formulations. Using colorimetry, the authors evaluated erythema and pigmentation following irradiation of cream-protected and non-protected skin of healthy subjects. UVB as well as UVA transmission decreased with increasing pityriacitrin concentrations. An increase of pityriacitrin concentration of 1.25, 2.5, and 5% was associated with slightly increasing SPFs of 1.4, 1.5, and 1.7, respectively. The *in vivo* tests confirmed the validity of the SPF of pityriacitrin 5% cream determined *in vitro*. Overall, the UV protective effect of pityriacitrin was very weak, suggesting that pityriacitrin likely is only an inferior cofactor in the development of hypopigmentation in pityriasis versicolor alba lesions following sun exposure.

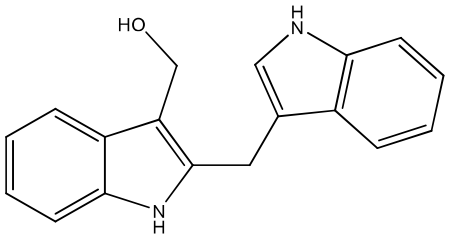
[0007] Further studies of the UV filtering effects of pityriacitrin were performed on human skin microflora. (Machowinski *et al*., 2006). The authors determined pityriacitrin has a UV-protective effect on *Candida albicans* and staphylococci with no toxicity in the ranges tested. The UV protective properties of pityrialactone have also been confirmed in a yeast model. (Mayser *et al*., 2003). Pityrialactone appears to be responsible for the yellow fluorescence of Tinea Versicolor under Wood's Light examination.

[0008] 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. Malassezin and Indirubin are tryptophan metabolites of *Malassezia* that may contribute to the depigmentation characteristic of *Malassezia* overgrowth.

[0009] The invention disclosed herein utilizes compounds produced by or derived from *Malassezia* yeast, including Malassezin, Indirubin, and chemical analogs thereof, as the basis for safe and efficacious skin brightening and skin darkening compositions. Photoprotective compositions comprising Malassezin, Indirubin, and chemical analogs thereof are also disclosed herein.

SUMMARY

[0010] In one aspect, the present disclosure provides a cosmetic method for brightening skin in a subject comprising contacting the subject with a composition, wherein the composition comprises one or more compounds selected from the group consisting of:



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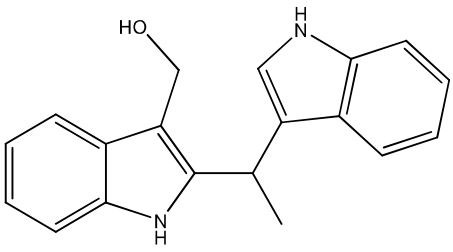

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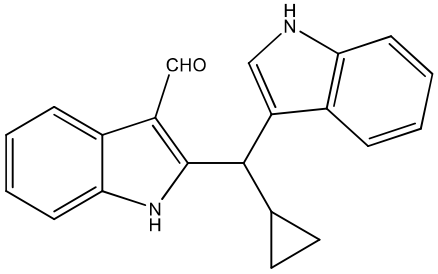

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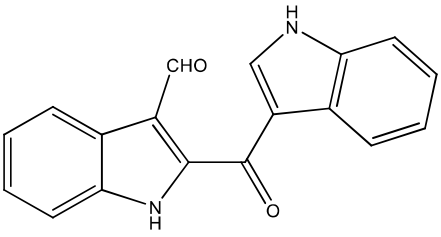

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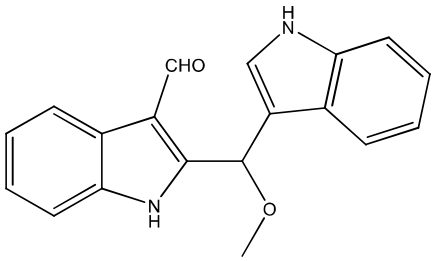

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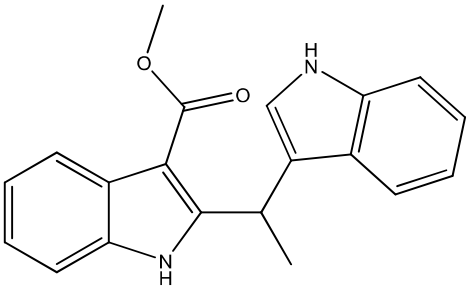

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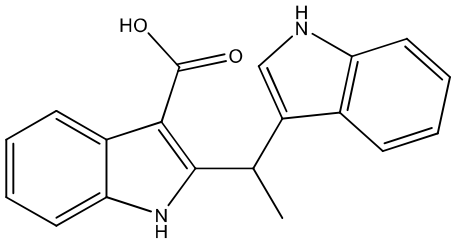

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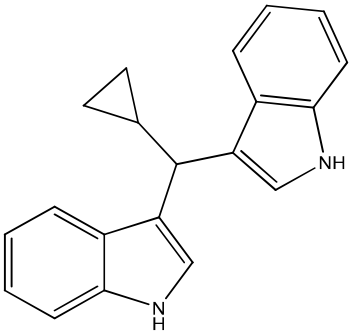

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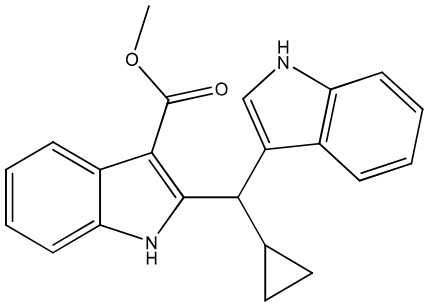

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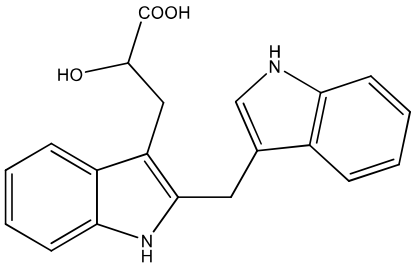

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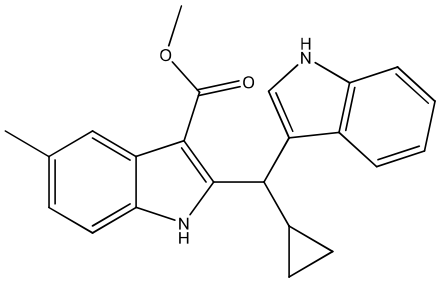

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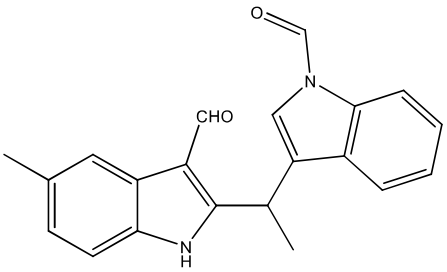

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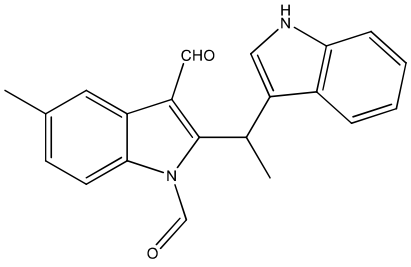

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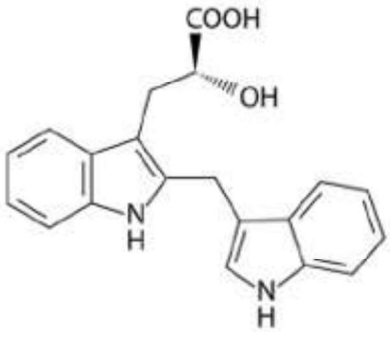

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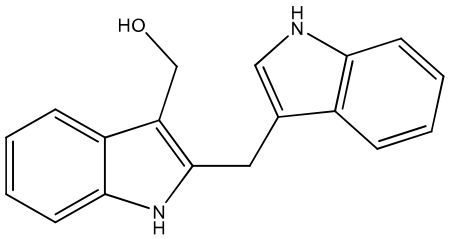
or a hydrate or pharmaceutically or cosmetically acceptable salt thereof.

[0010a] In another aspect, the present disclosure provides a composition comprising one or more compounds selected from the group consisting of: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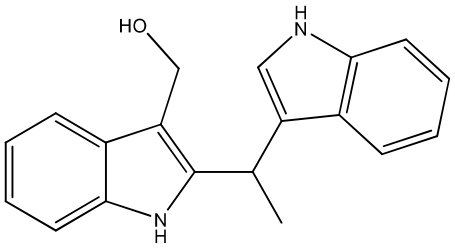
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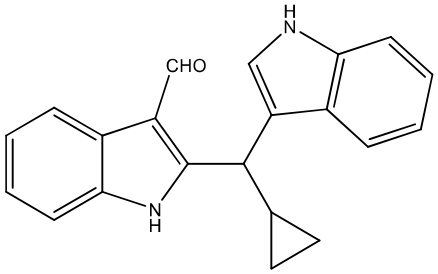
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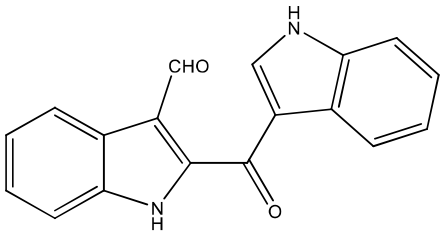
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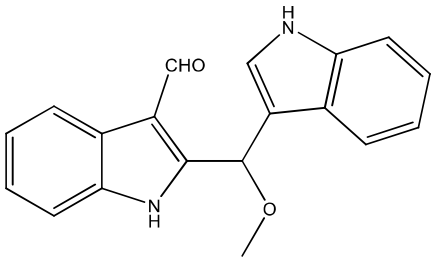
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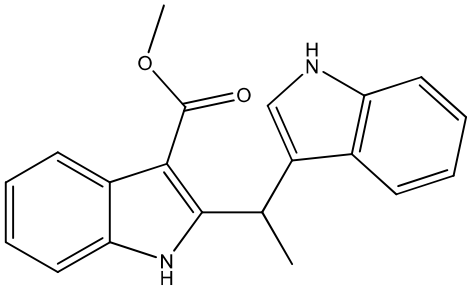
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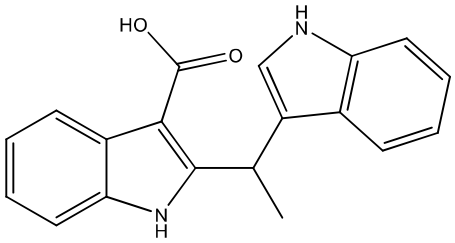
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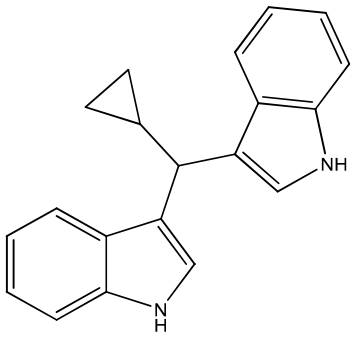
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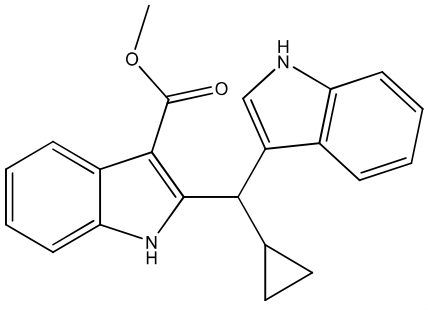
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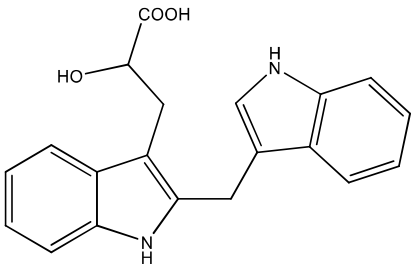
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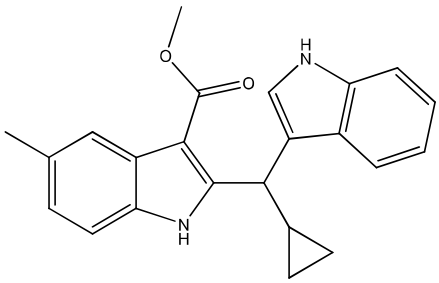
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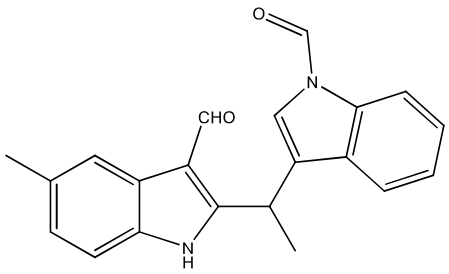
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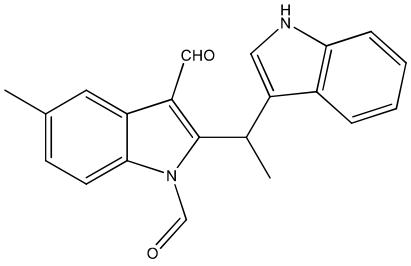
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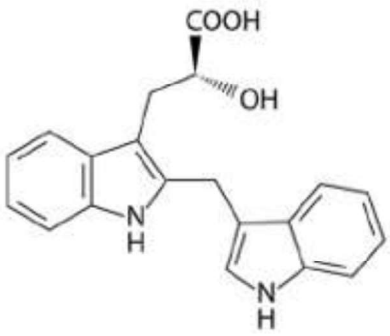
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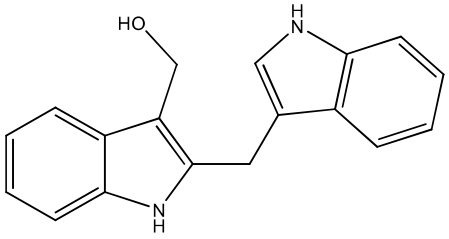
or a hydrate or pharmaceutically or cosmetically acceptable salt thereof.

[0010b] In yet another aspect, the present disclosure provides a composition comprising a compound selected from the group consisting of: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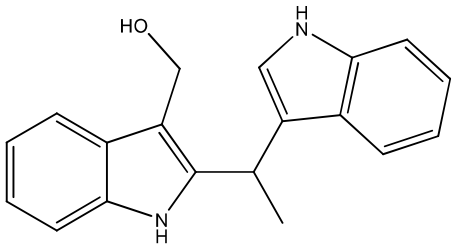
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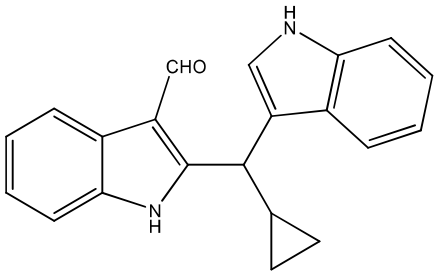
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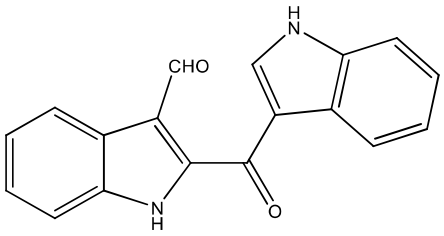
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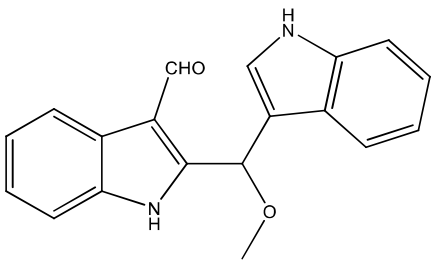
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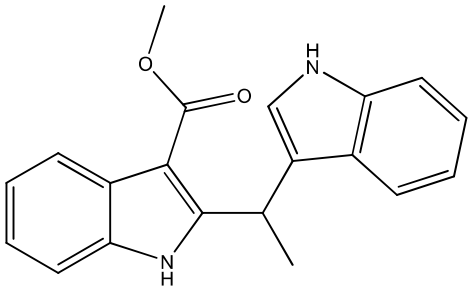
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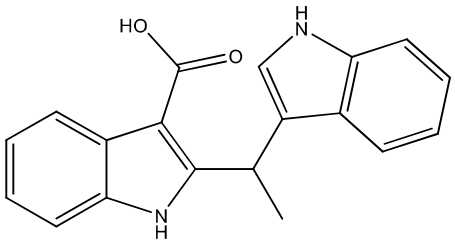

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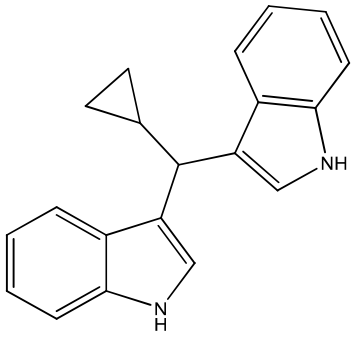

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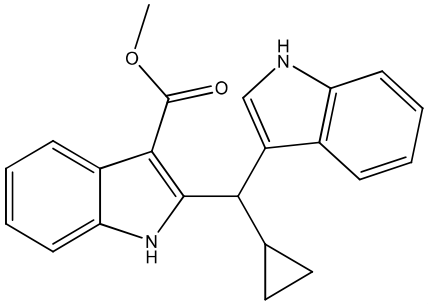

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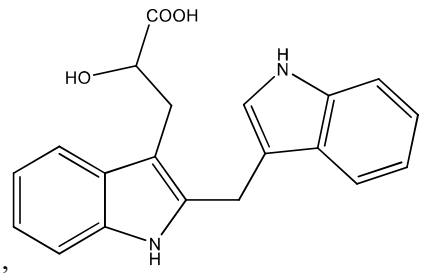

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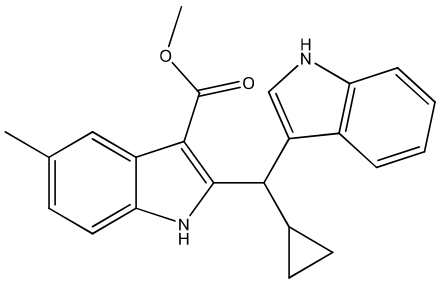

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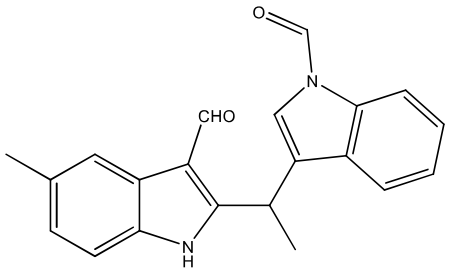

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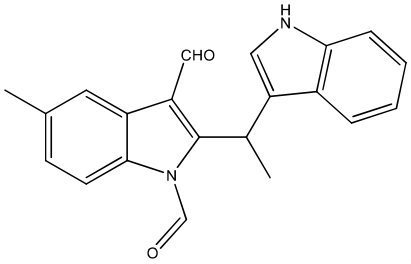

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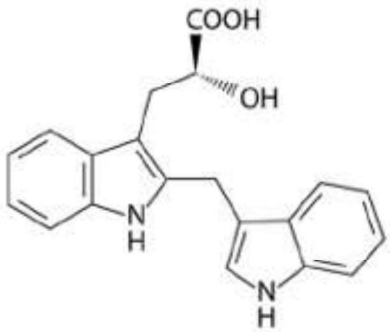

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or a pharmaceutically or cosmetically acceptable salt thereof.

[0010c] In a further aspect, the present disclosure provides use of a composition or a hydrate or pharmaceutically or cosmetically acceptable salt thereof as defined herein in the manufacture of a medicament for brightening skin in a subject.

[0010d] One example of the present disclosure is a composition. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0011] Another example of the present disclosure is a method for brightening skin in a subject. The method comprises contacting the subject with one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0012] A further example of the present disclosure is a method for inducing melanocyte apoptosis in a subject. The method comprises contacting the subject with one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0013] An additional example of the present disclosure is a method for modulating arylhydrocarbon receptor (AhR) activity in a subject. The method comprises contacting the subject with one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0014] Another example of the present disclosure is a method for modulating melanogenesis in a subject. The method comprises contacting the subject with one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0015] Another example of the present disclosure is a method for modulating melanin concentration in a subject. The method comprises contacting the subject with one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0016] An additional example of the present disclosure is a composition. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0017] A further example of the present disclosure is a composition for brightening skin. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0018] Another example of the present disclosure is a composition for inducing melanocyte apoptosis. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0019] An additional example of the present disclosure is a composition for modulating arylhydrocarbon receptor (AhR) activity. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0020] A further example of the present disclosure is a composition for modulating melanogenesis. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0021] Another example of the present disclosure is a composition for modulating melanin concentration. The composition comprises one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0022] An additional example of the present disclosure is a method for brightening skin in a subject. The method comprises contacting the subject with a composition, the composition comprising one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0023] 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 composition, the composition comprising one or more

of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

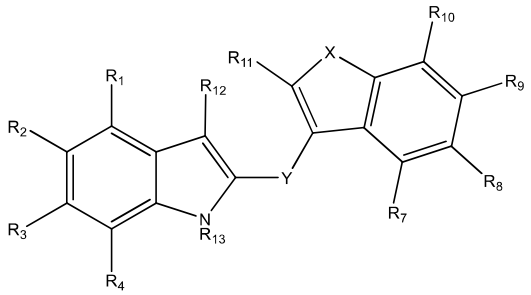
[0024] Another example of the present disclosure is a method for modulating arylhydrocarbon receptor (AhR) activity in a subject. The method comprises contacting the subject with a composition, the composition comprising one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0025] An additional example of the present disclosure is a method for modulating melanogenesis in a subject. The method comprises contacting the subject with a composition, the composition comprising one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0026] A further example of the present disclosure is a method for modulating melanin concentration in a subject. The method comprises contacting the subject with a composition, the composition comprising one or more of the compounds listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or pharmaceutically or cosmetically acceptable salt thereof.

[0027] Another example of the present disclosure is a composition. The composition comprises a *Malassezia* yeast and a cosmetically or pharmaceutically acceptable vehicle, diluent, or carrier.

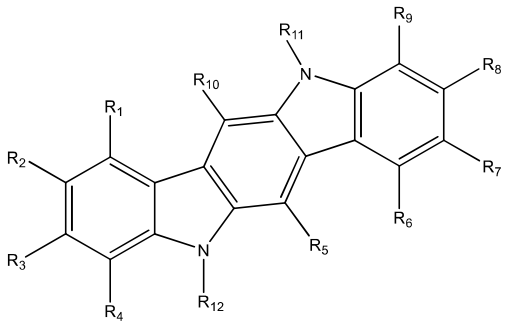
[0028] An additional example of the present disclosure is a composition. The composition comprises a compound having the structure of the following formula:



wherein:

X is selected from the group consisting of NR_{14} and O; Y is a covalent bond, CR_5R_6, O, or NR_{15}; R_1, R_2, R_3, R_4, R_7, R_8, R_9, R_{10}, and R_{11} are independently selected from the group consisting of hydrogen, halogen, CN, hydroxyl, R_{16}, or OR_{16}; R_{13}, R_{14}, and R_{15} are independently hydrogen or R_{16}; R_5 and R_6 are independently selected from the group consisting of hydrogen, hydroxyl, OR_{16}, R_{16}, and C_{3-6} cycloalkyl, or R_5 and R_6 combine to form an oxo (=O) group or a C_{3-6} cycloalkyl; R_{12} is selected from the group consisting of hydrogen, –COR^a, and R_{16}; each R_{16} is independently formyl, C_{1-9} alkyl, C_{2-9} alkenyl, or C_{2-9} alkynyl; and, R^a is selected from the group consisting of hydrogen, hydroxyl, and OR_{16}; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof, and a cosmetically or pharmaceutically acceptable vehicle, diluent, or carrier.

[0029] A further example of the present disclosure is a composition. The composition comprises a compound having the structure of the following formula:



wherein:

R_1, R_4, R_5, R_6, R_9, and R_{10} are independently selected from the group consisting of hydrogen, hydroxyl, halogen, CN, R_{13}, OR_{13}, $OCOR_{13}$ and -CHO; R_2 and R_3 are independently selected from the group consisting of hydrogen, hydroxyl, halogen, CN, R_{13}, OR_{13}, $OCOR_{13}$ and -CHO, or R_2 and R_3 combine to form a 5- or 6-membered heterocyclyl; R_7 and R_8 are independently selected from the group consisting of hydrogen, hydroxyl, halogen, CN, R_{13}, OR_{13}, $OCOR_{13}$ and -CHO, or R_7 and R_8 combine to form a 5- or 6-membered heterocyclyl; R_{11} and R_{12} are independently hydrogen or R_{13}; and, each R_{13} is independently $C_{1\text{-}9}$ alkyl, $C_{2\text{-}9}$ alkenyl, or $C_{2\text{-}9}$ alkynyl; or a crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof, and a cosmetically or pharmaceutically acceptable vehicle, diluent, or carrier.

[0030] Another example of the present disclosure is a composition. The composition comprises a compound listed in Table 1 or Fig. 3, or a chemical analog, crystalline form, hydrate, or cosmetically or pharmaceutically acceptable salt thereof, and a cosmetically or pharmaceutically acceptable vehicle, diluent, or carrier.

[0031] An additional example of the present disclosure is a method of treating or preventing UV-induced skin damage in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0032] A further example of the present disclosure is a method of treating or preventing UV-induced erythema in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0033] Another example of the present disclosure is a method of treating or preventing UV-induced aging of the skin in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0034] An additional example of the present disclosure is a method of treating or preventing sunburn in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0035] A further example of the present disclosure is a method of treating or preventing UV-induced hyperpigmentation in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0036] Another example of the present disclosure is a method for brightening skin in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0037] 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 compositions disclosed herein.

[0038] A further example of the present disclosure is a method for modulating arylhydrocarbon receptor (AhR) activity in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0039] Another example of the present disclosure is a method for modulating melanogenesis in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

[0040] An additional example of the present disclosure is a method for modulating melanin concentration in a subject. The method comprises contacting the subject with any of the compositions disclosed herein.

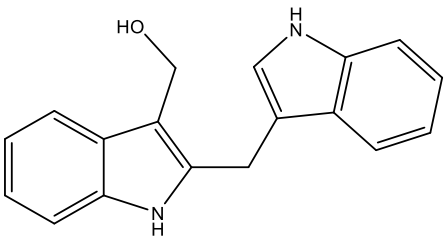
BRIEF DESCRIPTION OF THE DRAWINGS

[0041] 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.

[0042] Figs. 1-2 are tables showing mean tissue viability and melanin concentration data ascertained from separate experiments with MelanoDerm™ substrates treated with varying concentrations of the test articles shown.

CLAIMS

1. A cosmetic method for brightening skin in a subject comprising contacting the subject with a composition, wherein the composition comprises one or more compounds selected from the group consisting of:



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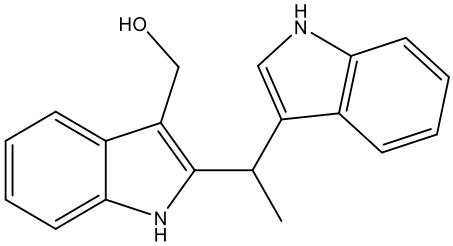

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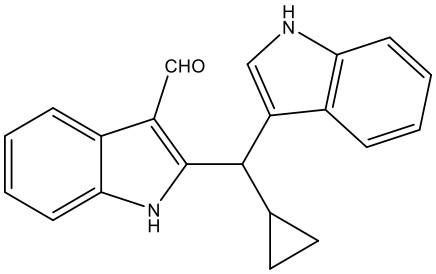

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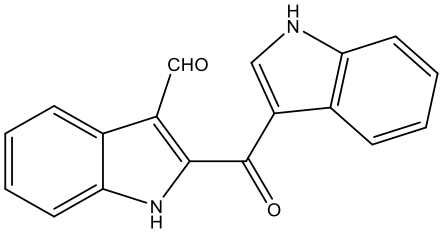

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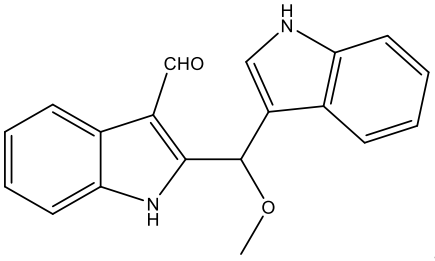

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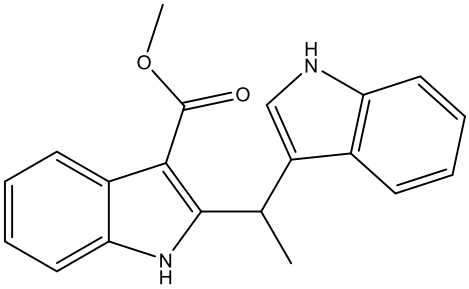

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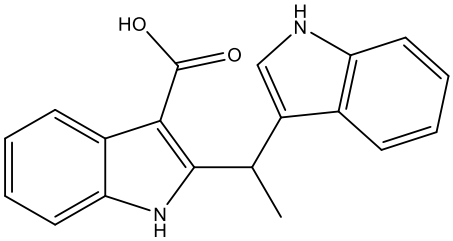

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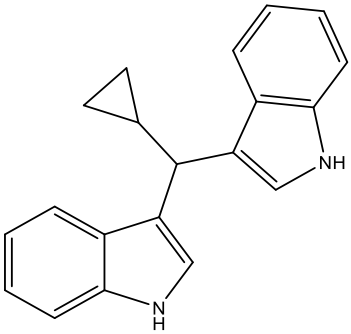

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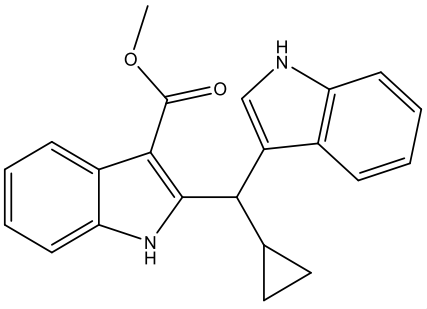

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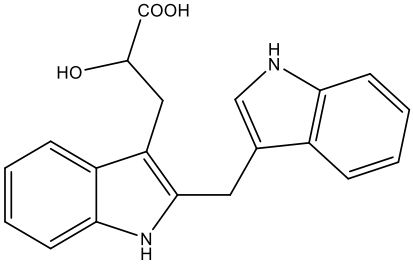

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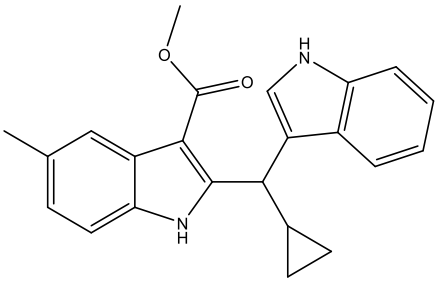

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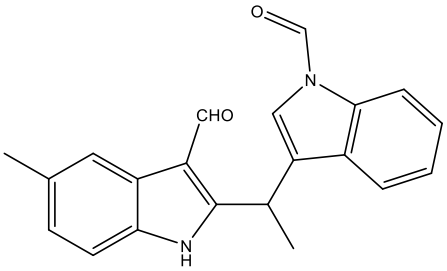

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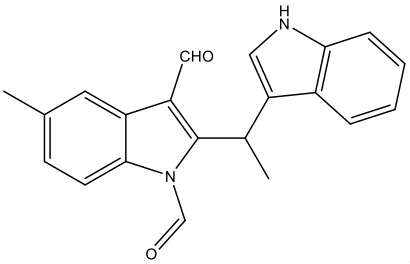

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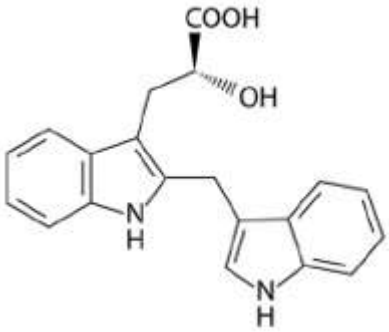

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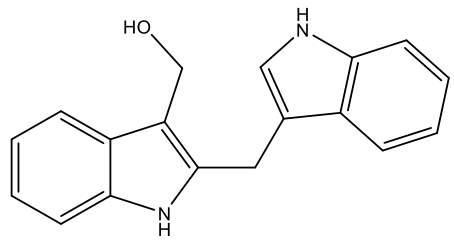
or a hydrate or pharmaceutically or cosmetically acceptable salt thereof.

2. The method of claim 1, wherein the composition comprises a compound selected from the group consisting of:



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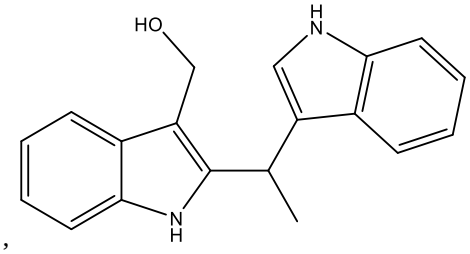

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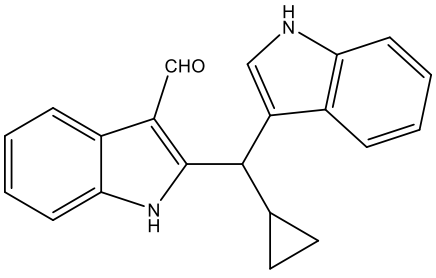

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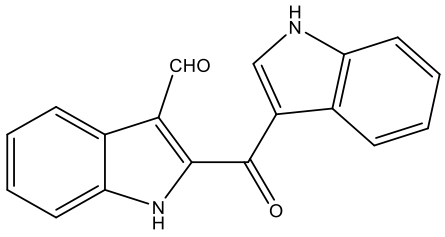

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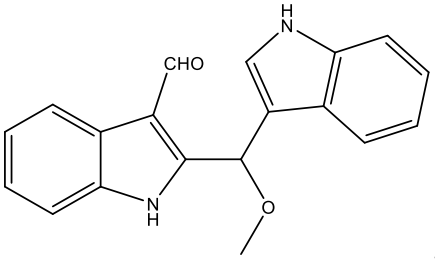

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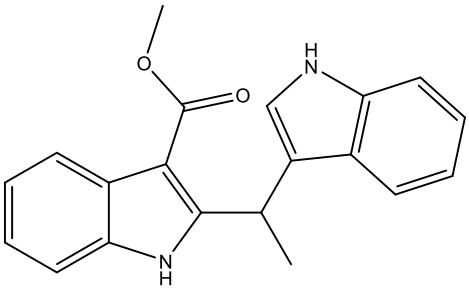

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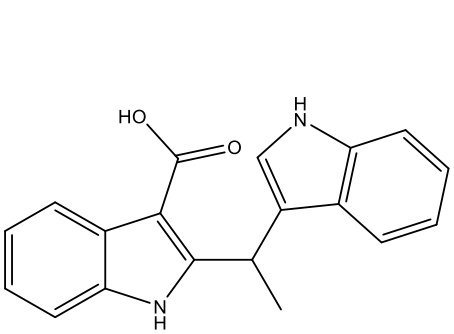

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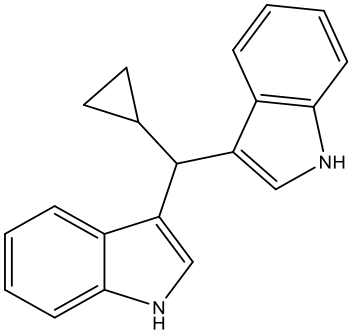

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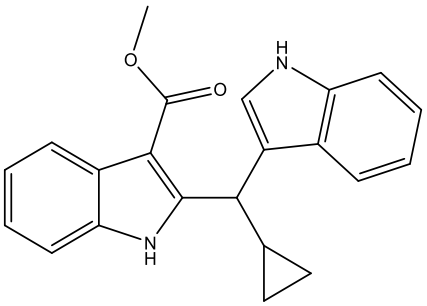

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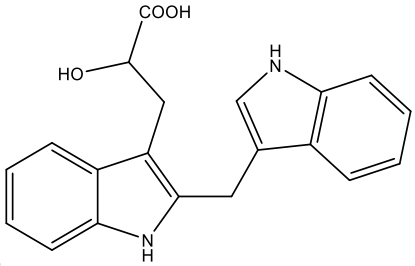

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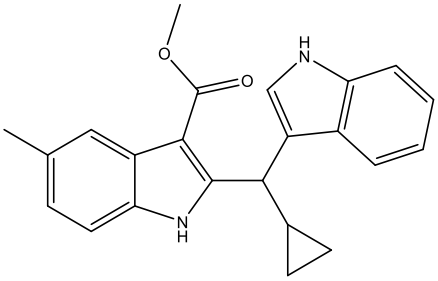

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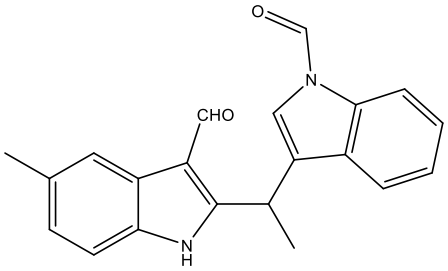

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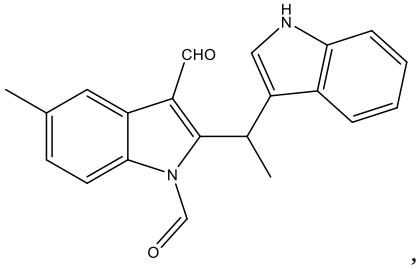

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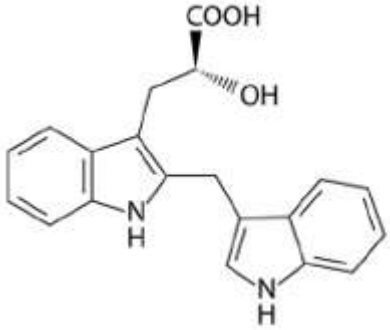

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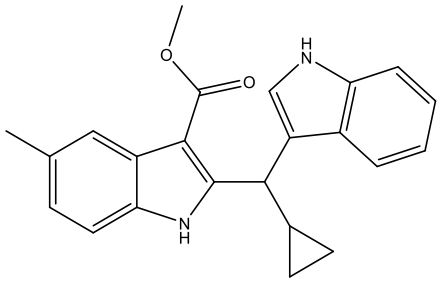
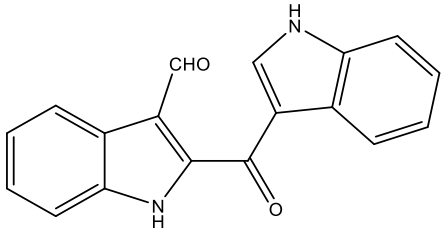
or a pharmaceutically or cosmetically acceptable salt thereof.

3. The method of claim 1, wherein the composition comprises a compound of the following structure:



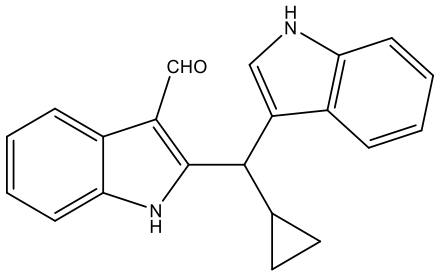
or a pharmaceutically or cosmetically acceptable salt thereof.

4. The method of claim 1, wherein the composition comprises a compound of the following structure:



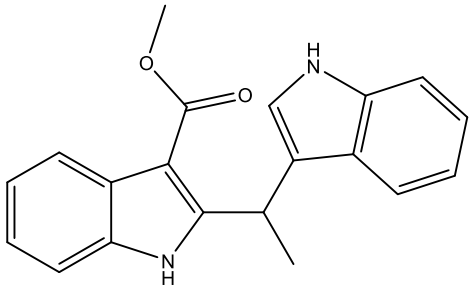
or a pharmaceutically or cosmetically acceptable salt thereof.

5. The method of claim 1, wherein the composition comprises a compound of the following structure:



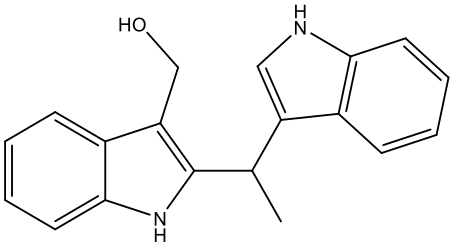
or a pharmaceutically or cosmetically acceptable salt thereof.

6. The method of claim 1, wherein the composition comprises a compound of the following structure:



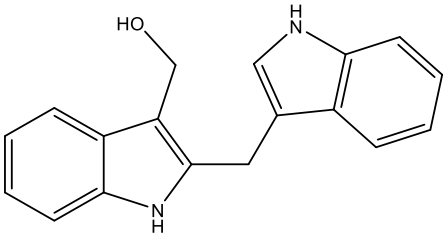
or a pharmaceutically or cosmetically acceptable salt thereof.

7. The method of claim 1, wherein the composition comprises a compound of the following structure:



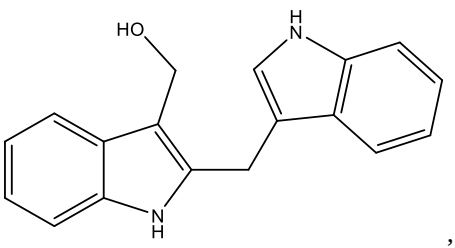
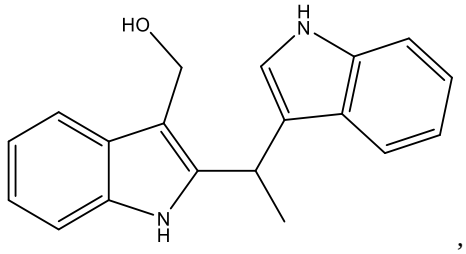
or a pharmaceutically or cosmetically acceptable salt thereof.

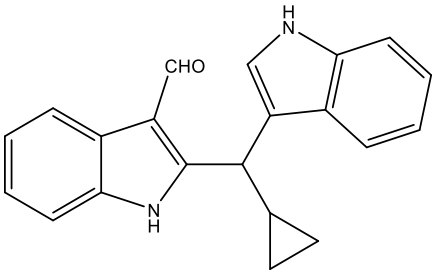
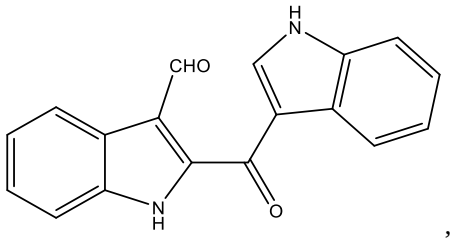
8. The method of claim 1, wherein the composition comprises a compound of the following structure:

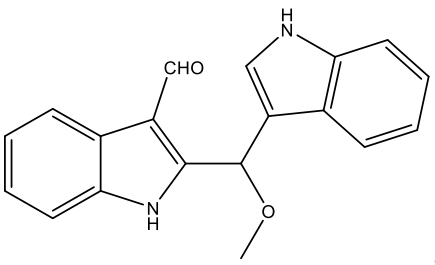
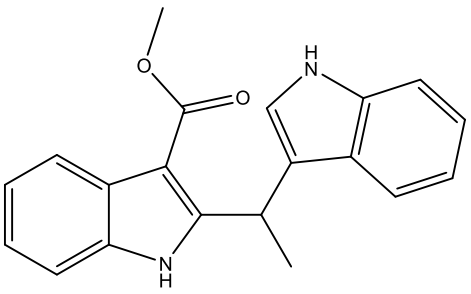


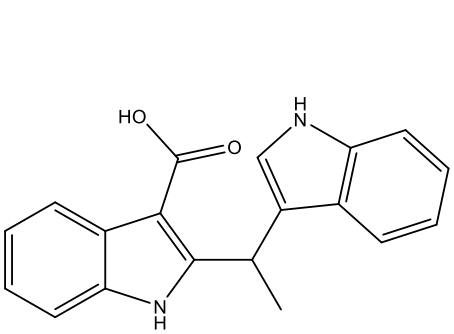
or a pharmaceutically or cosmetically acceptable salt thereof.

9. A composition comprising one or more compounds selected from the group consisting of:

, ,

, ,

, ,



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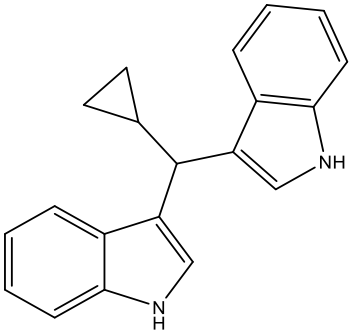

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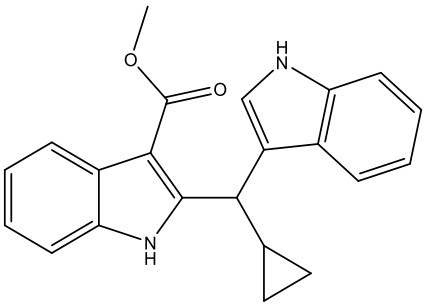

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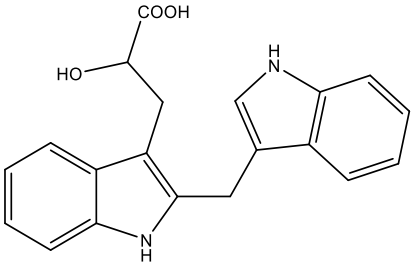

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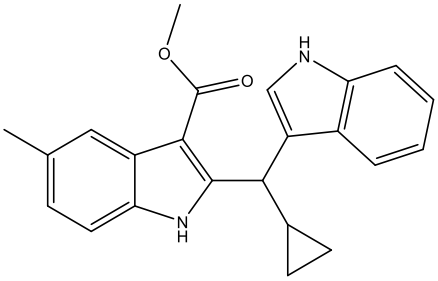

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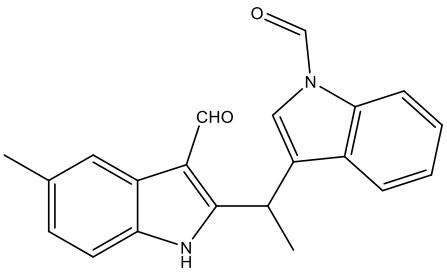

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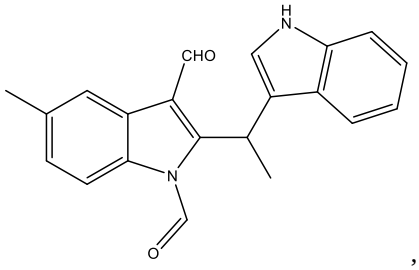

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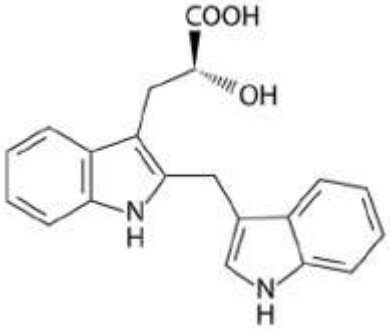

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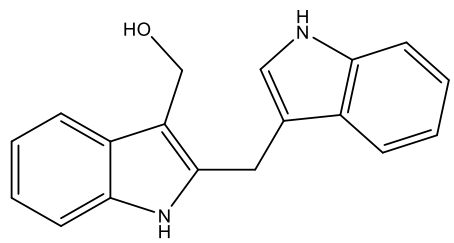
or a hydrate or pharmaceutically or cosmetically acceptable salt thereof.

10. A composition comprising a compound selected from the group consisting of: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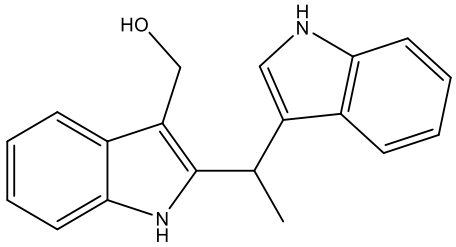
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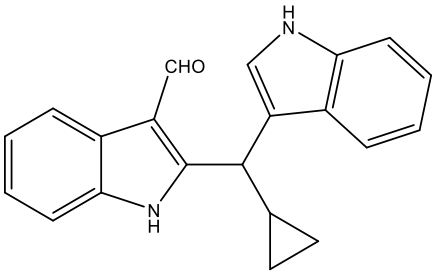
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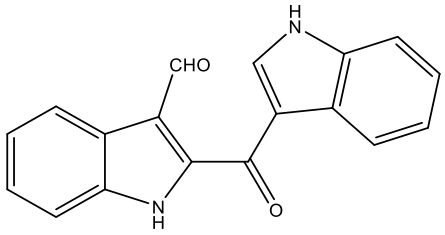
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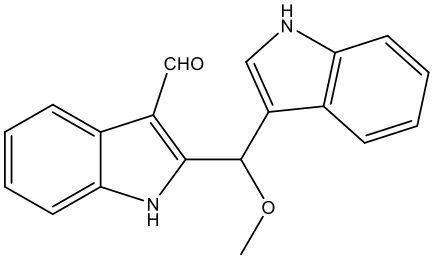
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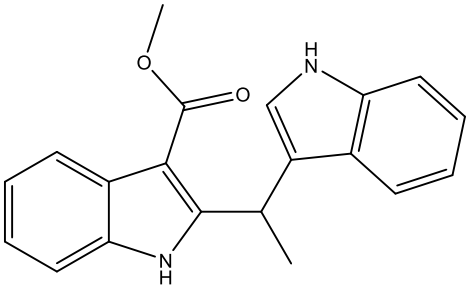
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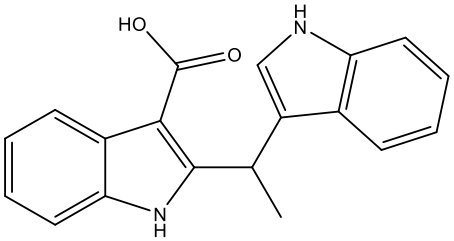
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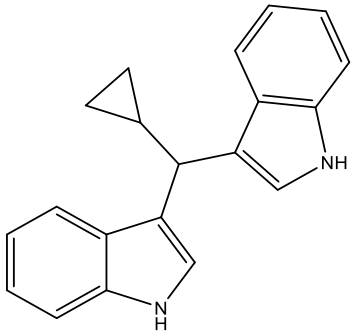
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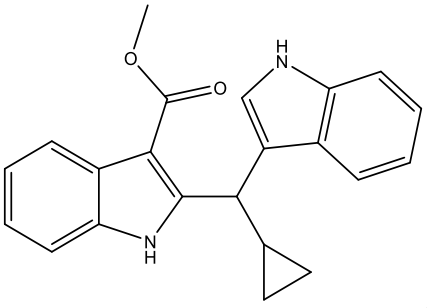
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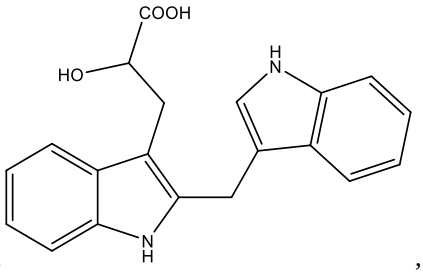
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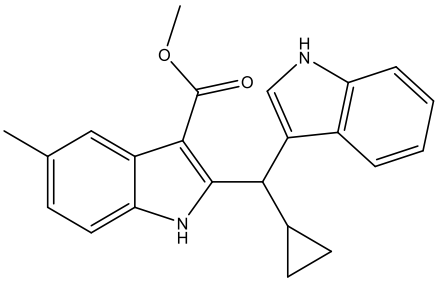

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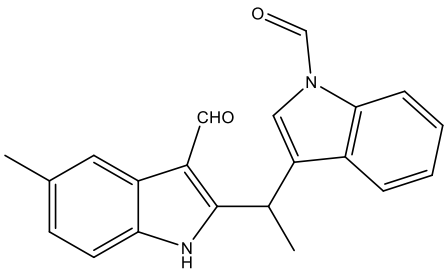

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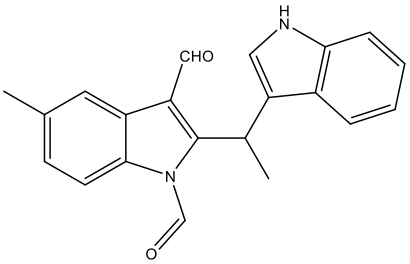

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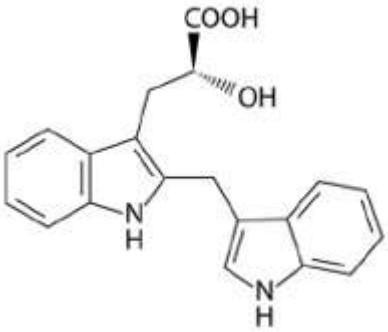
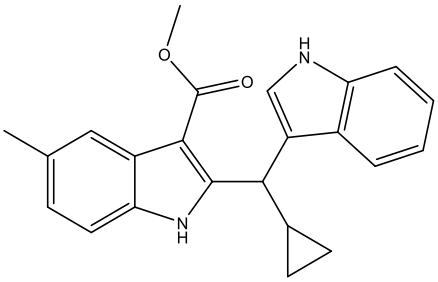


, and ,

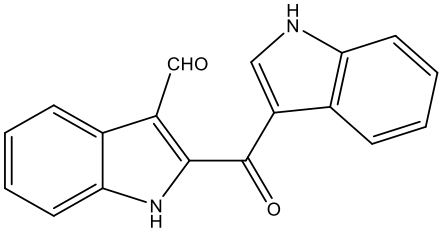
or a pharmaceutically or cosmetically acceptable salt thereof.

11. The composition of claim 9, wherein the composition comprises a compound of the following structure:



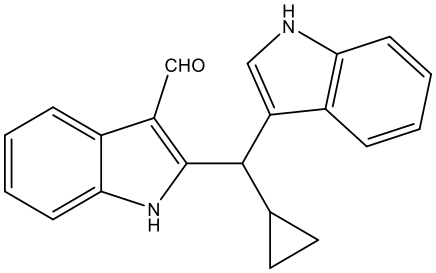
or a pharmaceutically or cosmetically acceptable salt thereof.

12. The composition of claim 9, wherein the composition comprises a compound of the following structure:



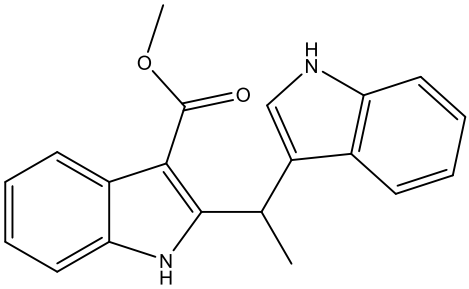
or a pharmaceutically or cosmetically acceptable salt thereof.

13. The composition of claim 9, wherein the composition comprises a compound of the following structure:



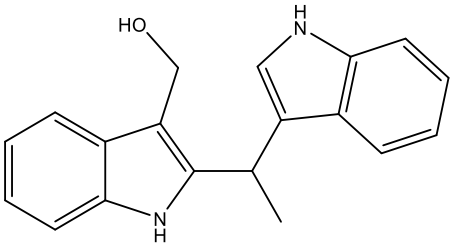
or a pharmaceutically or cosmetically acceptable salt thereof.

14. The composition of claim 9, wherein the composition comprises a compound of the following structure:



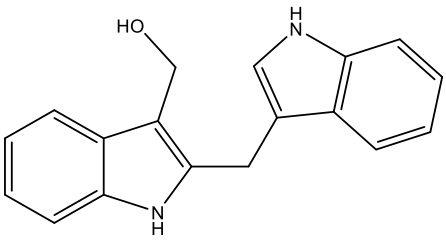
or a pharmaceutically or cosmetically acceptable salt thereof.

15. The composition of claim 9, wherein the composition comprises a compound of the following structure:



or a pharmaceutically or cosmetically acceptable salt thereof.

16. The composition of claim 9, wherein the composition comprises a compound of the following structure:



or a pharmaceutically or cosmetically acceptable salt thereof.

17. Use of a composition or a hydrate or pharmaceutically or cosmetically acceptable salt thereof as defined in claim 9 in the manufacture of a medicament for brightening skin in a subject.