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(54) INSECT REPELLENT AND ANTIFUNGAL COMPOSITION

(71) We, GORO IZAWA, of No. 7—9, 6-Chome, Zushi, Zushi-shi, Kanagawa-ken, Japan, TAMIO NISHIMURA, of No. 4063—3, Ikuta, Kawasaki-shi, Kanagawa-ken, Japan, and YOSHIO MIWA, of No. 10—25, 3-chome, Shimoochiai, Shinjuku-ku, Tokyo, Japan, all citizens of Japan, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The invention relates to an insect repellent and antifungal composition deriving its action from the nontoxic vapour evolved from an insect repellent and antifungal agent of high boiling point and low toxicity and thereby producing both insect repellent and antifungal effects over a long period of time. More particularly, this invention relates to an insect repellent and antifungal composition made by adding α -bromocinnamaldehyde to a hygroscopic substance like silica gel, or to a volatile substance like *p*-dichlorobenzene, the purpose being to produce an insect repellent and antifungal composition that exhibits a durable effect over a long period of time as a result of the minute quantity of vapour evolved therefrom, which vapour is nontoxic to human body.

According to the present invention there is provided an insect repellent and antifungal composition which comprises α -bromocinnamaldehyde together with a carrier other than a conventional liquid medium used in the preparation, isolation and purification of the active ingredient.

α -Bromocinnamaldehyde is a solid at ordinary (ambient) temperatures, and is a compound with high boiling point, its vapour pressure being ca. 0.001 mmHg at 50°C. The amount of vapour evolved from this substance is so minute that it cannot be measured and yet that vapour which is evolved shows antifungal and insect repellent activity. The vapour of α -bromocinnamaldehyde is able, as a result of its insect repellent activity, to reduce the harmful effect on sheep wool of

fiber-eating insects like *Attagenus japonicus* and clothes moth larvae, and shows insect prevention activity against ticks comparable to the action of the insecticide known as Dieldrin.

The oral toxicity of α -bromocinnamaldehyde in mice, LD₅₀, is 1,752 mg/kg, and the cutaneous toxicity is 2.220 mg/kg. In chronic tests using rats, histological examination during autopsy showed no changes in the internal organs. This evidence indicates that α -bromocinnamaldehyde has a low toxicity and that the very minute quantity of vapour evolved from it may be considered to be almost entirely nontoxic to the human body.

It has also been found that α -bromocinnamaldehyde has almost no effect on electrical properties (dielectric breakdown voltage and volume resistivity), that its vapour effectively permeates through paper or a polyethylene bag, that it does not corrode metals, and has no adverse effect on natural or synthetic fibers or on paper. The composition obtained by the addition of at least 0.001% by weight of α -bromocinnamaldehyde to a carrier e.g. silica gel or *p*-dichlorobenzene, shows excellent and durable effects over a long period of time.

The composition of the present invention may fall into one of the following classes having the following characteristics:—

(1) When a volatile insect repellent like *p*-dichlorobenzene or naphthalene is used as the carrier, the characteristics of this agent are, of course, utilized and the properties of the resulting vapour from the composition supplemented. The volatile insect repellent agents referred to above exhibit strong insect repellent activity with low toxicity but have no fungicidal action, and, indeed, their insect repellent activity disappears in a short time as a result of volatilization. In contrast, the insect repellent activity of α -bromocinnamaldehyde, in addition to its antifungal activity is very durable. This type of composition of the present invention retains its insect repellent and anti-fungal activities for a long period of time even after volatilization of the volatile insect repellent(s). Thus, this type of composition may be used effectively as an insect repellent

[Price 33p]

Price 75p

and antifungal agent for clothes, art objects, antiques and specimens.

(2) When hygroscopic substances like silica gel and Kaolin mineral earth are used as the carrier the hygroscopic substance will remove a large quantity of moisture (an important source of fungus production) so that a more perfect and long-term anti-fungal effect can be attained. Silica gel has numerous unseen capillaries (the capillaries of 1 g of silica gel are said to occupy an area of ca. 500 m² when extended) and any α -Bromocinnamaldehyde adsorbed inside these capillaries is retained there. Since α -bromocinnamaldehyde has a high boiling point, its rate of evaporation is extremely small and the insect repellent and antifungal effect of such a composition is maintained over a long period of time. In addition, the compositions of this invention with a silica gel carrier are light in weight (sp. gr. 0.6—0.7) and easy to handle.

None of the ingredients of such a composition are sublimable as is naphthalene, so that there is no fear of vapour crystallizing in a closed vessel and adhering to other objects. Such compositions can, therefore, be sealed in precision photochemical instruments such as cameras and microscopes without causing any harm to the lens, shutter, or other precision parts and still give the desired antifungal effect. Such compositions are also useful as antifungal agents for recording films and microfilms requiring permanent storage, and as desiccating antifungal agents for musical instruments such as the piano, violin or flute.

Carriers for use in the present composition are not limited to the carriers mentioned above but also include for example, powders such as charcoal powder.

The invention also provides a method of repelling insects or inhibiting the growth of fungus which method utilizes a composition in accordance with the invention or α -bromocinnamaldehyde.

The invention will now be further described and illustrated with reference to the following specific Examples.

Example 1.

When silica gel is used as a carrier, α -bromocinnamaldehyde is dissolved in an organic solvent with a suitable surfactant and

the solution is diluted with water to contain 100—30,000 μ g/ml of α -bromocinnamaldehyde. Jellied silica gel, obtained by final washing with water during the manufacture of the silica gel, is immersed in this solution of α -bromocinnamaldehyde for a suitable period of time, collected, and dried.

Example 2.

In the case in which talc is employed as a carrier, the above-described (Example 1) solution of α -bromocinnamaldehyde is sprayed onto the powder while stirring thoroughly and the powder is then dried. In this case, a solution in an organic solvent may be used as the spray.

Example 3.

In the case in which *p*-dichlorobenzene is utilized as a carrier, 1—10 parts of finely powdered α -bromocinnamaldehyde is mixed with 1,000 parts of crystalline powdered *p*-dichlorobenzene and the mixture formed into granules or beads. Since the melting point of α -bromocinnamaldehyde is 71.5—72°C, it may be added to fused *p*-dichlorobenzene, mixed thoroughly, and crystallized.

Example 4.

Test on the effect of α -bromocinnamaldehyde powder mixed with *p*-dichlorobenzene powder on ticks (*Tyrophagus dimidiatus* Hermann).

Test method: Two grams of each of the compositions shown in Table 1 was placed on a veneer board of 10 × 10 cm, a straw mat of 10 cm² and 5 cm in thickness was placed on it, and the straw mat was inoculated with 4,000 ticks (2 g, including feed). The whole was closed in a polyethylene bag and stored in a thermostatic room maintained at 25°C. After 24 hours, 1 week, and 1 month, straw was drawn from the upper, middle, and lower layers of the straw mat and the number of ticks present in 2 g of this straw was counted by the "heat chasing method". This number was compared with the number of live ticks in the untreated control to obtain the mortality rate and the effect of treatment was examined. The values given in Table 1 are average values from the results of two experiments.

Table 1 Test Result:

Sample	Index of No. of ticks decreased in 2 g of straw					
	24 hr.		7 days		30 days	
	No. %		No. %		No. %	
<i>p</i> -Dichlorobenzene alone	41.0	45.3%	7.0	94.6%	855.0	30.4%
<i>p</i> -Dichlorobenzene (95) + α -Br-cinnamaldehyde (5)	9.5	87.3	5.5	95.7	774.0	37.0
<i>p</i> -Dichlorobenzene (90) + α -Br-cinnamaldehyde (10)	2.5	96.7	24.0	81.4	350.15	71.5
Untreated control	75.0	—	129.0	—	1,228.0	—

Example 5.

Test on the insect repellent effect of α -bromocinnamaldehyde against fiber-eating insects.

Test method: the test insect (larvae of *Attagenus japonicus* and of the clothes moth) was placed in a 1-liter conical flask, 10 insects to a flask, ca. 50 mg of test sheep wool yarn was added, and α -bromocinnamaldehyde crys-

tals placed on a small dish was placed in it. The flask was stoppered to close it and maintained at 25°C for 7 days. The yarn was then taken out and weighed after naked-eye examination. The difference in weight of the yarn before the start and at the end of the experiment was taken as the amount of yarn eaten by the insect. The test was repeated five times.

Table 2 Test Result

Amount of α -Br-cinnamaldehyde (mg/liter)	Amount of yarn eaten (mean of 5 expt). (mg)	Macroscopic evaluation of insect damage
0	46.90	Extremely bad
1	15.44	Bad
10	4.34	Small
50	3.94	Small
100	1.62	Very small

Example 6.

Antifungal test on the vapour of a composition with silica gel as the carrier.

A solution containing 15% by weight of α -bromocinnamaldehyde was prepared with toluene and nonionic surfactant and this solution was diluted with water to make solution A containing 30,000 μ g/ml and solution B containing 15,000 μ g/ml of α -bromocinnamaldehyde. Jelly-like silica gel (water content,

ca. 70%) just before drying was immersed in each of these two solutions, collected, and dried. Antifungal tests on the vapour evolved from the thus-prepared composition were made by the following method and the results are given in Tables 3 and 4.

Test method: (Antifungal test). On a potato-agar medium, one loopful of spores of *Aspergillus niger* was streaked in 10 parallel

lines. The sample was placed in the lid of the dish, the dish containing the medium was placed on it with the agar surface down, and the medium was incubated at 27°C. Proliferation of the fungus was checked after 7 days. (Antifungal test): The agar media showing no sign of fungal growth after a suitable incubation period were replicated on a fresh agar plate, using flannel cloth, and the plate was incubated at 27°C for 7 days to observe the growth of the fungus.

Table 3. Antifungal test of vapour of the composition.

Sample	Quantity (mg)	Fungal growth after 7 days
A	200	Entirely no growth
B	200	Entirely no growth
Control (Silica gel alone)	200	Growth over entire surface

Sample A: Silica gel immersed in a solution containing 30,000 $\mu\text{g/ml}$ α -bromocinnamaldehyde and dried.

Sample B: Silica gel immersed in a solution containing 15,000 $\mu\text{g/ml}$ of α -bromocinnamaldehyde and dried.

Table 4. Antifungal test of vapour of the composition.

Sample	Quantity (mg)	Fungal growth after 7 days
A	200	No growth
B	200	No growth
Control	200	Growth over entire surface

Replicated 24 hours later. Samples A and B are the same as described in Table 3.

As can be seen, the vapour evolved from this composition had good antifungal activity.

Example 7.

Antifungal test of the vapour of a composition with talc as the carrier.

A 20% by weight solution of α -bromocinnamaldehyde was prepared with xylene and nonionic surfactant and 5 ml of this solution was prayed on 100 g of talc powder with thorough stirring. The dried talc powder and granules prepared from it were submitted to an antifungal test by the method described above and its result is given in Table 5.

Table 5 Antifungal test of vapour of the composition

Sample	Quantity (mg)	Fungal growth after (days)			
		3	7	14	21
C	100	—	—	—	—
	200	—	—	—	—
	500	—	—	—	—
D	100	—	—	—	—
	200	—	—	—	—
	500	—	—	—	—
Control	500	+	+	+	+

Sample C: Granular

Sample C: Powder

— : Complete inhibition

+ : fungal growth seen

Thus, 100, 200 and 500 mg of this composition completely inhibited the growth of fungus during 21 days of observation.

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Example 8.

Penetration test of vapour from a composition in accordance with the invention.

The composition described in Example 4 was placed in bags made of polyethylene film and of paper, 1 and 3 g, respectively, and the penetration effect of the vapour evolved from this composition was tested by the method described above. The result is given in Table 6.

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Table 6 Penetration of vapour from the composition

Sample	Quantity (g)	Fungal growth after (days)			
		48 hr	4	7	14
Polyethylene bag	1	—	—	—	—
Granules	3	—	—	—	—
Paper bag	—	—	—	—	—
	3	—	—	—	—
Polyethylene bag		1	—	—	—
		3	—	—	—
Powder	Paper bag	1	—	—	—
		3	—	—	—
Control		3	±	+	+

+ : Growth of fungus

— : Complete inhibition of growth

Thus, the vapour of the composition demonstrates its antifungal activity after passing through polyethylene or paper.

5 WHAT WE CLAIM IS:—

1. An insect repellent and antifungal composition which composition comprises α -bromocinnamaldehyde together with a carrier other than a conventional liquid medium used in the preparation, isolation and purification of the active ingredient.

2. A composition as claimed in claim 1, wherein the carrier is a volatile substance or a hygroscopic substance.

3. A composition as claimed in claim 2, wherein the carrier is *p*-dichlorobenzene or naphthalene.

4. A composition as claimed in claim 2, wherein the carrier is Kaolin mineral earth or silica gel.

5. A composition as claimed in claim 1, wherein the carrier is charcoal powder.

6. A composition as claimed in any one of the preceding claims, wherein the composition

contains at least 0.001% by weight of α -bromocinnamaldehyde. 25

7. A composition as claimed in claim 1, substantially as hereinbefore described in any one of Examples 1 to 5, 7 or 8.

8. A method of repelling insects or inhibiting the growth of fungus which method utilizes a composition as claimed in any one of the preceding claims of α -bromocinnamaldehyde. 30

9. A method as claimed in claim 8, substantially as hereinbefore described in any one of Examples 5, 6, 7, 8 or 9. 35

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Reference has been directed in pursuance of section 9, subsection (1) of the Patents Act 1949, to Patent No. 1,308,507.



Table 6 Penetration of vapour from the composition

Sample	Quantity (g)	Fungal growth after (days)			
		48 hr	4	7	14
Polyethylene bag	1	—	—	—	—
Granules	3	—	—	—	—
Paper bag	—	—	—	—	—
	3	—	—	—	—
Polyethylene bag	1	—	—	—	—
Powder	3	—	—	—	—
Paper bag	1	—	—	—	—
	3	—	—	—	—
Control	3	±	+	+	+

+ : Growth of fungus

— : Complete inhibition of growth

Thus, the vapour of the composition demonstrates its antifungal activity after passing through polyethylene or paper.

5 WHAT WE CLAIM IS:—

1. An insect repellent and antifungal composition which composition comprises α -bromocinnamaldehyde together with a carrier other than a conventional liquid medium used in the preparation, isolation and purification of the active ingredient.

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3. A composition as claimed in claim 2, wherein the carrier is *p*-dichlorobenzene or naphthalene.

4. A composition as claimed in claim 2, wherein the carrier is Kaolin mineral earth or silica gel.

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