

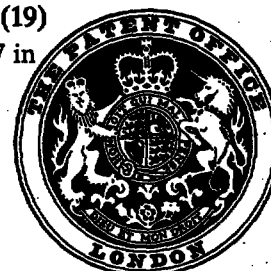
PATENT SPECIFICATION

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- (21) Application No. 18867/78/ (22) Filed 11 May 1978/ (19)
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(54) IMPROVEMENTS IN OR RELATING TO INSECT PEST REPELLENTS

(71) We, KAO SOAP CO. LTD., a Japanese Company of No 1-1, Kayaba-cho, Nihon-bashi, Chuo-ku, Tokyo, 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 present invention relates to insect pest repellents, and more particularly to insect pest repellents in which N,N-diethyltoluamide is an active repellent ingredient.

Among vectors, most mosquitoes inhabit warm or torrid zones, but they can inhabit and survive in relatively cold districts. The mosquitoes attack exposed skin surfaces during outdoor work, and often carry infectious diseases and endemic diseases.

In order to repel such insect pests, many studies on pest repellents have been made and, as a result, a variety of compounds possessing a repellent effect have been found. Among these, N,N-diethyltoluamide has been found to be the most suitable for practical use with human beings and is widely used at present in view of its durability after application and the strength of repellent effect produced.

However, N,N-diethyltoluamide has the disadvantage that it is absorbed from the skin into the human body when it is applied to the surface of the body, and consequently can no longer exercise a repellent effect. The repellent effect of N,N-diethyltoluamide lasts longer when it is employed in increased amounts, but the use of such large amounts gives the person using it a sticky feeling and is not acceptable in practice. In one attempt to inhibit the absorption of the compound from the skin into the body, it has been proposed to form on the skin a film which is insoluble in and therefore impervious to N,N-diethyltoluamide and subsequently coating the N,N-diethyltoluamide onto this film. In this case, however, no satisfactory results can be obtained because the film only fits the skin badly.

In order to overcome the difficulties referred to above, the present Applicants have carried out various studies, taking account of the facts that N,N-diethyltoluamide has a carbonyl group which can act as a proton acceptor and that the energy of the hydrogen bond formed in the carbonyl group is far smaller than that of a covalent bond. As a result of these studies, they have found that the repellent effect of N,N-diethyltoluamide is not in the least decreased whilst absorption of the compound from the skin into the body is significantly inhibited, by forming a complex with a proton donor.

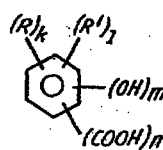
According to the invention, there is provided an insect pest repellent comprising N,N-diethyltoluamide as a repellent component, and a proton donor having at least one aromatic ring which is substituted directly by one or more hydroxy and/or carboxy groups.

Suitable proton donors for use in the present invention are aromatic compounds in which the aromatic rings are substituted directly by one or more hydroxy and/or carboxy groups, which proton donors have one of the formulae (I) and (II):-

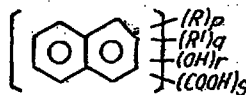
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(I)



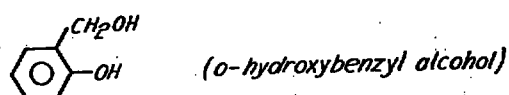
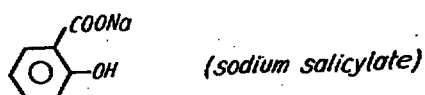
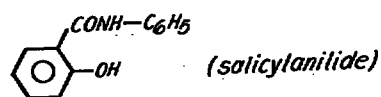
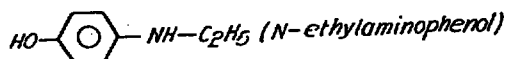
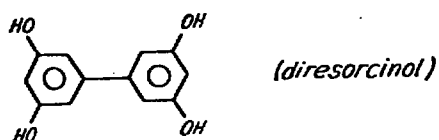
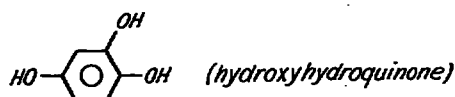
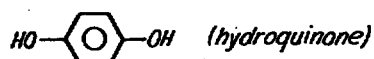
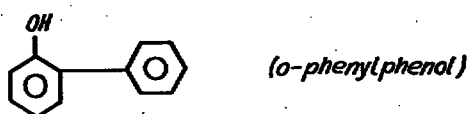
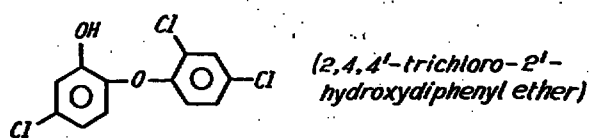
(II)

wherein R represents a substituted or unsubstituted alkyl group, a substituted or unsubstituted aromatic ring, a halogen atom, or one of the groups $-NH_2$, $-SO_3H$, $-COOM$, $-OM$ (M being an alkali metal) or $-CHO$; R' represents one of the groups $R''-COO-$, $R''-O-$, $R''-OOC-$, $R''-OCNH-$, $R''NHCO-$ or $R''NH-$ (R'' being a substituted or unsubstituted alkyl group or a substituted or unsubstituted aromatic ring; k, l, m and n are integral numbers having values of 0 to 6, and $m + n \geq 1$; and p, q, r and s respectively are integral numbers having values of 0 to 8, and $r + s \geq 1$.

These proton donors may be divided into the following classes:-

- 1) Compounds in which monocyclic aromatic compounds or polycyclic aromatic compounds not containing fused rings are substituted by hydroxy groups but not carboxy groups

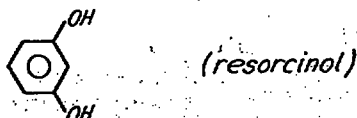
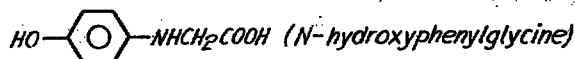
[n = 0 in the formula (I)], such as :-



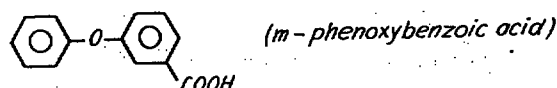
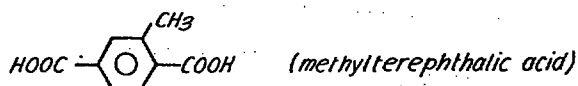
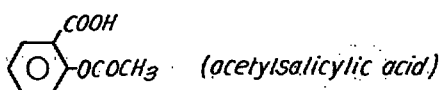
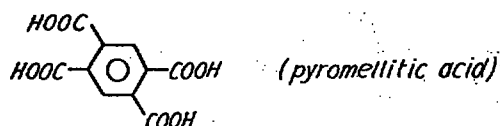
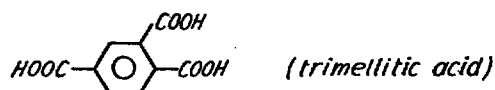
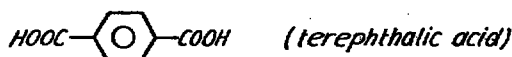
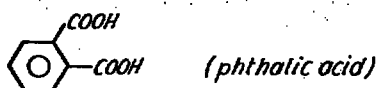
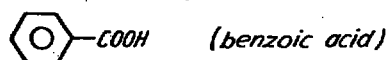
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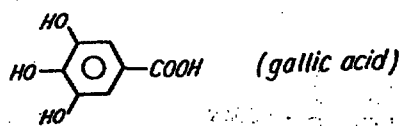
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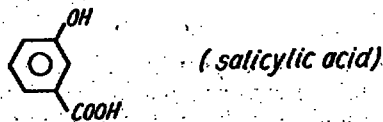
2) Compounds in which monocyclic aromatic compounds or polycyclic aromatic compounds not containing fused rings are substituted by carboxy groups but not by hydroxy groups [$m = 0$ in the formula (I)], such as:-



3) Compounds in which monocyclic aromatic compounds or polycyclic aromatic compounds not containing fused rings are substituted by both hydroxy and carboxy groups [both m and n are at least 1 in the formula (I)], such as:-

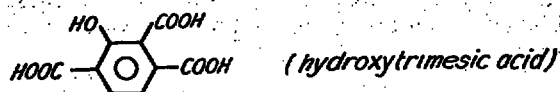


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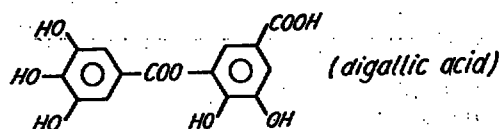
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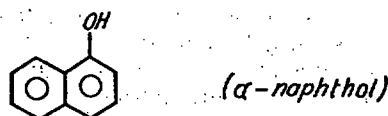
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tannic acid

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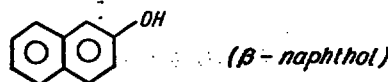
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4) Compounds in which polycyclic aromatic compounds containing fused rings are substituted by hydroxy groups but not carboxy groups [$s = 0$ in the formula (II)], such as :-



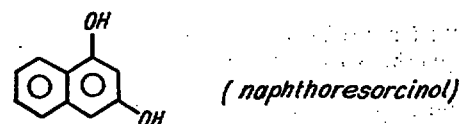
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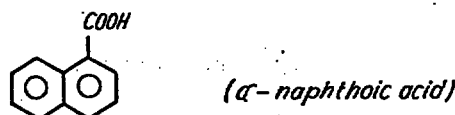
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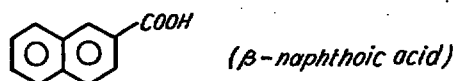
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5) Compounds in which polycyclic aromatic compounds containing fused rings are substituted by carboxy groups but not hydroxy groups [$r = 0$ in the formula (II)], examples being:-



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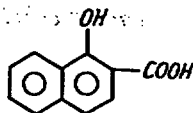
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6) Compounds in which polycyclic aromatic compounds containing fused rings are substituted by both hydroxy and carboxy groups [both r and s are at least 1 in the formula (II)], an example being:-

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(1-naphthol-2-carboxylic acid)

In order to produce an insect pest repellent according to the invention, N,N-diethyltoluamide may be mixed with any one of the above proton donors. Preferably, the mixing ratio of both compounds is such that the number of N,N-diethyltoluamide molecules is the same as that of the proton donor groups. From a practical standpoint, the proton donor is preferably used in an amount of 0.5 to 2.0 times the value of x which is calculated from the following equation:

$$x = \frac{\left[\begin{array}{l} \text{The amount of} \\ \text{N,N-diethyltoluamide} \\ \text{(g)} \end{array} \right] \times \left[\begin{array}{l} \text{the molecular weight} \\ \text{of a proton donor} \end{array} \right]}{191.26 \times \begin{array}{l} \text{the number of proton donor groups} \\ \text{in one proton donor molecule} \end{array}}$$

The insect pest repellents of the invention can be used in any of the forms generally used, such as solutions, lotions, creams, gels, sticks, pastes, aerosol sprays, foams and powders. The content of N,N-diethyltoluamide should preferably be in the range of 1 to 50% by weight.

The invention is illustrated by the following examples:-

Example 1 - Hair was clipped from the bodies of three Hartley strain female guinea-pigs, weighing 500 to 600 g. The test compositions were applied to the skin areas so exposed in an amount including 0.2 mg of N,N-diethyltoluamide/cm². At a time of 3 hours after application, N,N-diethyltoluamide was recovered from the skin surface using acetone and the residual amount was determined by gas chromatography.

COMPOSITION A

N,N-diethyltoluamide	6 g
2,4,4'-trichloro-2'-hydroxy-diphenyl ether (MW 290)	9 g
Ethanol	35 g
Water	50 g

CONTROL COMPOSITION

N,N-diethyltoluamide	6 g
Ethanol	44 g
Water	50 g

The results obtained are shown in Table 1 below. The recovery ratio in the Table indicates the weight % of N,N-diethyltoluamide recovered at 3 hours after application relative to that recovered immediately after application.

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Table 1

	Recovery ratio after 3 hours (%)	Mean value (%)
Control Composition	28.5 28.5 27.6	28.2
Composition A	73.4 80.3 82.1	78.6

EXAMPLE 2 - Using Composition B as set out below containing digallic acid as a proton donor, the residual ratio of N,N-diethyltoluamide at a time of 3 hours after application was determined in the same way as in Example 1. The results obtained are shown in the accompanying drawing, in which the residual ratio is graphed against the amount of digallic acid used by weight.

COMPOSITION B

N,N-diethyltoluamide	6 g
Digallic acid	0 - 3.36 g
Water	50 g
Ethanol	remainder
	100 g

EXAMPLE 3 - Guinea-pigs, which were treated with Composition C as set out below and the Control Composition (the same was used as in Example 1) in the same way as in Example 1, were fixed to a holder and placed in a cage in which 30 mosquitoes were released. The number of mosquitoes that sucked blood within 3 minutes was counted. The results obtained are shown in Table 2 below.

Table 2

	Number of mosquitoes that sucked blood		
	After 2 hours	After 4 hours	After 5 hours
Untreated	7	7	-
Control Composition	2*	7	7
Composition C	1*	0	3*

* indicates the number of the mosquitoes that sucked blood more than 1 minute after release in the cage.

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COMPOSITION C

	N,N-diethyltoluamide	6 g	
5	Digallic acid	1.68 g	
	Water	50 g	
10	Ethanol	remainder	10
		100 g	

15 **EXAMPLE 4** - The proton donors shown in Table 3 below were combined with N,N-diethyltoluamide and the residual ratio of N,N-diethyltoluamide (DET) at a time of 3 hours after application was determined in the same way as in Example 1. The results obtained are shown in Table 3. 15

Table 3

Name of compound	Proton donors		Composition ratio of proton donor to DET	Residual ratio of DET at 3 hours after application (%)
	Molecular weight	Number of proton donor groups		
2,4,4'-trichloro-2'-hydroxydiphenyl ether	290	1	1.5	81.2
o-phenylphenol	170.12	1	0.89	80.3
hydroquinone	110.11	2	0.58	58.3
benzoic acid	122.12	1	0.64	76.2
trimellitic acid	192.13	3	0.33	79.4
gallic acid	188.14	4	0.49	72.8
tannic acid	322.22	6	0.28	84.4
α -naphthol	144.16	1	0.75	73.1
β -naphthoic acid	172.18	1	0.90	61.2
1-naphthol-2-carboxylic acid	188.18	2	0.49	76.9
Control	-	-	-	28.5

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Example 5 (Aerosol)

	N,N-diethyltoluamide	6 (w/w %)	
5	tannic acid	1.5	
	perfume	trace	
10	propellant	50.0	10
	ethyl alcohol	remainder	
		100.0	

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Example 6 (Powder)

	N,N-diethyltoluamide	15.0 (w/w %)	
20	tannic acid	4.2	20
	colloidal silica	18.5	
25	perfume	trace	25
	talc	remainder	
		100.0	

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Example 7 (Lotion)

	N,N-diethyltoluamide	20.0 (w/w %)	
35	tannic acid	7.0	35
	perfume	trace	
40	isopropyl alcohol	remainder	40
		100.0	

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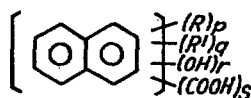
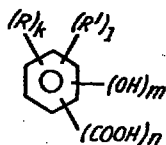
Example 8 (Spray)

	N,N-diethyltoluamide	3.0 (w/w %)	
50	tannic acid	0.8	50
	di-n-propyl isocinchomeronate	0.2	
55	N-octylbicycloheptenedicarboxyimide	1.0	55
	purified petroleum ether	remainder	
		100.0	

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WHAT WE CLAIM IS:-

1. An insect pest repellent comprising N,N-diethyltoluamide as a repellent component, and a proton donor having at least one aromatic ring which is directly substituted by one or more hydroxy and/or carboxy groups.
2. An insect pest repellent as claimed in Claim 1, wherein said proton donor is a compound represented by one of the formulae (I) and (II):-



where R is a substituted or unsubstituted alkyl group, a substituted or unsubstituted aromatic ring, a halogen atom, or one of the groups -NH_2 , $\text{-SO}_3\text{H}$, -COOM , -OM , (M being an alkali metal) or -CHO ; R' is one of the groups $\text{R}''\text{-COO-}$, $\text{R}''\text{-O-}$, $\text{R}''\text{-OOC-}$, $\text{R}''\text{OCNH-}$, $\text{R}''\text{NHCO-}$ or $\text{R}''\text{NH-}$ (R'' being a substituted or unsubstituted alkyl group or a substituted or unsubstituted aromatic ring); k, l, m and n respectively are integral numbers having values of 0 to 6, and $m + n \geq 1$; and p, q, r and s respectively are integral numbers having values of 0 to 8, and $r + s \geq 1$.

3. An insect pest repellent as claimed in Claim 1 or Claim 2, wherein the content of N,N-diethyltoluamide in the repellent is in the range of 1 to 50% by weight.

4. An insect pest repellent as claimed in any one of Claims 1 to 4, wherein the weight ratio of said proton donor to N,N-diethyltoluamide is 0.5 to 2.0 times the value of x calculated from the following equation:-

$$x = \frac{\left[\text{the amount of N, N-diethyltoluamide (g)} \right] \times \left[\text{the molecular weight of a proton donor} \right]}{191.26 \times \text{the number of proton donor groups in one proton donor molecule}}$$

5. An insect pest repellent as claimed in Claim 1, substantially as hereinbefore described with reference to any of the Examples.

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