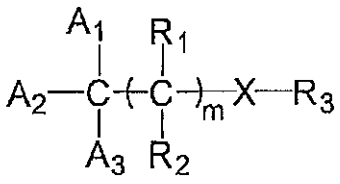
CLAIMS

[Claim 1] A melanin production inhibitor, comprising a compound represented by the following general formula (1) (excluding clotrimazole) and/or a pharmacologically acceptable salt thereof:

[Chem. 1]



(1)

where A1, A2, and A3 are each independently selected from a hydrogen atom, an aryl group which may have a substituent, and an aromatic heterocyclic group which may have a substituent, provided that at least one of A1, A2, and A3 is selected from the aryl group and the aromatic heterocyclic group, and a total number of carbon atoms included in A1, A2, and A3 is 6 to 50;

when two or more of A1, A2, and A3 each represent the aryl or the aromatic heterocyclic groups, the adjacent two aryl groups or aromatic heterocyclic groups may be bound to each other via an alkyl chain or an alkenyl chain to further form a ring;

m represents an integer of 0 to 2;

X represents a hetero atom, a hydrogen atom, or a carbon atom;

R1 and R2 are each independently selected from a hydrogen atom and oxo, provided that, when one of R1 and R2 represents the oxo, the other is absent;

R3 is selected from a hydrogen atom, and a hydrocarbon group having 1 to 8 carbon atoms, in which part of hydrogen atoms or carbon atoms may be substituted by a hetero atom, and a number of R3's corresponds to X;

provided that, when two or more R3's are present, the R3's are each independent of each other, and when two or more R3's are present, the adjacent two R3's may be bound to each other to form a ring together with X; and

a terminal of R3 may be bound to a carbon atom to which A1, A2, and A3 are bound, thereby forming a ring.

[Claim 2] The melanin production inhibitor according to claim 1, wherein X represents a hetero atom or a carbon atom.

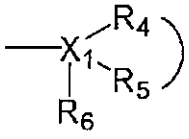
[Claim 3] The melanin production inhibitor according to claim 2, wherein the aryl group is selected from phenyl, biphenyl, and naphthyl, and the aromatic heterocyclic group is selected from pyridyl and quinolyl.

[Claim 4] The melanin production inhibitor according to claim 2 or 3, wherein X represents a nitrogen atom, an oxygen atom, or a carbon atom.

[Claim 5] The melanin production inhibitor according to any one of claims 2 to 4, wherein m represents 0.

[Claim 6] The melanin production inhibitor according to any one of claims 2 to 5, wherein -X-R3 represents a group represented by the following general formula (2):

[Chem. 2]



(2)

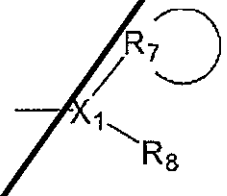
where X1 represents a carbon atom or a nitrogen atom;

R4 and R5 are bound to each other to form, together with X1, a heterocyclic ring or hydrocarbon ring which has 2 to 8 carbon atoms and may have a substituent; and

R6 represents a hydrogen atom, provided that R6 is absent when X1 represents a carbon atom and the heterocyclic ring or hydrocarbon ring represents an aromatic ring, and when X1 represents a nitrogen atom.

[Claim 7] The melanin production inhibitor according to any one of claims 2 to 5, wherein -X-R3 represents a group represented by the following general formula (3):

[Chem. 3]



(3)

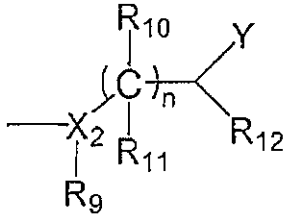
where X1 represents a carbon atom or a nitrogen atom;

R7 represents a hydrocarbon ring group which has 3 to 8 carbon atoms and may have a substituent; and

R8 represents a hydrogen atom, and a number of R8's corresponds to X1.

[Claim 8] The melanin production inhibitor according to any one of claims 2 to 5, wherein -X-R3 represents a group represented by the following general formula (4):

[Chem. 4]



(4)

where X2 represents a nitrogen atom or an oxygen atom;

n represents an integer of 0 to 5;

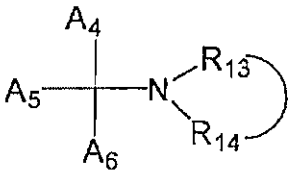
Y is selected from hydroxyl, amino, and an alkyloxy having 1 to 6 carbon atoms;

R9 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 6 carbon atoms when X2 represents a nitrogen atom, and R9 is absent when X2 represents an oxygen atom; and

R10, R11, and R12 are each independently selected from a hydrogen atom, hydroxyl, oxo, and a hydroxyalkyl having 1 to 5 carbon atoms, provided that, when one of R10 and R11 represents the oxo, the other is absent.

[Claim 9] The melanin production inhibitor according to claim 6, wherein the compound represented by the general formula (1) comprises a compound represented by the following general formula (5):

[Chem. 5]



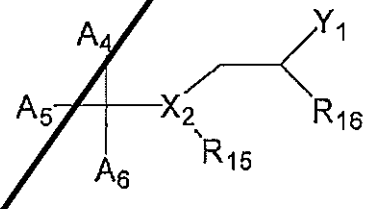
(5)

where A4, A5, and A6 are each independently selected from phenyl and pyridyl which may be substituted by methyl, methoxy, or hydroxyl; and

R13 and R14 are bound to each other to form, together with a nitrogen atom represented by N, a saturated heterocyclic ring which has 4 or 5 carbon atoms and may be substituted by hydroxyl or oxo.

[Claim 10] The melanin production inhibitor according to claim 8, wherein the compound represented by the general formula (1) comprises a compound represented by the following general formula (6):

[Chem. 6]



(6)

where A4, A5, and A6 are each independently selected from phenyl and pyridyl each of which may be substituted by methyl, methoxy, or hydroxyl;

X2 represents a nitrogen atom or an oxygen atom;

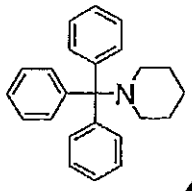
Y1 represents hydroxyl or amino;

R15 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 3 carbon atoms when X2 represents a nitrogen atom, and R15 is absent when X2 represents an oxygen atom; and

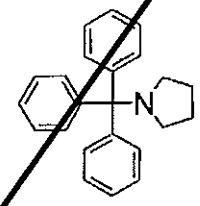
R16 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 3 carbon atoms.

[Claim 11] The melanin production inhibitor according to claim 9, wherein the compound represented by the general formula (5) is selected from 1-triphenylmethylpiperidine (Compound 5) and 1-triphenylmethylpyrrolidine (Compound 6).

[Chem. 7]



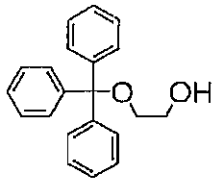
1-(Triphenylmethyl)piperidine (Compound 5)



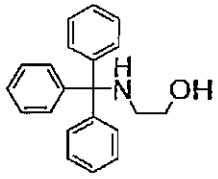
1-(Triphenylmethyl)pyrrolidine (Compound 6)

[Claim 12] The melanin production inhibitor according to claim 10, wherein the compound represented by the general formula (6) is selected from 2-(triphenylmethyloxy)ethanol (Compound 2), 2-(triphenylmethylamino)ethanol (Compound 3), and 2-(triphenylmethyloxy)ethylamine (Compound 4).

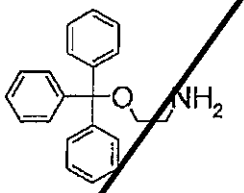
[Chem. 8]




2-(Triphenylmethyloxy)ethanol (Compound 2)




2-(Triphenylmethylamino)ethanol (Compound 3)

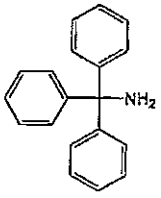



2-(Triphenylmethyloxy)ethylamine (Compound 4)

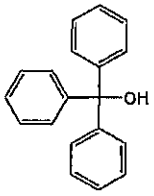
[Claim 13] The melanin production inhibitor according to claim 1,

wherein the compound represented by the general formula (1) is selected from triphenylmethylamine, triphenylmethanol, triphenylmethane, and aminodiphenylmethane.

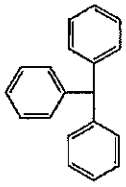
[Chem. 9]



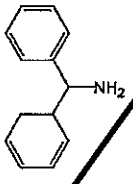

Triphenylmethylamine




Triphenylmethanol



Triphenylmethane




Aminodiphenylmethane

[Claim 14] The melanin production inhibitor according to any one of claims 1 to 10, wherein the compound represented by the general formula (1) is free of an imidazole skeleton.

[Claim 15] The melanin production inhibitor according to any one of claims 1 to 14, wherein the melanin production inhibitor has $MIC_{80}$ 10 times or more that of clotrimazole.

[Claim 16] The melanin production inhibitor according to any one of claims 1 to 15, wherein the melanin production inhibitor is free of an effect of inhibiting expression of tyrosinase protein at a minimum effective dose for melanin production inhibition.

[Claim 17] An external preparation for skin for melanin production inhibition, comprising the melanin production inhibitor according to any one of claims 1 to 16.

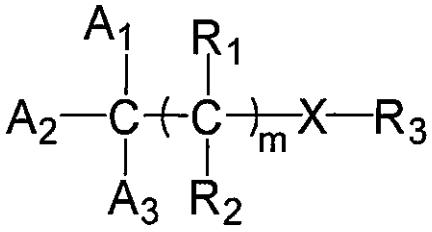
[Claim 18] The external preparation for skin according to claim 17, comprising the melanin production inhibitor in an amount of 0.001 w/w % to 10 w/w % with respect to a total amount of the external preparation for skin.

[Claim 19] The external preparation for skin according to claim 17 or 18, wherein the external preparation for skin is a cosmetic.

## Claims

[Claim 1]

A melanin production inhibitor, comprising a compound represented by the following general formula (1) and/or a pharmacologically acceptable salt thereof, wherein the compound represented by the general formula (1) is free of an imidazole skeleton:



(1)

where A1, A2, and A3 are each independently selected from an aryl group which may have a substituent selected from a linear or branched alkyl having 1 to 8 carbon atoms, a linear or branched alkyloxy having 1 to 8 carbon atoms, and hydroxyl; and pyridyl or quinolyl which may have a substituent selected from a linear or branched alkyl having 1 to 8 carbon atoms, a linear or branched alkyloxy having 1 to 8 carbon atoms, and hydroxyl, and a total number of carbon atoms included in A1, A2, and A3 is 6 to 50;

the adjacent two aryl, pyridyl or quinolyl may be bound to each other via an alkyl chain or an alkenyl chain to further form a ring;

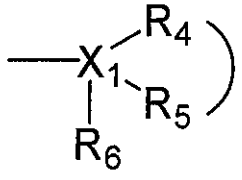
m represents an integer of 0;

X represents a nitrogen atom, or an oxygen atom;

R1 and R2 are absent;

R3 is a hydrogen atom, or -XR3 is selected from a group represented by the following general formula (2), a group represented by the following general formula (4) and a hydrogen atom, and a number of R3's corresponds to X;

provided that, when two or more R3's are present, the R3's are each independent of each other:



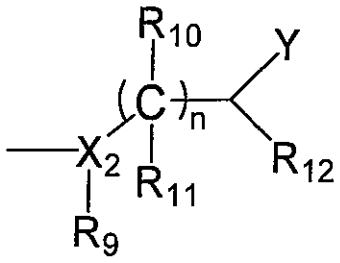
(2)

where X1 represents a nitrogen atom;

R4 and R5 are bound to each other to form, together with X1, a heterocyclic ring which has 2 to 8 carbon atoms (excluding aromatic heterocyclic group) which may

have a substituent; and

R6 is absent:



(4)

where X2 represents a nitrogen atom or an oxygen atom;

n represents an integer of 0 to 5;

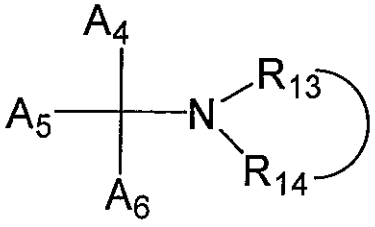
Y is selected from hydroxyl, amino, and an alkyloxy having 1 to 6 carbon atoms;

R9 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 6 carbon atoms when X2 represents a nitrogen atom, and R9 is absent when X2 represents an oxygen atom; and

R10 and R11 are each independently selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 5 carbon atoms, and R12 is selected from a hydrogen atom, hydroxyl, oxo, and a hydroxyalkyl having 1 to 5 carbon atoms.

[Claim 2]

The melanin production inhibitor according to claim 1, wherein the compound represented by the general formula (1) comprises a compound represented by the following general formula (5):



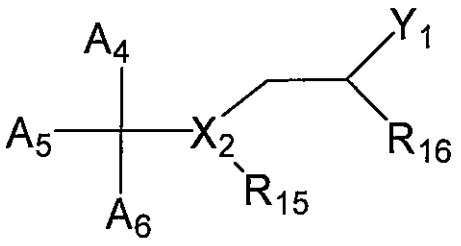
(5)

where A4, A5, and A6 are each independently selected from phenyl and pyridyl which may have a substituent selected from methyl, methoxy, and hydroxyl; and

R13 and R14 are bound to each other to form, together with a nitrogen atom represented by N, a saturated heterocyclic ring which has 4 or 5 carbon atoms and may have a substituent selected from hydroxyl and oxo.

[Claim 3]

The melanin production inhibitor according to claim 1, wherein the compound represented by the general formula (1) comprises a compound represented by the following general formula (6):




(6)

where A4, A5, and A6 are each independently selected from phenyl and pyridyl each of which may have a substituent selected from methyl, methoxy, and hydroxyl;

X2 represents a nitrogen atom or an oxygen atom;

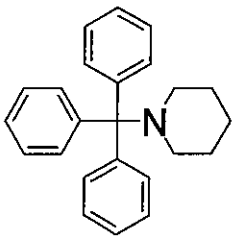
Y1 represents hydroxyl or amino;

R15 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 3 carbon atoms when X2 represents a nitrogen atom, and R15 is absent when X2 represents an oxygen atom; and

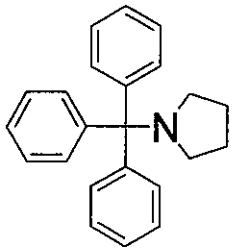
R16 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 3 carbon atoms.

[Claim 4]

The melanin production inhibitor according to claim 2, wherein the compound represented by the general formula (5) is selected from 1-(triphenylmethyl)piperidine (Compound 5) and 1-(triphenylmethyl)pyrrolidine (Compound 6).



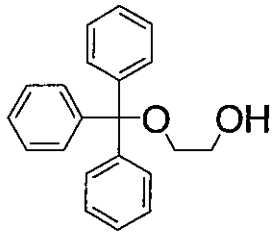

1-(Triphenylmethyl)piperidine (Compound 5)



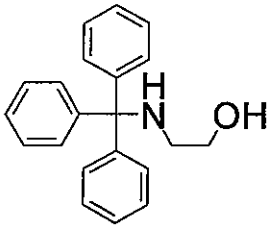
1-(Triphenylmethyl)pyrrolidine (Compound 6)

[Claim 5]

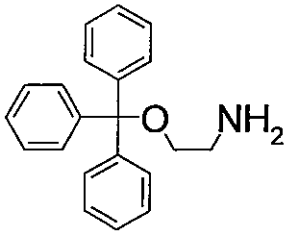
The melanin production inhibitor according to claim 3, wherein the compound represented by the general formula (6) is selected from 2-(triphenylmethyloxy)ethanol (Compound 2), 2-(triphenylmethylamino)ethanol (Compound 3), and 2-(triphenylmethyloxy)ethylamine (Compound 4).




2-(Triphenylmethyloxy)ethanol (Compound 2)



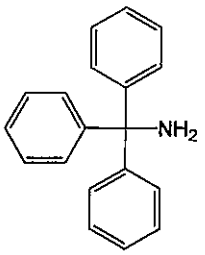

2-(Triphenylmethylamino)ethanol (Compound 3)



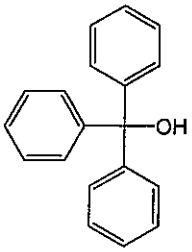

2-(Triphenylmethyloxy)ethylamine (Compound 4)

[Claim 6]

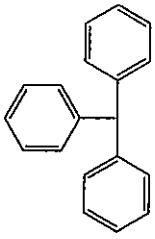
The melanin production inhibitor according to claim 1, wherein the compound represented by the general formula (1) is selected from triphenylmethylamine, triphenylmethanol, and triphenylmethane.




Triphenylmethylamine



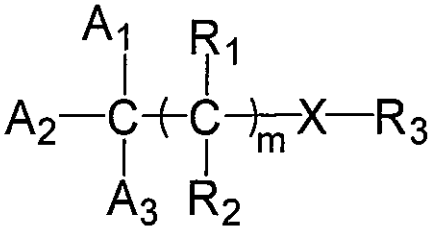

Triphenylmethanol



Triphenylmethane

[Claim 7]

A melanin production inhibitor, comprising a compound represented by the following general formula (1) and/or a pharmacologically acceptable salt thereof, wherein the compound represented by the general formula (1) is free of an imidazole skeleton:




(1)

where A1 represents a hydrogen atom, A2 and A3 are each independently selected from an aryl which may have a substituent selected from a linear or branched alkyl having 1 to 8 carbon atoms, a linear or branched alkyloxy having 1 to 8 carbon atoms, and hydroxyl; and pyridyl or quinolyl which may have a substituent selected from a linear or branched alkyl having 1 to 8 carbon atoms, a linear or branched

alkyloxy having 1 to 8 carbon atoms, and hydroxyl, and a total number of carbon atoms included in A1, A2, and A3 is 6 to 50;

the adjacent two aryl, pyridyl or quinolyl may be bound to each other via an alkyl chain or an alkenyl chain to further form a ring;

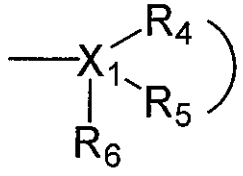
m represents an integer of 0;

X represents a nitrogen atom, or an oxygen atom;

R1 and R2 are absent;

R3 is a hydrogen atom, or -XR3 is selected from a group represented by the following general formula (2), and a group represented by the following general formula (4), and a number of R3's corresponds to X;

provided that, when two or more R3's are present, the R3's are each independent of each other:

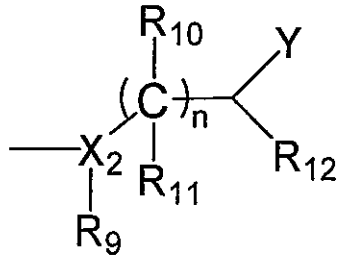


(2)

where X1 represents a nitrogen atom;

R4 and R5 are bound to each other to form, together with X1, a heterocyclic ring which has 2 to 8 carbon atoms (excluding aromatic heterocyclic group) which may have a substituent; and

R6 is absent:



(4)

where X2 represents a nitrogen atom or an oxygen atom;

n represents an integer of 0 to 5;

Y is selected from hydroxyl, amino, and an alkyloxy having 1 to 6 carbon atoms;

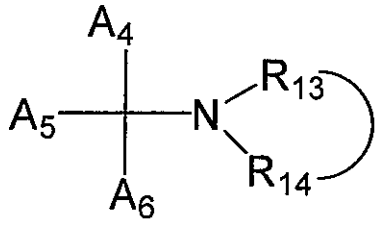
R9 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 6 carbon atoms when X2 represents a nitrogen atom, and R9 is absent when X2 represents an oxygen atom; and

R10 and R11 are each independently selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 5 carbon atoms, and R12 is selected from a hydrogen

atom, hydroxyl, oxo, and a hydroxyalkyl having 1 to 5 carbon atoms.

[Claim 8]

The melanin production inhibitor according to claim 7, wherein the compound represented by the general formula (1) comprises a compound represented by the following general formula (5):



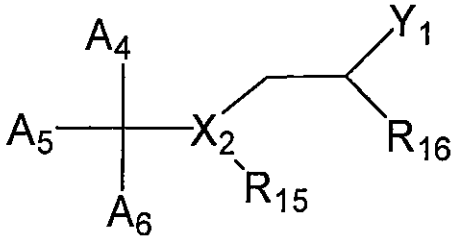

(5)

where A4 represents a hydrogen atom, A5 and A6 are each independently selected from phenyl and pyridyl which may have a substituent selected from methyl, methoxy, and hydroxyl; and

R13 and R14 are bound to each other to form, together with a nitrogen atom represented by N, a saturated heterocyclic ring which has 4 or 5 carbon atoms and may have a substituent selected from hydroxyl and oxo.

[Claim 9]

The melanin production inhibitor according to claim 7, wherein the compound represented by the general formula (1) comprises a compound represented by the following general formula (6):




(6)

where A4 represents a hydrogen atom, A5 and A6 are each independently selected from phenyl and pyridyl each of which may have a substituent selected from methyl, methoxy, and hydroxyl;

X2 represents a nitrogen atom or an oxygen atom;

Y1 represents hydroxyl or amino;

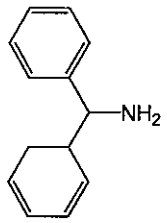
R15 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1 to 3 carbon atoms when X2 represents a nitrogen atom, and R15 is absent when X2 represents an oxygen atom; and

R16 is selected from a hydrogen atom, hydroxyl, and a hydroxyalkyl having 1

to 3 carbon atoms.

[Claim 10]

The melanin production inhibitor according to claim 7, wherein the compound represented by the general formula (1) is aminodiphenylmethane.




Aminodiphenylmethane

[Claim 11]

An external preparation for skin for melanin production inhibition, comprising the melanin production inhibitor according to any one of claims 1 to 10.

[Claim 12]

The external preparation for skin according to claim 11, comprising the melanin production inhibitor in an amount of 0.001 w/w % to 10 w/w % with respect to a total amount of the external preparation for skin.

[Claim 13]

The external preparation for skin according to claim 11 or 12, wherein the external preparation for skin is a cosmetic.