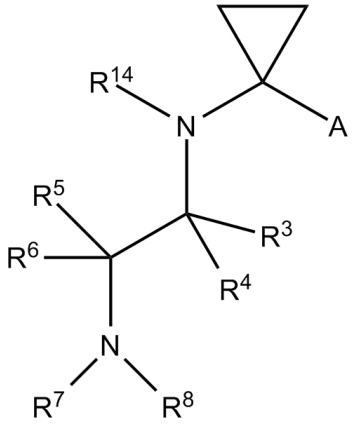
Claims

1. A compound of formula (XVI):



Formula (XVI)

wherein

R^{14} is selected from the group consisting of –C(O)-C_{1-8} alkyl; –C(O)-O-C_{1-8} alkyl; -C_{2}~~2~~$_{3}$-$_{8}$ alkyl~~; -H~~ and –$S(O)_2$-C_{1-8} alkyl;

R^3 is H, C_{1-5} alkyl, or a bond;

R^4 is H, C_{1-5} alkyl, or a bond;

R^5 is H, a bond, or C_{1-8} alkyl, wherein one methylene group optionally is replaced by -O-;

R^6 is H, a bond, or C_{1-8} alkyl, wherein one methylene group optionally is replaced by -O-;

R^7 is H, a bond,-OH, or C_{1-8} alkyl, wherein one or more methylene group optionally and individually is replaced by -O- and/or substituted with =O;

R^8 is H, a bond, -OH, or C_{1-8} alkyl, wherein one or more methylene group optionally and individually is replaced by -O- and/or substituted with =O;

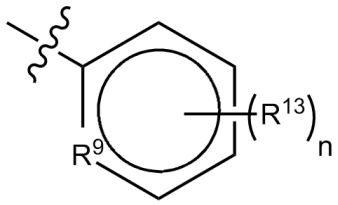
Anyone of R^3, R^4, R^5, R^6, R^7, and R^8 optionally is linked together to form a ring;

A is a phenyl or a pyridinyl, wherein the phenyl or pyridinyl is optionally substituted with one or more substituents R^{13} individually selected from the group consisting of halogen, -CX_3, -OCX_3, -CHX_2, -$OCHX_2$, -CH_2X, -OCH_2X, -CH_2CX_3, OCH_2CX_3, -C_{1-8} alkyl, -OC_{1-8} alkyl, -C_{3-7} cycloalkyl, -OC_{3-7} cycloalkyl, -CN, NO_2, –SO_2CH_3, and -SF_5; and

X is halogen;

or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein A is a moiety of formula (IX):



Formula (IX)

wherein

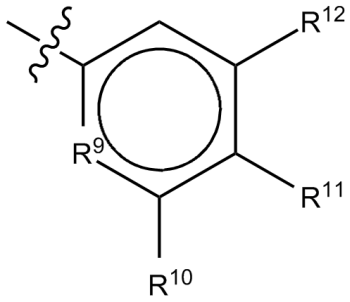
R^9 is -C(H)-, -N-, or -C(R^{13})-;

R^{13} is individually selected from the group consisting of halogen, -CX_3, -OCX_3, -CHX_2, -$OCHX_2$, -CH_2X, -OCH_2X, -CH_2CX_3, OCH_2CX_3, -C_{1-8} alkyl, -OC_{1-8} alkyl, -C_{3-7} cycloalkyl, -OC_{3-7} cycloalkyl, -CN, NO_2, –SO_2CH_3, and -SF_5;

n is an integer of 0 to 4; and

X is halogen.

3. The compound according to claim 1, wherein A is a moiety of formula (X):



Formula (X)

wherein

R^9 is -C(H)-, -N-, or -C(R^{13})-;

R^{10}, R^{11}, R^{12}, and R^{13} are individually selected from the group consisting of H, halogen, -CX_3, -OCX_3, -CHX_2, -$OCHX_2$, -CH_2X, -OCH_2X, -CH_2CX_3, OCH_2CX_3, -C_{1-8} alkyl, -OC_{1-8} alkyl, -C_{3-7} cycloalkyl, -OC_{3-7} cycloalkyl, -CN, NO_2, –SO_2CH_3, and -SF_5; and

X is halogen.

4. The compound according to claim 3, wherein

R^9 is -C(H)- or -N-;

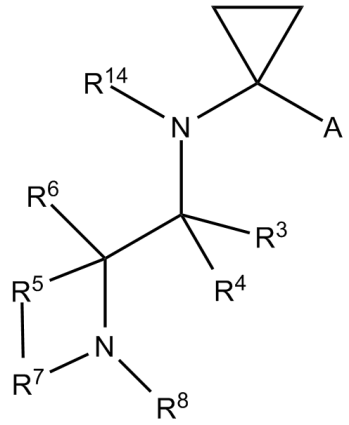
R^{10} is H or halogen;

R^{11} is H or halogen;

R^{12} is $-CX_3$, $-OCX_3$, H or halogen; and
X is halogen.

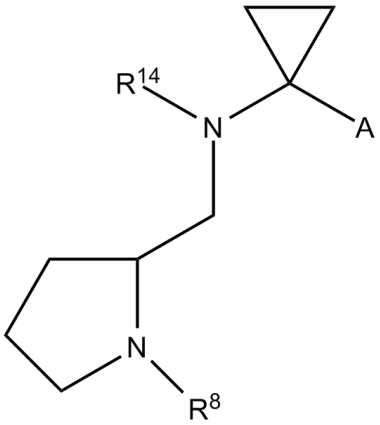
5. The compound according to any one of the preceding claims, wherein R^3 and R^4 are -H, R^5 and R^6 are methyl, and R^7 and R^8 are –H.

6. The compound according to any one of claims 1 to 4, wherein the compound is of formula (XVIII):



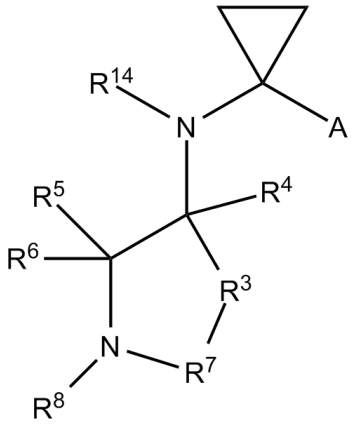
Formula (XVIII).

7. The compound according to any one of the claims 1 to 4, wherein the compound is of formula (XIX):



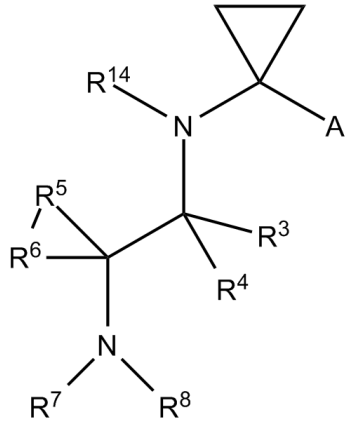
Formula (XIX).

8. The compound according to any one of claims 1 to 4, wherein the compound is of formula (XXI):



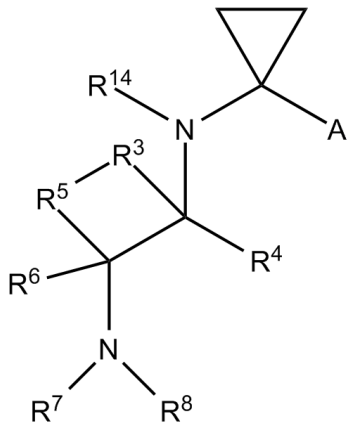
Formula (XXI).

9. The compound according to any one of claims 1 to 4, wherein the compound is of formula (XXII):



Formula (XXII).

10. The compound according to any one of claims 1 to 4, wherein the compound is of formula (XX):



Formula (XX).

11. The compound according to any one of the preceding claims, wherein R^{14} is -C(O)-OC_{1-4} alkyl.

12. The compound according to any one of the preceding claims, wherein R^{14} is C_{3-4} alkyl.

13. The compound according to ~~any one of the preceding~~ claim~~s~~ 3 or 4, wherein R^{12} is -CF_3, -OCF_3, or a halogen.

14. The compound according to ~~any one of the preceding~~ claim~~s~~ 3 or 4, wherein R^9 is -C(H)-, R^{10} is H, R^{11} is F and R^{12} is -CF_3.

15. The compound according to any one of the preceding claims, wherein the compound is selected from the group consisting of:

Methyl N-(2-(dimethylamino)ethyl)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl) carbamate;

Methyl (2-amino-2-methylpropyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

Methyl ((1-aminocyclopropyl)methyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl) carbamate;

Methyl 3-((1-(4-fluoro-3-(trifluoromethyl) phenyl) cyclopropyl) (methoxycarbonyl)amino)azetidine-1-carboxylate;

Methyl azetidin-3-yl(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

N-(cyclopropylmethyl)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)azetidin-3-amine;

Methyl (2-aminoethyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

N1-(cyclopropyl methyl)-N1-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)-2-methyl propane-1,2-diamine;

N-(2-amino-2-methylpropyl)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)cyclopropanecarboxamide;

N1-cyclopropyl-2-methyl-N1-(1-(3-(trifluoromethyl)phenyl)cyclopropyl)propane-1,2-diamine;

Methyl (2-amino-2-methylpropyl)(1-(3,5-dichlorophenyl)cyclopropyl)carbamate;

Methyl (2-amino-2-methylpropyl)(1-(3-bromophenyl)cyclopropyl)carbamate;

Methyl (2-amino-2-methylpropyl)(1-(3-chlorophenyl)cyclopropyl)carbamate;

1-((azetidin-2-ylmethyl)(1-(4-fluoro-3-(trifluoromethyl) phenyl)cyclopropyl)amino)-2-methyl propan-2-ol;

Methyl (2-amino-2-methylpropyl)(1-(3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

1-((1-(4-fluoro-3-(trifluoromethyl) phenyl)cyclopropyl)((1-methylazetidin-2-yl)methyl)amino)-2-methylpropan-2-ol;

Methyl (2-amino-2-methylpropyl)(1-(5-fluoro-4-(trifluoromethyl)pyridin-2-yl)cyclopropyl) carbamate;

N1-cyclobutyl-2-methyl-N1-(1-(3-(trifluoromethyl)phenyl)cyclopropyl)propane-1,2-diamine;

Ethyl (2-amino-2-methylpropyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

Methyl (2-amino-2-methylpropyl)(1-(4-fluoro-3-(trifluoromethoxy)phenyl)cyclopropyl)carbamate;

N-(2-amino-2-methylpropyl)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)methanesulfonamide;

Methyl (R)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Methyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Methyl (2-acetamido-2-methylpropyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

~~N1-(1-(4-fluoro-3-(trifluoromethyl)phenyl) cyclopropyl)-2-methylpropane-1,2-diamine;~~

Methyl (azetidin-2-ylmethyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)carbamate;

Methyl (S)-(1-(4-fluoro-3-(trifluoro methyl) phenyl)cyclopropyl) ((1-methylpyrrolidin-2-yl)methyl) carbamate;

Methyl (S)-(1-(4-fluoro-3-(trifluoromethoxy)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Methyl (R)-(1-(4-fluoro-3-(trifluoromethoxy)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Methyl (1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)((1-methylazetidin-2-yl)methyl)carbamate;

Methyl (R)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)((1-methylpyrrolidin-2-yl)methyl)carbamate;

Methyl (azetidin-2-ylmethyl)(1-(4-fluoro-3-(trifluoromethoxy)phenyl)cyclopropyl)carbamate;

Methyl (1-(4-fluoro-3-(trifluoromethyl) phenyl)cyclopropyl)(2-(hydroxyamino)-2-methylpropyl)carbamate;

Ethyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Ethyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)((1-methylpyrrolidin-2-yl)methyl) carbamate;

(S)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)-N-(pyrrolidin-2-ylmethyl) methanesulfonamide;

(S)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)-N-((1-methylpyrrolidin-2-yl)methyl)methanesulfonamide;

Ethyl (R)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Methyl (R)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(morpholin-3-ylmethyl) carbamate;

Methyl (R)-(1-(4-fluoro-3-(trifluoromethyl) phenyl)cyclopropyl)((4-methylmorpholin-3-yl)methyl)carbamate;

(R)-N-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)-N-(pyrrolidin-2-ylmethyl) methane sulphonamide;

Methyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(morpholin-3-ylmethyl) carbamate;

Methyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)((4-methylmorpholin-3-yl)methyl)carbamate;

Isopropyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Cyclopropyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

Methyl (R)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)((2-methyl pyrrolidin-2-yl)methyl)carbamate;

~~N-((1-amino cyclopropyl)methyl)-1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropan-1-amine;~~

Cyclopropylmethyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)(pyrrolidin-2-ylmethyl)carbamate;

N-((1-aminocyclopropyl)methyl)-N-(1-(4-fluoro-3-(trifluoromethyl)-phenyl)cyclopropyl)methanesulfonamide;

Methyl (S)-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)((2-methylpyrrolidin-2-yl)methyl)carbamate;

~~(1S, 2S)-N1-(1-(4-fluoro-3-(trifluoromethyl) phenyl)cyclopropyl)-cyclopentane-1,2-diamine;~~

~~(1R,2S)-N1-(1-(4-fluoro-3-(trifluoromethyl)phenyl)cyclopropyl)-cyclopentane-1,2-diamine;~~ and

Methyl (S)-(azetidin-2-ylmethyl)(1-(4-fluoro-3-(trifluoromethyl)phenyl)-cyclopropyl)carbamate.

16. A pharmaceutical composition comprising the compound according to any one of the preceding claims.

17. The compound according to any one of claims 1 to 15 or pharmaceutical composition according claim 16 for use in medicine.

18. The compound according to any one of claims 1 to 15 or pharmaceutical composition according to claim 16 for use in the treatment of inflammatory bowel disease (IBD), such as ulcerative colitis or Crohn’s disease.

19. The compound according to any one of claims 1 to 15 or pharmaceutical composition according to claim 16 for use in the treatment of hereditary xerocytosis.

20. The compound according to any one of claims 1 to 15 or pharmaceutical composition according to claim 16 for use in the treatment of acute respiratory distress syndrome (ARDS).

21. Use of the compound according to any one of claims 1 to 15 or pharmaceutical composition according claim 16 in the manufacture of a medicament for the treatment of inflammatory bowel disease (IBD), such as ulcerative colitis or Crohn’s disease.

22. Use of the compound according to any one of claims 1 to 15 or pharmaceutical composition according claim 16 in the manufacture of a medicament for the treatment of hereditary xerocytosis.

23. Use of the compound according to any one of claims 1 to 15 or pharmaceutical composition according claim 16 in the manufacture of a medicament for the treatment of acute respiratory distress syndrome (ARDS).