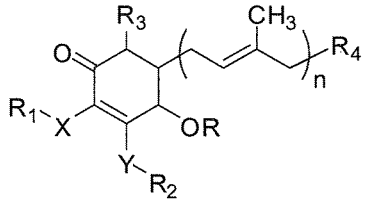
CLAIMS

1. A pharmaceutical composition for use in the treatment of a disease or condition associated with bone metastasis comprising administering to a subject in need thereof a therapeutically effective amount of a compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

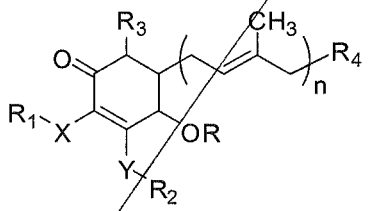
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

2. A pharmaceutical composition for use in the inhibition of hypercalcemia of malignancy in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a cyclohexenone compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

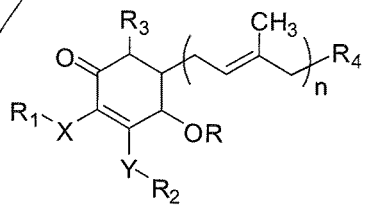
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

3. A pharmaceutical composition for use in the inhibition of bone resorption in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a cyclohexenone compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

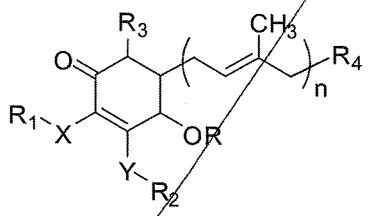
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

4. A pharmaceutical composition for use in the treatment of osteolytic lesions in a subject comprising administering to the subject in need thereof a therapeutically effective amount of a cyclohexenone compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

5. The composition of any of claims 1-4, wherein the subject has breast cancer or prostate cancer.

6. The composition of any one of claims 1-5, wherein R is a hydrogen, $C(=O)C_3H_8$, $C(=O)C_2H_5$, or $C(=O)CH_3$.

7. The composition of any one of claims 1-6, wherein each of R_1, R_2 and R_3 independently is a hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, or octyl.

8. The composition of any one of claims 7, wherein R_1 is a hydrogen or methyl.

9. The composition of any one of claims 1-8, wherein R_2 is a hydrogen or methyl.

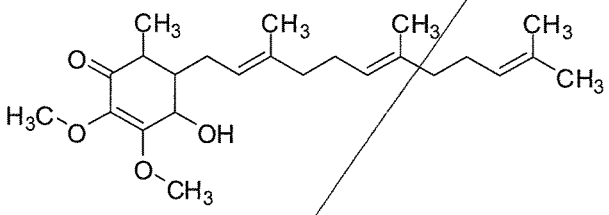
10. The composition of any one of claims 1-9, wherein R_4 is halogen, NH_2, $NHCH_3$, $N(CH_3)_2$, OCH_3, OC_2H_5, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, $C(=O)NHCH_3$, $C(=O)NHC_2H_5$, $C(=O)NH_2$, $OC(=O)CH_3$, $OC(=O)C_2H_5$, $OC(=O)OCH_3$, $OC(=O)OC_2H_5$, $OC(=O)NHCH_3$, $OC(=O)NHC_2H_5$, or $OC(=O)NH_2$.

11. The composition of any one of claims 1-9, wherein R_4 is $C_2H_5C(CH_3)_2OH$, $C_2H_5C(CH_3)_2OCH_3$, CH_2COOH, C_2H_5COOH, CH_2OH, C_2H_5OH, CH_2Ph, C_2H_5Ph, $CH_2CH=C(CH_3)(CHO)$, $CH_2CH=C(CH_3)(C(=O)CH_3)$, 5 or 6-membered lactone, aryl, or glucosyl, wherein 5 or 6-membered lactone, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

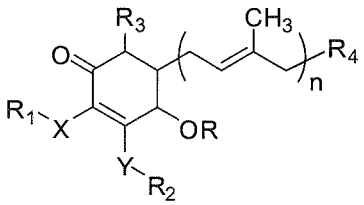
12. The composition of claim 11, wherein R_4 is C_1-C_8alkyl optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

13. The composition of claim 12, wherein R_4 is $CH_2CH=C(CH_3)_2$.

14. The composition of any one of claims 1-5, wherein said compound is



15. Use of a pharmaceutical composition in the manufacture of a medicament for treating a disease or condition associated with bone metastasis wherein said medicament comprises a therapeutically effective amount of a compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

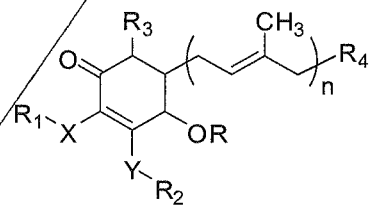
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

16. Use of a pharmaceutical composition in the manufacture of a medicament for inhibition of hypercalcemia of malignancy in a subject wherein said medicament comprises a therapeutically effective amount of a cyclohexenone compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

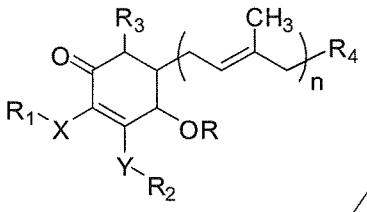
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

17. Use of a pharmaceutical composition in the manufacture of a medicament for inhibition of bone resorption in a subject wherein said medicament comprises a therapeutically effective amount of a cyclohexenone compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

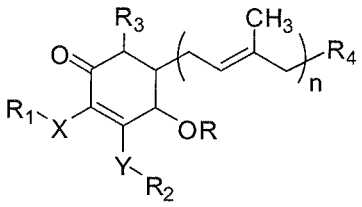
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

18. Use of a pharmaceutical composition in the manufacture of a medicament for treatment of osteolytic lesions in a subject wherein said medicament comprises a therapeutically effective amount of a cyclohexenone compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m = 1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

19. The use of any of claims 15-18, wherein the subject has breast cancer or prostate cancer.

20. The use of any one of claims 15-19, wherein R is a hydrogen, $C(=O)C_3H_8$, $C(=O)C_2H_5$, or $C(=O)CH_3$.

21. The use of any one of claims 15-20, wherein each of R_1, R_2 and R_3 independently is a hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, or octyl.

22. The use of claim 21, wherein R_1 is a hydrogen or methyl.

23. The composition of any one of claims 15-22, wherein R_2 is a hydrogen or methyl.

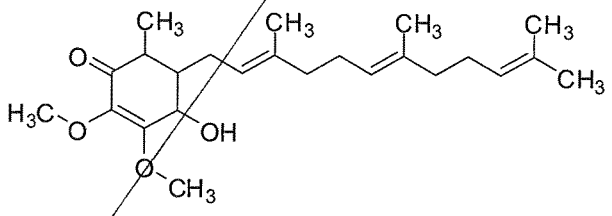
24. The composition of any one of claims 15-23, wherein R_4 is halogen, NH_2, $NHCH_3$, $N(CH_3)_2$, OCH_3, OC_2H_5, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, $C(=O)NHCH_3$, $C(=O)NHC_2H_5$, $C(=O)NH_2$, $OC(=O)CH_3$, $OC(=O)C_2H_5$, $OC(=O)OCH_3$, $OC(=O)OC_2H_5$, $OC(=O)NHCH_3$, $OC(=O)NHC_2H_5$, or $OC(=O)NH_2$.

25. The composition of any one of claims 15-23, wherein R_4 is $C_2H_5C(CH_3)_2OH$, $C_2H_5C(CH_3)_2OCH_3$, CH_2COOH, C_2H_5COOH, CH_2OH, C_2H_5OH, CH_2Ph, C_2H_5Ph, $CH_2CH=C(CH_3)(CHO)$, $CH_2CH=C(CH_3)(C(=O)CH_3)$, 5 or 6-membered lactone, aryl, or glucosyl, wherein 5 or 6-membered lactone, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

26. The composition of claim 25, wherein R_4 is C_1-C_8alkyl optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

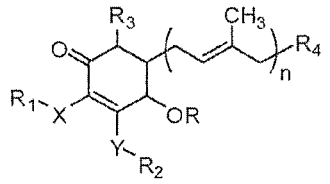
27. The composition of claim 26, wherein R_4 is $CH_2CH=C(CH_3)_2$.

28. The composition of any one of claims 15-19, wherein said compound is



CLAIMS

1. Use of a pharmaceutical composition in the manufacture of a medicament for treating a disease or condition associated with bone metastasis in a subject, wherein said medicament comprises a therapeutically effective amount



of a compound having the structure:

wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein the 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

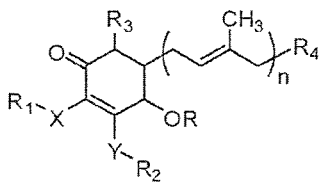
each of R_5 and R_6 is independently a hydrogen or C_1-C_8alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m=1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

2. Use of a pharmaceutical composition in the manufacture of a medicament for inhibiting hypercalcemia of malignancy, or inhibiting bone resorption, or treating osteolytic lesions in a subject, wherein said medicament comprises a therapeutically effective amount of a compound having the structure:



wherein each of X and Y independently is oxygen, NR_5 or sulfur;

R is a hydrogen or $C(=O)C_1$-C_8alkyl;

each of R_1, R_2 and R_3 independently is a hydrogen, methyl or $(CH_2)_m$—CH_3;

R_4 is NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, halogen, 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, glucosyl, wherein the 5 or 6-membered lactone, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, aryl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl;

each of R_5 and R_6 is independently a hydrogen or C_1-C_8 alkyl;

R_7 is a C_1-C_8alkyl, OR_5 or NR_5R_6;

m=1-12; and

n=1-12; or a pharmaceutically acceptable salt, metabolite, solvate or prodrug thereof.

3. The use of claim 1, wherein the subject has breast cancer or prostate cancer.

4. The use of claim 2, wherein the subject has breast cancer or prostate cancer.

5. The use claim 1, wherein R is a hydrogen, $C(=O)C_3H_8$, $C(=O)C_2H_5$, or $C(=O)CH_3$.

6. The use claim 2, wherein R is a hydrogen, $C(=O)C_3H_8$, $C(=O)C_2H_5$, or $C(=O)CH_3$.

7. The use of claim 1, wherein each of R_1, R_2 and R_3 independently is a hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, or octyl.

8. The use of claim 2, wherein each of R_1, R_2 and R_3 independently is a hydrogen, methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, or octyl.

9. The use of claim 1, wherein R_4 is halogen, NH_2, $NHCH_3$, $N(CH_3)_2$, OCH_3, OC_2H_5, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, $C(=O)NHCH_3$, $C(=O)NHC_2H_5$, $C(=O)NH_2$, $OC(=O)CH_3$, $OC(=O)C_2H_5$, $OC(=O)OCH_3$, $OC(=O)OC_2H_5$, $OC(=O)NHCH_3$, $OC(=O)NHC_2H_5$, or $OC(=O)NH_2$.

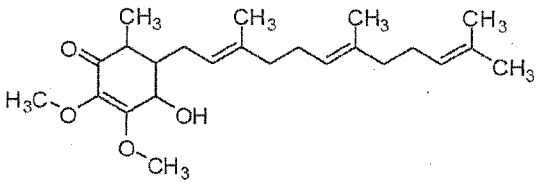
10. The method of claim 1, wherein R_4 is $C_2H_5C(CH_3)_2OH$, $C_2H_5C(CH_3)_2OCH_3$, CH_2COOH, C_2H_5COOH, CH_2OH, C_2H_5OH, CH_2Ph, C_2H_5Ph, $CH_2CH=C(CH_3)(CHO)$,

$CH_2CH=C(CH_3)(C(=O)CH_3)$, 5 or 6-membered lactone, aryl, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, or glucosyl, wherein the 5 or 6-membered lactone, aryl, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

11. The use of claim 10, wherein R_4 is C_1-C_8alkyl optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

12. The use of claim 11, wherein R_4 is $CH_2CH=C(CH_3)_2$.

13. The use of claim 1, wherein said compound is



14. The use of claim 1, wherein said subject is human.

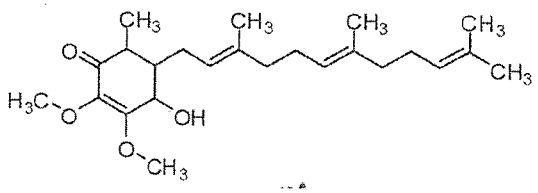
15. The use of claim 2, wherein R_4 is halogen, NH_2, $NHCH_3$, $N(CH_3)_2$, OCH_3, OC_2H_5, $C(=O)CH_3$, $C(=O)C_2H_5$, $C(=O)OCH_3$, $C(=O)OC_2H_5$, $C(=O)NHCH_3$, $C(=O)NHC_2H_5$, $C(=O)NH_2$, $OC(=O)CH_3$, $OC(=O)C_2H_5$, $OC(=O)OCH_3$, $OC(=O)OC_2H_5$, $OC(=O)NHCH_3$, $OC(=O)NHC_2H_5$, or $OC(=O)NH_2$.

16. The use of claim 2, wherein R_4 is $C_2H_5C(CH_3)_2OH$, $C_2H_5C(CH_3)_2OCH_3$, CH_2COOH, C_2H_5COOH, CH_2OH, C_2H_5OH, CH_2Ph, C_2H_5Ph, $CH_2CH=C(CH_3)(CHO)$, $CH_2CH=C(CH_3)(C(=O)CH_3)$, 5 or 6-membered lactone, aryl, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, or glucosyl, wherein the 5 or 6-membered lactone, aryl, C_1-C_8alkyl, C_2-C_8alkenyl, C_2-C_8alkynyl, and glucosyl are optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

17. The use of claim 16, wherein R_4 is C_1-C_8alkyl optionally substituted with one or more substituents selected from NR_5R_6, OR_5, $OC(=O)R_7$, $C(=O)OR_5$, $C(=O)R_5$, $C(=O)NR_5R_6$, C_1-C_8 alkyl, C_2-C_8 alkenyl, C_2-C_8 alkynyl, C_3-C_8 cycloalkyl, and C_1-C_8 haloalkyl.

18. The use of claim 17, wherein R_4 is $CH_2CH=C(CH_3)_2$.

19. The use of claim 2, wherein said compound is



20. The use of claim 2, wherein said subject is human.