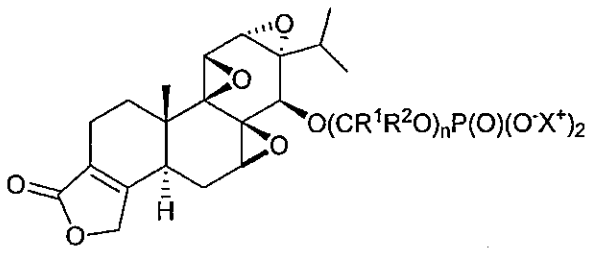
CLAIMS

What is claimed is:

1. A compound of formula I:



I

wherein:

each R^1 is independently H, $(C_1\text{-}C_6)$alkyl, aryl$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl or aryl; and each R^2 is independently H, $(C_1\text{-}C_6)$alkyl, aryl$(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl or aryl; or R^1 and R^2 together with the atom to which they are attached form a $(C_3\text{-}C_7)$cycloalkyl; wherein any alkyl or cycloalkyl of R^1 or R^2 may be optionally substituted with one or more groups selected from halo, $(C_1\text{-}C_6)$alkoxy and NR^aR^b and wherein any aryl of R^1 or R^2 may be optionally substituted with one or more groups selected from halo, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, NR^aR^b, nitro and cyano;

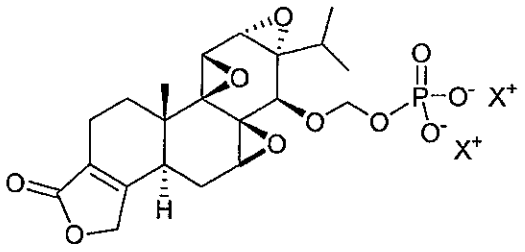
R^a and R^b are each independently selected from H, $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_6)$cycloalkyl and aryl; or R^a and R^b together with the nitrogen to which they are attached form a pyrrolidino, piperidino, piperazino, azetidino, morpholino, or thiomorpholino;

n is 1, 2 or 3; and

each X is H;

or a salt thereof.

2. A compound of claim 1 which is a compound of formula Ia:



Ia

wherein X^+ is a pharmaceutically acceptable organic cation or inorganic cation.

3. The compound of claim 1wherein R^1 is H or $(C_1$-$C_6)$alkyl.

4. The compound of claim 1wherein R^1 is H.

5. The compound of claim 1wherein R^1 is $(C_1$-$C_6)$alkyl.

6. The compound of claim 1wherein R^1 is methyl or ethyl.

7. The compound of claim 1or any one of claims 2-6 wherein R^2 is H or $(C_1$-$C_6)$alkyl.

8. The compound of claim 1or any one of claims 2-6 wherein R^2 is H.

9. The compound of claim 1or any one of claims 2-8 wherein each X^+ is H.

10. The compound of claim 1or any one of claims 2-8 wherein each X^+ is lithium, sodium, potassium, magnesium, calcium, barium, zinc or aluminium.

11. The compound of claim 1or any one of claims 2-8 wherein each X^+ is of the formula HY^+ wherein Y is ammonia, triethylamine, tromethamine, triethanolamine, ethylenediamine, glucamine, N-methylglucamine, glycine, lysine, ornithine, arginine, ethanolamine or choline.

12. The compound of any one of claims 1-8 wherein X^+ is selected from Li^+, K^+ and Na^+.

13. The compound of any one of claims 1-8 wherein each X^+ is Na^+.

14. The compound 14-O-phosphonooxymethyltriptolide disodium salt, 14-O-phosphonooxyethyltriptolide disodium salt or 14-O-phosphonooxypropyltriptolide disodium salt.

15. The compound 14-O-phosphonooxymethyltriptolide disodium salt.

16. A pharmaceutical composition comprising a compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

17. A compound of formula I as described in as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof for use in medical therapy.

18. A method for treating cancer in a mammal, comprising administering a compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof, to the mammal.

19. The method of claim 18 wherein the cancer is selected from pancreatic cancer, bile duct carcinoma, neuroblastoma, colon cancer, breast cancer, myeloma, gastric cancer, liver cancer, glioblastoma, ovarian cancer, colorectal cancer, non-Hodgkin lymphoma, lung cancer, prostate cancer, small-cell lung cancer, large cell lung cancer, kidney cancer, esophageal cancer, stomach cancer, cervical cancer or lymphoma tumors.

20. The method of claim 18 wherein the cancer is pancreatic cancer or neuroblastoma.

21. A compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof for use in the prophylactic or therapeutic treatment of cancer.

22. The use of a compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the treatment of cancer.

23. The use of claim 21 or claim 22 wherein the cancer is selected from pancreatic cancer, bile duct carcinoma, neuroblastoma, colon cancer, breast cancer, myeloma, gastric cancer, liver cancer, glioblastoma, ovarian cancer, colorectal cancer, non-Hodgkin lymphoma, lung cancer, prostate cancer, small-cell lung cancer, large cell lung cancer, kidney cancer, esophageal cancer, stomach cancer, cervical cancer and lymphoma tumors.

24. The use of claim 21 or claim 22 wherein the cancer is pancreatic cancer or neuroblastoma.

25. A method for inhibiting cancer cell growth in HSP70-expressing cancer in a mammal comprising administering an inhibitory effective amount of a compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof, to the mammal.

26. The method of claim 25 wherein the HSP70-expressing cancer is pancreatic cancer, breast cancer, colon cancer, gastric cancer, liver cancer, neuroblastoma or glioblastoma.

27. The method of claim 25 wherein the HSP70-expressing cancer is neuroblastoma or pancreatic cancer.

28. A compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof for use in the prophylactic or therapeutic inhibition of cancer cell growth in HSP70-expressing cancer.

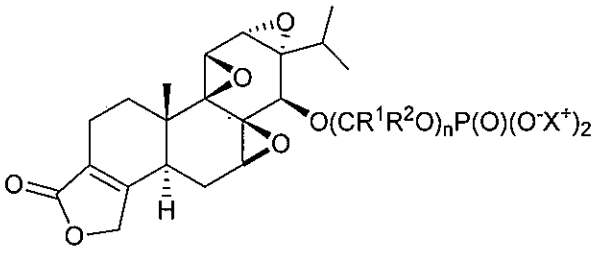
29. The use of a compound of formula I as described in any one of claims 1-15, or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for the inhibition of cancer cell growth in an HSP70-expressing cancer.

30. The use of claim 28 or claim 29 wherein the HSP70-expressing cancer is pancreatic cancer, breast cancer, colon cancer, gastric cancer, liver cancer, neuroblastoma or glioblastoma.

31. The use of claim 28 or claim 29 wherein the HSP70-expressing cancer is neuroblastoma or pancreatic cancer.

Claims

1. A compound of formula I:



I

wherein:

each R^1 is independently H, (C_1-C_6)alkyl, aryl(C_1-C_6)alkyl-, (C_3-C_6)cycloalkyl or aryl; and each R^2 is independently H, (C_1-C_6)alkyl, aryl(C_1-C_6)alkyl-, (C_3-C_6)cycloalkyl or aryl; or R^1 and R^2 together with the atom to which they are attached form a (C_3-C_7)cycloalkyl; wherein any alkyl or cycloalkyl of R^1 or R^2 may be optionally substituted with one or more groups selected from halo, (C_1-C_6)alkoxy and NR^aR^b and wherein any aryl of R^1 or R^2 may be optionally substituted with one or more groups selected from halo, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, NR^aR^b, nitro and cyano;

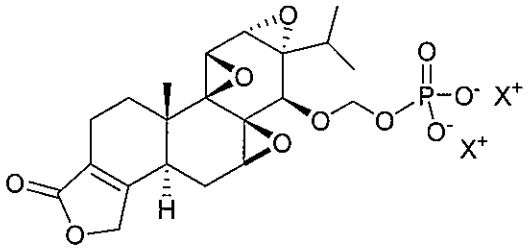
R^a and R^b are each independently selected from H, (C_1-C_6)alkyl, (C_3-C_6)cycloalkyl and aryl; or R^a and R^b together with the nitrogen to which they are attached form a pyrrolidino, piperidino, piperazino, azetidino, morpholino, or thiomorpholino;

n is 1, 2 or 3; and

each X is H;

or a salt thereof.

2. A compound of claim 1 which is a compound of formula Ia:



Ia

wherein X^+ is a pharmaceutically acceptable organic cation or inorganic cation.

3. The compound of claim 1 wherein R^1 is H or $(C_1\text{-}C_6)$alkyl.

4. The compound of claim 1 wherein R^1 is H.

5. The compound of claim 1 wherein R^1 is $(C_1\text{-}C_6)$alkyl.

6. The compound of claim 1 wherein R^1 is methyl or ethyl

7. The compound of claim 1wherein R^2 is H or $(C_1\text{-}C_6)$alkyl.

8. The compound of claim 1wherein R^2 is H.

9. The compound of claim 1wherein each X^+ is H.

10. The compound of claim 1 wherein each X^+ is lithium, sodium, potassium, magnesium, calcium, barium, zinc or aluminium.

11. The compound of claim 1 wherein each X^+ is of the formula HY^+ wherein Y is ammonia, triethylamine, tromethamine, triethanolamine, ethylenediamine, glucamine, N-methylglucamine, glycine, lysine, ornithine, arginine, ethanolamine or choline.

12. The compound of claim 1 wherein X^+ is selected from Li^+, K^+ and Na^+.

13. The compound of claim 1 wherein each X^+ is Na^+.

14. The compound of claim 1 which is 14-O-phosphonooxymethyltriptolide disodium salt, 14-O-phosphonooxyethyltriptolide disodium salt or 14-O-phosphonooxypropyltriptolide disodium salt.

15. The compound of claim 1 which is 14-O-phosphonooxy-methyltriptolide disodium salt.

16. A pharmaceutical composition comprising a compound of formula I as described in claim 1, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.