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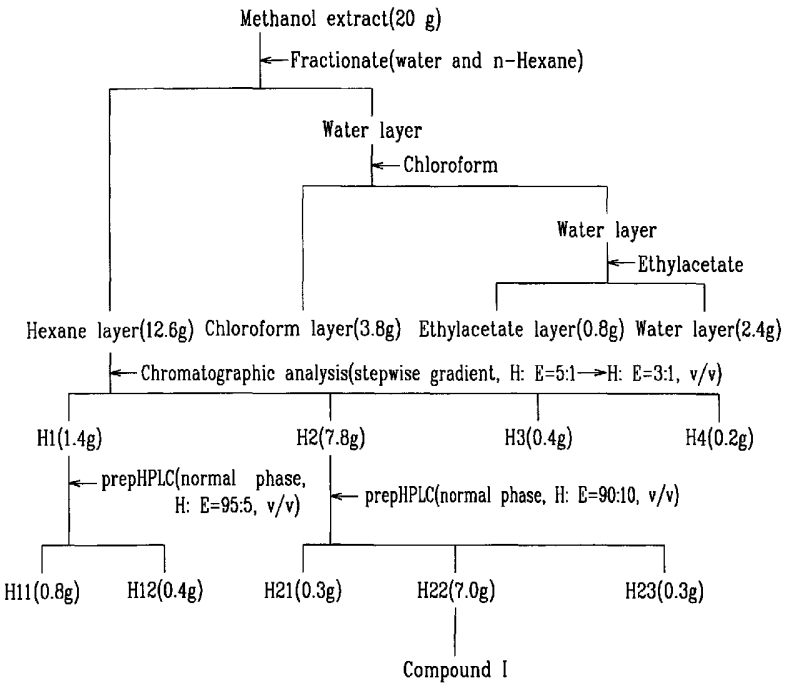

(57) Abstract: The present invention relates to an antibacterial composition comprising plant extracts, and more particularly to an extract of one or more kinds of plants selected from a group consisting of Foeniculum vulgare, Illicium verum, Asarum heterotropoides, Cinnamomum plants, and cloves, and an antibacterial compound therefrom.

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ANTIBACTERIAL COMPOSITION COMPRISING PLANT EXTRACT

BACKGROUND OF THE INVENTION

(a) Field of the Invention

The present invention relates to an antibacterial composition comprising plant extracts, more particularly to an antibacterial composition comprising an extract of one or more kinds of plants selected from a group consisting of *Foeniculum vulgare*, *Illicium verum*, *Asarum heterotropoides*, *Cinnamomum* plants, and cloves, or a compound derived therefrom, having antibacterial activity for *Candida* and *five species containing Trichophyton* .

(b) Description of the Related Art

Skin diseases caused by fungi are generically called dermatomycosis. Particularly, those caused by a dermatophyte that invades corneous tissues such as keratin, hair, fingernails, toenails, etc. and are parasitic thereon are called dermatophytosis, Tinea, or superficial fungal infection (Ribbon, J. W. (1998) Medical Mycology. *In* The pathogenic fungi and the pathogenic actinomyces. 2nd Ed. W.B Saunders Company. Philadelphia, London, Toronto.).

Superficial fungal infections are referred to differently according to the invaded skin region, for example Tinea manus & Tinea pedis for hand and foot, Tinea faciale for face, Tinea crusis for the groin, Tinea capitis for the head, Tinea ungrium or Onychomy-cosis for fingernails and toenails, and Tinea corporis for the other regions (Rezabek, G.H. and Friedman, A. D. 1992. *Drugs* 43(5):674-682.; Kamalam, A. and Thambiah, A.S. 1976. *Sabouraudia*

14(2):129-148).

Major causes for superficial fungal infection are *Microsporum*, *epidermophyton*, *Trichophyton*, *candida* species, and *Malassezia furfur*. *Microsporum* mainly invades skin and hair; *epidermophyton* invades skin and nails; and *Trichophyton* invades skin, hair, and nails (Weitzman, I. and Summerbell, R. C. 1995. The dermatophytes. *Clinical Microbiology* Review 8(2):240-259). *Candida* causes disease on skin and mucous membranes, and *Malassezia furfur* causes tinea versicolor, which causes spots.

Superficial fungal infection-causing bacteria are parasitic on keratin of the upper part of epithelial cells and cause superficial diseases, but sometimes they may cause inflammation below the upper part of the epithelial cells, or cause dermatophytid.

Pathogenic fungi have a worldwide distribution, and cause diseases in animals including humans. Pathogenic fungi do not always cause disease by contact, and whether or not infection occurs therewith depends on the kinds of infecting fungi, age of host, immune condition, existence and nonexistence of complications, health condition of skin, nutrition, or hormone conditions (Brash, J. and Gottkehaskamp, D. 1992. The effect of selected human steroid hormones upon the growth of dermatophytes with different adaptation to man. *Mycopathologia* 120(2): 87-92).

Most skin and subsidiary organ infections with *Dematophyte spp* fungi are called Dermatophytosis. These fungi groups locally inhabit the epidermis keratin layer, and some species invade and inhabit animal tissue. For

convenience, they are divided into Anthrophillic (parasitic on humans), Zoophilic (parasitic on animals) and Ziophilic (saprophyte parasitic in soil) according to the host (Gupta, A. K. Einarson, T. R. Summerbell, R. C. and Shear, N. H. 1998. A North American perspective of Drugs. 55(5): 645-674).

Superficial fungal infection is treated using local and general anti-fungals in principal, and according to circumstances, a keratin-solvent is simultaneously applied. Even after symptoms and skin disease disappear, approximately 2 to 4 weeks of treatment is required. However, there is high possibility of Tinea pedis treatment failing or of recurrence due to carelessness or physical properties and immunodeficiency of the patient.

Although various anti-fungals have been used to treat dermatomycosis, there is an effort to discover safer and superior anti-fungals from natural substances due to the high relapse rate and the increase in understanding of skin toxicity.

SUMMARY OF THE INVENTION

Accordingly, it is an object of the present invention to provide a plant extract having antibacterial activity for fungi.

It is another object of the present invention to provide a plant extract having antibacterial activity for *Trichophyton* and *Candida*.

It is another object of the present invention to provide a plant-derived compound having antibacterial activity for *Trichophyton* and *Candida*.

It is another object of the present invention to provide an anti-fungal

composition that is safe to skin and has superior anti-fungal activity.

In order to achieve these objects, the present invention provides an antibacterial composition comprising an extract of one or more kinds of plants selected from a group consisting of *Foeniculum vulgare*, *Illicium verum*, *Asarum heterotropoides*, *Cinnamomum* plants, and cloves.

The present invention also provides an antibacterial composition comprising a compound selected from a group consisting of fenchone, eugenol, isoeugenol, methyleugenol, cinnamyl alcohol, cinnamic aldehyde, and a mixture thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows a process for separating eugenol from a methanol extract of cloves.

Fig. 2 shows a process for separating eugenol and isoeugenol from clove oil.

DETAILED DESCRIPTION AND THE PREFERRED EMBODIMENTS

The present inventors discovered that *Foeniculum vulgare*, *Asarum heterotropoides*, *Cinnamomum sp.* plants, and cloves have anti-fungal activities, and completed the present invention.

Foeniculum vulgare is known to have almost the same major ingredients as *Illicium verum* (Changmin Kim, Minkyo Shin, Dukkyun Ann, Kyungsun Lee, etc. 1998. Medicine Dictionary, vol. 9, Jungdam, 5813-5816; vol. 10, 6597-6603).

Cinnamomum sp. plants include *Cinnamomum sieboldii*, *C. cassia*, *C. zeylanica*, a cinnamon tree, and *C. laureirii*. In herbal medicine, pellicles (roots, trunks, branches) of *Lauraceae* plants are called *C. sieboldii* for those stripped thickly from branches and dried, *C. cassia* for those stripped from smaller bark and dried, and *Cinnamomi Ramulus* for those stripped from very slim branches and dried. Those stripped from the bark of *Cinnamomum* belonging to the *Lauraceae* family, and when dried are called *C. cassia* or *Cinnamomum sieboldii*.

The scientifical name of cloves is *Eugenia caryophyllata* or *Syzygium aromaticum*, and the essential oil therefrom is commonly used as clove bud or leaf oil. In particular, clove bud oil is a plant oil obtained only from the buds of cloves.

The plant extract of the present invention is prepared by a common extraction method, preferably by mixing the pulverized plant with distilled water, alcohol, or organic solvent; fractioning the mixture; and removing the solvent. The alcohol is preferably C1-5; more preferably ethanol, methanol, propanol, or butanol; and most preferably methanol. The organic solvent is preferably hexane, chloroform, or ethyl acetate, and most preferably hexane. The extraction region is the flower, branch, trunk, bud, root, bark, fruit, seed, plant body, etc., and *Foeniculum vulgare* extract is preferably from its fruit, *Asarum heterotropoides* extract is preferably from its root, and *Cinnamomum sp.* plants and clove extracts are preferably from their root. However, the extraction region is not limited thereto.

In addition, the plants of the present invention can be made into essential oil. Plant essential oil is extracted by common essential oil extraction methods, or marketed essential oil can be used. Representative extraction methods include distillation and expression using water or vapor. Marketed essential oil includes fennel sweet oil (*Foeniculum vulgare* oil), Cinnamon oil (*C. cassia* oil), and clove bud oil (clove oil).

The plant extracts and essential oils of the present invention were applied to *Candida* or *Trichophyton*, which cause athlete's foot. As a result, all of them showed excellent anti-fungal activity, and *Asarum heterotropoides* extract, clove extract, *C. cassia* extract, and clove oil showed the best anti-fungal activities.

In addition, the present invention provides a plant-derived anti-fungal compound. The anti-fungal compound includes clove-derived compounds eugenol and isoeugenol, a *Foeniculum vulgare*-derived compound (+)-fenchone, and *Cinnamomum sieboldii*-derived compounds cinnamyl alcohol, cinnamic aldehyde, and methyl eugenol. The anti-fungal compounds can be purchased as marketed compounds, or they can be separated and purified from the plants.

The present invention also provides an antibacterial composition comprising plant extracts or anti-fungal compounds. The antibacterial composition has growth-inhibition activity for pathogenic fungi, and it preferably has growth-inhibition activity for *Trichophyton* and *Candida*.

The anti-fungal composition of the present invention has antibacterial

effects for pathogenic fungi as shown in Table 1. Representative pathogenic fungi include *Trichophyton rubrum*, KCTC 6345; *Microsporum audouinii*, KCTC 6346; *Trichophyton ferrugineum*, KCTC 6351; *Epidermophyton floccosum*, KCTC 6586; *Trichophyton mentagrophytes*, KCTC 6077; and *Candida albicans*, KCTC 7728.

Table 1

Fungi (species name)		Ecology	Hair-Invasion	Attack region
Microsporum sp.	*M. audouinii*	Anthrophillic	External parasitism	Head
	M. canis	Zoophilic	External parasitism	Head, hair, face, body
	M. gypseum	Ziophilic	External parasitism	head
	M. fulvum	Ziophilic	External parasitism	
	M. cookei	Ziophilic		
	M. distortum	Zoophilic		
Epidermophyton sp.	*E. floccosum*	Anthrophillic		Tinea, foot, nails
Trichophyton sp.	*T. rubrum*	Anthrophillic		barba, face, body, tinea, foot, nails
	T. mentagrophytes	Zoophilic	External parasitism	Head, hair, face, body, tinea, foot, nails
	T. ferrugineum	Anthrophillic	External parasitism	Head, body
	T. violaceum	Anthrophillic	Internal parasitism	Head, nails
	T. verrucosum	Zoophilic	External parasitism	Head, hair
	T. tonsurans	Anthrophillic	Internal parasitism	Head
	T. schoenleinii	Anthrophillic	Internal parasitism	Head, favus
	T. simii	Zoophilic	Internal parasitism	Head
	T. terrestre	Ziophilic		
	T. gallinase	Zoophilic		
	T. megninii	Anthrophillic		

The anti-fungal composition of the present invention can be used for inhibiting growth of pathogenic fungi, and preferably it is used as a cleaner, a

treating agent for dermatomycosis such as athlete's foot, a disinfectant, etc.

The preparations of the anti-fungal composition, although not limited thereto, are preferably plasters, granules, lotions, liniments, limonades, aromatic waters, powders, syrups, eye ointments, liquids, solutions, aerosols, extracts, elixirs, ointments, fluid extracts, emulsions, suspensions, infusions, decoctions, ophthalmic solutions, tablets, suppositories, injections, spirits, cataplasma, capsules, creams, troches, tinctures, pastes, or pills.

The anti-fungal composition may further comprise pharmaceutically acceptable vehicles according to its preparation and use method, and the contents of plant extracts or essential oils in the composition are preferably 1 to 20 wt%. A dose of the composition is preferably 10 to 50 mg and the frequency is preferably one to three times per day, but it is preferably controlled according to the degree of disease and health condition of the patient.

The present invention will now be explained in more detail with reference to the following Examples. However, these are to illustrate the present invention and the present invention is not limited to them.

Example 1.

Preparation of antibacterial plant extract

Fruits of *Foeniculum vulgare*, roots of *Asarum heterotropoides*, buds of *Cinnamomum sieboldii* or *Eugenia caryophyllata*, and *C. cassia* were purchased, and methanol extracts were obtained from each. All of the methanol extracts were prepared by the same method, and methanol extraction method of *Foeniculum vulgare* fruit is hereinafter explained as an

example.

300 g of *Foeniculum vulgare* fruit were finely pulverized with a mixer and introduced into a 500 ml Erlenmeyer flask, 200 ml of methanol were mixed therewith, and the mixture was left for 2 days. It was then filtered under reduced pressure, and the filtrate was concentrated with a rotary vacuum condenser (EYELA autojack NAJ-160, Japan). The pulverized substance was filtered through a filtering paper and mixed with methanol again to finally prepare a methanol extract.

Example 2.

Preparation of antibacterial plant essential oil

Foeniculum vulgare oil, *Cinnamomum sieboldii* oil, *C. cassia* oil, and clove oil were purchased from Jin-a Perfume Inc.

The essential oils were prepared by steam distillation, as follows.. A small amount of distilled water was added to each of the *Foeniculum vulgare*, *Cinnamomum sieboldii*, and cloves, and they were finely pulverized with a mixer and introduced into 3L concentration flasks, respectively. The temperature of the flask was set to approximately 70 ℃ on a heating mantle, and flasks containing 40 ml each (1/1, v/v) of diethyl ether and hexane were set to 30 to 40 ℃ (approximately 38℃), and they were all heated for 2 hours. The amount of sample required for one distillation was 250 g, and after extraction, a small amount of sodium hydroxide anhydride (Na_2SO_4) was added to the flasks and they were left in a desiccator to remove moisture from the extracts, and then the extracts were passed through a Toyo No. 2 filter to

concentrate them.

Example 3.

Measurement of fungi growth-inhibition activity

The six species of *Trichophyton rubrum*, KCTC 6345; *Microsporum audouinii*, KCTC 6346; *Trichophyton ferrugineum*, KCTC 6351; *Epidermophyton floccosum*, KCTC 6586; *Trichophyton mentagrophytes*, KCTC 6077; and *Candida albicans,* KCTC 7728 were obtained from the Korean Collection for Type Cultures, KCTC. Growth-inhibition activities were examined by a paper disc diffusion method.

The strains were inoculated on a Sabouraud's agar medium, and each methanol extract (from Example 1) was dissolved in methanol and applied to a paper disc or each essential oil (from Example 2) was directly applied to a paper disc. The paper discs were mounted on each of the mediums inoculated with the various fungi, the fungi were aerobically cultured for 5 days at 28 ℃, and antibacterial activities were confirmed by the size of a clear zone formed around the paper discs.

Table 2 shows growth-inhibition activities of the 5 species of bacteria causing *Trichophytia* and 1 species of *Candida* caused by the methanol extracts and essential oils, when each paper disc was applied with an appropriate concentration of methanol extract or essential oil.

Table 2.

Treating concentration, mg/paper	Clear zone, mm					
	Microsporum audouinii	*Trichophyton ferrugineum*	*Candida albicans*	*Trichophyton mentagrophytes*	*Epidermophyton floccosum*	*Trichophyton rubrum*

Foeniculum vulgare	50	11	10	9	9	10	12
Foeniculum vulgare oil	100	14	17	14	14	15	14
	50	13	11	11	10	10	10
	10	8	9	9	8	9	9
Asarum heterotropoides	20	16	15	20	17	18	16
	10	16	15	16	16	15	15
Cinnamomum sieboldii	10	28	27	37	35	30	28
Cinnamomum sieboldii oil	50	25	24	26	26	25	23
Clove	10	30	28	30	30	22	24
Clove oil	10	25	26	24	22	25	20

When the diameter of the clear zone generated by the methanol extract or the essential oil was 10 mm or more, fungi growth-inhibition activity was judged to exist. As shown in Table 2, *Foeniculum vulgare* methanol extract showed antibacterial activity for *Microsporum audouinii* when 50 mg thereof were applied, *Foeniculum vulgare* oil showed antibacterial activity when 100 mg and 50 mg were applied, and *Asarum heterotropoides* showed activity when 10 mg or more were applied. In addition, *Cinnamomum sieboldii* methanol extract and oil formed very strong clear zones when 10 mg and 50 mg respectively were applied, and clove methanol extract and oil also formed a very broad clear zone when 10 mg were applied. They showed similar aspects of antibacterial activities in other fungi.

Example 4.

Separation of anti-fungal compound

(1) Separation of eugenol

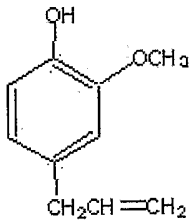
Clove methanol extract (20 g) was fractionated with hexane (800 ml), chloroform (800 ml), ethylacetate (800 ml), and a water layer to obtain 12.6 g of

hexane, 3.8 g of chloroform, 0.8 g of ethylacetate, and 2.4 g of the water layer. Antibacterial activity of each fraction was examined, and it was confirmed that the hexane fraction showed antibacterial activity.

A chromatographic analysis with a silica gel column (Merck 230 mesh, 600g, diameter 5.5 x 70 g) and a stepwise gradient with hexane-ethyl acetate (hexane: ethylacetate = 5:1 ->3:1, v/v) were performed on 12.6 g of the hexane fraction to obtain effluents. TLC (Thin Layer Chromatography) was performed on the effluents, and if migration of spot is same, they were gathered and concentrated to separate them into H1 (1.4 g), H2 (27 g), H3 (0.4 g), and H4 (0.2 g) fractions. Antibacterial activity of each fraction was examined, and results showed antibacterial activities in the H1 and H2 fractions. Since H2 showed a larger yield than H1, the antibacterial substance was isolated in H2.

High-speed liquid chromatography (Spectra System P2000) was performed on H2. Hexane : ethyl acetate (9:1.v/v) solvent was dripped into a column (μ Porasil, inner diameter 19mm X length 300 mm) at a rate of 3 ml per minute, and effluent was detected at 242 nm to obtain a compound I. The compound I was identified as eugenol of Chemical Formula 1 as a result of an analysis on the basis of a spectroscopic analysis such as EI-MS, ^{1}H and ^{13}C-NMR, etc.

(Chemical Formula 1)



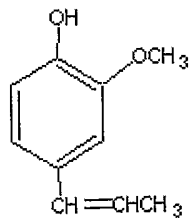
(2) Separation of isoeugenol and eugenol from clove oil

Isoeugenol and eugenol were separated from 1 mg of clove oil (Fig. 2).

Analytical HPLC (μ Porasil: diameter 10 ㎛, inner diameter 3.9 mm X length 300 m) was performed on clove oil at a rate of 2 ml per minute, absorbance of 242 nm, solvent condition of hexane : ethylacetate 9:1 (v/v) to separate isoeugenol and eugenol. Under the same conditions, compounds H1, H2, and H3 were purified using a fractioning column (μ Porasil, resin diameter 10 ㎛, inner diameter 19 mm X length 300 mm). These three kinds of compounds (H1, H2, H3) were examined for their antibacterial activities, and H2 and H3 were confirmed to have antibacterial activities.

Isoeugenol and eugenol were purchased from Sigma, and EI-MS of H2 and H3 were compared with those of the standard isoeugenol and eugenol products. As a result, H2 was identified as eugenol, and H3 as isoeugenol. Isoeugenol is represented by the Chemical Formula 2.

(Chemical Formula 2)



Example 5.

Examination of Antifungal activities of compounds

Antifungal activities of eugenol and isoeugenol were examined, and those of *Foeniculum vulgare* oil-derived Fenchone, *Cinnamomum sieboldii*-derived cinnamyl alcohol, and cinnamic aldehyde were examined by the same method.

Table 3.

Treating concentration, mg/paper		Clear zone, mm					
		Microsporum audouinii	*Trichophyton ferrugineum*	*Candida albicans*	*Trichophyton mentagrophytes*	*Epidermophyton floccosum*	*Trichophyton rubrum*
Fenchone	50	16	12	13	15	14	13
	10	9	11	10	9	9	10
Eugenol	10	31	31	30	28	25	26
Isoeugenol	10	25	25	24	23	24	22
Cinnamyl alcohol	10	28	28	28	27	25	29
Cinnamic aldehyde	10	48	38	44	40	35	40
Methyleugenol	5	32	25	25	23	30	31
	2.5	30	26	23	25	28	27
	1.25	15	15	13	14	14	16
Clotrimazole	5	35	33	25	36	27	28
	2.5	23	30	22	18	24	23
	1.25	21	23	22	19	18	18

In Table 3, clotrimazole is a positive control. For *Microsporum audouinii*, fenchone showed very strong inhibition activity when 50 mg per paper disc were applied, eugenol and isoeugenol showed very strong activities when 10 mg were applied, and cinnamyl alcohol showed strong activity when 25 mg or more were applied. Cinnamic aldehyde and methyleugenol showed the strongest antifungal activities. The diameter of the clear zone from each compound differed slightly according to application concentration and strains,

but overall growth-inhibition activities thereof showed similar results.

Example 6.

Clinical Test

(1) Clinical test for *Foeniculum vulgare* oil

Foeniculum vulgare oil was dissolved in ethanol to prepare a 5% *Foeniculum vulgare* oil composition, and a clinical test was performed with 5 adult men whose feet were infected with *Trichophyton*.

The *Foeniculum vulgare* oil composition was sprayed on the subjects' feet once every day for 3 seconds (0.15 g of *Foeniculum vulgare* oil applied) to examine the progress of *Trichophyton* over time.

Subjects having serious athlete's foot showed the following effects according to use time.

(1) 1 day of treatment: Sore oozing from splitted or pressed skin such as eczema disappeared.

(2) 2 days: Split region was slowly healed.

(3) 3 days: Keratin formed around athlete's foot region, and pain around athlete's foot region disappeared.

(4) 4 days: Keratin formation was very conspicuous, and athlete's foot seemed to be completely healed.

For those not having serious athlete's foot, treatment twice per day could cause sufficient keratin formation and athlete's foot could be completely healed.

In addition, during application of *Foeniculum vulgare*, particular

symptom and side effects were not observed on the skin of the subjects.

Accordingly, *Foeniculum vulgare* oil composition causes keratinization of athlete's foot tissues to change growth conditions of *Trichophyton*, thereby treating athlete's foot.

According to the present invention, antibacterial extracts were separated from *Foeniculum vulgare*, *Illicium verum*, *Asarum heterotropoides*, *Cinnamomum sp.* plants, and cloves, and the antibacterial compounds fenchone, eugenol, isoeugenol, methyleugenol, cinnamyl alcohol, and cinnamic aldehyde were identified. The antibacterial extracts and compounds can be used as natural antibacterial compounds without toxicity because they have very strong antibacterial activities for *Trichophyton* and *Candida*.

WHAT IS CLAIMED IS:

1. An antibacterial composition comprising an extract of one or more kinds of plants selected from a group consisting of *Foeniculum vulgare*, *Illicium verum*, *Asarum heterotropoides*, *Cinnamomum sp.* plants, and cloves.

2. The antibacterial composition according to Claim 1, wherein the *Cinnamomum sp.* plant is one or more kinds selected from a group consisting of *Cinnamomum sieboldii*, *C. cassia*, *C. zeylanica*, a cinnamon tree, and *C. laureirii*.

3. The antibacterial composition according to Claim 1, wherein the extract is prepared using at least one solvent selected from a group consisting of an organic solvent, distilled water, and alcohol.

4. The antibacterial composition according to Claim 1, wherein the extract is at least one selected from a group consisting of *Foeniculum vulgare* oil, *Illicium verum* oil, *Asarum heterotropoides* oil, *Cinnamomum sieboldii* oil, *C. cassia* oil, clove oil, and clove bud oil.

5. The antibacterial composition according to Claim 1, wherein the composition has antibacterial activity for *Trichophyton* or *Candida*.

6. The antibacterial composition according to Claim 1, wherein the composition has antibacterial activity for one or more kinds of fungi selected from a group consisting of *Trichophyton rubrum, Microsporum audouinii, Trichophyton ferrugineum, Epidermophyton floccosum, Trichophyton mentagrophytes, and Candida albicans*.

7. An antibacterial composition comprising a compound selected

from fenchone, eugenol, isoeugenol, methyleugenol, cinnamyl alcohol, cinnamic aldehyde, and a mixture thereof.

8. The antibacterial composition according to Claim 7, wherein the composition has antibacterial activity for *Trichophyton* and *Candida*.

9. The antibacterial composition according to Claim 7 for treating athlete's foot.

FIG.1

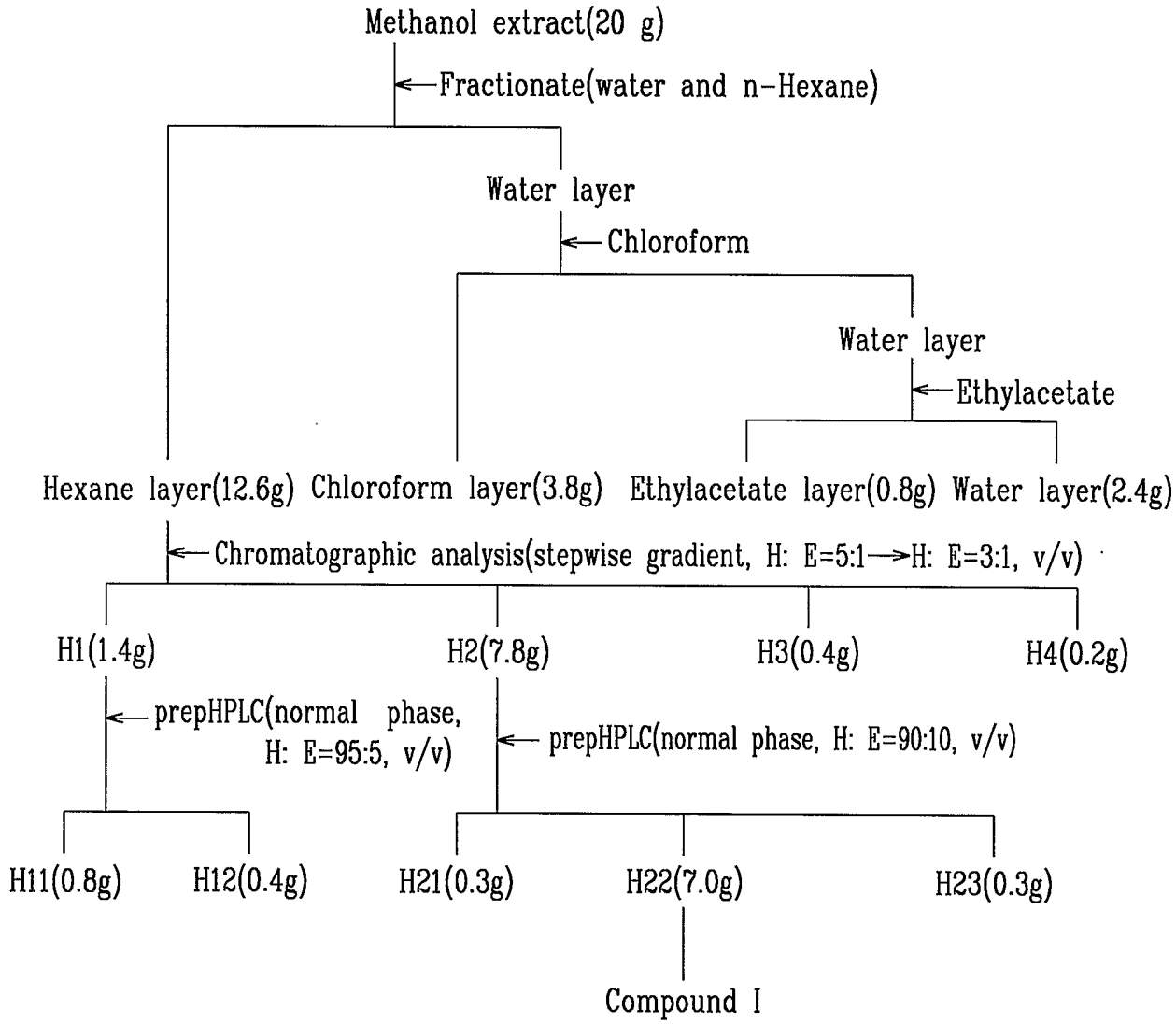
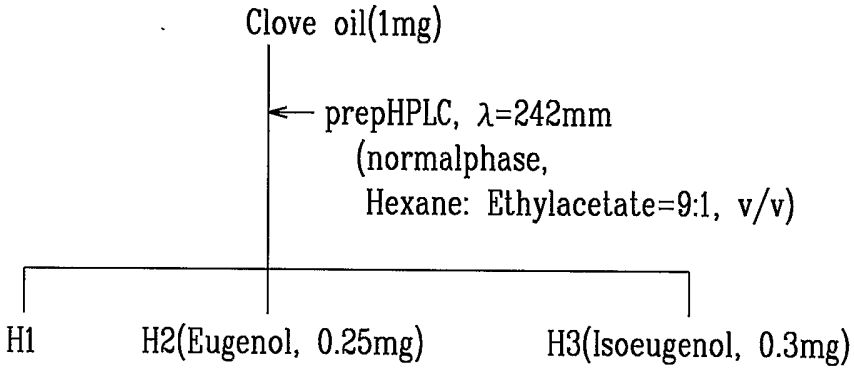

Methanol extract(20 g)
Fractionate(water and n-Hexane)
Water layer
Chloroform
Water layer
Ethylacetate
Hexane layer(12.6g)
Chloroform layer(3.8g)
Ethylacetate layer(0.8g)
Water layer(2.4g)
Chromatographic analysis(stepwise gradient, H: E=5:1→H: E=3:1, v/v)
H1(1.4g)
H2(7.8g)
H3(0.4g)
H4(0.2g)
prepHPLC(normal phase, H: E=95:5, v/v)
prepHPLC(normal phase, H: E=90:10, v/v)
H11(0.8g)
H12(0.4g)
H21(0.3g)
H22(7.0g)
H23(0.3g)
Compound I

FIG.2


Clove oil(1mg)
prepHPLC, λ=242mm
(normalphase,
Hexane: Ethylacetate=9:1, v/v)
H1
H2(Eugenol, 0.25mg)
H3(Isoeugenol, 0.3mg)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR 02/00826

CLASSIFICATION OF SUBJECT MATTER

IPC[7]: A61K 35/78

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC[7]: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPI, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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X	JP 04 005237 A (NONOKAWA SHOJI YG) 9 January 1992 (09.01.92) (abstract) World Patents Index [online]. London, U.K.: Derwent Publications, Ltd. [retrieved on 2002-07-09]. Retrieved from: Questel/Orbit, Paris, France. DW 9230, Accession No. 92-060692.	1-4,7
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☒ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
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„E" earlier application or patent but published on or after the international filing date
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Date of the actual completion of the international search	Date of mailing of the international search report
9 July 2002 (09.07.2002)	22 July 2002 (22.07.2002)
Name and mailing adress of the ISA/AT Austrian Patent Office Kohlmarkt 8-10; A-1014 Vienna Facsimile No. 1/53424/535	Authorized officer WOLF K. Telephone No. 1/53424/436

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR 02/00826

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Internal application No.
PCT/KR 02/00826-0

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