Claims

1. Use of at least one compound in the manufacture of a medicament for preventing, treating or inhibiting mycobacterial infections, wherein the at least one compound is selected from the group consisting of:

N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);

3,5,4'-trihydroxy-trans-stilbene (Resveratrol);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta*[e]*-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and

[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR).

2. The use of claim 1, wherein the bacterial infection is an intracellular bacterial infection.

3. The use of claim 1, wherein the mycobacteria is selected from the group consisting of *M. tuberculosis, M. bovis, M. bovis BCG, M. africanum, M. canetti, M. caprae, M. microti, M. leprae, M. avium, M. paratuberculosis* and *M. pinnipedii*.

4. The use of claim 3, wherein the mycobacteria are *M. tuberculosis*.

5. The use of claim 3, wherein the mycobacteria are drug resistant *M. tuberculosis*.

6. The use of any one of the preceding claims, wherein methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644) is S-(+)-methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644).

7. The use of any one of the preceding claims, wherein the medicament further comprises an anti-tuberculosis drug which is to be administered together or separately with any one of the at least one compound.

8. The use of claim 7, wherein the anti-tuberculosis drug is selected from the group consisting of isoniazid, pyrazinamide, rifampicin, ethionamide, rifabutin, amikacin, ethambutol, PA824, bedaquiline, streptomycin, kanamycin, fluoroquinolone antibiotic and combinations thereof.

9. The use of any one of the preceding claims, wherein the at least one compound is selected from the group consisting of N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin) and 3,5,4'-trihydroxy-trans-stilbene (Resveratrol).

10. The use of any one of the preceding claims, wherein the concentration of the compound is about 1 to about 100 mg/Kg of body weight of the patient.

11. The use of any one of the preceding claims, wherein the route of administration is selected from the group consisting of systemic administration, oral administration, intravenous administration and parenteral administration.

12. Use of at least one compound in the manufacture of a medicament for increasing the acidity of bacterial phagosomes to inhibit mycobacterial growth in a cell, wherein the use comprises contacting the cell with at least one of the compounds selected from the group consisting of:

N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);

3,5,4'-trihydroxy-trans-stilbene (Resveratrol);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and

[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR).

13. Use of at least one compound in the manufacture of a medicament for increasing mitrochondrial reactive oxygen species (mROS) generation to inhibit mycobacterial growth in a cell, wherein the use comprises contacting the cell with at least one of the compounds selected from the group consisting of:

N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);

3,5,4'-trihydroxy-trans-stilbene (Resveratrol);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and

[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR).

14. The use of claim 13, wherein the mycobacteria are drug resistant *M. tuberculosis*.

15. A pharmaceutical composition comprising:

at least one of the compounds selected from the group consisting of:

N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and
[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR);
and anti-tuberculosis drug.

16. Use of at least one compound in the manufacture of a medicament for eliciting an immune response to an intracellular mycobacteria, wherein the at least one compound is selected from the group consisting of:
N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);
3,5,4'-trihydroxy-trans-stilbene (Resveratrol);
methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);
2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);
2',5'-Dideoxyadenosine;
4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);
(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);
N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);
3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);
(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);
(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and
[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR).

Claims

1. Use of at least one compound in the manufacture of a medicament for preventing, treating or inhibiting mycobacterial infections, wherein the at least one compound is selected from the group consisting of:

N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);

3,5,4'-trihydroxy-trans-stilbene (Resveratrol);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and

[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR); wherein the medicament further comprises an anti-tuberculosis drug; wherein the anti-tuberculosis drug is selected from the group consisting of isoniazid, pyrazinamide, rifampicin, ethionamide, rifabutin, amikacin, ethambutol, PA824, bedaquiline, streptomycin, kanamycin, fluoroquinolone antibiotic and combinations thereof.

2. The use of claim 1, wherein the mycobacterial infection is an intracellular bacterial infection.

3. The use of claim 1, wherein the mycobacteria is selected from the group consisting of *M. tuberculosis, M. bovis, M. bovis BCG, M. africanum, M. canetti, M. caprae, M. microti, M. leprae, M. avium, M. paratuberculosis* and *M. pinnipedii*.

4. The use of claim 3, wherein the mycobacteria are *M. tuberculosis*.

5. The use of claim 3, wherein the mycobacteria are drug resistant *M. tuberculosis*.

6. The use of any one of the preceding claims, wherein methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644) is S-(+)-methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644).

7. The use of any one of the preceding claims, wherein the medicament further comprises an anti-tuberculosis drug which is to be administered together or separately with any one of the at least one compound.

8. The use of any one of the preceding claims, wherein the at least one compound is selected from the group consisting of N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin) and 3,5,4'-trihydroxy-trans-stilbene (Resveratrol).

9. The use of any one of the preceding claims, wherein the concentration of the compound is about 250 mg/kg or about 500 mg/kg of body weight of the patient.

10. The use of any one of the preceding claims, wherein the route of administration is selected from the group consisting of systemic administration, oral administration, intravenous administration and parenteral administration.

11. Use of at least one compound in the manufacture of a medicament for inhibiting mycobacterial growth in a cell, wherein the use comprises contacting the cell with at least one of the compounds selected from the group consisting of:
N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);
3,5,4'-trihydroxy-trans-stilbene (Resveratrol);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and

[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR); wherein the medicament further comprises an anti-tuberculosis drug; wherein the anti-tuberculosis drug is selected from the group consisting of isoniazid, pyrazinamide, rifampicin, ethionamide, rifabutin, amikacin, ethambutol, PA824, bedaquiline, streptomycin, kanamycin, fluoroquinolone antibiotic and combinations thereof.

12. The use of claim 11, wherein the mycobacteria are drug resistant *M. tuberculosis*.

13. A pharmaceutical composition comprising:

at least one of the compounds selected from the group consisting of:

N,N-dimethyl imidodicarbonimidic diamide hydrochloride (Metformin);

methyl 2,6-dimethyl-5-nitro-4-[2-(trifluoromethyl)phenyl]-1,4-dihydropyridine-3-carboxylate (Bay K8644);

2,5-Dimethyl-4-[2-(phenylmethyl)benzoyl]-1H-pyrrole-3-carboxylic acid methyl ester (FPL 64176);

2',5'-Dideoxyadenosine;

4-[4-(4-chlorophenyl)-4-hydroxypiperidin-1-yl]- N,N-dimethyl-2,2-diphenylbutanamide hydrochloride (Loperamide);

(5R,6S,8S)-Hexyl 6-hydroxy-5-methyl-13-oxo-6,7,8,13,14,15-hexahydro-5H-16-oxa-4b,8a,14-triaza-5,8-methanodibenzo[*b,h*]cycloocta[*jkl*]cyclopenta[*e*]-as-indacene-6-carboxylate (KT 5720);

N-(dicyclopropylmethyl)-4,5-dihydro-1,3-oxazol-2-amine (Rilmenidine);

3-(2-methoxyethyl) 5-propan-2-yl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nimodipine);

(RS)-ethyl methyl 2,6-dimethyl-4-(3-nitrophenyl)-1,4-dihydropyridine-3,5-dicarboxylate (Nitrendipine);

(2-{4-[(2-butyl-1-benzofuran-3-yl)carbonyl]-2,6-diiodophenoxy}ethyl)diethylamine (Amiodarone); and

[(2R,3S,4R,5R)-5-(4-Carbamoyl-5-aminoimidazol-1-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate (AICAR);

and anti-tuberculosis drug; wherein the anti-tuberculosis drug is selected from the group consisting of isoniazid, pyrazinamide, rifampicin, ethionamide, rifabutin, amikacin, ethambutol, PA824, bedaquiline, streptomycin, kanamycin, fluoroquinolone antibiotic and combinations thereof.