Thus, there exists a need for novel skin brightening agents and formulations that exhibit higher levels of safety and/or efficacy than agents currently on the market.

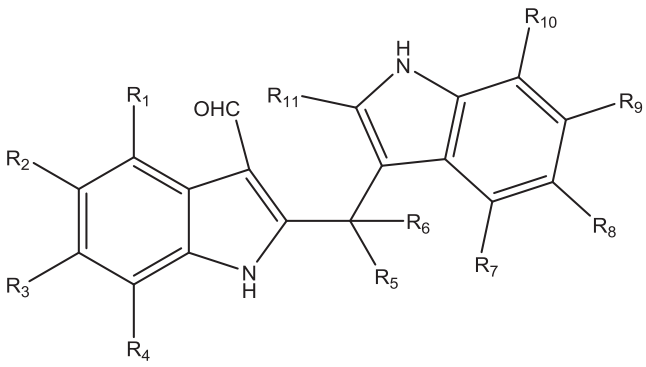
[0004] *Malassezia* is a genus of lipophilic yeast commonly found in the normal flora of human skin. *Malassezia* is responsible for a number of skin diseases, including tinea versicolor (pityriasis versicolor), seborrheic dermatitis, and atopic dermatitis.

[0005] Tinea versicolor is a non-contagious skin disease caused by *Malassezia* overgrowth that locally alters pigmentation levels. *Malassezia* yeasts have two metabolic pathways for synthesizing melanin and tryptophan-derived indole pigments. The indole pigments include malassezin, a tryptophan metabolite of *Malassezia* that may elicit melanocyte apoptosis and contribute to the depigmentation characteristic of *Malassezia* overgrowth.

[0006] The invention disclosed herein utilizes compounds produced by *Malassezia* yeast, including malassezin, and chemical analogs thereof, as the basis for safe and efficacious skin brightening compositions.

SUMMARY

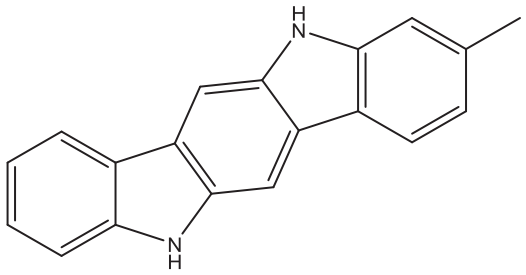
[0006a] In one aspect, the present disclosure refers to a compound having the structure of formula (II):



(II)

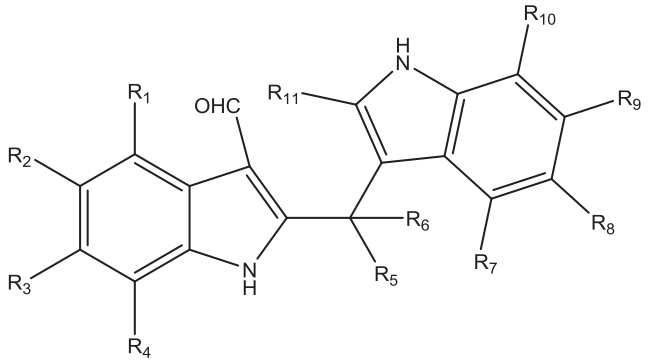
wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl, and at least one of R1, R2, R3, R4, R5, R6, R7, R8, R9, R10 and R11 is methyl; or a hydrate or cosmetically acceptable salt thereof.

[0006b] In another aspect ,the present disclosure refers to a compound having the following structure:



or a hydrate or cosmetically acceptable salt thereof.

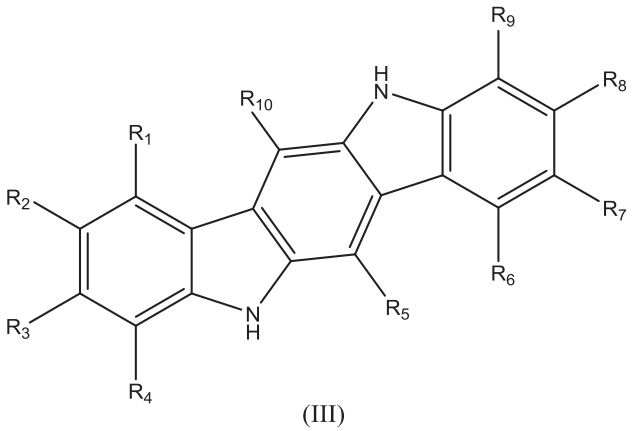
[0006c] In yet another aspect, the present disclosure refers to a cosmetic method for brightening skin in a subject comprising, contacting the subject with a compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a hydrate or cosmetically acceptable salt thereof.

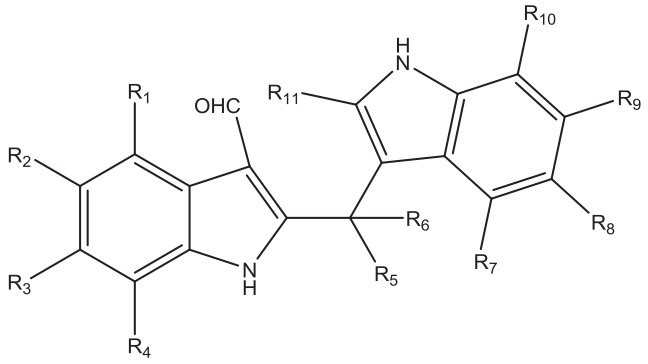
[0006d] In yet another aspect, the present disclosure refers to a cosmetic method for brightening skin in a subject comprising, contacting the subject with a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a hydrate or cosmetically acceptable salt thereof.

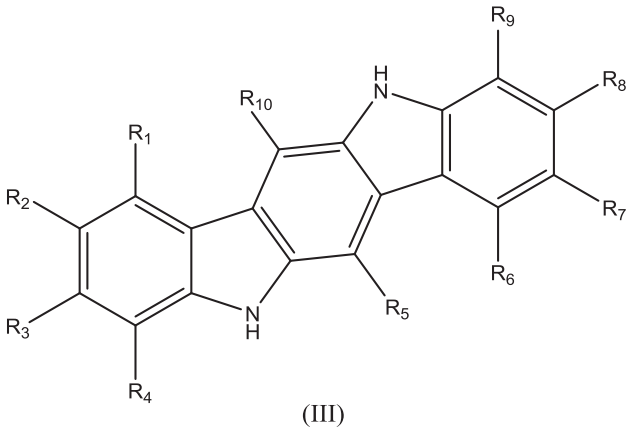
[0006e] In yet another aspect, the present disclosure refers to a cosmetic composition comprising, as active ingredient, a compound having the structure of formula (II)



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a hydrate or cosmetically acceptable salt thereof, and a cosmetically acceptable vehicle, diluent or carrier.

[0006f] In yet another aspect, the present disclosure refers to a cosmetic composition comprising, as active ingredient, a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a hydrate or cosmetically acceptable salt thereof, and a cosmetically acceptable vehicle, diluent or carrier.

[0006g] In yet another aspect, the present disclosure refers to a cosmetic method for brightening skin in a subject comprising contacting the subject with the composition as described herein.

[0007] One example of the present disclosure is a compound for brightening skin. The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0008] Another example of the present disclosure is a compound for inducing melanocyte apoptosis. The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0009] A further example of the present disclosure is a compound for modulating melanocyte activity. The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0010] An additional example of the present disclosure is a compound for agonizing the arylhydrocarbon receptor (AhR). The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0011] Another example of the present disclosure is a compound for improving hyperpigmentation caused by a hyperpigmentation disorder. The

compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0012] A further example of the present disclosure is a compound for modulating melanin production. The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0013] An additional example of the present disclosure is a compound for modulating melanosome biogenesis. The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0014] Another example of the present disclosure is a compound for modulating melanosome transfer. The compound is a chemical analog of a compound produced by a *Malassezia* yeast, or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0015] A further example of the present disclosure is a composition. The composition comprises a *Malassezia* yeast and a cosmetically or pharmaceutically acceptable vehicle, diluent or carrier.

[0016] An additional example of the present disclosure is a composition. The composition comprises a compound isolated or isolatable from a

Malassezia yeast and a cosmetically or pharmaceutically acceptable vehicle, diluent or carrier.

[0017] Another example of the present disclosure is a composition. The composition comprises any of the compounds, including analogs, disclosed herein and a cosmetically or pharmaceutically acceptable vehicle, diluent or carrier.

[0018] A further example of the present disclosure is a method of brightening skin in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0019] An additional example of the present disclosure is a method for inducing melanocyte apoptosis in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0020] Another example of the present disclosure is a method for modulating melanocyte activity in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0021] A further example of the present disclosure is a method for agonizing an arylhydrocarbon receptor (AhR) in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

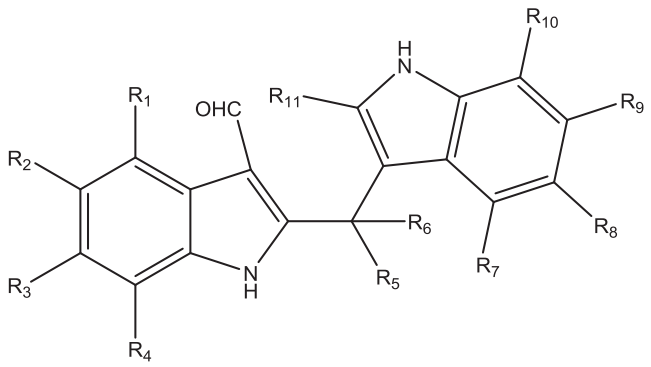
[0022] An additional example of the present disclosure is a method for improving hyperpigmentation caused by a hyperpigmentation disorder in a subject in need thereof. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0023] Another example of the present disclosure is a method for modulating melanin production in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0024] A further example of the present disclosure is a method for modulating melanosome biogenesis in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0025] An additional example of the present disclosure is a method for modulating melanosome transfer in a subject. The method comprises contacting the subject with any of the compounds or compositions disclosed herein.

[0026] In one example, there is provided a compound having the structure of formula (II):



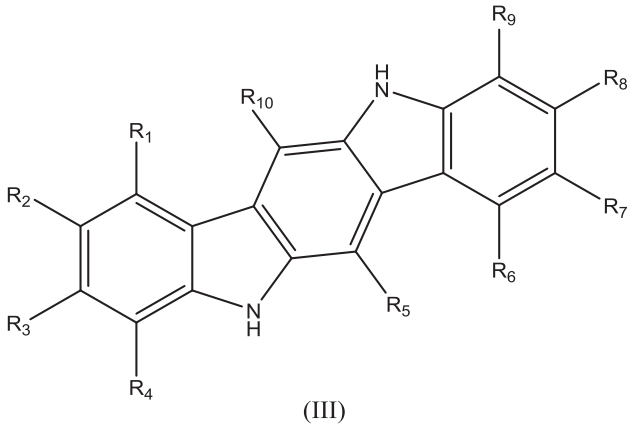
(II)

wherein:

R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl, and at least one of R1, R2,

R3, R4, R5, R6, R7, R8, R9, R10 and R11 is methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

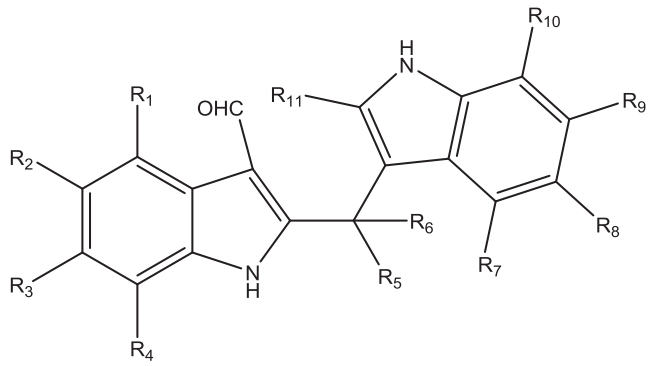
[0027] In one example, there is provided a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl, and at least one of R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 is methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

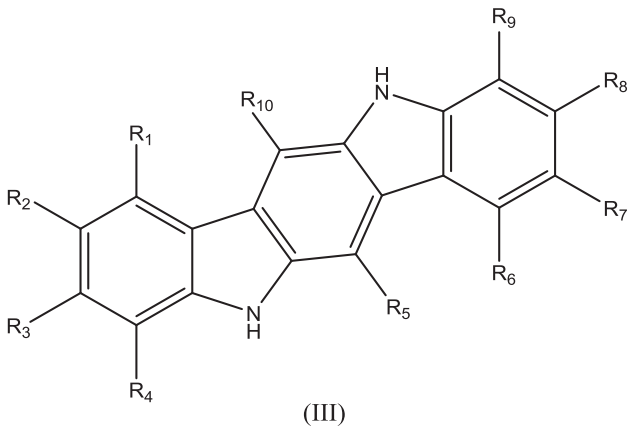
[0028] In one example, there is provided a compound for brightening skin, the compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

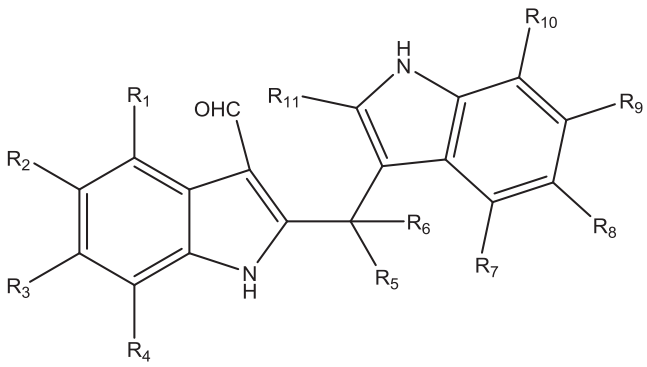
[0029] In one example, there is provided a compound for brightening skin, the compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

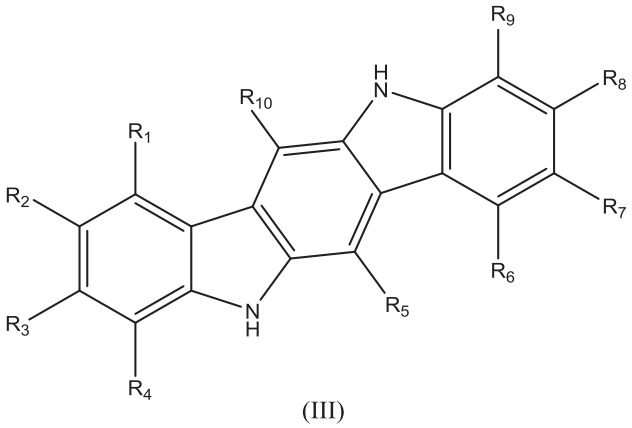
[0030] In one example, there is provided a compound for inducing melanocyte apoptosis, the compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

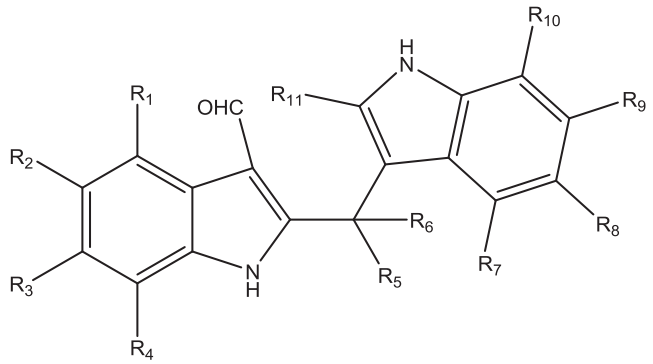
[0031] In one example, there is provided a compound for inducing melanocyte apoptosis, the compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

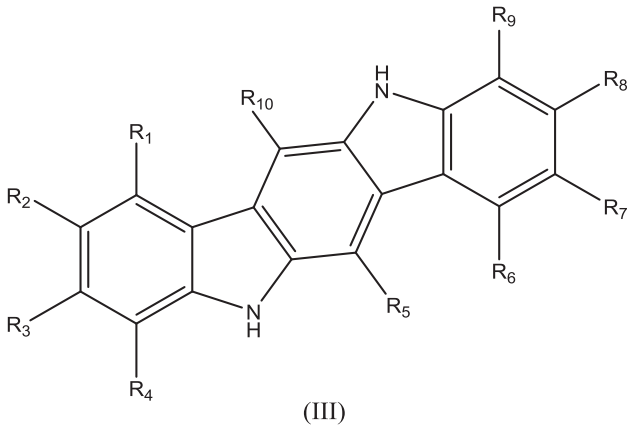
[0032] In one example, there is provided a compound for agonizing the arylhydrocarbon receptor (AhR), the compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

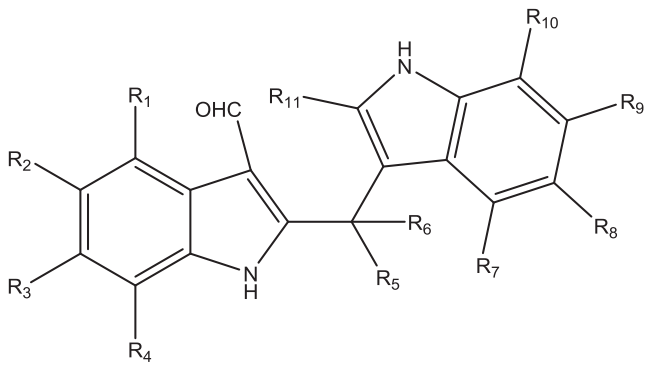
[0033] In one example, there is provided a compound for agonizing the arylhydrocarbon receptor (AhR), the compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

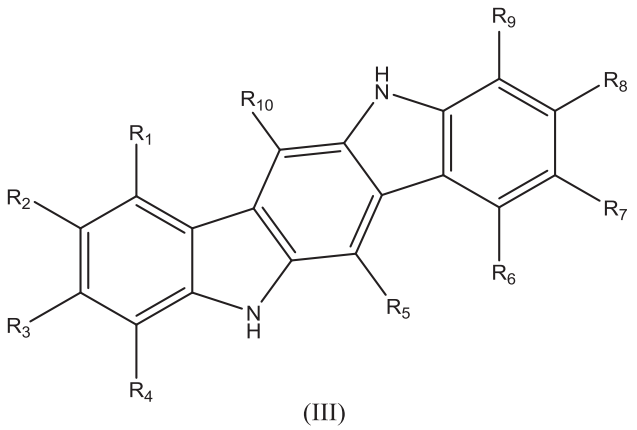
[0034] In one example, there is provided a composition comprising a compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof, and a cosmetically or pharmaceutically acceptable vehicle, diluent or carrier.

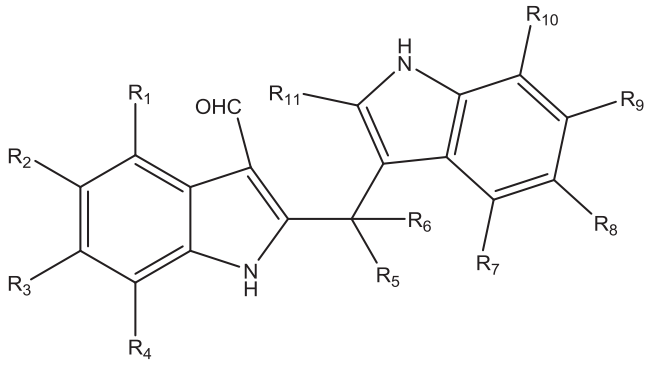
[0035] In one example, there is provided a composition comprising a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof, and a cosmetically or pharmaceutically acceptable vehicle, diluent or carrier.

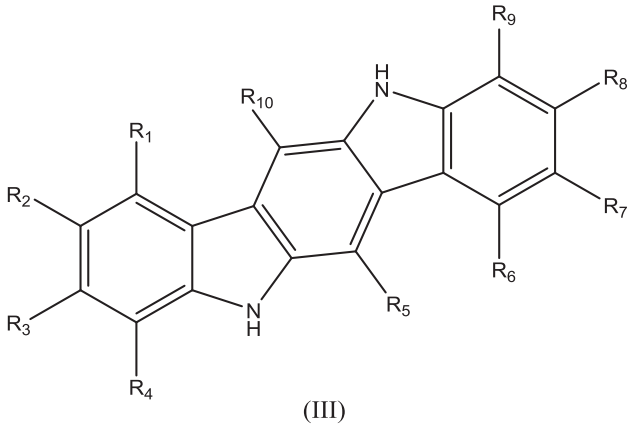
[0036] A further example of the present disclosure is a method for brightening skin in a subject. The method comprises: contacting the subject with a compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

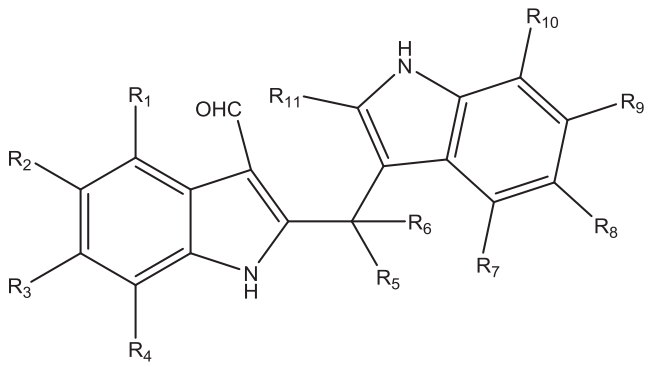
[0037] An additional example of the present disclosure is a method for brightening skin in a subject. The method comprises: contacting the subject with a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

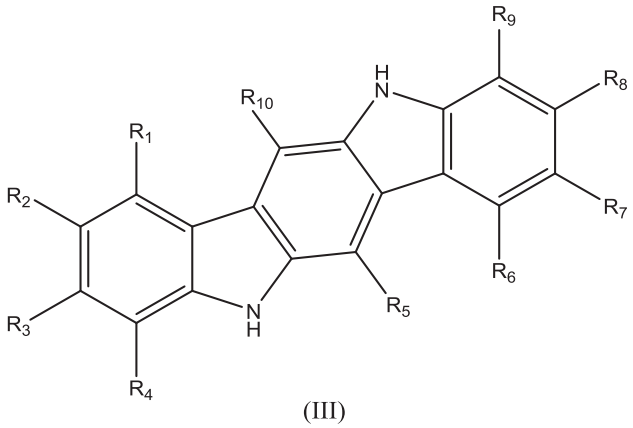
[0038] Another example of the present disclosure is a method for inducing melanocyte apoptosis in a subject. The method comprises: contacting the subject with a compound having the structure of formula (II)



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

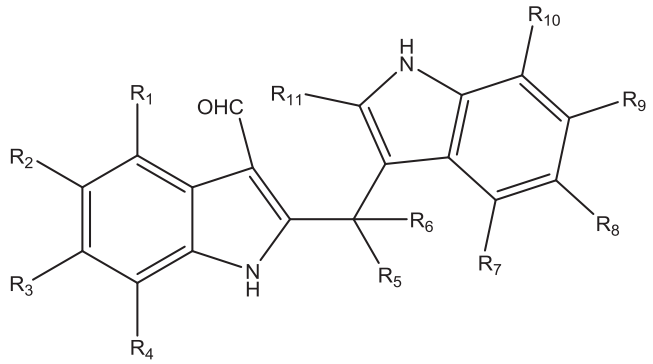
[0039] A further example of the present disclosure is a method for inducing melanocyte apoptosis in a subject. The method comprises: contacting the subject with a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

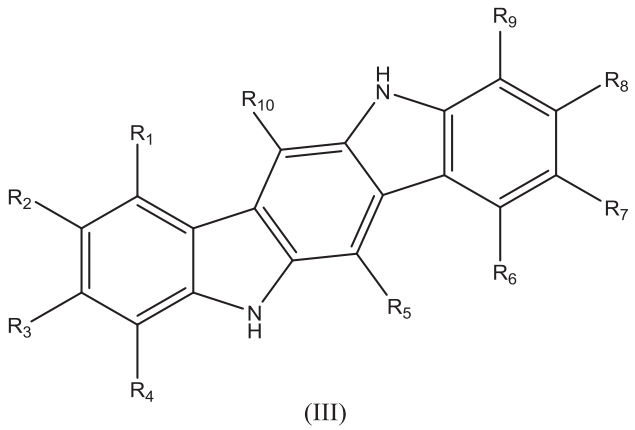
[0040] Another example of the present disclosure is a method for agonizing an arylhydrocarbon receptor (AhR) in a subject. The method comprises: contacting the subject with a compound having the structure of formula (II):



(II)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

[0041] A further example of the present disclosure is a method for agonizing an arylhydrocarbon receptor (AhR) in a subject. The method comprises: contacting the subject with a compound having the structure of formula (III):



(III)

wherein: R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

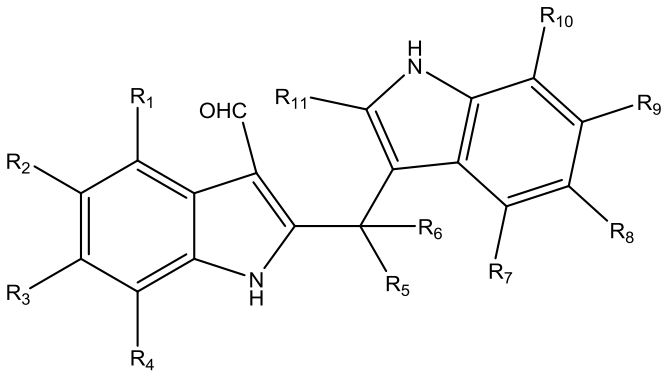
[0042] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the Office upon request and payment of the necessary fee.

[0043] Fig. 1A is a schematic diagram of the skin's component layers. The inset diagram shows the cellular makeup of the epidermis and dermis. Fig. 1B is a schematic diagram showing potential mechanisms of action of hypopigmentation-causing agents.

[0044] Fig. 2 is a set of synthetic schemes for malassezin and malassezin derivatives: Fig. 2A: malassezin and indolo[3,2-b] carbazole; Fig. 2B: compounds I and IV; Fig. 2C: compound II.

WHAT IS CLAIMED IS:

1. A compound having the structure of formula (II):



(II)

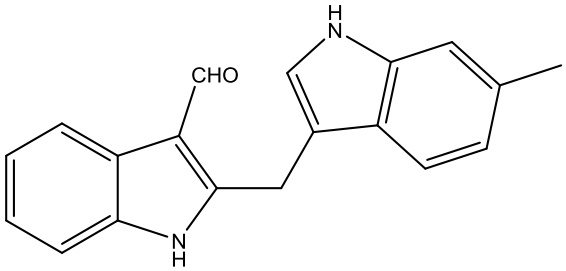
wherein:

R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl, and

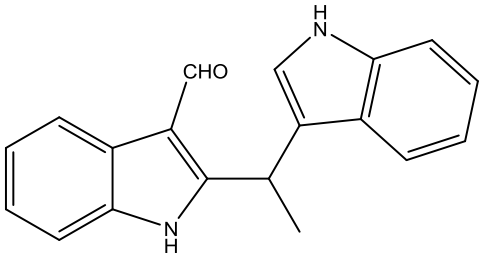
at least one of R1, R2, R3, R4, R5, R6, R7, R8, R9, R10 and R11 is methyl;

or a hydrate or cosmetically acceptable salt thereof.

2. The compound of claim 1, wherein the compound is selected from the group consisting of:

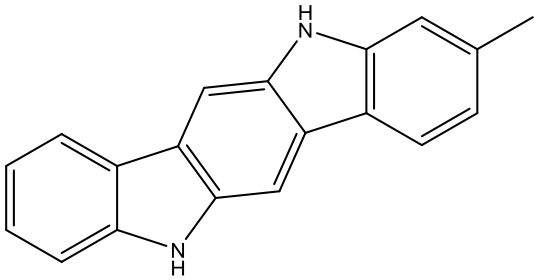


and



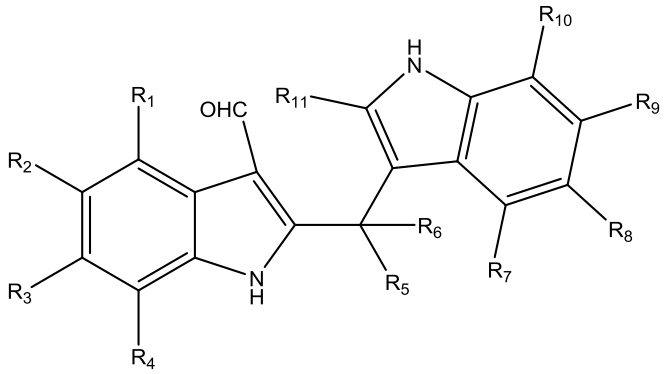
and hydrates and cosmetically acceptable salts thereof.

3. A compound having the following structure:



or a hydrate or cosmetically acceptable salt thereof.

4. A cosmetic method for brightening skin in a subject comprising, contacting the subject with a compound having the structure of formula (II):



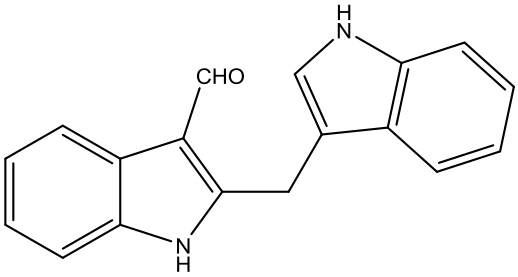
(II)

wherein:

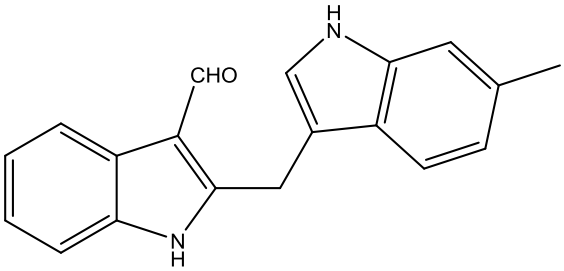
R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl;

or a hydrate or cosmetically acceptable salt thereof.

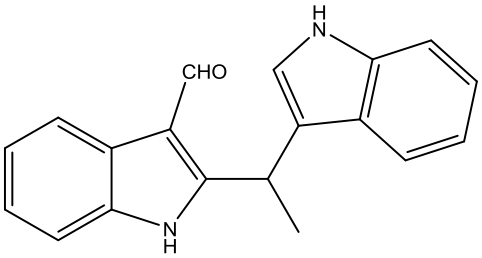
5. The cosmetic method of claim 4, wherein the compound is selected from the group consisting of:



,

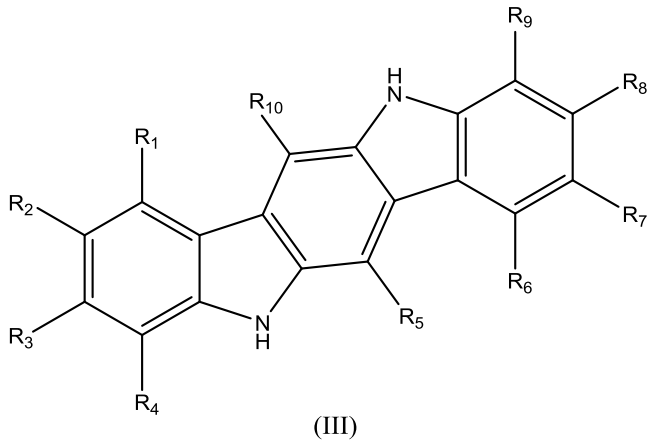


and



and hydrates and cosmetically acceptable salts thereof.

6. A cosmetic method for brightening skin in a subject comprising, contacting the subject with a compound having the structure of formula (III):



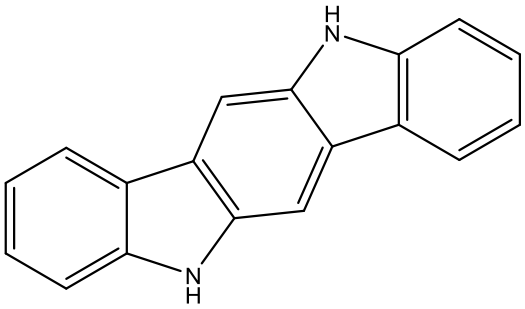
(III)

wherein:

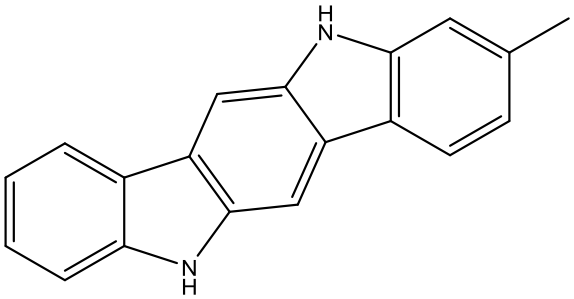
R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl;

or a hydrate or cosmetically acceptable salt thereof.

7. The cosmetic method of claim 6, wherein the compound is selected from the group consisting of:

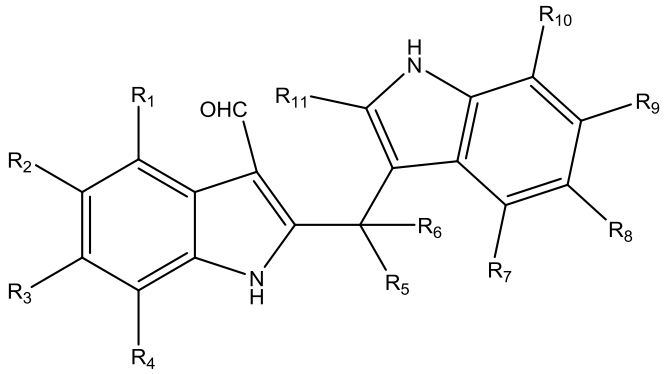


and



and hydrates and cosmetically acceptable salts thereof.

8. A cosmetic composition comprising, as active ingredient, a compound having the structure of formula (II)



(II)

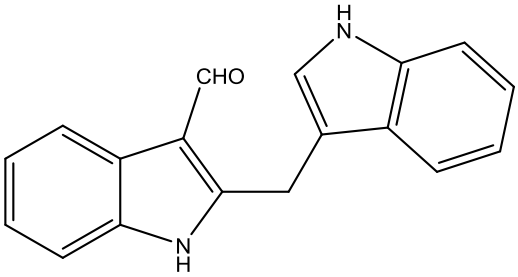
wherein:

R1, R2, R3, R4, R5, R6, R7, R8, R9, R10, and R11 are independently selected from the group consisting of hydrogen and methyl;

or a hydrate or cosmetically acceptable salt thereof,

and a cosmetically acceptable vehicle, diluent or carrier.

9. A composition according to claim 8, wherein the compound is selected from the group consisting of:



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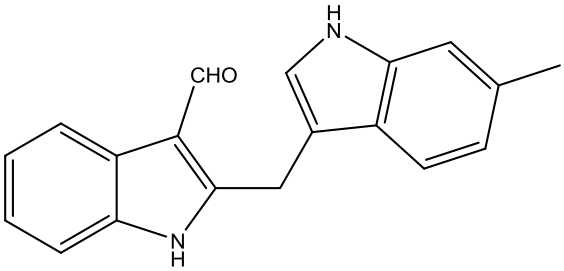

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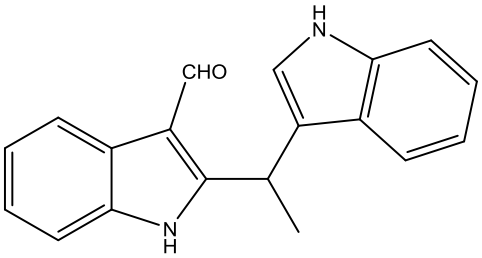
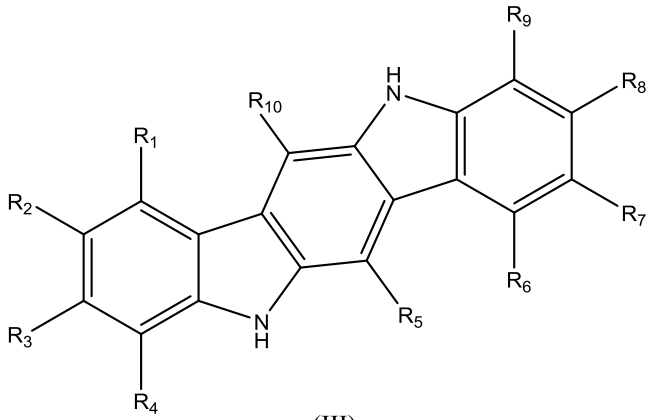


and hydrates and cosmetically acceptable salts thereof.

10. A cosmetic composition comprising, as active ingredient, a compound having the structure of formula (III):



(III)

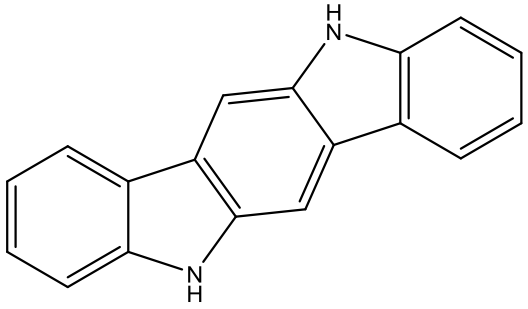
wherein:

R1, R2, R3, R4, R5, R6, R7, R8, R9, and R10 are independently selected from the group consisting of hydrogen and methyl;

or a hydrate or cosmetically acceptable salt thereof,

and a cosmetically acceptable vehicle, diluent or carrier.

11. The cosmetic composition of claim 10, wherein the compound is selected from the group consisting of:



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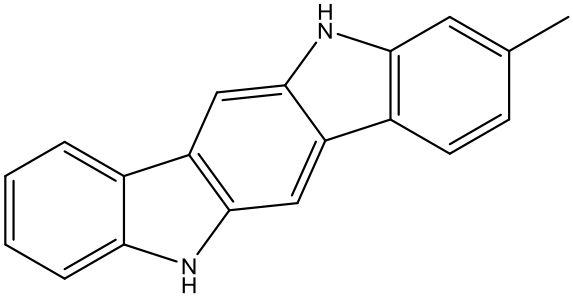
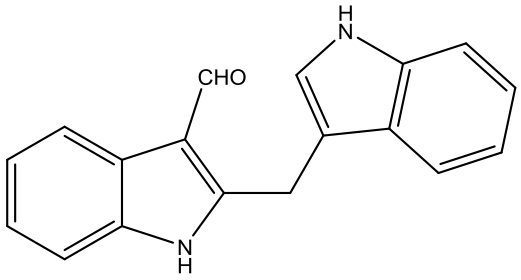


and hydrates and cosmetically acceptable salts thereof.

12. The cosmetic method of claim 4, wherein the subject is contacted with the compound having the structure of formula (II) or a cosmetically acceptable salt thereof.

13. The cosmetic method of claim 5, wherein the subject is contacted with a compound selected from the group consisting of:



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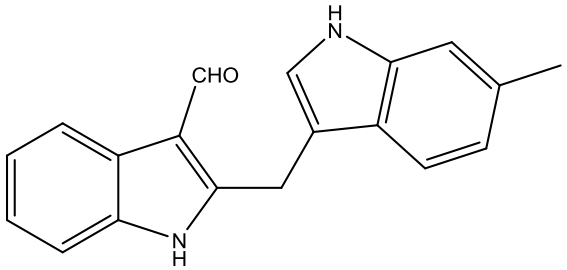

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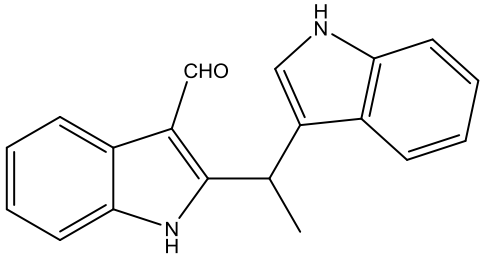

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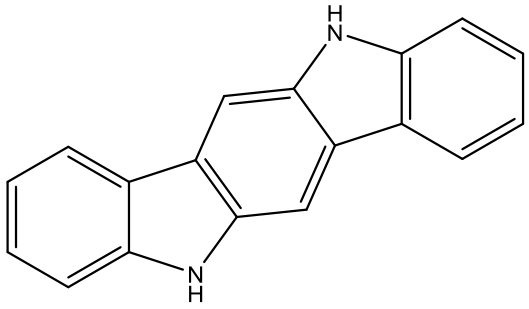
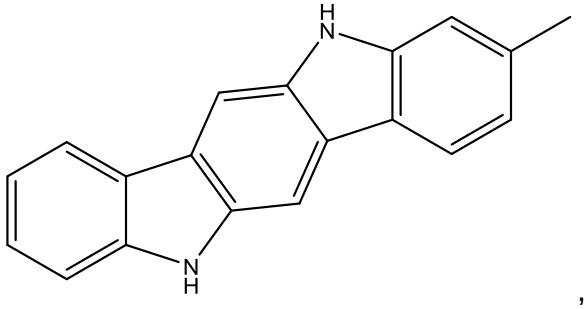
and cosmetically acceptable salts thereof.

14. The cosmetic method of claim 6, wherein the subject is contacted with the compound having the structure of formula (III) or a cosmetically acceptable salt thereof.

15. The cosmetic method of claim 7, wherein the subject is contacted with a compound selected from the group consisting of:



and



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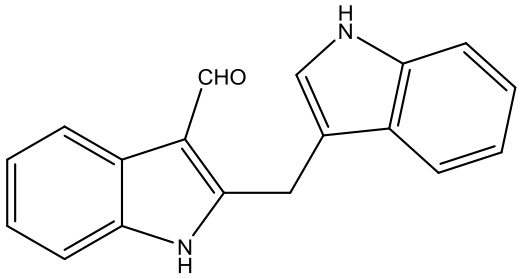
and cosmetically acceptable salts thereof.

16. A cosmetic method for brightening skin in a subject comprising contacting the subject with the composition of claim 8.

17. The cosmetic method of claim 16, wherein the composition comprises, as active ingredient, the compound having the structure of formula (II) or a cosmetically acceptable salt thereof.

18. A cosmetic method for brightening skin in a subject comprising contacting the subject with the composition of claim 9.

19. The cosmetic method of claim 18, wherein the composition comprises, as active ingredient, a compound selected from the group consisting of:



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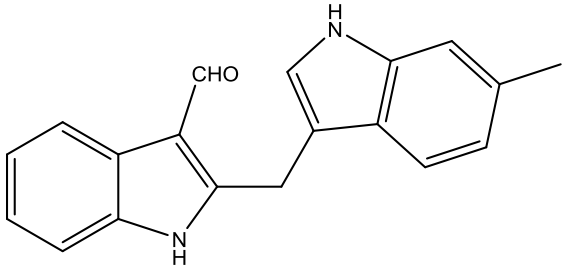

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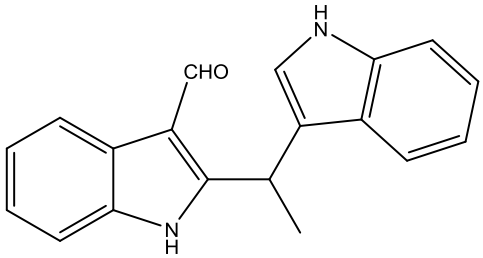

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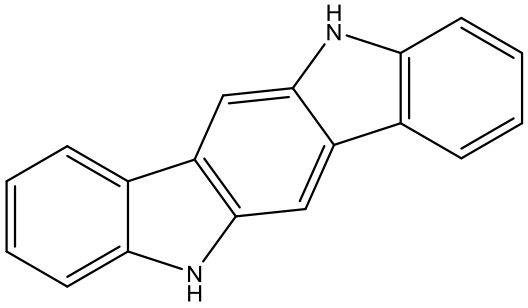
and cosmetically acceptable salts thereof.

20. A cosmetic method for brightening skin in a subject comprising contacting the subject with the composition of claim 10.

21. The cosmetic method of claim 20, wherein the composition comprises, as active ingredient, the compound having the structure of formula (III) or a cosmetically acceptable salt thereof.

22. A cosmetic method for brightening skin in a subject comprising contacting the subject with the composition of claim 11.

23. The cosmetic method of claim 22, wherein the composition comprises, as active ingredient, a compound selected from the group consisting of:



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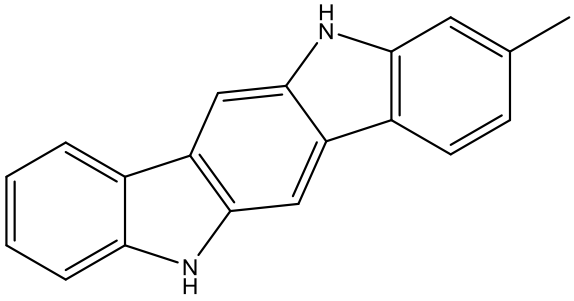

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and cosmetically acceptable salts thereof.