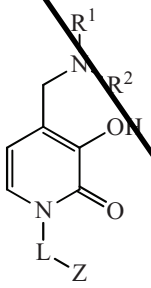
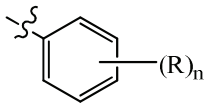
CLAIMS

1. The use of a compound for treating an inflammatory epithelial disease, the compound having the formula:



wherein Z has the formula:



R represents from 0 to 5 substitutions for hydrogen;
the index n is an integer from 0 to 5;
L is chosen from CH_2 or SO_2;
R^1 and R^2 are each independently chosen from:

i) hydrogen;
ii) substituted or unsubstituted C_1-C_{10} linear, branched, or cyclic alkyl;
iii) substituted or unsubstituted C_2-C_{10} linear, branched, or cyclic alkenyl;
iv) substituted or unsubstituted C_2-C_{10} linear or branched alkynyl;
v) substituted or unsubstituted C_6 or C_{10} aryl;
vi) substituted or unsubstituted C_1-C_9 heterocyclic;
vii) substituted or unsubstituted C_1-C_9 heteroaryl; or
viii) R^1 and R^2 can be taken together to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring having from form 2 to 20 carbon atoms and from 1 to 7 heteroatoms; or

a pharmaceutically acceptable salt thereof.

2. The use according to Claim 1, wherein the one or more compounds are in the form of a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

3. The use according to either one of Claims 1 or 2, wherein L is CH_2.

4. The use according to either one of Claims 1 or 2, wherein L is SO_2.

5. The use according to any of one of Claims 1 to 4, wherein each R is a substitution for hydrogen independently chosen from:

i) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;
ii) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkenyl;
iii) substituted or unsubstituted C_2-C_{12} linear or C_3-C_{12} branched alkynyl;

iv) C_6 or C_{10} substituted or unsubstituted aryl;

v) C_1-C_9 substituted or unsubstituted heterocyclic;

vi) C_1-C_{11} substituted or unsubstituted heteroaryl;

vii) halogen;

viii) $-[C(R^{23a})(R^{23b})]_xOR^{10}$;

R^{10} is chosen from:

a) –H;

b) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

c) C_6 or C_{10} substituted or unsubstituted aryl or alkylenearyl;

d) C_1-C_9 substituted or unsubstituted heterocyclic;

e) C_1-C_{11} substituted or unsubstituted heteroaryl;

ix) $-[C(R^{23a})(R^{23b})]_xN(R^{11a})(R^{11b})$;

R^{11a} and R^{11b} are each independently chosen from:

a) –H;

b) $-OR^{12}$;

R^{12} is hydrogen or C_1-C4 linear alkyl;

c) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

d) C_6 or C_{10} substituted or unsubstituted aryl;

e) C_1-C_9 substituted or unsubstituted heterocyclic;

f) C_1-C_{11} substituted or unsubstituted heteroaryl; or

g) R^{11a} and R^{11b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

x) $-[C(R^{23a})(R^{23b})]_xC(O)R^{13}$;

R^{13} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $-OR^{14}$;

R^{14} is hydrogen, substituted or unsubstituted C_1-C_4 linear alkyl, C_6 or C_{10} substituted or unsubstituted aryl, C_1-C_9 substituted or unsubstituted heterocyclic, C_1-C_{11} substituted or unsubstituted heteroaryl;

c) $-N(R^{15a})(R^{15b})$;

R^{15a} and R^{15b} are each independently hydrogen, substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{15a} and R^{15b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xi) $-[C(R^{23a})(R^{23b})]_xOC(O)R^{16}$;

R^{16} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $-N(R^{17a})(R^{17b})$;

R^{17a} and R^{17b} are each independently hydrogen, substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or

unsubstituted heteroaryl; or R^{17a} and R^{17b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xii) $-[C(R^{23a})(R^{23b})]_xNR^{18}C(O)R^{19}$;

R^{18} is:

a) –H; or

b) substituted or unsubstituted C_1-C4 linear, C_3-C_4 branched, or C_3-C_4 cyclic alkyl;

R^{19} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $-N(R^{20a})(R^{20b})$;

R^{20a} and R^{20b} are each independently hydrogen, substituted or unsubstituted C_1-C_4 linear or C_2-C_4 branched alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{20a} and R^{20b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xiii) $-[C(R^{23a})(R^{23b})]_xCN$;

xiv) $-[C(R^{23a})(R^{23b})]_xNO_2$;

xv) $-[C(R^{23a})(R^{23b})]_xR^{21}$;

R^{21} is C_1-C_{10} linear, branched, or cyclic alkyl substituted by from 1 to 21 halogen atoms chosen from –F, –Cl, –Br, or –I;

xvi) $-[C(R^{23a})(R^{23b})]_xSO_2R^{22}$;

R^{22} is hydrogen, hydroxyl, substituted or unsubstituted C_1-C_4 linear or C_2-C_4 branched alkyl; substituted or unsubstituted C_6, C_{10}, or C_{14} aryl; C_7-C_{15} alkylenearyl; C_1-C_9 substituted or unsubstituted heterocyclic; or C_1-C_{11} substituted or unsubstituted heteroaryl;

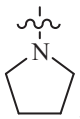
R^{23a} and R^{23b} are each independently hydrogen or C_1-C_4 alkyl; and

the index x is an integer from 0 to 5.

6. The use according to any of one of Claims 1 to 5, wherein R^1 and R^2 are taken together to form a 5-member substituted or unsubstituted C_1-C_4 heterocyclic or a substituted or unsubstituted C_1-C_4 heteroaryl ring.

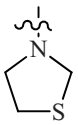
7. The use according to any of one of Claims 1 to 6, wherein R^1 and R^2 are taken together to form a ring having the formula:

i)



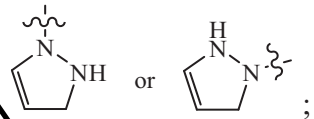
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ii)

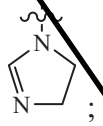


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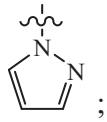
ii)


;

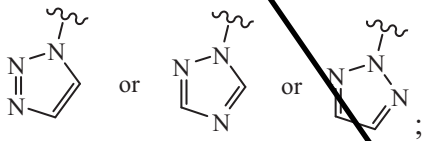
iii)


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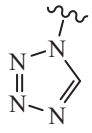
iv)


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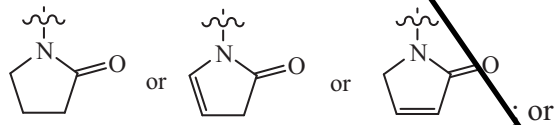
v)


;

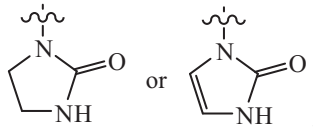
vi)


;

vii)


; or

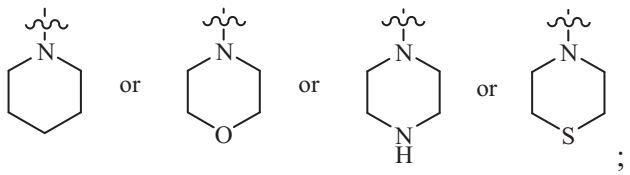
viii)


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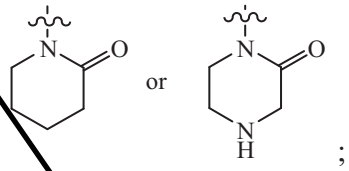
8. The use according to any of one of Claims 1 to 5, wherein R^1 and R^2 are taken together to form a substituted or unsubstituted C_4-C_{11} heterocyclic or a substituted or unsubstituted C_4-C_{11} heteroaryl ring.

9. The use according to any of one of Claims 1 to 5, wherein R^1 and R^2 are taken together to form a ring having the formula:

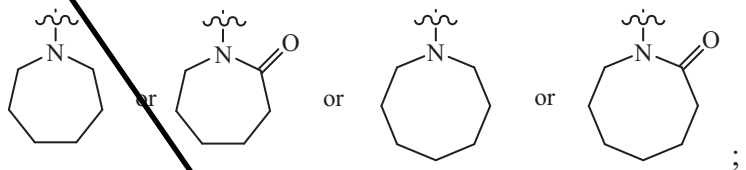
i)


;

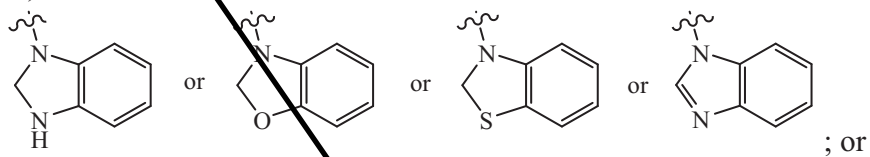
ii)


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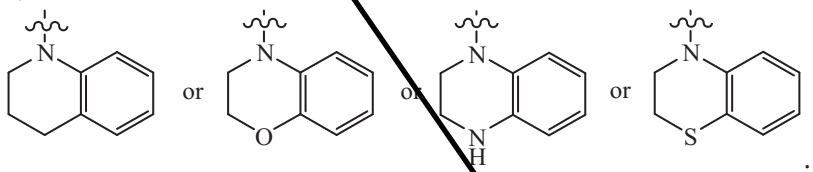
iii)


;

iv)


; or

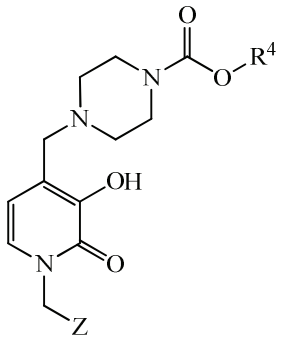
v)


.

10. The use according to any of one of Claims 1 to 5, wherein R^1 and R^2 are taken together to form a ring chosen from pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-(pyrdin-2-yl)pyrrolidin-1-yl, 2-methylcarboxypyrrolidin-1-yl, 2-(methoxymethyl)pyrrolidin-1-yl, thiazolidin-3-yl, 1*H*-imidazol-1-yl, piperidin-1-yl, 4-benzylpiperidin-1-yl, 1,4'-bipiperidinyl-1'-yl, piperazin-1-yl, 4-benzylpiperazin-1-yl, 4-(2-methoxyphenyl)-piperazin-1-ylmethyl, 4-(6-chloropyridazin-3-yl)piperazin-1-yl, 1,4-dioxa-8-azaspiro[4,5]dec-8-yl, morpholin-4-yl, thiomorpholin-4-yl, azepan-1-yl, azocan-1-yl, and 3,4-dihydroquinolin-1(2*H*)-yl.

11. The use according to any of one of Claims 1 to 5, wherein R^2 is hydrogen and R^1 is chosen from benzyl, 4-methoxybenzyl, 4-fluorobenzyl, 4-chlorobenzyl, 4-methylbenzyl, 2-(pyridin-2-yl)ethyl, [1,3]dioxolan-2-ylmethyl, tetrahydrofuran-2-ylmethyl, 2-methoxyethyl, 1-hydroxy-2-methylpropan-2-yl, pyridin-4-ylmethyl, furan-2-ylmethyl, 2-(methylthio)ethyl, 1-phenylethyl, 3-imidazol-1-ylpropyl, cycloheptyl, 4-methylcyclohexyl, 1-benzylpiperidin-4-yl, azepan-2-on-3-yl, and 1-benzyl-pyrrolidin-3-yl.

12. The use according to Claim 1, wherein the one or more compounds have the formula:



R^4 is C_1-C_4 linear alkyl or C_3-C_4 branched alkyl;

or a pharmaceutically acceptable salt thereof.

13. The use according to Claim 12, wherein R^4 is methyl.

14. The use according to Claim 12, wherein R^4 is ethyl.

15. The use according to Claim 12, wherein R^4 is *tert*-butyl.

16. The use according to any one of Claims 12 to 15, wherein Z is 4-chlorophenyl.

17. The use according to any one of Claims 12 to 15, wherein Z is chosen from 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, or 4-fluorophenyl.

18. The use according to any one of Claims 12 to 15, wherein Z is chosen from 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 2,5-dichlorophenyl, and 2,6-dichlorophenyl.

19. The use according to Claim 1, wherein the compound is chosen from is *tert*-butyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}-piperazine-1-carboxylate or a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

20. The use according to Claim 1, wherein the compound is chosen from:
Methyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate; and
tert-Butyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate.

21. The use according to any of Claims 1 to 20, wherein the inflammatory epithelial disease is a disease affecting intestinal epithelial tissue.

22. The use according to any one of Claims 1 to 20, wherein the disease is Crohn's disease.

23. The use according to any one of Claims 1 to 20, wherein the disease is ulcerative colitis.

24. The use according to any one of Claims 1 to 20, wherein the disease is collagenous colitis.

25. The use according to any one of Claims 1 to 20, wherein the disease is lymphocytic colitis.

26. The use according to any one of Claims 1 to 20, wherein the disease is ischemic colitis.

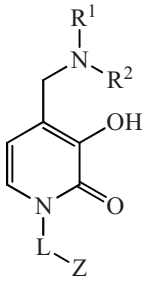
27. The use according to any one of Claims 1 to 20, wherein the disease is diversion colitis.

28. The use according to any one of Claims 1 to 20, wherein the disease is Behçet's syndrome.

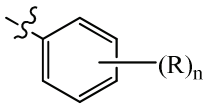
29. The use according to any one of Claims 1 to 20, wherein the disease is indeterminate colitis.

30. The use according to any one of Claims 1 to 20, wherein the inflammatory epithelial disease is chosen from a disease affecting the respiratory tract, mucosa, skin, GI tract, lining of major organs and endocrine glands, vascular tissue, and combinations thereof.

31. A composition for treating inflammatory epithelial disease, comprising
a) an effective amount of one or more compounds having the formula:



wherein Z has the formula:



R represents from 0 to 5 substitutions for hydrogen;
the index n is an integer from 0 to 5;
L is chosen from CH_2 or SO_2;
R^1 and R^2 are each independently chosen from:

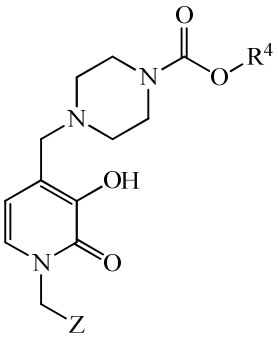
i) hydrogen;
ii) substituted or unsubstituted C_1-C_{10} linear, branched, or cyclic alkyl;
iii) substituted or unsubstituted C_2-C_{10} linear, branched, or cyclic alkenyl;
iv) substituted or unsubstituted C_2-C_{10} linear or branched alkynyl;
v) substituted or unsubstituted C_6 or C_{10} aryl;
vi) substituted or unsubstituted C_1-C_9 heterocyclic;
vii) substituted or unsubstituted C_1-C_9 heteroaryl; or
viii) R^1 and R^2 can be taken together to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring having from form 2 to 20 carbon atoms and from 1 to 7 heteroatoms; or

a pharmaceutically acceptable salt thereof; and

b) one or more excipients.

32. The composition according to Claim 31, wherein the one or more compounds are in the form of a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

33. The composition according to Claim 31, wherein the one or more compounds have the formula:



wherein Z is phenyl substituted with from 1 to 5 halogens chosen from fluorine and chlorine;
R^4 is C_1-C_4 linear alkyl or C_3-C_4 branched alkyl; or
a pharmaceutically acceptable salt thereof.

34. The composition according to any one of Claims 31 to 33, wherein R^4 is methyl.

35. The composition according to any one of Claims 31 to 33, wherein R^4 is ethyl.

36. The composition according to any one of Claims 31 to 33, wherein R^4 is *tert*-butyl.

37. The composition according to any one of Claims 31 to 33, wherein Z is 4-chlorophenyl.

38. The composition according to any one of Claims 31 to 33, wherein Z is chosen from 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, or 4-fluorophenyl.

39. The composition according to any one of Claims 31 to 33, wherein the one or more compounds is *tert*-butyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}-piperazine-1-carboxylate or a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

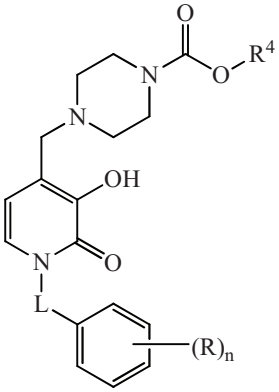
40. The composition according to any one of Claims 31 to 39, further comprising one or more chemotherapeutic compounds.

41. The composition according to Claim 40, wherein the one or more chemotherapeutic compounds are chosen from 6-hydroxymethylacylfulvene, cyclophosphamide, dacarbazine, carmustine, doxorubicin, and methotrexate.

42. The composition according to Claim 33, wherein the inflammatory epithelial disease is chosen from Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischemic colitis, diversion colitis, Behçet's syndrome, and indeterminate colitis

43. A composition for treating a subject with colitis, comprising

a) an effective amount of one or more compounds having the formula:



wherein L is chosen from CH_2 or SO_2;

R represents from 0 to 5 substitutions for hydrogen;

the index n is an integer from 0 to 5;

R^1 and R^2 are each independently chosen from:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_{10} linear, branched, or cyclic alkyl;

iii) substituted or unsubstituted C_2-C_{10} linear, branched, or cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_{10} linear or branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heterocyclic;

vii) substituted or unsubstituted C_1-C_9 heteroaryl; or

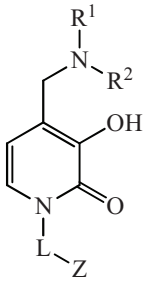
viii) R^1 and R^2 can be taken together to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring having from form 2 to 20 carbon atoms and from 1 to 7 heteroatoms;

R^4 is C_1-C_4 linear or C_3-C_4 branched alkyl; or
a pharmaceutically acceptable salt thereof; and

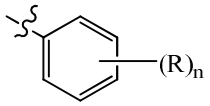
b) one or more excipients.

44. The composition according to Claim 43, wherein the compound is chosen from is *tert*-butyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}-piperazine-1-carboxylate or a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

45. The use of a compound for making a medicament for treating an inflammatory epithelial disease, the compound having the formula:



wherein Z has the formula:



R represents from 0 to 5 substitutions for hydrogen;
the index n is an integer from 0 to 5;
L is chosen from CH_2 or SO_2;
R^1 and R^2 are each independently chosen from:

ix) hydrogen;
x) substituted or unsubstituted C_1-C_{10} linear, branched, or cyclic alkyl;
xi) substituted or unsubstituted C_2-C_{10} linear, branched, or cyclic alkenyl;
xii) substituted or unsubstituted C_2-C_{10} linear or branched alkynyl;
xiii) substituted or unsubstituted C_6 or C_{10} aryl;
xiv) substituted or unsubstituted C_1-C_9 heterocyclic;
xv) substituted or unsubstituted C_1-C_9 heteroaryl; or
xvi) R^1 and R^2 can be taken together to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring having from form 2 to 20 carbon atoms and from 1 to 7 heteroatoms; or

a pharmaceutically acceptable salt thereof.

46. The use according to Claim 45, wherein the one or more compounds are in the form of a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

47. The use according to either one of Claims 45 or 46, wherein L is CH_2.

48. The use according to either one of Claims 45 or 46, wherein L is SO_2.

49. The use according to any of one of Claims 45 to 48, wherein each R is a substitution for hydrogen independently chosen from:

i) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

ii) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkenyl;

iii) substituted or unsubstituted C_2-C_{12} linear or C_3-C_{12} branched alkynyl;

iv) C_6 or C_{10} substituted or unsubstituted aryl;

v) C_1-C_9 substituted or unsubstituted heterocyclic;

vi) C_1-C_{11} substituted or unsubstituted heteroaryl;

vii) halogen;

viii) $–[C(R^{23a})(R^{23b})]_xOR^{10}$;

R^{10} is chosen from:

a) –H;

b) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

c) C_6 or C_{10} substituted or unsubstituted aryl or alkylenearyl;

d) C_1-C_9 substituted or unsubstituted heterocyclic;

e) C_1-C_{11} substituted or unsubstituted heteroaryl;

ix) $–[C(R^{23a})(R^{23b})]_xN(R^{11a})(R^{11b})$;

R^{11a} and R^{11b} are each independently chosen from:

a) –H;

b) $–OR^{12}$;

R^{12} is hydrogen or C_1-C4 linear alkyl;

c) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

d) C_6 or C_{10} substituted or unsubstituted aryl;

e) C_1-C_9 substituted or unsubstituted heterocyclic;

f) C_1-C_{11} substituted or unsubstituted heteroaryl; or

g) R^{11a} and R^{11b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

x) $–[C(R^{23a})(R^{23b})]_xC(O)R^{13}$;

R^{13} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $–OR^{14}$;

R^{14} is hydrogen, substituted or unsubstituted C_1-C_4 linear alkyl, C_6 or C_{10} substituted or unsubstituted aryl, C_1-C_9 substituted or unsubstituted heterocyclic, C_1-C_{11} substituted or unsubstituted heteroaryl;

c) $–N(R^{15a})(R^{15b})$;

R^{15a} and R^{15b} are each independently hydrogen, substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{15a} and R^{15b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xi) $–[C(R^{23a})(R^{23b})]_xOC(O)R^{16}$;

R^{16} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $–N(R^{17a})(R^{17b})$;

R^{17a} and R^{17b} are each independently hydrogen, substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{17a} and R^{17b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xii) $–[C(R^{23a})(R^{23b})]_xNR^{18}C(O)R^{19}$;

R^{18} is:

a) –H; or

b) substituted or unsubstituted C_1-C4 linear, C_3-C_4 branched, or C_3-C_4 cyclic alkyl;

$R^{19}$is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $–N(R^{20a})(R^{20b})$;

R^{20a} and R^{20b} are each independently hydrogen, substituted or unsubstituted C_1-C_4 linear or C_2-C_4 branched alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{20a} and R^{20b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xiii) $–[C(R^{23a})(R^{23b})]_xCN$;

xiv) $–[C(R^{23a})(R^{23b})]_xNO_2$;

xv) $–[C(R^{23a})(R^{23b})]_xR^{21}$;

R^{21} is C_1-C_{10} linear, branched, or cyclic alkyl substituted by from 1 to 21 halogen atoms chosen from –F, –Cl, –Br, or –I;

xvi) $–[C(R^{23a})(R^{23b})]_xSO_2R^{22}$;

R^{22} is hydrogen, hydroxyl, substituted or unsubstituted C_1-C_4 linear or C_2-C_4 branched alkyl; substituted or unsubstituted C_6, C_{10}, or C_{14} aryl; C_7-C_{15} alkylenearyl; C_1-C_9 substituted or unsubstituted heterocyclic; or C_1-C_{11} substituted or unsubstituted heteroaryl;

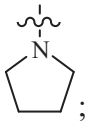
R^{23a} and R^{23b} are each independently hydrogen or C_1-C_4 alkyl; and

the index x is an integer from 0 to 5.

50. The use according to any of one of Claims 45 to 49, wherein R^1 and R^2 are taken together to form a 5-member substituted or unsubstituted C_1-C_4 heterocyclic or a substituted or unsubstituted C_1-C_4 heteroaryl ring.

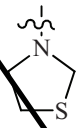
51. The use according to any of one of Claims 45 to 50, wherein R^1 and R^2 are taken together to form a ring having the formula:

i)



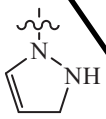
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ii)

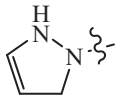


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ii)

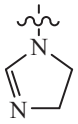


or



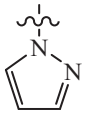
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iii)



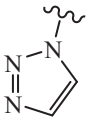
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iv)

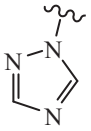


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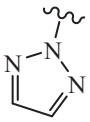
v)



or

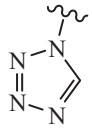


or



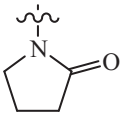
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vi)

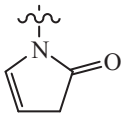


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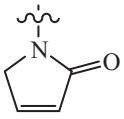
vii)



or

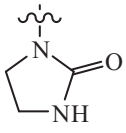


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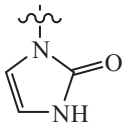


; or

viii)



or

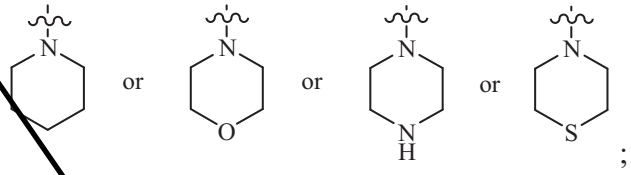


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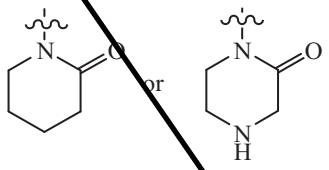
52. The use according to any of one of Claims 45 to 49, wherein R^1 and R^2 are taken together to form a substituted or unsubstituted C_4-C_{11} heterocyclic or a substituted or unsubstituted C_4-C_{11} heteroaryl ring.

53. The use according to any of one of Claims 45 to 49, wherein R^1 and R^2 are taken together to form a ring having the formula:

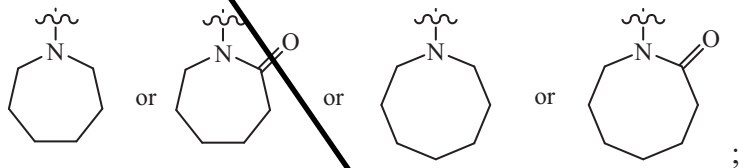
i)



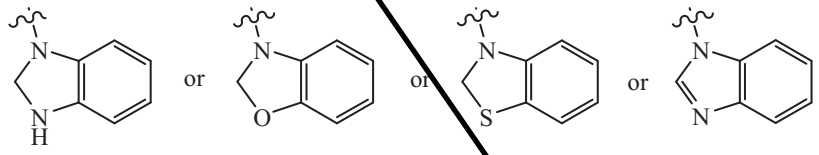
ii)



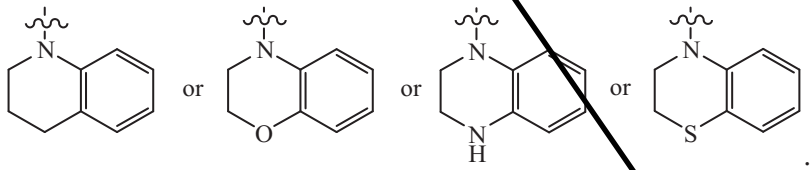
iii)



iv)



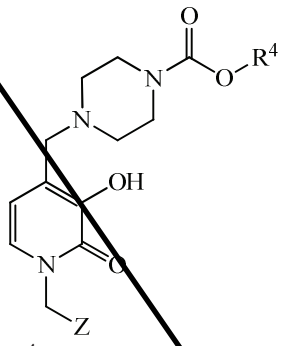
v)



54. The use according to any of one of Claims 45 to 49, wherein R^1 and R^2 are taken together to form a ring chosen from pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-(pyrdin-2-yl)pyrrolidin-1-yl, 2-methylcarboxypyrrolidin-1-yl, 2-(methoxymethyl)pyrrolidin-1-yl, thiazolidin-3-yl, 1*H*-imidazol-1-yl, piperidin-1-yl, 4-benzylpiperidin-1-yl, 1,4'-bipiperidinyl-1'-yl, piperazin-1-yl, 4-benzylpiperazin-1-yl, 4-(2-methoxyphenyl)-piperazin-1-ylmethyl, 4-(6-chloropyridazin-3-yl)piperazin-1-yl, 1,4-dioxa-8-azaspiro[4,5]dec-8-yl, morpholin-4-yl, thiomorpholin-4-yl, azepan-1-yl, azocan-1-yl, and 3,4-dihydroquinolin-1(2*H*)-yl.

55. The use according to any of one of Claims 45 to 49, wherein R^2 is hydrogen and R^1 is chosen from benzyl, 4-methoxybenzyl, 4-fluorobenzyl, 4-chlorobenzyl, 4-methylbenzyl, 2-(pyridin-2-yl)ethyl, [1,3]dioxolan-2-ylmethyl, tetrahydrofuran-2-ylmethyl, 2-methoxyethyl, 1-hydroxy-2-methylpropan-2-yl, pyridin-4-ylmethyl, furan-2-ylmethyl, 2-(methylthio)ethyl, 1-phenylethyl, 3-imidazol-1-ylpropyl, cycloheptyl, 4-methylcyclohexyl, 1-benzylpiperidin-4-yl, azepan-2-on-3-yl, and 1-benzyl-pyrrolidin-3-yl.

56. The use according to Claim 45, wherein the one or more compounds have the formula:



R^4 is C_1-C_4 linear alkyl or C_3-C_4 branched alkyl;
or a pharmaceutically acceptable salt thereof.

57. The use according to Claim 56, wherein R^4 is methyl.

58. The use according to Claim 56, wherein R^4 is ethyl.

59. The use according to Claim 56, wherein R^4 is *tert*-butyl.

60. The use according to any one of Claims 56 to 59, wherein Z is 4-chlorophenyl.

61. The use according to any one of Claims 56 to 59, wherein Z is chosen from 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, or 4-fluorophenyl.

62. The use according to any one of Claims 56 to 59, wherein Z is chosen from 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 2,5-dichlorophenyl, and 2,6-dichlorophenyl.

62. The use according to Claim 45, wherein the compound is chosen from is *tert*-butyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}-piperazine-1-carboxylate or a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

63. The use according to Claim 45, wherein the compound is chosen from:
Methyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

tert-Butyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Methyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
Ethyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;
tert-Butyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate; and
tert-Butyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate.

64. The use according to any one of Claims 45 to 63, wherein the inflammatory epithelial disease is a disease affecting intestinal epithelial tissue.

65. The use according to any one of Claims 45 to 63, wherein the disease is Crohn's disease.

66. The use according to any one of Claims 45 to 63, wherein the disease is ulcerative colitis.

67. The use according to any one of Claims 45 to 63, wherein the disease is collagenous colitis.

68. The use according to any one of Claims 45 to 63, wherein the disease is lymphocytic colitis.

69. The use according to any one of Claims 45 to 63, wherein the disease is ischemic colitis.

70. The use according to any one of Claims 45 to 63, wherein the disease is diversion colitis.

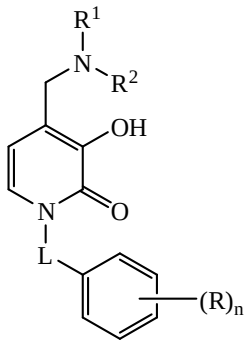
71. The use according to any one of Claims 45 to 63, wherein the disease is Behçet's syndrome.

72. The use according to any one of Claims 45 to 63, wherein the disease is indeterminate colitis.

73. The use according to any one of Claims 45 to 63, wherein the inflammatory epithelial disease is chosen from a disease affecting the respiratory tract, mucosa, skin, GI tract, lining of major organs and endocrine glands, vascular tissue, and combinations thereof.

CLAIMS

1. Use of a composition in the manufacture of a medicament for treating a subject for an inflammatory epithelial disease, the composition comprising an effective amount of one or more compounds having the formula:



wherein L is chosen from CH_2 or SO_2;

R represents from 0 to 5 substitutions for hydrogen;

the index n is an integer from 0 to 5;

R^1 and R^2 are each independently chosen from:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_{10} linear, branched, or cyclic alkyl;

iii) substituted or unsubstituted C_2-C_{10} linear, branched, or cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_{10} linear or branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heterocyclic;

vii) substituted or unsubstituted C_1-C_9 heteroaryl; or

viii) R^1 and R^2 can be taken together to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring having from form 2 to 20 carbon atoms and from 1 to 7 heteroatoms; or

a pharmaceutically acceptable salt thereof.

2. The use of a composition according to Claim 1, wherein the one or more compounds are in the form of a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

3. The use of a composition according to Claim 1, wherein the inflammatory epithelial disease is a disease affecting intestinal epithelial tissue.

4. The use of a composition according to Claim 3, wherein the disease is Crohn's disease.

5. The use of a composition according to Claim 3, wherein the disease is ulcerative colitis.

6. The use of a composition according to Claim 3, wherein the disease is collagenous colitis.

7. The use of a composition according to Claim 3, wherein the disease is lymphocytic colitis.

8. The use of a composition according to Claim 3, wherein the disease is ischemic colitis.

9. The use of a composition according to Claim 3, wherein the disease is diversion colitis.

10. The use of a composition according to Claim 3, wherein the disease is Behçet's syndrome.

11. The use of a composition according to Claim 3, wherein the disease is indeterminate colitis.

12. The use of a composition according to Claim 1, wherein the inflammatory epithelial disease is chosen from a disease affecting the respiratory tract, mucosa, skin, GI tract, lining of major organs and endocrine glands, vascular tissue, and combinations thereof.

13. The use of a composition according to Claim 1, wherein L is CH_2.

14. The use of a composition according to Claim 1, wherein L is SO_2.

15. The use of a composition according to Claim 1, wherein each R is a substitution for hydrogen independently chosen from:

i) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

ii) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkenyl;

iii) substituted or unsubstituted C_2-C_{12} linear or C_3-C_{12} branched alkynyl;

iv) C_6 or C_{10} substituted or unsubstituted aryl;

v) C_1-C_9 substituted or unsubstituted heterocyclic;

vi) C_1-C_{11} substituted or unsubstituted heteroaryl;

vii) halogen;

viii) $-[C(R^{23a})(R^{23b})]_xOR^{10}$;

R^{10} is chosen from:

a) –H;

b) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

c) C_6 or C_{10} substituted or unsubstituted aryl or alkylenearyl;

d) C_1-C_9 substituted or unsubstituted heterocyclic;

e) C_1-C_{11} substituted or unsubstituted heteroaryl;

ix) $-[C(R^{23a})(R^{23b})]_xN(R^{11a})(R^{11b})$;

R^{11a} and R^{11b} are each independently chosen from:

a) –H;

b) $-OR^{12}$;

R^{12} is hydrogen or C_1-C4 linear alkyl;

c) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

d) C_6 or C_{10} substituted or unsubstituted aryl;

e) C_1-C_9 substituted or unsubstituted heterocyclic;

f) C_1-C_{11} substituted or unsubstituted heteroaryl; or

g) R^{11a} and R^{11b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

x) $-[C(R^{23a})(R^{23b})]_xC(O)R^{13}$;

R^{13} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $-OR^{14}$;

R^{14} is hydrogen, substituted or unsubstituted C_1-C_4 linear alkyl, C_6 or C_{10} substituted or unsubstituted aryl, C_1-C_9 substituted or unsubstituted heterocyclic, C_1-C_{11} substituted or unsubstituted heteroaryl;

c) $-N(R^{15a})(R^{15b})$;

R^{15a} and R^{15b} are each independently hydrogen, substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{15a} and R^{15b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xi) $-[C(R^{23a})(R^{23b})]_xOC(O)R^{16}$;

R^{16} is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $-N(R^{17a})(R^{17b})$;

R^{17a} and R^{17b} are each independently hydrogen, substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl; C_6 or C_{10} substituted or unsubstituted aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{17a} and R^{17b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xii) $-[C(R^{23a})(R^{23b})]_xNR^{18}C(O)R^{19}$;

R^{18} is:

a) –H; or

b) substituted or unsubstituted C_1-C4 linear, C_3-C_4 branched, or C_3-C_4 cyclic alkyl;

$R^{19}$is:

a) substituted or unsubstituted C_1-C_{12} linear, C_3-C_{12} branched, or C_3-C_{12} cyclic alkyl;

b) $-N(R^{20a})(R^{20b})$;

R^{20a} and R^{20b} are each independently hydrogen, substituted or unsubstituted C_1-C_4 linear or C_2-C_4 branched alkyl; C_6 or C_{10} substituted or unsubstituted

aryl; C_1-C_9 substituted or unsubstituted heterocyclic; C_1-C_{11} substituted or unsubstituted heteroaryl; or R^{20a} and R^{20b} can be taken together to form a substituted or unsubstituted ring having from 3 to 10 carbon atoms and from 0 to 3 heteroatoms chosen from oxygen, nitrogen, and sulfur;

xiii) $-[C(R^{23a})(R^{23b})]_xCN$;

xiv) $-[C(R^{23a})(R^{23b})]_xNO_2$;

xv) $-[C(R^{23a})(R^{23b})]_xR^{21}$;

R^{21} is C_1-C_{10} linear, branched, or cyclic alkyl substituted by from 1 to 21 halogen atoms chosen from –F, –Cl, –Br, or –I;

xvi) $-[C(R^{23a})(R^{23b})]_xSO_2R^{22}$;

R^{22} is hydrogen, hydroxyl, substituted or unsubstituted C_1-C_4 linear or C_2-C_4 branched alkyl; substituted or unsubstituted C_6, C_{10}, or C_{14} aryl; C_7-C_{15} alkylenearyl; C_1-C_9 substituted or unsubstituted heterocyclic; or C_1-C_{11} substituted or unsubstituted heteroaryl;

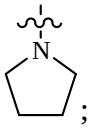
R^{23a} and R^{23b} are each independently hydrogen or C_1-C_4 alkyl; and

the index x is an integer from 0 to 5.

16. The use of a composition according to Claim 1, wherein R^1 and R^2 are taken together to form a 5-member substituted or unsubstituted C_1-C_4 heterocyclic or a substituted or unsubstituted C_1-C_4 heteroaryl ring.

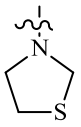
17. The use of a composition according to Claim 16, wherein R^1 and R^2 are taken together to form a ring having the formula:

i)



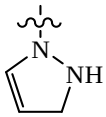
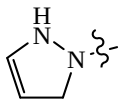
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ii)

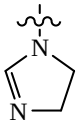


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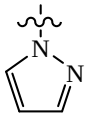
ii)

 or  ;

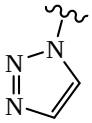
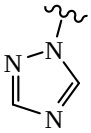
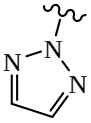
iii)

 ;

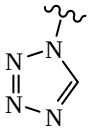
iv)

 ;

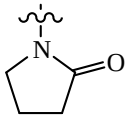
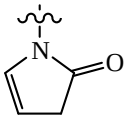
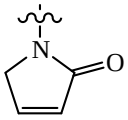
v)

 or  or  ;

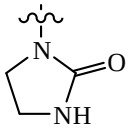
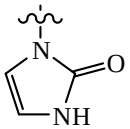
vi)

 ;

vii)

 or  or  ; or

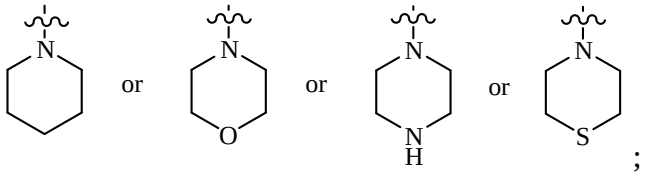
viii)

 or  .

18. The use of a composition according to Claim 1, wherein R^1 and R^2 are taken together to form a substituted or unsubstituted C_4-C_{11} heterocyclic or a substituted or unsubstituted C_4-C_{11} heteroaryl ring.

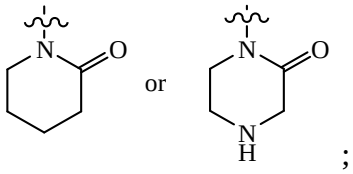
19. The use of a composition according to Claim 18, wherein R^1 and R^2 are taken together to form a ring having the formula:

i)



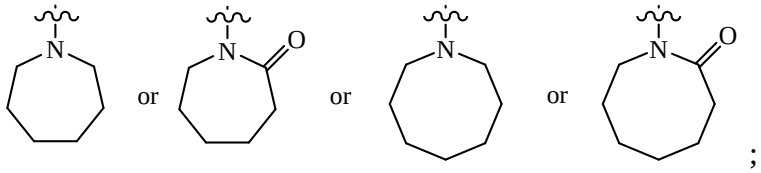
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ii)



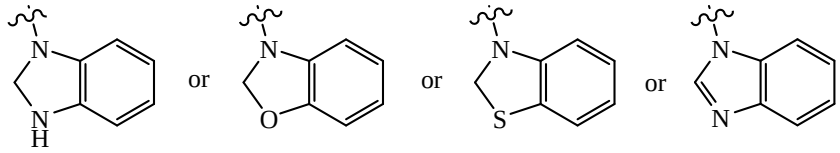
;

iii)



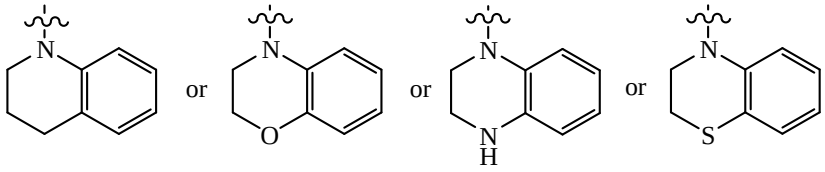
;

iv)



; or

v)

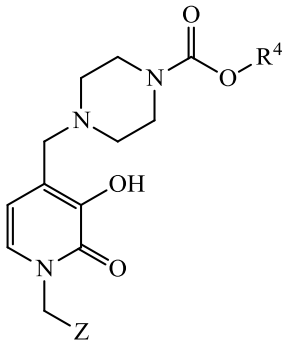


.

20. The use of a composition according to Claim 1, wherein R^1 and R^2 are taken together to form a ring chosen from pyrrolidin-1-yl, 3-hydroxypyrrolidin-1-yl, 2-(pyrdin-2-yl)pyrrolidin-1-yl, 2-methylcarboxypyrrolidin-1-yl, 2-(methoxymethyl)pyrrolidin-1-yl, thiazolidin-3-yl, 1*H*-imidazol-1-yl, piperidin-1-yl, 4-benzylpiperidin-1-yl, 1,4'-bipiperidinyl-1'-yl, piperazin-1-yl, 4-benzylpiperazin-1-yl, 4-(2-methoxyphenyl)-piperazin-1-ylmethyl, 4-(6-chloropyridazin-3-yl)piperazin-1-yl, 1,4-dioxa-8-azaspiro[4,5]dec-8-yl, morpholin-4-yl, thiomorpholin-4-yl, azepan-1-yl, azocan-1-yl, and 3,4-dihydroquinolin-1(2*H*)-yl.

21. The use of a composition according to Claim 1, wherein R^2 is hydrogen and R^1 is chosen from benzyl, 4-methoxybenzyl, 4-fluorobenzyl, 4-chlorobenzyl, 4-methylbenzyl, 2-(pyridin-2-yl)ethyl, [1,3]dioxolan-2-ylmethyl, tetrahydrofuran-2-ylmethyl, 2-methoxyethyl, 1-hydroxy-2-methylpropan-2-yl, pyridin-4-ylmethyl, furan-2-ylmethyl, 2-(methylthio)ethyl, 1-phenylethyl, 3-imidazol-1-ylpropyl, cycloheptyl, 4-methylcyclohexyl, 1-benzylpiperidin-4-yl, azepan-2-on-3-yl, and 1-benzyl-pyrrolidin-3-yl.

22. The use of a composition according to Claim 1, wherein the one or more compounds have the formula:



wherein Z is phenyl substituted with from 1 to 5 halogens chosen from fluorine and chlorine; R^4 is C_1-C_4 linear alkyl or C_3-C_4 branched alkyl; or
a pharmaceutically acceptable salt thereof.

23. The use of a composition according to Claim 22, wherein R^4 is methyl.

24. The use of a composition according to Claim 22, wherein R^4 is ethyl.

25. The use of a composition according to Claim 22, wherein R^4 is *tert*-butyl.

26. The use of a composition according to Claim 22, wherein Z is 4-chlorophenyl.

27. The use of a composition according to Claim 22, wherein Z is chosen from 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, or 4-fluorophenyl.

28. The use of a composition according to Claim 22, wherein Z is chosen from 2,3-difluorophenyl, 2,4-difluorophenyl, 2,5-difluorophenyl, 2,6-difluorophenyl, 2,3-dichlorophenyl, 2,4-dichlorophenyl, 2,5-dichlorophenyl, and 2,6-dichlorophenyl.

29. The use of a composition according to Claim 1, wherein the one or more compounds is *tert*-butyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}-piperazine-1-carboxylate or a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

30. The use of a composition according to Claim 1, wherein the one or more compounds is chosen from:

Methyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Methyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Methyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

tert-Butyl 4-{[1-(3-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

tert-Butyl 4-{[1-(2-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Methyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Methyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Methyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

Ethyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

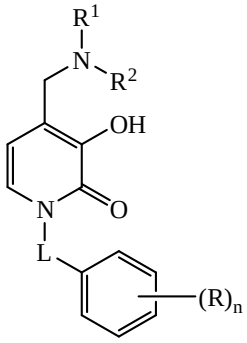
tert-Butyl 4-{[1-(4-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate;

tert-Butyl 4-{[1-(3-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate; and

tert-Butyl 4-{[1-(2-fluorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}piperazine-1-carboxylate.

31. A composition for use in treating a subject for an inflammatory epithelial disease, comprising

a) an effective amount of one or more compounds having the formula:



wherein L is chosen from CH_2 or SO_2;

R represents from 0 to 5 substitutions for hydrogen;

the index n is an integer from 0 to 5;

R^1 and R^2 are each independently chosen from:

i) hydrogen;

ii) substituted or unsubstituted C_1-C_{10} linear, branched, or cyclic alkyl;

iii) substituted or unsubstituted C_2-C_{10} linear, branched, or cyclic alkenyl;

iv) substituted or unsubstituted C_2-C_{10} linear or branched alkynyl;

v) substituted or unsubstituted C_6 or C_{10} aryl;

vi) substituted or unsubstituted C_1-C_9 heterocyclic;

vii) substituted or unsubstituted C_1-C_9 heteroaryl; or

i) R^1 and R^2 can be taken together to form a substituted or unsubstituted heterocyclic or substituted or unsubstituted heteroaryl ring having from form 2 to 20 carbon atoms and from 1 to 7 heteroatoms;

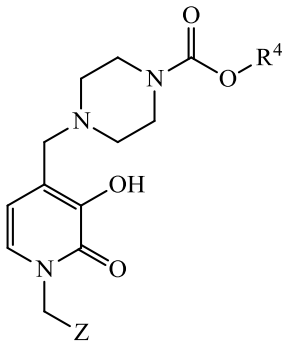
R^4 is C_1-C_4 linear or C_3-C_4 branched alkyl; or

a pharmaceutically acceptable salt thereof; and

b) one or more excipients.

32. The composition according to Claim 31, wherein the one or more compounds are in the form of a pharmaceutically acceptable salt chosen from hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

33. The composition according to Claim 31, wherein the one or more compounds have the formula:



wherein Z is phenyl substituted with from 1 to 5 halogens chosen from fluorine and chlorine;

R^4 is C_1-C_4 linear alkyl or C_3-C_4 branched alkyl; or

a pharmaceutically acceptable salt thereof.

34. The composition according to Claim 33, wherein R^4 is methyl.

35. The composition according to Claim 33, wherein R^4 is ethyl.

36. The composition according to Claim 33, wherein R^4 is *tert*-butyl.

37. The composition according to Claim 33, wherein Z is 4-chlorophenyl.

38. The composition according to Claim 33, wherein Z is chosen from 2-chlorophenyl, 3-chlorophenyl, 2-fluorophenyl, 3-fluorophenyl, or 4-fluorophenyl.

39. The composition according to Claim 31, wherein the one or more compounds is *tert*-butyl 4-{[1-(4-chlorobenzyl)-3-hydroxy-2-oxo-1,2-dihydropyridin-4-yl]methyl}-piperazine-1-carboxylate or a pharmaceutically acceptable salt hydrochloride salt, hydrogen sulfate salt, sulfate salt, p-toluenesulfonyl salt, methansulfonyl salt and mixtures thereof.

40. The composition according to Claim 31, further comprising one or more chemotherapeutic compounds.

41. The composition according to Claim 40, wherein the one or more chemotherapeutic compounds are chosen from 6-hydroxymethylacylfulvene, cyclophosphamide, dacarbazine, carmustine, doxorubicin, and methotrexate.

42. The composition according to Claim 31, wherein the inflammatory epithelial disease is chosen from Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischemic colitis, diversion colitis, Behçet's syndrome, and indeterminate colitis