CLAIMS

1. Use of a topical composition comprising a therapeutically effective amount of a vitamin D compound and a carrier, formulated to be delivered to epidermis while substantially avoiding dermis delivery, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the effective amount is equivalent to 0.1 to 100 µg of the vitamin D compound per 75 kg body weight.

2. The use of claim 1, wherein the carrier comprises 20-45% (w/w) propylene glycol and 55-80% (w/w) anhydrous absolute ethanol.

3. The use of claim 2, wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25: 75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

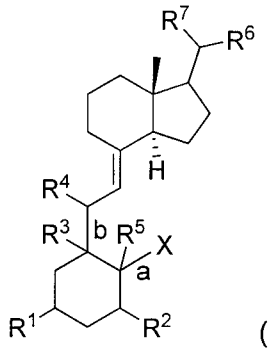
4. Use of a topical composition comprising a therapeutically effective amount of a vitamin D compound and a carrier, formulated to be delivered to epidermis while substantially avoiding dermis delivery, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the carrier comprises propylene glycol and anhydrous absolute ethanol; wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25: 75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

5. Use of a topical composition comprising a therapeutically effective amount of a vitamin D compound and a carrier, formulated to be delivered to epidermis while substantially avoiding dermis delivery, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol, and about 60% (w/w) anhydrous absolute ethanol.

6. The use of claim 3 or 4, wherein the carrier comprises about 40% (w/w) propylene glycol and about 60% (w/w) anhydrous absolute ethanol.

7. The use of claim 1, wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol, and about 60% (w/w) anhydrous absolute ethanol.

8. The use of any one of claims 1-7, wherein the vitamin D compound is represented by Formula (I):



(I)

wherein

a and b are each independently a single or double bond;

X is -CH_2 when a is a double bond, or X is hydrogen or a hydroxyl substituted alkyl when a is a single bond;

R^1 is hydrogen, hydroxyl, alkoxyl, tri-alkyl silyl or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^2 is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^3 is absent when b is a double bond or R^3 is hydrogen, hydroxyl or alkyl, or R^3 and R^1 together with the carbon atoms to which they are attached may be linked to form 5-7 membered carbocyclic ring when b is a single bond;

R^4 is absent when b is a double bond orhydrogen, halogen or hydroxyl when b is a single bond;

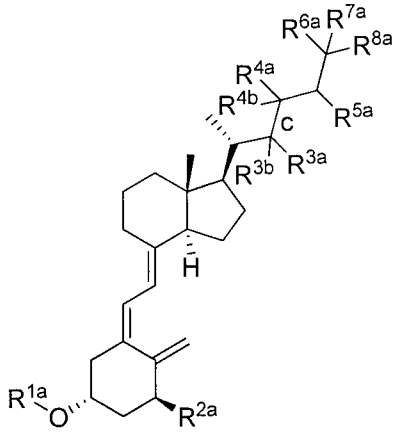
R^5 is absent when a is a double bond or R^5 is hydrogen, halogen or hydroxyl when a is a single bond;

R^6 is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclicyl, alkyl-O-alkyl, alkyl-CO_2-alkyl optionally substituted with one to five, hydroxyl, oxo, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties;

R^7 is alkyl optionally substituted with one to three hydroxyl, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties; and,

R' and R" are each, independently, hydrogen, hydroxyl, halogen, alkyl or alkoxyl, and pharmaceutically acceptable salts thereof.

9. The use of claim 8, wherein the vitamin D compound is represented by Formula (II):



(II)

wherein

c is a single or double bond;

R^{1a} is hydrogen or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{2a} is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{3a} and R^{4a} are absent when c is a double bond, or are each independently hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties when c is a single bond; and

R^{3b}, R^{4b}, R^{5a}, R^{6a}, R^{7a} and R^{8a} are each, independently, hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties, or any two of R^{6a}, R^{7a} and R^{8a} may be linked to form a 3-7 membered carbocyclic ring, and pharmaceutically acceptable salts thereof.

10. The use of any one of claims 1-9, wherein the vitamin D compound is 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

11. The use of any one of claims 1-9, wherein the vitamin D compound is 1,25-dihydroxyvitamin D3.

12. The use of any one of claims 1-9, wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

13. The use of any one of claims 1-12, wherein the vitamin D compound exhibits similar or identical gene regulation profile as equivalent amount of calcitriol in normal keratinocytes.

14. The use of any one of claims 1-12, wherein the vitamin D compound promotes the expression of one or more genes whose expression levels are promoted by an equivalent amount of calcitriol.

15. The use of any one of claims 1-12, wherein the vitamin D compound inhibits the expression of one or more genes whose expression levels are inhibited by an equivalent amount of calcitriol.

16. The use of any one of claims 1-12, wherein the vitamin D compound modulates the expression of HSPA2 or HSF4 mRNA, HSPB1 or DNAJC6 mRNA in normal keratinocytes.

17. The use of any one of claims 1-12, wherein the vitamin D compound modulates the expression of SLC1A1, KCNB2, oKCNN4 protein or SLC1A3 protein in normal keratinocytes.

18. The use of any one of claims 1-12, wherein the vitamin D compound decreases the expression of one or more proteins selected from the group consisting of Crk II, Growth Factor Independence1, Serine Threonine Protein Phosphatase 1b, Cathepsin D, Transforming Growth Factorb pan, WAVE, Protein Tyrosine Phosphatase PEST, and CD40 by at least about 2-fold.

19. The use of any one of claims 1-12, wherein the vitamin D compound induces overexpression of one or more proteins selected from the group consisting of BACH1, CENPE, cMyc, C-src tryosine kinase (Csk), CtBP1, Dimethyl Histone H3 diMeLys4, Dimethyl Histone H3 diMeLys9, Estrogen Receptor, FKHRL1 FOXO3a, FOXP2, HDAC2, HDAC6, MAP Kinase Activated Protein Kinase2 MAPKAPK2, MAP Kinase ERK1, Melanocortin3 Receptor, Proliferating Cell Protein Ki67, S100, SHPTP2, Sin3A, ARTS, ASAP1 Centaurin b4, Cofilin, Connexin 32, Dystrophin, Focal Adhesion Kinase pp125FAK, gTubulin, Myosin IX Myr5,

Neurofilament 200, p120ctn, PAD14, Par4 Prostate Apoptosis Response 4, ROCK1, Uvomorulin ECadherin, Vitronectin, Bclx, BclxL, BID, Bmf, DcR2, ERK5 BIG MAPKBMK1, Integrin-linked kinase (ILK), Protein Kinase Ba, PUMA bbc3, Amyloid Precursor Protein, Presenilin1, Glutamic Acid Decarboxylase 65, Glutamic Acid Decarboxylase GAD65 67, Nitric Oxide Synthase bNOS, Substance P Receptor, Synaptopodin, Tumor Necrosis Factor a, and Ubiquitin Cterminal Hydrolase L1 by at least about 2-fold.

20. The use of any one of claims 1-12, wherein the vitamin D compound induces overexpression in normal keratinocytes of one or more of: GST, Keratin 1, Keratin 17, Galectin 1, S100 A9 (Calprotectin), or S100 A13.

21. Use of a topical composition comprising a therapeutically effective amount of calcitriol and a carrier, formulated to be delivered to epidermis while substantially avoiding dermis delivery, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the carrier comprises propylene glycol and anhydrous absolute ethanol, and wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25: 75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

22. The use of claim 21, wherein the carrier comprises about 40% (w/w) propylene glycol and about 60% (w/w) anhydrous absolute ethanol.

23. Use of a topical composition comprising a therapeutically effective amount of calcitriol and a carrier, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the carrier comprises about 40% (w/w) propylene glycol and about 60% (w/w) anhydrous absolute ethanol.

24. Use of a topical composition comprising a therapeutically effective amount of calcitriol and a carrier, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol, and about 60% (w/w) anhydrous absolute ethanol.

25. The use of any one of claims 1-23, wherein the individual is a primate.

26. The use of claim 25, wherein the individual is a human.

27. The use of any one of claims 1-26, wherein alopecia has not commenced in the individual.

28. The use of claim 27, wherein the individual is undergoing or about to undergo chemotherapy.

29. The use of claim 28, wherein the topical composition is to be administered to the individual prior to chemotherapy.

30. The use of claim 28, wherein the topical composition is to be administered to the individual concurrently with chemotherapy.

31. The use of claim 28, wherein the topical composition is to be administered to the individual after the commencement of chemotherapy, but prior to the commencement of alopecia.

32. The use of any one of claims 1-31, wherein the topical composition does not substantially reduce the efficacy of chemotherapy.

33. The use of any one of claims 1-32, wherein chemotherapy is systemic chemotherapy.

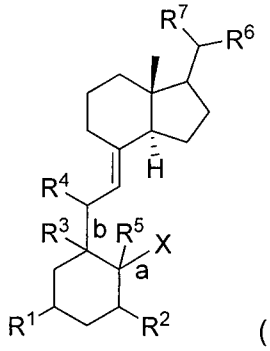
34. The use of any one of claims 1-33, wherein chemotherapy includes one or more of: an Anthracycline, 5-FU, Tamoxifen, Irinotecan, Paclitaxel (Taxol), Carboplatin, Etoposide, Cytoxan/Cyclophosphamide, Cisplatin, Erlotinib (Tarceva), Gemcitabine, Staurosporin, Vincristine, Imatinib (Gleevec), Gefitinib (Iressa), Sorafenib, Dasatinib, Dactinomycin, Hexamethamelamine (HMM, altretamine), Ifosfamide, bleomycin, methotrexate, Docetaxel (Taxotere), Vindesine, Vinorelbine, Topotecan, Amsacrine, Cytarabine, Busulphan, Melphalan, Vinblastine, Lomustine(CCNU), Thiotepa, Gemcitabine, Carmustine(BCNU), Mitroxantrone, Mitomycin C, Procarbazine, 6-Mercaptopurine, Sreptozotocin, Fludarabine, Raltitrexate (Tomudex), Capecitabine, and equivalents thereof.

35. The use of claim 34, wherein the Anthracycline is selected from the group consisting of Adriamycin (Doxorubicin), Daunorubicin, Epirubicin, Idarubicin, and Valrubicin.

36. The use of any one of claims 1-35, wherein the vitamin D compound is to be topically administered to the individual at a dosage volume equivalent to about 0.1 μg of calcitriol/cm^2.

37. The use of any one of claims 1-36, wherein the total dose is equivalent to about 2-100 μg of calcitriol/75 kg body weight.

38. Use of a topical composition comprising a therapeutically effective amount of a vitamin D compound and a carrier, in the manufacture of a medicament for preventing or treating chemotherapy-induced alopecia in an individual, wherein the vitamin D compound is represented by Formula (I):



(I)

wherein

a and b are each independently a single or double bond;

X is -CH_2 when a is a double bond, or X is hydrogen or a hydroxyl substituted alkyl when a is a single bond;

R^1 is hydrogen, hydroxyl, alkoxyl, tri-alkyl silyl or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^2 is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^3 is absent when b is a double bond or R^3 is hydrogen, hydroxyl or alkyl, or R^3 and R^1 together with the carbon atoms to which they are attached may be linked to form 5-7 membered carbocyclic ring when b is a single bond;

R^4 is absent when b is a double bond orhydrogen, halogen or hydroxyl when b is a single bond;

R^5 is absent when a is a double bond or R^5 is hydrogen, halogen or hydroxyl when a is a single bond;

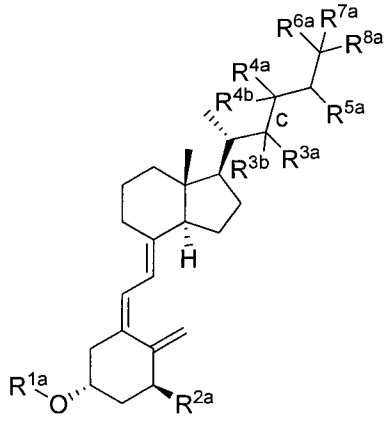
R^6 is alkyl, cycloalkyl, heterocyclicyl, alkyl-O-alkyl, alkyl-CO_2-alkyl optionally substituted with one to five, hydroxyl, oxo, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties;

R^7 is alkyl optionally substituted with one to three hydroxyl, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties; and,

R' and R" are each, independently, hydrogen, hydroxyl, halogen, alkyl or alkoxyl, and pharmaceutically acceptable salts thereof;

wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

39. The use of claim 38, wherein the vitamin D compound is represented by Formula (II):



(II)

wherein

c is a single bond;

R^{1a} is hydrogen or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{2a} is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{3a} and R^{4a} are each independently hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties; and

R^{3b}, R^{4b}, R^{5a}, R^{6a}, R^{7a} and R^{8a} are each, independently, hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties, or any two of R^{6a}, R^{7a} and R^{8a} may be linked to form a 3-7 membered carbocyclic ring, and pharmaceutically acceptable salts thereof.

40. The use of any one of claims 1-39, wherein said vitamin D compound is to be topically administered to the individual at an effective concentration of:

(1) about 50 μg/mL, and does not cause toxicity after at least about 25 consecutive days of drug administration; or

(2) about 100 μg/mL, and does not cause toxicity after at least about 7 consecutive days of drug administration.

41. The use of any one of claims 38-40, wherein the vitamin D compound:

(1) exhibits similar or identical gene regulation profile as equivalent amount of calcitriol in normal keratinocyte;

(2) modulates the expression of one or more genes whose expression levels are modulated by an equivalent amount of calcitriol;

(3) modulates the expression of HSPA2 or HSF4 mRNA, HSPB1 or DNAJC6 mRNA in normal keratinocytes;

(4) modulates the expression of SLC1A1, KCNB2, or KCNN4 protein or SLC1A3 protein in normal keratinocytes;

(5) modulates the expression of one or more proteins selected from the group consisting of Crk II, Growth Factor Independence1, Serine Threonine Protein Phosphatase 1b, Cathepsin D, Transforming Growth Factorb pan, WAVE, Protein Tyrosine Phosphatase PEST, and CD40 by at least about 2-fold;

(6) induces overexpression of one or more proteins selected from the group consisting of BACH1, CENPE, cMyc, C-src tryosine kinase (Csk), CtBP1, Dimethyl Histone H3 diMeLys4, Dimethyl Histone H3 diMeLys9, Estrogen Receptor, FKHRL1 FOXO3a, FOXP2, HDAC2, HDAC6, MAP Kinase Activated Protein Kinase2 MAPKAPK2, MAP Kinase ERK1, Melanocortin3 Receptor, Proliferating Cell Protein Ki67, S100, SHPTP2, Sin3A, ARTS, ASAP1 Centaurin b4, Cofilin, Connexin 32, Dystrophin, Focal Adhesion Kinase pp125FAK, gTubulin, Myosin IX Myr5, Neurofilament 200, p120ctn, PAD14, Par4 Prostate Apoptosis Response 4, ROCK1, Uvomorulin ECadherin, Vitronectin, Bclx, BclxL, BID, Bmf, DcR2, ERK5 BIG MAPKBMK1, Integrin-linked kinase (ILK), Protein Kinase Ba, PUMA bbc3, Amyloid Precursor Protein, Presenilin1, Glutamic Acid Decarboxylase 65, Glutamic Acid Decarboxylase GAD65 67, Nitric Oxide Synthase bNOS, Substance P Receptor, Synaptopodin, Tumor Necrosis Factor a, and Ubiquitin Cterminal Hydrolase L1 by at least about 2-fold; or,

(7) induces overexpression in normal keratinocytes of one or more of: GST, Keratin 1, Keratin 17, Galectin 1, S100 A9 (Calprotectin), or S100 A13;

wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

42. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of a vitamin D compound and a carrier, wherein said vitamin D compound is formulated to be delivered to epidermis while substantially avoiding dermis delivery, and wherein the effective amount is equivalent to 0.1 to 100 µg of the vitamin D compound per 75 kg body weight.

43. The topical pharmaceutical composition of claim 42, wherein the carrier comprises 20-45% (w/w) propylene glycol and 55-80% (w/w) anhydrous absolute ethanol.

44. The topical pharmaceutical composition of claim 42, wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25: 75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

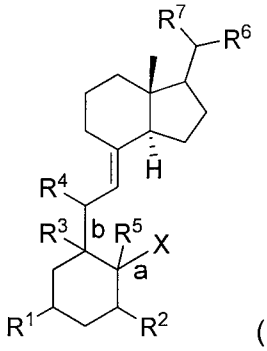
45. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of a vitamin D compound and a carrier, wherein said vitamin D compound is formulated to be delivered to epidermis while substantially avoiding dermis delivery; wherein the carrier comprises propylene glycol and anhydrous absolute ethanol; and wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25: 75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

46. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of a vitamin D compound and a carrier, wherein said vitamin D compound is formulated to be delivered to epidermis while substantially avoiding dermis delivery; and wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol, and about 60% (w/w) anhydrous absolute ethanol.

47. The topical pharmaceutical composition of claim 43 or 45, wherein the carrier comprises about 40% (w/w) propylene glycol and about 60% (w/w) anhydrous absolute ethanol.

48. The topical pharmaceutical composition of claim 42, wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol, and about 60% (w/w) anhydrous absolute ethanol.

49. The topical pharmaceutical composition of any one of claims 42-45, 47 and 48, wherein the vitamin D compound is represented by Formula (I):



(I)

wherein

a and b are each independently a single or double bond;

X is $-CH_2$ when a is a double bond, or X is hydrogen or a hydroxyl substituted alkyl when a is a single bond;

R^1 is hydrogen, hydroxyl, alkoxyl, tri-alkyl silyl or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^2 is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^3 is absent when b is a double bond or R^3 is hydrogen, hydroxyl or alkyl, or R^3 and R^1 together with the carbon atoms to which they are attached may be linked to form 5-7 membered carbocyclic ring when b is a single bond;

R^4 is absent when b is a double bond orhydrogen, halogen or hydroxyl when b is a single bond;

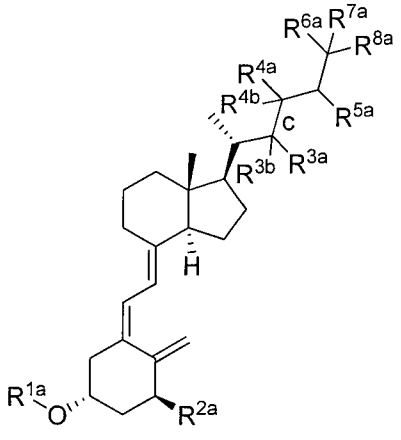
R^5 is absent when a is a double bond or R^5 is hydrogen, halogen or hydroxyl when a is a single bond;

R^6 is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclicyl, alkyl-O-alkyl, alkyl-CO_2-alkyl optionally substituted with one to five, hydroxyl, oxo, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties;

R^7 is alkyl optionally substituted with one to three hydroxyl, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties; and,

R' and R" are each, independently, hydrogen, hydroxyl, halogen, alkyl or alkoxyl, and pharmaceutically acceptable salts thereof.

50. The topical pharmaceutical composition of claim 49, wherein the vitamin D compound is represented by Formula (II):



(II)

wherein

c is a single or double bond;

R^{1a} is hydrogen or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{2a} is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{3a} and R^{4a} are absent when c is a double bond, or are each independently hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties when c is a single bond; and

R^{3b}, R^{4b}, R^{5a}, R^{6a}, R^{7a} and R^{8a} are each, independently, hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties, or any two of R^{6a}, R^{7a} and R^{8a} may be linked to form a 3-7 membered carbocyclic ring, and pharmaceutically acceptable salts thereof.

51. The topical pharmaceutical composition of any one of claims 42-45 and 47-50, wherein the vitamin D compound is 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

52. The topical pharmaceutical composition of claim 51, wherein the vitamin D compound is 1,25-dihydroxyvitamin D3.

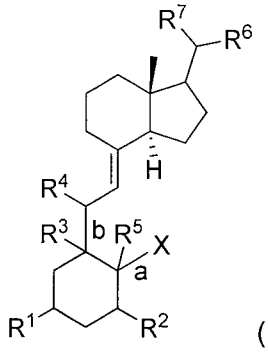
53. The topical pharmaceutical composition of any one of claims 42-45 and 47-50, wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

54. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of calcitriol and a carrier, formulated to be delivered to epidermis while substantially avoiding dermis delivery, wherein the carrier comprises propylene glycol and anhydrous absolute ethanol; and wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25: 75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

55. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of calcitriol and a carrier, wherein the carrier comprises about 40% (w/w) propylene glycol and about 60% (w/w) anhydrous absolute ethanol.

56. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of calcitriol and a carrier, wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol, and about 60% (w/w) anhydrous absolute ethanol.

57. A topical pharmaceutical composition for use in the prevention or treatment of chemotherapy-induced alopecia in an individual, comprising a therapeutically effective amount of a vitamin D compound, wherein said vitamin D compound is represented by Formula (I):



(I)

wherein

a and b are each independently a single or double bond;

X is -CH_2 when a is a double bond, or X is hydrogen or a hydroxyl substituted alkyl when a is a single bond;

R^1 is hydrogen, hydroxyl, alkoxyl, tri-alkyl silyl or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^2 is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^3 is absent when b is a double bond or R^3 is hydrogen, hydroxyl or alkyl, or R^3 and R^1 together with the carbon atoms to which they are attached may be linked to form 5-7 membered carbocyclic ring when b is a single bond;

R^4 is absent when b is a double bond orhydrogen, halogen or hydroxyl when b is a single bond;

R^5 is absent when a is a double bond or R^5 is hydrogen, halogen or hydroxyl when a is a single bond;

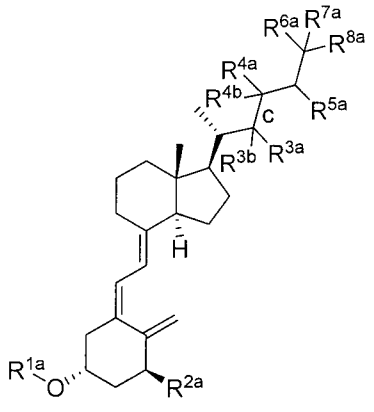
R^6 is alkyl, cycloalkyl, heterocyclicyl, alkyl-O-alkyl, alkyl-CO_2-alkyl optionally substituted with one to five, hydroxyl, oxo, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties;

R^7 is alkyl optionally substituted with one to three hydroxyl, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties; and,

R' and R" are each, independently, hydrogen, hydroxyl, halogen, alkyl or alkoxyl, and pharmaceutically acceptable salts thereof;

wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

58. The topical pharmaceutical composition of claim 57, wherein the vitamin D compound is represented by Formula (II):



(II)

wherein

c is a single bond;

R^{1a} is hydrogen or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{2a} is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{3a} and R^{4a} are each independently hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties; and

R^{3b}, R^{4b}, R^{5a}, R^{6a}, R^{7a} and R^{8a} are each, independently, hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties, or any two of R^{6a}, R^{7a} and R^{8a} may be linked to form a 3-7 membered carbocyclic ring, and pharmaceutically acceptable salts thereof.

59. The topical pharmaceutical composition of any one of claims 42-58, wherein said vitamin D compound is to be topically administered to the individual at an effective concentration of:

(1) about 50 μg/mL, and does not cause toxicity after at least about 25 consecutive days of drug administration; or

(2) about 100 μg/mL, and does not cause toxicity after at least about 7 consecutive days of drug administration.

60. The topical pharmaceutical composition of any one of claims 42-59, wherein said therapeutically effective amount of the vitamin D compound is to be co-administered with a chemotherapeutic agent, wherein the vitamin D compound does not substantially interfere with the efficacy of the chemotherapeutic agent.

61. The topical pharmaceutical composition of any one of claims 42-59 the vitamin D compound:

(1) exhibits similar or identical gene regulation profile as equivalent amount of calcitriol in normal keratinocytes;

(2) modulates the expression of one or more genes whose expression levels are modulated by an equivalent amount of calcitriol;

(3) modulates the expression of HSPA2 or HSF4 mRNA, HSPB1 or DNAJC6 mRNA in normal keratinocytes;

(4) modulates the expression of SLC1A1, KCNB2, or KCNN4 protein, SLC1A3 protein in normal keratinocytes;

(5) modulates the expression of one or more proteins in Table 3-1 and Table 3-2 by at least about 2-fold;

(6) induces overexpression of one or more proteins in Tables 3-3, 3-4, 3-5 or 3-6 after about 24-hour exposure of normal keratinocytes to said vitamin D compound; or,

(7) induces overexpression in normal keratinocytes of one or more of: GST, Keratin 1, Keratin 17, Galectin 1, S100 A9 (Calprotectin), or S100 A13;

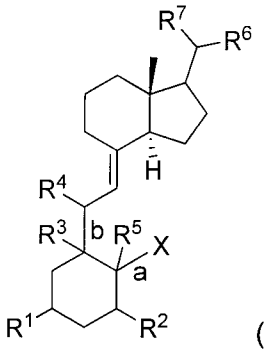
wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

62. A topical pharmaceutical composition comprising a therapeutically effective amount of a vitamin D compound and a carrier, wherein the vitamin D compound is formulated to be delivered to epidermis while substantially avoiding dermis delivery; wherein the carrier comprises propylene glycol and anhydrous absolute ethanol; and wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25:75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

63. The topical pharmaceutical composition of claim 62, wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is about 40:60.

64. A topical pharmaceutical composition comprising a therapeutically effective amount of a vitamin D compound and a carrier, wherein the vitamin D compound is formulated to be delivered to epidermis while substantially avoiding dermis delivery; and wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol^{TM}, and about 60% (w/w) anhydrous absolute ethanol.

65. The topical pharmaceutical composition of any one of claims 62-64, wherein the vitamin D compound is compound is represented by Formula (I):



(I)

wherein

a and b are each independently a single or double bond;

X is $-CH_2$ when a is a double bond, or X is hydrogen or a hydroxyl substituted alkyl when a is a single bond;

R^1 is hydrogen, hydroxyl, alkoxyl, tri-alkyl silyl or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^2 is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^3 is absent when b is a double bond or R^3 is hydrogen, hydroxyl or alkyl, or R^3 and R^1 together with the carbon atoms to which they are attached may be linked to form 5-7 membered carbocyclic ring when b is a single bond;

R^4 is absent when b is a double bond or hydrogen, halogen or hydroxyl when b is a single bond;

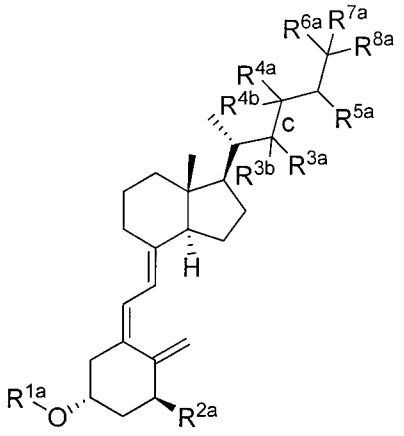
R^5 is absent when a is a double bond or R^5 is hydrogen, halogen or hydroxyl when a is a single bond;

R^6 is alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclicyl, alkyl-O-alkyl, alkyl-CO_2-alkyl optionally substituted with one to five, hydroxyl, oxo, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties;

R^7 is alkyl optionally substituted with one to three hydroxyl, halogen, alkoxyl, aryl, heteroaryl, cyano, nitro or -NR'R" moieties; and,

R' and R" are each, independently, hydrogen, hydroxyl, halogen, alkyl or alkoxyl, and pharmaceutically acceptable salts thereof.

66. The topical pharmaceutical composition of any one of claims 62-64, wherein the vitamin D compound is represented by Formula (II):



(II)

wherein

c is a single or double bond;

R^{1a} is hydrogen or alkyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{2a} is hydrogen, hydroxyl, -O-trialkyl silyl, or alkyl, alkoxyl or alkenyl, optionally substituted with one to three halogen, hydroxyl, cyano or -NR'R" moieties;

R^{3a} and R^{4a} are absent when c is a double bond, or are each independently hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties when c is a single bond; and

R^{3b}, R^{4b}, R^{5a}, R^{6a}, R^{7a} and R^{8a} are each, independently, hydrogen, hydroxyl, halogen, alkoxyl or alkyl optionally substituted with one to three hydroxyl or halogen moieties, or any two of R^{6a}, R^{7a} and R^{8a} may be linked to form a 3-7 membered carbocyclic ring, and pharmaceutically acceptable salts thereof.

67. The topical pharmaceutical composition of any one of claims 62-64, wherein the vitamin D compound is 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α-hydroxyvitamin D3; 1α,24-dihydroxyvitamin D3, or MC 903.

68. The topical pharmaceutical composition of claim 67, wherein the vitamin D compound is 1,25-dihydroxyvitamin D3.

69. The topical pharmaceutical composition of any one of claims 62-66, wherein the vitamin D compound is not 1,25-dihydroxyvitamin D3; 1,25-dihydroxy-16-ene-23-yne-cholecalciferol; 1α,24-dihydroxyvitamin D3, or MC 903.

70. The topical pharmaceutical composition of any one of claims 62-66 and 69, wherein the vitamin D compound exhibits similar or identical gene regulation profile as equivalent amount of calcitriol in normal keratinocytes.

71. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound promotes the expression of one or more genes whose expression levels are promoted by an equivalent amount of calcitriol.

72. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound inhibits the expression of one or more genes whose expression levels are inhibited by an equivalent amount of calcitriol.

73. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound modulates the expression of HSPA2 or HSF4 mRNA, HSPB1 or DNAJC6 mRNA in normal keratinocytes.

74. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound modulates the expression of SLC1A1, KCNB2, oKCNN4 protein or SLC1A3 protein in normal keratinocytes.

75. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound decreases the expression of one or more proteins selected from the group consisting of Crk II, Growth Factor Independence1, Serine Threonine Protein Phosphatase 1b, Cathepsin D, Transforming Growth Factorb pan, WAVE, Protein Tyrosine Phosphatase PEST and CD40 by at least about 2-fold.

76. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound induces overexpression of one or more proteins selected from the group consisting of BACH1, CENPE, cMyc, C-src tryosine kinase (Csk), CtBP1, Dimethyl Histone H3 diMeLys4, Dimethyl Histone H3 diMeLys9, Estrogen Receptor, FKHRL1 FOXO3a, FOXP2,

HDAC2, HDAC6, MAP Kinase Activated Protein Kinase2 MAPKAPK2, MAP Kinase ERK1, Melanocortin3 Receptor, Proliferating Cell Protein Ki67, S100, SHPTP2, Sin3A, ARTS, ASAP1 Centaurin b4, Cofilin, Connexin 32, Dystrophin, Focal Adhesion Kinase pp125FAK, gTubulin, Myosin IX Myr5, Neurofilament 200, p120ctn, PAD14, Par4 Prostate Apoptosis Response 4, ROCK1, Uvomorulin ECadherin, Vitronectin, Bclx, BclxL, BID, Bmf, DcR2, ERK5 BIG MAPKBMK1, Integrin-linked kinase (ILK), Protein Kinase Ba, PUMA bbc3, Amyloid Precursor Protein, Presenilin1, Glutamic Acid Decarboxylase 65, Glutamic Acid Decarboxylase GAD65 67, Nitric Oxide Synthase bNOS, Substance P Receptor, Synaptopodin, Tumor Nerosis Factor a and Ubiquitin Cterminal Hydrolase L1 by at least about 2-fold.

77. The topical pharmaceutical composition of any one of claims 62-66 and 70, wherein the vitamin D compound induces overexpression in normal keratinocytes of one or more of: GST, Keratin 1, Keratin 17, Galectin 1, S100 A9 (Calprotectin), or S100 A13.

78. A topical pharmaceutical composition comprising a therapeutically effective amount of calcitriol and a carrier, formulated to be delivered to epidermis while substantially avoiding dermis delivery, wherein the carrier comprises propylene glycol and anhydrous absolute ethanol; and wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is selected from the group consisting of 20:80; 25:75; 30:70; 35:65; 36:64; 37:63; 38:62; 39:61; 40:60; 41:59; 42:58; 43:57; 44:56; and 45:55.

79. The topical pharmaceutical composition of claim 78, wherein the % (w/w) ratio of propylene glycol to anhydrous absolute ethanol is about 40:60.

80. A topical pharmaceutical composition comprising a therapeutically effective amount of calcitriol and a carrier, wherein the carrier comprises about 40% (w/w) propylene glycol and about 60% (w/w) anhydrous absolute ethanol.

81. A topical pharmaceutical composition comprising a therapeutically effective amount of calcitriol and a carrier, wherein the carrier comprises about 30% (w/w) propylene glycol, about 10% (w/w) ethoxydiglycol or transcutol™, and about 60% (w/w) anhydrous absolute ethanol.

82. The topical pharmaceutical composition of any one of claims 62-80, wherein said calcitriol, when topically administered to the individual at an effective concentration of:

(1) about 50 μg/mL, does not cause toxicity after at least about 25 consecutive days of drug administration; or

(2) about 100 μg/mL, does not cause toxicity after at least about 7 consecutive days of drug administration.

83. The topical pharmaceutical composition of any one of claims 62-81, wherein said therapeutically effective amount of the calcitriol, when co-administered with a chemotherapeutic agent, does not substantially interfere with the efficacy of the chemotherapeutic agent.