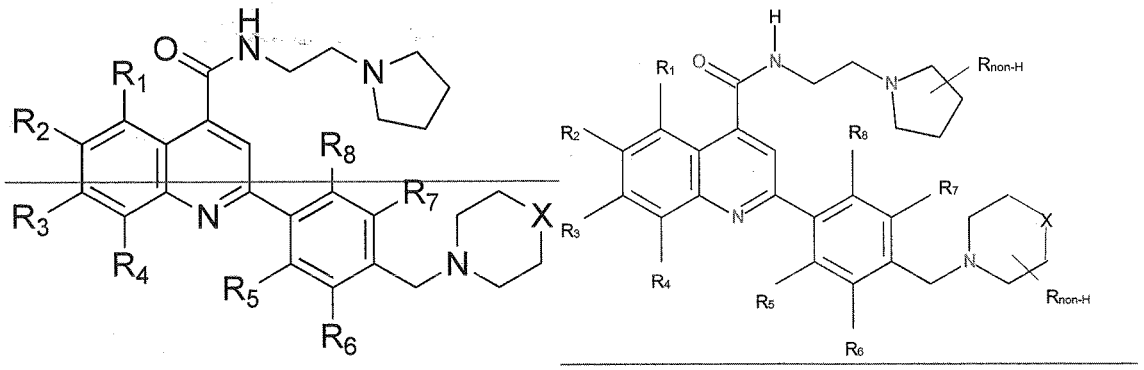
stage; which can be used for single-dose treatment; and/or which can be used for prophylactic treatment.

The present invention provides a novel class of class of quinolone-4-carboxamide compounds *Plasmodium falciparum* 3D7 inhibitors having potential as anti-malarial agents. The novel class of quinolone-4-carboxamide compounds according to the present invention have potential for the treatment of *Plasmodium falciparum*, *Plasmodium vivax*, *Plasmodium ovale, Plasmodium malariae* and *Plasmodium knowlesi* infections. In particular the novel class of class of quinolone-4-carboxamide compounds according to the present invention have potential for the treatment of *Plasmodium falciparum infections*; *Plasmodium falciparum and Plasmodium vivax infections; Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae* and *Plasmodium knowlesi* infections.

Desirable properties of compounds of formula (I) according to the present invention include: potency against *Plasmodium falciparum* 3D7; low toxicity in MRC-5 or HepG2 cells ; both desirable *Plasmodium falciparum* (*Pf*) 3D7 potency and low toxicity in MRC-5 or HepG2 ; desirable *Plasmodium falciparum* and *Plasmodium vivax* (*Pv*) activity against clinical isolates; desirable transmission blocking activity; gametocyte inhibitory potential; activity against dormant liver stage forms; good biopharmaceutical properties such as physical stability; good solubility profiles; appropriate metabolic stability; desirable ADME properties (adsorption, distribution, metabolism, excretion).

Summary of the Invention

According to a first aspect the present invention provides compounds of formula (I)



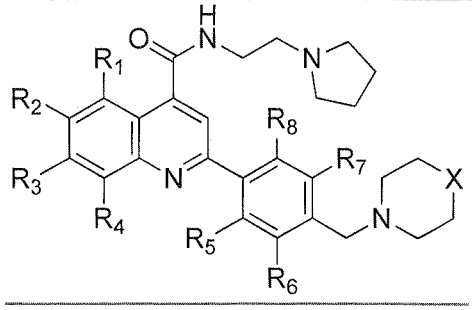
I

wherein R^1, R^2, R^3 R^4, R^5, R^6, R^7 and R^8 are independently of each other selected from: H, Cl or F; wherein the pyrrolidinyl, morpholinyl or thiomorpholinyl dioxide heterocyclic groups are independently optionally substituted, wherein optionally substituted indicates that the particular group or groups may have one or more non-hydrogen substituents (R_{non-H}), and wherein the pyrrolidinyl, morpholinyl and/or thiomorpholinyl dioxide groups in compounds of formula may have one or more Cl, F or $-(C_1-C_3)$ alkyl optional substituent groups; and

wherein X is –O- or -SO2- ;

or a pharmaceutically acceptable salt, hydrate, or polymorph thereof.

The present disclosure additionally provides compounds of formula (I)

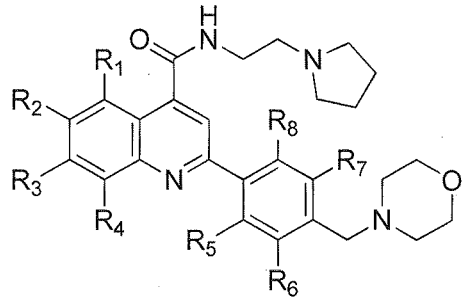


I

wherein R^1, R^2, R^3 R^4, R^5, R^6, R^7 and R^8 are independently of each other selected from: H, Cl or F; wherein the pyrrolidinyl, morpholinyl or thiomorpholinyl dioxide heterocyclic groups are independently optionally substituted by one or more Cl, F or $-(C_1-C_3)$ alkyl groups; and wherein X is –O- or $-SO_2-$; or a pharmaceutically acceptable salt, hydrate, or polymorph thereof.

The present disclosure additionally provides compounds of formula (I) wherein ~~wherein~~ R^1, R^2, R^3 R^4, R^5, R^6, R^7 and R^8 are independently of each other selected from: H, Cl or F; wherein the pyrrolidinyl, morpholinyl or thiomorpholinyl dioxide heterocyclic groups are independently optionally substituted by one or more Cl, F or $-(C_1-C_3)$ alkyl groups; and
wherein X is –O- or $-SO_2-$; or a pharmaceutically acceptable salt, hydrate, or polymorph thereof.

Also disclosed are compounds of formula (I) wherein X is –O-, compounds of formula (IA):

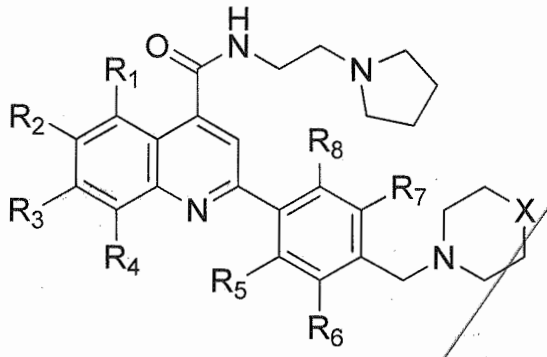


IA

or a pharmaceutically acceptable salt, hydrate, solvate, isomer, prodrug or polymorph thereof wherein R^1, R^2, R^3 R^4, R^5, R^6, R^7 and R^8 are independently of each other selected from: H, Cl or F; and wherein the pyrrolidinyl or morpholinyl groups are independently optionally substituted by one or more Cl, F or $-(C_1-C_3)$ alkyl groups.

Claims

1. A compound of formula I



I

wherein R^1, R^2, R^3 R^4, R^5, R^6, R^7 and R^8 are independently of each other selected from: H, Cl or F; wherein the pyrrolidinyl, morpholinyl or thiomorpholinyl dioxide heterocyclic groups are independently optionally substituted by one or more Cl, F or $-(C_1-C_3)$ alkyl groups; and

wherein X is –O- or $-SO_2-$;

or a pharmaceutically acceptable salt, hydrate, or polymorph thereof.

2. A compound according to claim 1 wherein X is –O-.

3. A compound according claim 1 or 2 wherein R^1 and R^2 are independently selected from H or F.

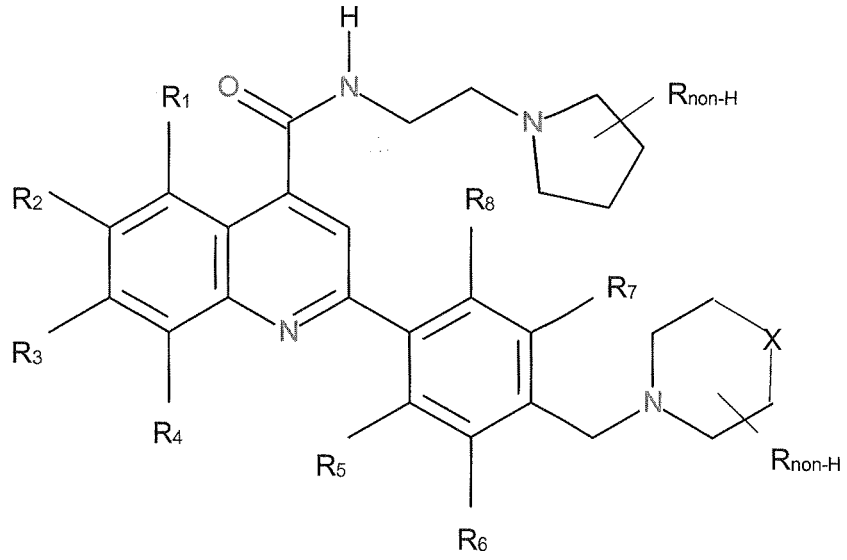
4. A compound according claim 1 or 2 wherein R^1 and R^2 are independently selected from H or Cl.

5. A compound according any of claims 1 or 4 wherein R^3 and R^4 are each independently selected from H or F.

6. A compound according to any of claims 1 to 5 wherein the quinoline ring is mono- or di-substituted with F or Cl or a mixture thereof.

Claims

1. A compound of formula I



I

wherein R^1, R^2, R^3, R^4, R^5, R^6, R^7 and R^8 are independently of each other selected from: H, Cl or F; wherein the pyrrolidinyl, morpholinyl or thiomorpholinyl dioxide heterocyclic groups are independently optionally substituted, wherein optionally substituted indicates that the particular group or groups may have one or more non-hydrogen substituents (R_{non-H}), and wherein the pyrrolidinyl, morpholinyl and/or thiomorpholinyl dioxide groups in compounds of formula may have one or more Cl, F or $-(C_1-C_3)$ alkyl optional substituent groups; and

wherein X is –O- or $-SO_2-$;

or a pharmaceutically acceptable salt, hydrate, or polymorph thereof.

2. A compound according to claim 1 wherein X is –O-.

3. A compound according claim 1 or 2 wherein R^1 and R^2 are independently selected from H or F.

4. A compound according claim 1 or 2 wherein R^1 and R^2 are independently selected from H or Cl.

5. A compound according any of claims 1 or 4 wherein R^3 and R^4 are each independently selected from H or F.

6. A compound according to any of claims 1 to 5 wherein the quinoline ring is mono- or di-substituted with F or Cl or a mixture thereof.