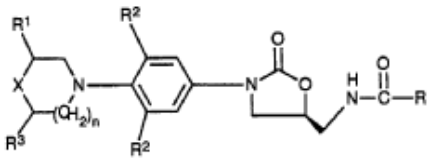
1. (WO1995007271) SUBSTITUTED OXAZINE AND THIAZINE OXAZOLIDINONE ANTIMICROBIALS

PCT Biblio. Data | Description | Claims | National Phase | Notices | Drawings | Documents

What is Claimed:

1. A compound of structural Formula I:



or pharmaceuticaUy acceptable salts thereof wherein:
X is O, S, SO, SO_2, SNR^{10} or $S(O)NR^{10}$;
R is (a) hydrogen,
(b) C- Cg alkyl optionally substituted with one or more of the foUowing: F, CI, hydroxy, C_j-Cg alkoxy, C_j-Cg acyloxy or -O-CH_2-Ph,
(c) Cg-Cg cycloalkyl,
(d) amino,
(e) $C_{-j^{\wedge}}$-Cg alkylamino,
(f) $-_{j^{\wedge}}$-Cg dialkylamino or
(g) C_1-C_8 alkoxy;
R^1 is H, except when X is O then R^1 can be H, CH_3, CN, CO_2H, CO_2R or

$(CH_2)_mR^n$ (m is 1 or 2);
R^2 is independently H, F or CI;
R^3 is H except when X is O and R^1 is CH_3 then R^3 can be H or CH_3;
R is independently H, C_1-C_4 alkyl (optionaUy substituted with chloro, fluoro, hydroxy, C_j-Cg alkoxy, amino, C_j-Cg alkylamino, or C_j-Cg dialkylamino) orp-toluenesulfonyl;
R^{11} is hydrogen, OH, OR, OCOR, NH_2, NHCOR or $N(R^{10})_2$; and
n is 0, 1 or 2.

2. The compound of Claim 1 wherein X is O.

3. The compound of Claim 2 wherein each R is fluorine.

4. The compound of Claim 1 wherein n is 1 and X is S, SO or SO_2.

5. The compound of Claim 1 which is an opticaUy pure enantiomer having the S- configuration at C5 of the oxazoUdinone ring.

6. The compound of Claim 1 wherein one R is hydrogen and the other is fluorine.

7. The compound of Claim 1 wherein R is methyl, OCHg, CHC1 , CH OH or hydrogen.

8. The compound of Claim 1 which is:
(a) (-S)-N-[[3-[3-fluoro-4-(4-thiomorphoUnyl)phenyl]-2-oxo-5-oxazoUdinyl] methyl]acetamide;
(b) (S)-N-[[3-[3-fluoro-4-(1, l-dioxothiomorphoUn-4-yl)phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide;
(c) (S)-N-[[3-[3-fluoro-4-(l-oxothiomorpholin-4-yl)phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide;
(d) (S)-N-t[3-[3,5-difluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl] acetamide;
(e) (S)-N-[[3-[3-fluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl] acetamide;
(f) (S)-N-[[3-[3-fluoro-4-[l-[(p-toluenesulfonyl)imino]thiomorphoUn-4-yl]phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide;
(g) (S)-N-[[3-[3-fluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl]hydroxyacetamide;

(g) (S) N-[[3-[3-fluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl]hydroxyacetamide;
(h) (S)-N-[[3-[3-fluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl]formamide;
(i) (S)-N-[[3-[3-fluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl]methylcarbamate; or
(j) (S)-N-[[3-[3-fluoro-4-morphoUnyl]phenyl]-2-oxo-5-oxazoUdinyl]methyl]dichloroacetamide.

9. The compound of Claim 1 where n is 0 and X is O, S, SO or SO_2.

10. The compound of Claim 9 wherein one R is hydrogen and the other is fluorine.

11. The compound of Claim 9 which is:
(a) (S)-N-[[3-[3-fluoro-4-(3-thiazoUdinyl)phenyl]-2-oxo-5-oxazoUdinyl]methyl] acetamide;
(b) (S)-N-[[3-[3-fluoro-4-(1, l-dioxothiazoUdin-3-yl)phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide;
(c) (S)-N-[[3-[3-fluoro-4-(l-oxothiazoUdin-3-yl)phenyl]-2-oxo-5-oxazoUdinyl] methyl]acetamide; or
(d) (S)-N-[[3-[3-fluoro-4-(3-oxazoUdinyl)]phenyl]-2-oxo-5-oxazoUdinyl] methyl] acetamide.

12. The compound of Claim 1 where n is 2 and X is O, S, SO or SO_2.

13. The compound of Claim 12 wherein one R is hydrogen and the other is fluorine.

14. The compound of Claim 12 which is:
(a) (S)-N-[[3-[3-fluoro-4-(hexahydrothiazepin-4-yl)phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide;
(b) (S)-N-[[3-[3-fluoro-4-(1, l-dioxohexahydrothiazepin-4-yl)phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide;
(c) (S)-N-[[3-[3-fluoro-4-(l-oxohexahydrothiazepin-4-yl)phenyl]-2-oxo-5-oxazoUdinyl]methyl]acetamide; or
(d) (S)-N-[[3-[3-fluoro-4-(hexahydrooxazepin-4-yl)]phenyl]-2-oxo-5-oxazoUdinyl]methyl] acetamide.

15. A use of a compound of Formula I as shown in Claim 1 in the preparation of a medicament useful in treating microbial infections in patients comprising:
administering to a patient in need thereof an effective amount thereof .

16. The use of Claim 15 wherein said compound of Formula I is administered oraUy, parenteraUy or topically in a pharmaceutical composition.

17. The use of Claim 15 wherein said compound is administered in an amount of from about 0.1 to about 100 mg/kg of body weight/day.

18. The use of Claim 17 wherein said compound is administered in an amount of from about 3.0 to about 50 mg/kg of body weight day.

19. The use of Claim 15 wherein said microbial infection is caused by
staphylococci, streptococci, enterococci, Bacteroides spp. , Clostridia spp. ,
Mycobacterium tuberculosis, Mycobacterium avium or Mycobacterium spp..