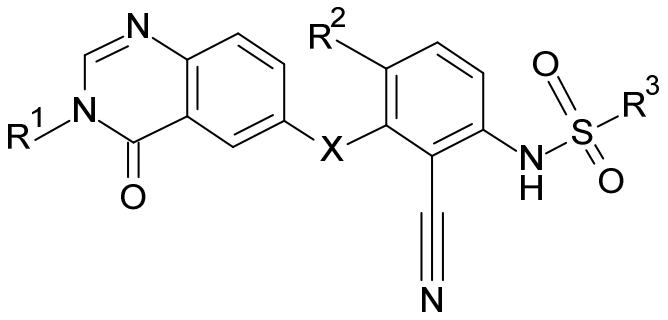
Claims

1. A compound of formula (I)



(I)

wherein

R^1 is C_{1-6}-alkyl;

X is selected from

i) -NH-, and

ii) -O-;

R^2 is selected from

iii) H,

iv) cyano, and

v) halogen;

R^3 is selected from

vi) NR^4R^5, and

vii) CHR^6R^7;

R^4 is selected from

viii) C_{1-6}-alkyl,

ix) C_{3-8}-cycloalkyl, and

x) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

R^5 is selected from

xi) C_{1-6}-alkyl,

xii) C_{3-8}-cycloalkyl, and

xiii) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

or R^4 and R^5 together with the nitrogen atom to which they are attached form an heterocycloalkyl optionally substituted with R^8, wherein the heterocycloalkyl is selected from pyrrolidinyl and piperidinyl;

R^6 is selected from

xiv) C_{1-6}-alkyl,

xv) C_{3-8}-cycloalkyl, and

xvi) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

R^7 is selected from

xvii) C_{1-6}-alkyl,

xviii) C_{3-8}-cycloalkyl, and

xix) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

or R^6 and R^7 together with the carbon atom to which they are attached form a C_{3-8}-cycloalkyl optionally substituted with R^8;

R^8 is halogen;

with the proviso that N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]-3-fluoro-pyrrolidine-1-sulfonamide is excluded

or a pharmaceutically acceptable salt thereof.

2. A compound according to claim 1, wherein

R^1 is C_{1-6}-alkyl;

X is selected from

i) -NH-, and

ii) -O-;

R^2 is selected from

iii) H, and

iv) halogen;

R^3 is selected from

v) NR^4R^5, and

vi) CHR^6R^7;

R^4 is selected from

vii) C_{1-6}-alkyl,

viii) C_{3-8}-cycloalkyl, and

ix) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

R^5 is selected from

x) C_{1-6}-alkyl,

xi) C_{3-8}-cycloalkyl, and

xii) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

or R^4 and R^5 together with the nitrogen atom to which they are attached form an heterocycloalkyl optionally substituted with R^8, wherein the heterocycloalkyl is selected from pyrrolidinyl and piperidinyl;

R^6 is selected from

xiii) C_{1-6}-alkyl,

xiv) C_{3-8}-cycloalkyl, and

xv) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

R^7 is selected from

xvi) C_{1-6}-alkyl,

xvii) C_{3-8}-cycloalkyl, and

xviii) C_{3-8}-cycloalkyl-C_{1-6}-alkyl;

or R^6 and R^7 together with the carbon atom to which they are attached form a cyclopentyl or a cyclohexyl ring optionally substituted with R^8;

R^8 is halogen;

with the proviso that (3R)-N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]-3-fluoro-pyrrolidine-1-sulfonamide is excluded

or a pharmaceutically acceptable salt thereof.

3. A compound according to claim 1 or 2, wherein

R^1 is methyl;

X is selected from

i) -NH-, and

ii) -O-;

R^2 is selected from

iii) H,

iv) chloro, and

v) fluoro;

R^3 is selected from

vi) NR^4R^5, and

vii) CHR^6R^7;

R^4 is selected from

viii) methyl,

ix) ethyl,

x) propyl,

xi) cyclopropyl, and

xii) cyclopropylmethyl;

R^5 is selected from

xiii) methyl,

xiv) ethyl,

xv) propyl,

xvi) cyclopropyl, and

xvii) cyclopropylmethyl;

or R^4 and R^5 together with the nitrogen atom to which they are attached form an heterocycloalkyl optionally substituted with R^8, wherein the heterocycloalkyl is selected from pyrrolidinyl and piperidinyl;

R^6 is selected from

xviii) methyl,

xix) ethyl,

xx) propyl,

xxi) cyclopropyl, and

xxii) cyclopropylmethyl;

R^7 is selected from

xxiii) methyl,

xxiv) ethyl,

xxv) propyl,

xxvi) cyclopropyl, and

xxvii) cyclopropylmethyl;

or R^6 and R^7 together with the carbon atom to which they are attached form a cyclopentyl or a cyclohexyl ring optionally substituted with R^8;

R^8 is fluoro;

with the proviso that (3R)-N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]-3-fluoro-pyrrolidine-1-sulfonamide is excluded

or a pharmaceutically acceptable salt thereof.

4. A compound according to any one of claims 1 to 3, wherein R^2 is selected from

i) H,

ii) chloro, and

iii) fluoro.

5. A compound according to any one of claims 1 to 4, wherein R^4 is methyl.

6. A compound according to any one of claims 1 to 5, wherein R^5 is ethyl.

7. A compound according to any one of claims 1 to 6, wherein R^4 and R^5 together with the nitrogen atom to which they are attached form an heterocycloalkyl optionally substituted with R^8, wherein the heterocycloalkyl is selected from pyrrolidinyl and piperidinyl.

8. A compound according to any one of claims 1 to 7, wherein R^4 and R^5 together with the nitrogen atom to which they are attached form an unsubstituted heterocycloalkyl, wherein the heterocycloalkyl is pyrrolidinyl.

9. A compound according to any one of claims 1 to 8, wherein R^6 and R^7 are independently selected from

i) methyl,

ii) ethyl,

iii) propyl,

iv) cyclopropyl, and

v) cyclopropylmethyl.

10. A compound according to any one of claims 1 to 9, wherein R^6 and R^7 together with the nitrogen atom to which they are attached form a cyclopentyl or a cyclohexyl ring.

11. A compound according to any one of claims 1 to 10, wherein R^8 is fluoro.

12. A compound according to any one of claims 1 to 11, wherein the compound is selected from

6-[2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]-6-fluoro-phenoxy]-3-methyl-4-oxo-quinazoline;

6-[6-chloro-2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]phenoxy]-3-methyl-4-oxo-quinazoline;

(3R)-N-[4-chloro-2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]-3-fluoro-pyrrolidine-1-sulfonamide;

N-[4-chloro-2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]pyrrolidine-1-sulfonamide;

6-[2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]phenoxy]-3-methyl-4-oxo-quinazoline;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]pyrrolidine-1-sulfonamide;

(3R)-N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]-3-fluoro-pyrrolidine-1-sulfonamide;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]cyclopentanesulfonamide;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]cyclohexanesulfonamide;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]butane-2-sulfonamide;

6-[2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]anilino]-3-methyl-4-oxo-quinazoline;

(3R)-N-[2-cyano-3-[(3-methyl-4-oxo-quinazolin-6-yl)amino]phenyl]-3-fluoro-pyrrolidine-1-sulfonamide;

6-[6-chloro-2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]anilino]-3-methyl-4-oxo-quinazoline;

N-[4-chloro-2-cyano-3-[(3-methyl-4-oxo-quinazolin-6-yl)amino]phenyl]pyrrolidine-1-sulfonamide;

N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]pyrrolidine-1-sulfonamide;

N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]cyclopentanesulfonamide; and

6-[2-cyano-3-(dimethylsulfamoylamino)-6-fluoro-phenoxy]-3-methyl-4-oxo-quinazoline;

or a pharmaceutically acceptable salt thereof.

13. A compound according to any one of claims 1 to 12, wherein the compound is selected from

6-[2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]-6-fluoro-phenoxy]-3-methyl-4-oxo-quinazoline;

6-[6-chloro-2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]phenoxy]-3-methyl-4-oxo-quinazoline;

N-[4-chloro-2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]pyrrolidine-1-sulfonamide;

6-[2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]phenoxy]-3-methyl-4-oxo-quinazoline;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]pyrrolidine-1-sulfonamide;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]cyclopentanesulfonamide;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]cyclohexanesulfonamide;

N-[2-cyano-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]butane-2-sulfonamide;

6-[2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]anilino]-3-methyl-4-oxo-quinazoline;

6-[6-chloro-2-cyano-3-[[ethyl(methyl)sulfamoyl]amino]anilino]-3-methyl-4-oxo-quinazoline;

N-[4-chloro-2-cyano-3-[(3-methyl-4-oxo-quinazolin-6-yl)amino]phenyl]pyrrolidine-1-sulfonamide;

N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]pyrrolidine-1-sulfonamide;

N-[2-cyano-4-fluoro-3-(3-methyl-4-oxo-quinazolin-6-yl)oxy-phenyl]cyclopentanesulfonamide; and

6-[2-cyano-3-(dimethylsulfamoylamino)-6-fluoro-phenoxy]-3-methyl-4-oxo-quinazoline;

or a pharmaceutically acceptable salt thereof.

14. A compound according to any one of claims 1 to 13 for use as therapeutically active substance.

15. A pharmaceutical composition comprising a compound according to any one of claims 1 to 13 and a therapeutically inert carrier.

16. A compound according to any one of claims 1 to 13 for use in the treatment or prophylaxis of thyroid cancer, colorectal cancer, brain cancer, melanoma or NSCLC.

17. The use of a compound according to any one of claims 1 to 13 for the treatment or prophylaxis of thyroid cancer, colorectal cancer, brain cancer, melanoma or NSCLC.

18. The use of a compound according to any one of claims 1 to 13 for the preparation of a medicament for the treatment or prophylaxis of thyroid cancer, colorectal cancer, brain cancer, melanoma or NSCLC.

19. A method for the treatment or prophylaxis of thyroid cancer, colorectal cancer, brain cancer, melanoma or NSCLC, which method comprises administering an effective amount of a compound as defined in any one of claims 1 to 13 to a patient in need thereof.

~~20. The invention as hereinbefore described.~~

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