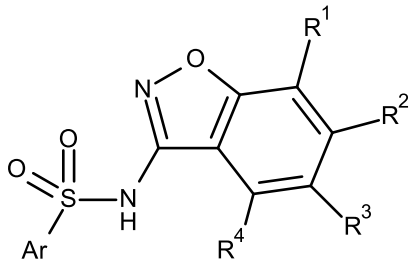
Claims

1. A compound of formula (I)~~, or a pharmaceutically acceptable salt thereof, for use in a method of therapy~~:



(I)

or a pharmaceutically acceptable salt thereof, wherein:

R^1, R^2, R^3 and R^4 are independently selected from:

(i) H;

(ii) C_{1-3} alkyl, optionally substituted by:

hydroxy,

C_{1-2} alkoxy, ~~optionally substituted by one or more fluoro groups,~~

NH_2,

phenyl,

C_{5-6} heteroaryl,

C_{1-4} alkyl carbamoyl, or

acylamido~~, or~~

~~one or more fluoro groups~~;

(iii) C_{1-3} alkoxy, optionally substituted by C_{3-6} cycloalkyl or by one or more fluoro groups;

(iv) C_{3-6} cycloalkyl;

(v) halo;

(vi) COR^C, where R^C is selected from $NR^{N1}R^{N2}$, where R^{N1} and R^{N2} are independently selected from H and methyl;

(vii) cyano, NH_2, or NO_2; and

(viii) phenyl or C_{5-6} heteroaryl, optionally substituted by methyl, ~~cyano,~~ hydroxy or methoxy;

Ar is a phenyl, ~~napthyl or C_{5-10} heteroaryl group, which groups are~~ optionally substituted by one or more groups selected from:

(i) C_{1-4} alkyl, optionally substituted by hydroxy, C_{1-2} alkoxy, NH_2, C_{1-4} alkyl carbamoyl, or by one or more fluoro groups;

(ii) C_{3-6} cycloalkyl;

(iii) hydroxy; cyano; $NR^{N3}R^{N4}$, where R^{N3} and R^{N4} are independently selected from H and methyl; or acylamido;

(iv) halo;

(v) C_{1-3} alkoxy, optionally substituted by hydroxy, $C(O)NH_2$, C_{3-6} cycloalkyl, phenyl, C_{5-6} heteroaryl, or by one or more fluoro groups;

(vi) phenoxy, optionally substituted by fluoro;

(vii) phenyl or C_{5-6} heteroaryl; or

(viii) SF_5 or SO_2CH_3;

~~**(ix)** $-(CH_2)_n-Y-$, where Y is O or CH_2, and n is 2 or 3; or~~

~~**(x)** C_{1-4} alkyl ester~~.

~~2. The compound or salt for use according to claim 1,~~ and wherein at least one of R^1, R^2, R^3 and R^4 is not H.

2. ~~3.~~ The compound or salt ~~for use~~ according to ~~either~~ claim 1 ~~or claim 2~~, wherein at least one of R^1, R^2, R^3 and R^4 is C_{1-3} alkyl, optionally substituted by:

hydroxy,

C_{1-2} alkoxy~~, optionally substituted by one or more fluoro groups~~,

NH_2,

phenyl,

C_{5-6} heteroaryl,

C_{1-4} alkyl carbamoyl, or

acylamido~~, or~~

~~one or more fluoro groups~~.

3. ~~4.~~ The compound or salt ~~for use~~ according to any one of claims 1 to 2 ~~claims 1 to 3~~, wherein at least one of R^1, R^2, R^3 and R^4 is C_{1-3} alkoxy, optionally substituted by C_{3-6} cycloalkyl or one or ~~of~~ more fluoro groups.

4. ~~5.~~ The compound or salt ~~for use~~ according to any one of claims 1 to 3 ~~claims 1 to 4~~, wherein at least one of R^1, R^2, R^3 and R^4 is

(a) C_{3-6} cycloalkyl;

(b)

~~6. The compound or salt for use according to any one of claims 1 to 5, wherein at least one of R^1, R^2, R^3 and R^4 is halo;~~

~~7. The compound or salt for use according to any one of claims 1 to 6, wherein at least one of R^1, R^2, R^3 and R^4 is COR^C, where R^C is selected from $NR^{N1}R^{N2}$, where R^{N1} and R^{N2} are independently selected from H and methyl;~~

(c)

~~8. The compound or salt for use according to any one of claims 1 to 7, wherein at least one of R^1, R^2, R^3 and R^4 is cyano, NH_2 or NO_2;~~ ; or

(d)

~~9. The compound or salt for use according to any one of claims 1 to 8, wherein at least one of R^1, R^2, R^3 and R^4 is~~ phenyl or C_{5-6} heteroaryl, optionally substituted by methyl, cyano, hydroxy or methoxy.

5. ~~10.~~ The compound or salt ~~for use~~ according to claim 1, wherein:

(a) R^4 is methoxy, R^2 is CH_2OCH_3 or $CH_2OCH_2CH_3$, and R^1 and R^3 are H;

(b) R^4 is methoxy, R^2 is phenyl, optionally substituted by methyl or methoxy, and R^1 and R^3 are H;

(c) R^4 is methoxy, R^2 is C_{5-6} heteroaryl, optionally substituted by methyl;

(d) R^4 is methoxy and R^1, R^2 and R^3 are H;

(e) R^4 is chloro, R^2 is C_{1-3} alkyl or bromo, and R^1 and R^3 are H;

(f) R^4 is chloro and R^1, R^2 and R^4 are H; or

(g) R^3 is C_{1-3} alkyl and R^1, R^2 and R^4 are H.

~~11. The compound or salt for use according to any one of claims 1 to 10, wherein Ar is:~~

~~(a) phenyl, which may be optionally substituted;~~

~~(b) napthyl, which may be optionally substituted; or~~

~~(c) a C_{5-10} heteroaryl group, which may be optionally substituted.~~

6. ~~12.~~ The compound or salt ~~for use~~ according to any one of claims 1 to 5 ~~claim 11~~, wherein Ar is substituted by C_{1-4} alkyl, optionally substituted by hydroxy, C_{1-2} alkoxy, NH_2, C_{1-4} alkyl carbamoyl, or one or more fluoro groups.

7. The compound or salt according to any one of claims 1 to 5, wherein Ar is substituted by C_{1-3} alkoxy, optionally substituted by hydroxy, $C(O)NH_2$, C_{3-6} cycloalkyl, phenyl, C_{5-6} heteroaryl, or one of more fluoro groups.

8. ~~13.~~ The compound or salt ~~for use~~ according to any one of claims 1 to 5 ~~claim 11~~, wherein Ar is substituted by

(a) C_{3-6} cycloalkyl~~.~~;

(b)

~~14. The compound or salt for use according to claim 11, wherein Ar is substituted by~~ hydroxy;

(c) cyano;

(d) $NR^{N3}R^{N4}$, where R^{N3} and R^{N4} are independently selected from H and methyl; or acylamido~~.~~;(e)

~~15. The compound or salt for use according to claim 11, wherein Ar is substituted by halo.~~

~~16. The compound or salt for use according to claim 11, wherein Ar is substituted by C_{1-3} alkoxy, optionally substituted by hydroxy, $C(O)NH_2$, C_{3-6} cycloalkyl, phenyl, C_{5-6} heteroaryl, or one of more fluoro groups.~~

~~17. The compound or salt for use according to claim 11, wherein Ar is substituted by~~ phenoxy, optionally substituted by fluoro~~.~~;

(f)

~~18. The compound or salt for use according to claim 11, wherein Ar is substituted by~~ phenyl or C_{5-6} heteroaryl~~.~~ ; or

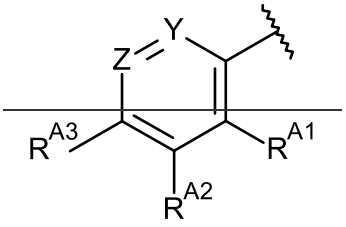
(g)

~~19. The compound or salt for use according to claim 11, wherein Ar is substituted by~~ SF_5 or SO_2CH_3.

~~20. The compound or salt for use according to claim 11, wherein Ar is substituted by -$(CH_2)_n$-Y-, where Y is O or CH_2, and n is 2 or 3.~~

~~21. The compound or salt for use according to claim 11, wherein Ar is substituted by C_{1-4} alkyl ester.~~

~~22. The compound or salt for use according to any one of claims 1 to 10, wherein Ar is represented by the formula (Ar-1):~~



~~(Ar-1)~~

~~where Y is either N or C-R^{A4}, and Z is either N or C-R^{A5}; and R^{A1}, R^{A2}, R^{A3}, R^{A4} (if present) and R^{A5} (if present) are independently selected from H and the optional substituents for Ar.~~

~~23. The compound or salt for use according to claim 22, wherein:~~

~~(a) R^{A2} is ethyl; or~~

~~(b) R^{A3} is selected from cycloalkyl; phenoxy; phenyl; C_{5-6} heteroaryl; SF_5; and SO_2CH_3.~~

9. ~~24.~~ The compound or salt ~~for use~~ according to any one of claims 1 to 5 ~~claims 1 to 10~~, wherein Ar is:

(a) 5-ethyl-2-methoxyphenyl;

(b) 5-CF_3-2-methoxyphenyl; or

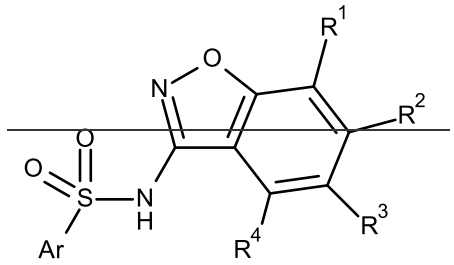
(c) 2,6-dimethoxyphenyl.

~~25. The compound or salt for use according to claim 1, with the proviso that when:~~

~~R^1, R^2, R^3 and R^4 are H,~~

~~Ar is not 4-aminophenyl.~~

~~26. A compound of formula (I), or a pharmaceutical salt thereof:~~



~~(I),~~

~~wherein R^1, R^2, R^3, R^4 and Ar are as defined in any one of claim 1 to 25.~~

~~27. A compound according to claim 26, wherein:~~

~~(a) at least one of R^1, R^2, R^3 and R^4 is not H;~~

~~(b) R^3 is not CF_3;~~

~~(c) R^3 is not substituted C_{1-3} alkyl;~~

~~(d) R^3 is ethyl or propyl;~~

~~(e) R^3 is not C_{1-3} alkyl, optionally substituted by hydroxy, C_{1-2} alkoxy, NH_2, phenyl, C_{5-6} heteroaryl, C_{1-4} alkyl carbamoyl, acylamido or by one or more fluoro groups;~~

~~(f) R^4 is methoxy;~~

~~(g) R^4 is Cl, and R^1, R^2 and R^3 are H;~~

~~(h) R^4 is Cl, and R^2 is C_{1-3} alkyl or bromo, and R^1 and R^3 are H; or~~

~~(i) R^3 is C_{1-3} alkyl and R^1, R^2 and R^4 are H.~~

~~28. A compound according to claim 26, with the proviso that when:~~

~~(a) R^1, R^2 and R^3 are H, and R^4 is methoxy,~~

~~Ar is not unsubstituted napthyl;~~

~~(b) R^1, R^2, R^3 and R^4 are H,~~

~~Ar is not 2,4,6-trimethylphenyl;~~

~~(c) R^1, R^2 and R^4 are H, and R^3 is CF_3,~~

~~Ar is not 2-(difluromethoxy)phenyl;~~

~~(d) R^1, R^2, R^3 and R^4 are H,~~

~~Ar is not 4-fluoro-3-methyl-phenyl; or~~

~~(e) R^1, R^2, R^3 and R^4 are H,~~

~~Ar is not 4-aminophenyl.~~

10. A pharmaceutical composition comprising a compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

11. A compound or salt according to any one of claims 1 to 9, for use in a method of therapy.

12. A compound or salt according to any one of claims 1 to 9, for use in the treatment of cancer.

13. A compound or salt for use according to claim 12, wherein the cancer is selected from leukemia, acute lymphocytic leukemia, acute myeloid leukemia, chronic lymphocytic leukemia, chronic myeloid leukemia, non-Hodgkin’s leukemia, Hodgkin’s disease, prostate cancer, lung cancer, melanoma, breast cancer, colon and rectal cancer, colon cancer, squamous cell carcinoma and gastric cancer.

14. A compound or salt for use according to claim 12, wherein the compound is administered simultaneously or sequentially with radiotherapy and / or chemotherapy.