disease, nephrotic syndrome, or melanoma invasion. However, the compound is not disclosed to be effective for treating or preventing photodermatoses (excluding protoporphyria), hypopigmentary disease (excluding vitiligo vulgaris), adverse effects of phototherapy, gray hair, and the like, based on a mechanism mainly involving an increase of pigmentation.

PRIOR ART REFERENCES

PATENT DOCUMENTS

[0014]

Patent Document 1: WO2014/160015

Patent Document 2: WO2018/142318

Patent Document 3: WOO2008/025094

Patent Document 4: WO2009/103816

Patent Document 5: WO2015/067503

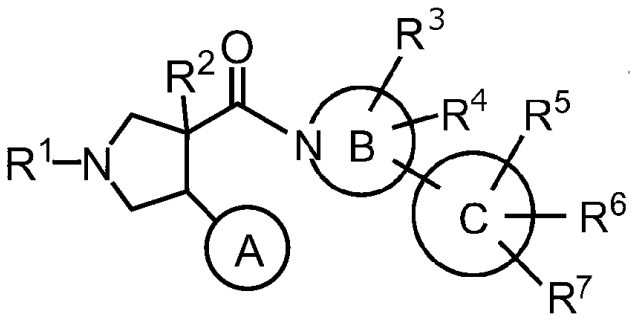
Patent Document 6: WO2008/025094

Patent Document 7: WO2015/182723

Patent Document 8: WO2020/138481

SUMMARY

[0014a] In a first aspect, the present disclosure refers to a use of a compound represented by general formula [I], or a pharmaceutically acceptable salt or cocrystal thereof, in the manufacture of a medicament for treating or preventing a condition (excluding protoporphyria and vitiligo vulgaris) that is treatable or preventable by promotion of melanin production:



[I]

wherein ring A represents an optionally substituted aryl group or an optionally substituted heteroaryl group,

wherein each substituent in the optionally substituted aryl group and the optionally substituted heteroaryl group corresponds to 1 to 3 groups independently selected from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, a cycloalkyl group, an alkoxy group, a haloalkoxy group, and an alkyleneoxy group;

R^1 represents an optionally substituted alkyl group, an optionally substituted cycloalkyl group, an optionally substituted aliphatic heterocyclic group, an optionally substituted and optionally partially hydrogenated aryl group, an optionally substituted heteroaryl group, or a carbamoyl group optionally substituted with 1 to 2 alkyl groups,

wherein a substituent in the optionally substituted alkyl group corresponds to 1 to 3 groups independently selected from the group consisting of a halogen atom; a hydroxyl group; an oxo group; a cyano group; a cycloalkyl group; an alkoxy group; an alkanoyl group; a carbamoyl group optionally substituted with 1 to 2 alkyl groups; an aliphatic heterocyclic group; an aliphatic heterocyclic carbonyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, and an alkoxyalkyl group; an alkylsulfonyl group; an aliphatic heterocyclic sulfonyl group; and an alkyleneoxy

group, and

each substituent in the optionally substituted cycloalkyl group, the optionally substituted aliphatic heterocyclic group, the optionally substituted and optionally partially hydrogenated aryl group, and the optionally substituted heteroaryl group corresponds to 1 to 3 groups independently selected from the group consisting of a halogen atom; a hydroxyl group; an oxo group; a cyano group; an alkyl group; a haloalkyl group; a cycloalkyl group; an alkoxy group; a hydroxyalkyl group; an alkoxyalkyl group; an alkanoyl group; a carbamoyl group optionally substituted with 1 to 2 alkyl groups; an aliphatic heterocyclic group; an aliphatic heterocyclic carbonyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, and an alkoxyalkyl group; an alkylsulfonyl group; an aliphatic heterocyclic sulfonyl group; and an alkyleneoxy group;

R^2 represents a halogen atom, an alkyl group, or an alkoxy group;

ring B represents a nitrogen-containing aliphatic heterocyclic group optionally partially including a double bond,

ring C represents an aryl group or a heteroaryl group,

R^3 and R^4 each independently represent a group selected from the group consisting of a hydrogen atom, a halogen atom, a cyano group, an alkyl group, a haloalkyl group, a cyanoalkyl group, a hydroxyalkyl group, an alkoxyalkyl group, a carboxyl group, a carbamoyl group optionally substituted with 1 to 2 alkyl groups, and an alkoxy group;

R^5 represents an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted cycloalkyl group, an optionally substituted cycloalkenyl group, an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted aliphatic heterocyclic group, an optionally substituted alkoxy group, an amino group optionally substituted with 1 to 2 alkyl

groups optionally substituted with a carboxyl group, or a carbamoyl group optionally substituted with 1 to 2 alkyl groups optionally substituted with a carboxyl group,

wherein a substituent in the optionally substituted alkyl group corresponds to 1 to 2 groups independently selected from the group consisting of a hydroxyl group; an oxo group; a cyano group; an alkoxy group; an alkanoyl group; a carboxyl group; an alkoxycarbonyl group; an aliphatic heterocyclic carbonyl group optionally substituted with a carboxyl group; a heteroaryl group optionally substituted with a hydroxyl group or a oxo group; an aliphatic heterocyclic group optionally substituted with 1 to 2 oxo groups; a carbamoyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group (the alkyl moiety is optionally substituted with a hydroxyl group, an alkoxy group, or a carboxyl group) and a hydroxyl group; an alkylsulfonyl group; an aminosulfonyl group optionally substituted with 1 to 2 alkyl groups; an aminosulfonylaminocarbonyl group optionally substituted with 1 to 2 alkyl groups; an alkylsulfonylaminocarbonyl group; and an amino group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group, an alkanoyl group, and an alkylsulfonyl group, and

each substituent in the optionally substituted alkenyl group, the optionally substituted cycloalkyl group, the optionally substituted cycloalkenyl group, the optionally substituted aryl group, the optionally substituted heteroaryl group, the optionally substituted aliphatic heterocyclic group, and the optionally substituted alkoxy group corresponds to 1 to 2 groups independently selected from the group consisting of a hydroxyl group; an oxo group; a cyano group; an alkyl group optionally substituted with a carboxyl group; an alkoxy group; an alkanoyl group; a carboxyl group; an alkoxycarbonyl group; an aliphatic heterocyclic carbonyl group optionally substituted with a carboxyl group; a heteroaryl group optionally substituted with a hydroxyl group or a oxo group; an aliphatic heterocyclic group

optionally substituted with 1 to 2 oxo groups; a carbamoyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group (the alkyl moiety is optionally substituted with a hydroxyl group, an alkoxy group, or a carboxyl group) and a hydroxyl group; an alkylsulfonyl group; an aminosulfonyl group optionally substituted with 1 to 2 alkyl groups; an aminosulfonylaminocarbonyl group optionally substituted with 1 to 2 alkyl groups; an alkylsulfonylaminocarbonyl group; and an amino group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group, an alkanoyl group, and an alkylsulfonyl group; and

R^6 and R^7 each independently represent a group selected from the group consisting of a hydrogen atom, a halogen atom, a cyano group, an alkyl group, a haloalkyl group, and a haloalkoxy group.

Problems to be solved by the invention

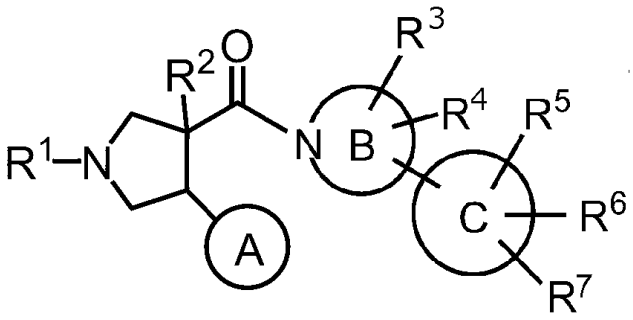
[0015]

There are few methods for fundamentally treating photodermatoses, and a method for preventing the skin from being exposed to sunlight is mainly adopted for avoiding any symptom from being developed or alleviating any symptom. In particular, a patient suffering from photodermatoses induced by visible light also tends to avoid outings in daylight, and quality of life (QOL) of the patient is known to be remarkably impaired.

While analogues of α-melanocyte-stimulating hormones (α-MSHs) as ligands of MCR have been developed as treating agents of photodermatoses and the like

CLAIMS

1. Use of a compound represented by general formula [I], or a pharmaceutically acceptable salt or cocrystal thereof, in the manufacture of a medicament for treating or preventing a condition (excluding protoporphyria and vitiligo vulgaris) that is treatable or preventable by promotion of melanin production:



[I]

wherein ring A represents an optionally substituted aryl group or an optionally substituted heteroaryl group,

wherein each substituent in the optionally substituted aryl group and the optionally substituted heteroaryl group corresponds to 1 to 3 groups independently selected from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, a cycloalkyl group, an alkoxy group, a haloalkoxy group, and an alkyleneoxy group;

R^1 represents an optionally substituted alkyl group, an optionally substituted cycloalkyl group, an optionally substituted aliphatic heterocyclic group, an optionally substituted and optionally partially hydrogenated aryl group, an optionally substituted heteroaryl group, or a carbamoyl group optionally substituted with 1 to 2 alkyl groups,

wherein a substituent in the optionally substituted alkyl group corresponds to 1 to 3 groups independently selected from the group consisting of a halogen atom; a

hydroxyl group; an oxo group; a cyano group; a cycloalkyl group; an alkoxy group; an alkanoyl group; a carbamoyl group optionally substituted with 1 to 2 alkyl groups; an aliphatic heterocyclic group; an aliphatic heterocyclic carbonyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, and an alkoxyalkyl group; an alkylsulfonyl group; an aliphatic heterocyclic sulfonyl group; and an alkyleneoxy group, and

each substituent in the optionally substituted cycloalkyl group, the optionally substituted aliphatic heterocyclic group, the optionally substituted and optionally partially hydrogenated aryl group, and the optionally substituted heteroaryl group corresponds to 1 to 3 groups independently selected from the group consisting of a halogen atom; a hydroxyl group; an oxo group; a cyano group; an alkyl group; a haloalkyl group; a cycloalkyl group; an alkoxy group; a hydroxyalkyl group; an alkoxyalkyl group; an alkanoyl group; a carbamoyl group optionally substituted with 1 to 2 alkyl groups; an aliphatic heterocyclic group; an aliphatic heterocyclic carbonyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of a halogen atom, an alkyl group, a haloalkyl group, and an alkoxyalkyl group; an alkylsulfonyl group; an aliphatic heterocyclic sulfonyl group; and an alkyleneoxy group;

R^2 represents a halogen atom, an alkyl group, or an alkoxy group;

ring B represents a nitrogen-containing aliphatic heterocyclic group optionally partially including a double bond,

ring C represents an aryl group or a heteroaryl group,

R^3 and R^4 each independently represent a group selected from the group consisting of a hydrogen atom, a halogen atom, a cyano group, an alkyl group, a haloalkyl group, a cyanoalkyl group, a hydroxyalkyl group, an alkoxyalkyl group, a carboxyl group, a carbamoyl group optionally substituted with 1 to 2 alkyl groups, and an alkoxy

group;

R^5 represents an optionally substituted alkyl group, an optionally substituted alkenyl group, an optionally substituted cycloalkyl group, an optionally substituted cycloalkenyl group, an optionally substituted aryl group, an optionally substituted heteroaryl group, an optionally substituted aliphatic heterocyclic group, an optionally substituted alkoxy group, an amino group optionally substituted with 1 to 2 alkyl groups optionally substituted with a carboxyl group, or a carbamoyl group optionally substituted with 1 to 2 alkyl groups optionally substituted with a carboxyl group,

wherein a substituent in the optionally substituted alkyl group corresponds to 1 to 2 groups independently selected from the group consisting of a hydroxyl group; an oxo group; a cyano group; an alkoxy group; an alkanoyl group; a carboxyl group; an alkoxycarbonyl group; an aliphatic heterocyclic carbonyl group optionally substituted with a carboxyl group; a heteroaryl group optionally substituted with a hydroxyl group or a oxo group; an aliphatic heterocyclic group optionally substituted with 1 to 2 oxo groups; a carbamoyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group (the alkyl moiety is optionally substituted with a hydroxyl group, an alkoxy group, or a carboxyl group) and a hydroxyl group; an alkylsulfonyl group; an aminosulfonyl group optionally substituted with 1 to 2 alkyl groups; an aminosulfonylaminocarbonyl group optionally substituted with 1 to 2 alkyl groups; an alkylsulfonylaminocarbonyl group; and an amino group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group, an alkanoyl group, and an alkylsulfonyl group, and

each substituent in the optionally substituted alkenyl group, the optionally substituted cycloalkyl group, the optionally substituted cycloalkenyl group, the optionally substituted aryl group, the optionally substituted heteroaryl group, the optionally substituted aliphatic heterocyclic group, and the optionally substituted

alkoxy group corresponds to 1 to 2 groups independently selected from the group consisting of a hydroxyl group; an oxo group; a cyano group; an alkyl group optionally substituted with a carboxyl group; an alkoxy group; an alkanoyl group; a carboxyl group; an alkoxycarbonyl group; an aliphatic heterocyclic carbonyl group optionally substituted with a carboxyl group; a heteroaryl group optionally substituted with a hydroxyl group or a oxo group; an aliphatic heterocyclic group optionally substituted with 1 to 2 oxo groups; a carbamoyl group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group (the alkyl moiety is optionally substituted with a hydroxyl group, an alkoxy group, or a carboxyl group) and a hydroxyl group; an alkylsulfonyl group; an aminosulfonyl group optionally substituted with 1 to 2 alkyl groups; an aminosulfonylaminocarbonyl group optionally substituted with 1 to 2 alkyl groups; an alkylsulfonylaminocarbonyl group; and an amino group optionally substituted with 1 to 2 groups independently selected from the group consisting of an alkyl group, an alkanoyl group, and an alkylsulfonyl group; and

R^6 and R^7 each independently represent a group selected from the group consisting of a hydrogen atom, a halogen atom, a cyano group, an alkyl group, a haloalkyl group, and a haloalkoxy group.

2. The use according to claim 1, wherein, in the general formula [I],

ring A is a phenyl group optionally substituted with an alkoxy group,

R^1 is a 5- to 6-membered monocyclic cycloalkyl group optionally substituted with a group selected from the group consisting of an alkoxy group and a cyano group,

R^2 is a halogen atom or an alkoxy group,

ring B is a pyrrolidinyl group, and R^3 is an alkoxyalkyl group and R^4 is a hydrogen atom or a halogen atom,

ring C is a phenyl group,

R^5 is a piperidinyl group substituted with a carboxyl group,

R^6 is a halogen atom or a haloalkyl group, and

R^7 is a hydrogen atom.

3. The use according to claim 1, wherein the compound represented by the general formula [I] is 1-{2-[(3S,4R)-1-{[(3R,4R)-1-cyclopentyl-3-fluoro-4-(4-methoxyphenyl)pyrrolidin-3-yl]carbonyl}-4-(methoxymethyl)pyrrolidin-3-yl]-5-(trifluoromethyl)phenyl}piperidine-4-carboxylic acid.

4. The use according to any one of claims 1 to 3, wherein the condition is photodermatoses (excluding protoporphyria).

5. The use according to claim 4, wherein the photodermatoses is photoallergic dermatitis, hydroa vacciniforme, DNA repair disorder, or porphyria (excluding protoporphyria).

6. The use according to claim 5, wherein

the photoallergic dermatitis is solar urticaria, polymorphous light eruption, chronic actinic dermatitis, photoallergic contact dermatitis, or photoallergic drug eruption, and

the DNA repair disorder is xeroderma pigmentosum, Cockayne syndrome, Bloom syndrome, Werner syndrome, Rothmund-Thomson syndrome, Trichothiodystrophy, UV-sensitive syndrome, Fanconi anemia or Ataxia telangiectasia.

7. The use according to claim 5, wherein

the porphyria is congenital erythropoietic porphyria, variegate porphyria, acute intermittent porphyria, porphyria cutanea tarda or hereditary coproporphyria.

8. The use according to any one of claims 1 to 3, wherein the condition is hypopigmentary disease (excluding vitiligo vulgaris).

9. The use according to claim 8, wherein the hypopigmentary disease is selected from

congenital hypopigmentary diseases including oculocutaneous albinism, piebaldism, nevus depigmentosus, hypomelanosis of Ito, phenylketonuria, tuberous sclerosis, dyschromatosis symmetrica hereditaria, Waardenburg syndrome, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome, Griscelli syndrome, and Tietz syndrome, and acquired hypopigmentary diseases such as leukoderma Sutton, Vogt-Koyanagi-Harada syndrome, leukoderma senile, leukoderma after sea bathing, and leukoderma syphiliticum.

10. The use according to any one of claims 1 to 3, wherein the condition is an adverse effect of phototherapy.

11. The use according to any one of claims 1 to 3, wherein the condition is gray hair.