide, zinc acetate, zinc pyrithione, hinokitiolato zinc, zinc chloride and zinc dipicolinate and said component (b) being at least one member selected from the group consisting of hinokitiol and hinokitiol sodium salt.

29. A cosmetic as claimed in Claim 28, wherein based on the total amount of zinc oxide and hinokitiol, zinc oxide is used in an amount of about 50 to 99.9% by weight and hinokitiol in an amount of about 50 to 0.1% by weight.

This Sheet Has Been Replaced

