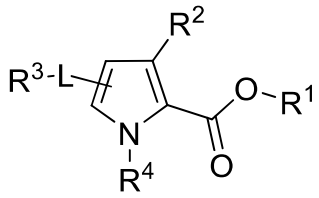
Provided herein are novel pyrrole derivatives for use in the treatment of conditions in which targeting of the ACC pathway or inhibition of AC carboxylase can be therapeutically useful.

It has now been found that certain pyrrole derivatives are novel and potent ACC inhibitors and can therefore be used in the treatment or prevention of these diseases.

SUMMARY

Thus the present disclosure is directed to new compounds that possess ACC inhibitory activity. Accordingly in one aspect, there is provided a pyrrole derivative, which pyrrole derivative is a compound of Formula (I), or a pharmaceutically acceptable salt, or a solvate, or a *N*-oxide, or a tautomer, or a stereoisomer, or an isotopically-labelled derivative thereof :



Formula (I)

wherein:

- R^1 is selected from the group consisting of a hydrogen atom, a linear or branched C_{1-4} alkyl group, a linear or branched C_{1-4} haloalkyl group, a linear or branched C_{1-10} hydroxyalkyl group, a –$(CH_2)_{0-3}$ –(C_{3-7} monocyclic cycloalkyl group), a –$(CH_2)_{0-3}$– (monocyclic or bicyclic C_{6-14} aryl group), a –$(CH_2)_{0-3}$–(4- to 7-membered heterocyclyl group containing at least one heteroatom selected from N, O and S), a –$(CH_2)_{0-3}$ – (monocyclic or bicyclic 5- to 14-membered heteroaryl group containing at least one heteroatom selected from N, O and S), a -$(CH_2)_{0-4}$-$[(CH_2)_{1-3}$-O$]_{1-5}$-R^a group, a -$(CR^aR^b)_{1-3}$-OC(O)-R^5 group and a -$(CH_2)_{1-3}$-C(O)NR^5R^a group,

  wherein the cycloalkyl, aryl, heterocyclyl and heteroaryl groups are unsubstituted or substituted by one or more substituents selected from a halogen atom, a linear or branched C_{1-4} alkyl group and an oxo group;

- R^2 is selected from the group consisting of a hydrogen atom, halogen atom, a –CN group and a linear or branched C_{1-4} alkyl group;

- R^3 represents a linear or branched C_{9-20} alkyl group,

  wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, a hydroxyl group, a linear or branched C_{1-4} alkyl group, a linear or branched C_{1-6} alkoxy group and a linear or branched C_{1-4} hydroxyalkyl group;

- R^4 is selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group;

- R^5 is selected from the group consisting of a hydrogen atom, a linear or branched C_{1-10} alkyl group, a -O-(linear or branched C_{1-10} alkyl group), a -O–$(CH_2)_{0-3}$–(C_{3-7} monocyclic cycloalkyl group), a -O–$(CH_2)_{0-3}$–(monocyclic or bicyclic C_{6-14} aryl group), a -$(CH_2)_{0-3}C(O)OR^a$ group and a –O-$[(CH_2)_{1-3}\text{-}O]_{1-5}\text{-}R^a$ group;

  wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, hydroxyl group and an amino group;

- R^a and R^b are independently selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group; wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom and hydroxyl group; and

- L represents a direct bond, a –$(CH_2)_{0-4}$-O- group, a –$(CH_2)_{0-4}$-S- group, a –$(CH_2)_{0-4}$-NR_a- group, a –$C(O)NR^a$- group, a –$NR^aC(O)$- group or a carbonyl group; wherein when R^2 represents a hydrogen atom, L represents a–$(CH_2)_{0-4}$-O- group or a–$C(O)NR^a$- group.

The disclosure further provides synthetic processes and intermediates described herein, which are useful for preparing said pyrrole derivatives.

The disclosure is also directed to a pyrrole derivative of the disclosure as described herein for use in the treatment of the human or animal body by therapy.

The disclosure also provides a pharmaceutical composition comprising the pyrrole derivatives of the disclosure and a pharmaceutically-acceptable diluent or carrier.

In another aspect, the present disclosure refers to a pyrrole derivative as described herein for use in the treatment of a pathological condition or disease susceptible to amelioration by inhibition of Acetyl-CoA carboxylase.

The disclosure is also directed to the pyrrole derivatives of the disclosure as described herein, for use in the treatment of a pathological condition or disease susceptible to amelioration by inhibiton of Acetyl-CoA carboxylase (ACC), in particular wherein the pathological condition or disease is selected from a dermatological disease, an inflammatory or autoimmune-mediated disease and a metabolism/endocrine function disorder. More in particular wherein the pathological condition or disease is selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, rosacea, Rhinophyma-type rosacea, seborrhea, seborrheic dermatitis, sebaceous gland hyperplasia, Meibomian gland dysfunction of facial rosacea, mitogenic alopecia, oily skin, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis, postular psoriasis and palmoplantar pustulosis; preferably in the treatment of acne vulgaris, acne conglobata, inflammatory acne, choracne, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis and postular psoriasis.

In another aspect, the present disclosure refers to use of a pyrrole derivative as described herein in the manufacture of a medicament for treating a pathological condition or disease susceptible to amelioration by inhibition of Acetyl-CoA carboxylase. In yet another aspect, the present disclosure refers to use of pyrrole derivative as described herein in the manufacture of a medicament for treating a pathological condition or disease selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, rosacea, Rhinophyma-type rosacea, seborrhea, seborrheic dermatitis, sebaceous gland hyperplasia, Meibomian gland dysfunction of facial rosacea, mitogenic alopecia, oily skin, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis, postular psoriasis and palmoplantar pustulosis.

The disclosure is also directed to use of the pyrrole derivatives of the disclosure as described herein, in the manufacture of a medicament for treatment of a pathological condition or disease susceptible to amelioration by inhibiton of Acetyl-CoA carboxylase (ACC), in particular wherein the pathological condition or disease is selected from a dermatological disease, an inflammatory or autoimmune-mediated disease and a metabolism/endocrine function disorder. More in particular wherein the pathological condition or disease is selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, rosacea, Rhinophyma-type rosacea, seborrhea, seborrheic dermatitis, sebaceous gland hyperplasia, Meibomian gland dysfunction of facial rosacea, mitogenic alopecia, oily skin, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis, postular psoriasis and palmoplantar pustulosis; preferably in the treatment of acne vulgaris, acne conglobata, inflammatory acne, choracne, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis and postular psoriasis.

In yet another aspect, the present disclosure refers to use of a pyrrole derivative as described herein in the manufacture of a medicament for treating a pathological condition or disease selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis and postular psoriasis. In yet another aspect, the present disclosure refers to a pharmaceutical composition comprising a pyrrole derivative as described herein in association with a pharmaceutically acceptable diluent or carrier.

The disclosure also provides a method of treatment of a pathological condition or disease susceptible to amelioration by inhibiton of Acetyl-CoA carboxylase (ACC), in particular wherein the pathological condition or disease is selected from a dermatological disease, an inflammatory or autoimmune-mediated disease and a metabolism/endocrine function disorder. More in particular wherein the pathological condition or disease is selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, rosacea, Rhinophyma-type rosacea, seborrhea, seborrheic dermatitis, sebaceous gland hyperplasia, Meibomian gland dysfunction of facial rosacea, mitogenic alopecia, oily skin, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis, postular psoriasis and palmoplantar pustulosis; preferably in the treatment of acne vulgaris, acne conglobata, inflammatory acne,

choracne, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis and postular psoriasis.

In a further aspect, the present disclosure refers to a combination product comprising (i) at least one pyrrole derivative as described herein, and (ii) one or more active ingredients selected from:

a) Corticoids and glucocorticoids ;
b) Dihydrofolate reductase inhibitors ;
c) Dihydroorotate dehydrogenase (DHODH) inhibitors ;
d) Purine antagonists ;
e) Antimalarials ;
f) Calcineurin inhibitors ;
g) Inosine-monophosphate dehydrogenase (IMPDH) inhibitors ;
h) Fumaric acid esters ;
i) Vitamine D3 derivatives ;
j) Retinoids ;
k) Anti-tumor necrosis factor-alpha (Anti-TNF-alpha) monoclonal antibodies ;
l) Soluble Tumor necrosis factor-alpha (TNF-alpha) receptors ;
m) Anti-Interleukin 6 Receptor (IL-6R) antibody ;
n) Anti-Interleukin 12 (IL-12) / Interleukin 23 (IL-23) antibody ;
o) Anti-Interleukin 17 Receptor (IL-17R) antibody ;
p) Anti-CD20 (B lymphocyte protein) antibody ;
q) Anti-Interleukin 5 (IL-5) antibody ;
r) Anti-Interleukin 5 Receptor (IL-5R) antibody ;
s) Anti-Interleukin 13 (IL-13) antibody ;
t) Anti-Interleukin 4 Receptor (IL-4R) / Interleukin 13 Receptor (IL-13R) antibody ;
u) Anti-Interleukin 17 (IL-17) antibody ;
v) An anti-IL-23 antibody ;
w) Anti-Interleukin 1 Receptor (IL-1R) antibody;
x) Anti-Inmunoglobuline E (IgE) antibody ;
y) Anti-B-cell activating factor (BAFF) ;
z) Anti-CD19 (B lymphocyte protein) monoclonal antibody ;
aa) Kappa opioid agonists ;
bb) Neurokinin receptor 1 antagonists ;
cc) Dihydropteroate synthase inhibitors ;

dd) Histamine 1 (H1) receptor antagonists ;
ee) Cysteinyl leukotriene (CysLT) receptor antagonists ;
ff) Chemoattractant receptor homologous molecule expressed on TH2 cells (CRTh2) antagonists ;
gg) Topical anti-septics ;
hh) Antibiotics ;
ii) Azelaic acid;
jj) α-hydroxy acids ;
kk) β-hydroxy acids ; and
ll) A PDE4 inhibitor.

The disclosure also provides a combination product comprising (i) the pyrrole derivatives of the disclosure as described herein; and (ii) one or more additional active substances.

DETAILED DESCRIPTION OF THE INVENTION

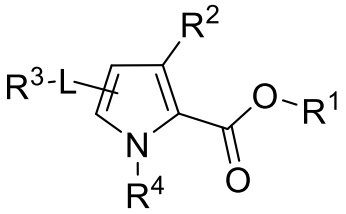
When describing the pyrrole derivatives, compositions, combinations and methods of the invention, the following terms have the following meanings, unless otherwise indicated.

As used herein the term C_{1-10} alkyl embraces linear or branched radicals having 1 to 10 carbon atoms. Examples include methyl, ethyl, *n*-propyl, i-propyl, *n*-butyl, *i*-butyl, *s*-butyl, *t*-butyl, *n*-pentyl, 1-methylbutyl, 2-methylbutyl, isopentyl, 1-ethylpropyl, 1,1-dimethylpropyl, 1,2-dimethylpropyl, *n*-hexyl, 1-ethylbutyl, 2-ethylbutyl, 1,1-dimethylbutyl, 1,2-dimethylbutyl, 1,3-dimethylbutyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl, 2-methylpentyl, 3-methylpentyl, iso-hexyl, heptyl, octyl, nonyl and decyl radicals. Such alkyl radical is typically unsubstituted or substituted by 1, 2 or 3 substituents which may be the same or different.

As used herein the term C_{1-4} alkyl embraces unsubstituted or substituted, linear or branched radicals having 1 to 4 carbon atoms. Analogously, the term C_{1-3} alkyl embraces linear or branched radicals having 1 to 3 carbon atoms and the term C_{1-2} alkyl embraces linear or branched radicals having 1 to 2 carbon atoms. Analogously, the term C_{2-4} alkyl embraces linear or branched radicals having 2 to 4 carbon atoms. Examples of C_{1-4} alkyl include methyl, ethyl, *n*-propyl, *i*-propyl, *n*-butyl, *i*-butyl, *sec*-butyl or *t*-butyl. Such alkyl radical is typically unsubstituted or substituted by 1,

CLAIMS

1. A pyrrole derivative, which pyrrole derivative is a compound of Formula (I), or a pharmaceutically acceptable salt, or a solvate, or a *N*-oxide, or a tautomer, or a stereoisomer, or an isotopically-labelled derivative thereof :



Formula (I)

wherein:

- R^1 is selected from the group consisting of a hydrogen atom, a linear or branched C_{1-4} alkyl group, a linear or branched C_{1-4} haloalkyl group, a linear or branched C_{1-10} hydroxyalkyl group, a $–(CH_2)_{0-3}–$(C_{3-7} monocyclic cycloalkyl group), a $–(CH_2)_{0-3}$ –(monocyclic or bicyclic C_{6-14} aryl group), a $–(CH_2)_{0-3}–$(4- to 7-membered heterocyclyl group containing at least one heteroatom selected from N, O and S), a $–(CH_2)_{0-3}–$(monocyclic or bicyclic 5- to 14-membered heteroaryl group containing at least one heteroatom selected from N, O and S), a $-(CH_2)_{0-4}-[(CH_2)_{1-3}-O]_{1-5}-R^a$ group, a $-(CR^aR^b)_{1-3}-OC(O)-R^5$ group and a $-(CH_2)_{1-3}-C(O)NR^5R^a$ group,

  wherein the cycloalkyl, aryl, heterocyclyl and heteroaryl groups are unsubstituted or substituted by one or more substituents selected from a halogen atom, a linear or branched C_{1-4} alkyl group and an oxo group;

- R^2 is selected from the group consisting of a hydrogen atom, halogen atom, a –CN group and a linear or branched C_{1-4} alkyl group;

- R^3 represents a linear or branched C_{9-20} alkyl group,

  wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, a hydroxyl group, a linear or branched C_{1-4} alkyl

group, a linear or branched C_{1-6} alkoxy group and a linear or branched C_{1-4} hydroxyalkyl group;

- R^4 is selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group;

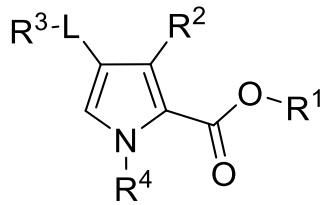
- R^5 is selected from the group consisting of a hydrogen atom, linear or branched C_{1-10} alkyl group, a -O-(linear or branched C_{1-10} alkyl group), a -O–$(CH_2)_{0-3}$–(C_{3-7} monocyclic cycloalkyl group), a -O–$(CH_2)_{0-3}$–(monocyclic or bicyclic C_{6-14} aryl group), a -$(CH_2)_{0-3}$C(O)OR^a group and a –O-[$(CH_2)_{1-3}$-O]$_{1-5}$-R^a group;

  wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, hydroxyl group and an amino group;

- R^a and R^b are independently selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group; wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom and a hydroxyl group; and

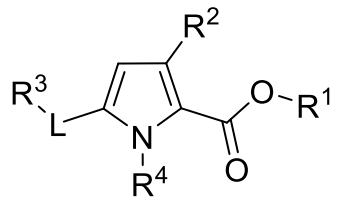
- L represents a direct bond, a –$(CH_2)_{0-4}$-O- group, a –$(CH_2)_{0-4}$-S- group, a –$(CH_2)_{0-4}$-NR_a- group, a –C(O)NR^a- group, a –NR^aC(O)- group or a carbonyl group; wherein when R^2 represents a hydrogen atom, L represents a–$(CH_2)_{0-4}$-O- group or a–C(O)NR^a- group.

2. A pyrrole derivative according to claim 1 wherein the compound of Formula (I) is represented by Formula (Ia):



Formula (Ia)

3. A pyrrole derivative according to claim 1 wherein the compound of Formula (I) is represented by Formula (Ib):



Formula (Ib)

4. A pyrrole derivative according to claims 1 to 3, wherein R^2 represents a halogen atom.

5. A pyrrole derivative according to claim 4 wherein R^2 represents a fluorine or chlorine atom.

6. A pyrrole derivative according to claims 1 to 5, wherein R^3 represents a linear or branched C_{9-20} alkyl group,

wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, a hydroxyl group, a linear or branched C_{1-4} alkyl group and a linear or branched C_{1-3} alkoxy group.

7. A pyrrole derivative according to claims 1 to 6, wherein L represents a direct bond or –O-.

8. A pyrrole derivative according to claim 1, wherein:

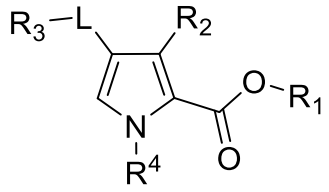
- R^2 represents a halogen atom;

- R^3 represents a linear or branched C_{9-20} alkyl group,
  wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, a hydroxyl group, a linear or branched C_{1-4} alkyl group and a linear or branched C_{1-3} alkoxy group; and

- L represents a direct bond or –O-.

9. A pyrrole derivative according to claim 8, wherein R^2 represents a fluorine or chlorine atom.

10. A pyrrole derivative according to claim 1 wherein the compound of Formula (I) is represented by Formula (Ia):



Formula (Ia)

wherein:

- R^1 is selected from the group consisting of a hydrogen atom, a linear or branched C_{1-4} alkyl group, a linear or branched C_{1-4} haloalkyl group, a linear or branched C_{2-10} hydroxyalkyl group, a cyclohexyl group, a $–CH_2–$phenyl group, a $–(CH_2)_{1-2}–$(5- to 6-membered heterocyclyl group containing at least one heteroatom selected from N, O and S), a $-(CH_2CH_2O)_{1-4}-R^a$ group, a $-(CR^aR^b)_{1-3}-OC(O)-R^5$ group and a $-(CH_2)_{1-3}-C(O)NR^5R^a$ group,

  wherein the cyclohexyl, phenyl and heterocyclyl groups are unsubstituted or substituted by one or more substituents selected from a halogen atom, a linear or branched C_{1-4} alkyl group and an oxo group;

- R^2 represents a halogen atom;

- R^3 represents a linear or branched C_{10-17} alkyl group, wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom, a hydroxyl group, a linear or branched C_{1-4} alkyl group and a linear or branched C_{1-3} alkoxy group;

- R^4 represents a hydrogen atom;

- R^5 is selected from the group consisting of a -O-(linear or branched C_{1-10} alkyl group), a -O–cyclohexyl group, a $-O–CH_2–$phenyl group, a $-(CH_2)_{1-2}C(O)OR^a$ group, a $–O-(CH_2CH_2O)_{1-3}-R^a$ group and a $–O-CH_2CH_2CH_2O-R^a$ group;

- R^a is selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group, wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom and hydroxyl group;

- R^b represents a hydrogen atom; and

- L represents a direct bond or –O-.

11. A pyrrole derivative according to claim 10, wherein:

- R^1 is selected from the group consisting of a hydrogen atom, a linear or branched C_{1-3} haloalkyl group, a linear or branched C_{3-9} hydroxyalkyl group, a $–(CH_2)_{1-2}–$(5-membered heterocyclyl group containing at least one heteroatom selected from N and O), a $-(CH_2CH_2O)_2-R^a$ group, a $-(CR^aR^b)-OC(O)-R^5$ group and a $-(CH_2)-C(O)NR^5R^a$ group, wherein the heterocyclyl group is unsubstituted or substituted by one or more substituents selected from a linear or branched C_{1-4} alkyl group and an oxo group;

- R^2 represents a fluorine atom or a chlorine atom;

- R^3 represents a linear or branched C_{10-17} alkyl group, wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a fluorine atom, a linear or branched C_{1-4} alkyl group and a linear or branched C_{1-3} alkoxy group;

- R^5 is selected from the group consisting of a -O-(linear or branched C_{2-4} alkyl group), a -O–cyclohexyl group, a $-O–CH_2–$phenyl group, a $-(CH_2)-C(O)OR^a$ group, a $–O-(CH_2CH_2O)_{1-2}-R^a$ group and a $–O-CH_2CH_2CH_2O-R^a$ group;

- R^a is selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group; wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a halogen atom and hydroxyl group.

12. A pyrrole derivative according to claim 1, wherein:

- R^1 is selected from the group consisting of a hydrogen atom, a linear or branched C_{1-4} alkyl group, a $-CH_2CF_3$ group, a $-(CH_2)_{2-9}-OH$ group, a $–CH_2-CH(OH)-CH_2-OH$, a $–CH(CH_2OH)_2$ group, a cyclohexyl group, a $–(CH_2)_2–$(2,5-dioxopyrrolidin-1-yl) group, a $–(CH_2)_2–$(2-oxopyrrolidin-1-yl) group, a $–(CH_2)–$(5-methyl-2-oxo-1,3-dioxol-4-yl) group, a $–CH_2–$phenyl group, a $-(CH_2CH_2O)_{2-4}-R^a$ group, a $-CH(CH_3)-OC(O)OCH(CH_3)_2$ group, a $-CH(CH_3)-OC(O)OC(CH_3)_3$ group, a $-CH(CH_3)-OC(O)O(CH_2)_8CH_3$ group, a $-CH(CH_3)-OC(O)O$-cyclohexyl group, a $-CH(CH_3)-OC(O)O-CH_2$-phenyl group, a $-CH(CH_3)-OC(O)O(CH_2CH_2O)_{1-2}-R^a$ group, a $-CH(CH_3)-OC(O)O(CH_2)_3OH$ group, a $-(CH_2)_2-OC(O)C(NH_2)-CH(CH_3)_2$ group and a $-CH_2-C(O)N(CH_3)CH_2CO_2R^a$ group;

- R^2 represents a hydrogen atom, methyl group, fluorine atom, chlorine atom, bromine atom or a –CN group;

- R^3 represents a linear C_{9-18} alkyl group,

  wherein the alkyl group is unsubstituted or substituted by one or more substituents selected from a fluorine atom, a linear or branched C_{1-4} alkyl group, and a linear or branched C_{1-3} alkoxy group;

- R^4 is selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group;

- R^a is selected from the group consisting of a hydrogen atom and a linear or branched C_{1-4} alkyl group;

- L represents a direct bond, –O-, –S- or a carbonyl group; wherein when R^2 represents a hydrogen atom, L represents a –O-.

13. A pyrrole derivative according to claims 1 to 12 wherein the compound of Formula (I) is one of:

4-(Dodecyloxy)-1H-pyrrole-2-carboxylic acid

Ethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-(2,5-Dioxopyrrolidin-1-yl)ethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-(2-Oxopyrrolidin-1-yl)ethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2,2,2-trifluoroethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-Hydroxyethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-(2-(2-(2-hydroxyethoxy)ethoxy)ethoxy)ethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

1-((isopropoxycarbonyl)oxy)ethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-((2-ethoxy-2-oxoethyl)(methyl)amino)-2-oxoethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-((L-valyl)oxy)ethyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 4-(dodecyloxy)-1H-pyrrole-2-carboxylate

4-Decyl-3-fluoro-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-undecyl-1H-pyrrole-2-carboxylic acid

4-Dodecyl-3-fluoro-1H-pyrrole-2-carboxylic acid

2,2,2-trifluoroethyl 4-dodecyl-3-fluoro-1H-pyrrole-2-carboxylate

2-(2-ethoxyethoxy)ethyl 4-dodecyl-3-fluoro-1H-pyrrole-2-carboxylate

1-((Isopropoxycarbonyl)oxy)ethyl 4-dodecyl-3-fluoro-1H-pyrrole-2-carboxylate

1-(((2-Methoxyethoxy)carbonyl)oxy)ethyl 4-dodecyl-3-fluoro-1H-pyrrole-2-carboxylate

4-oxo-3,5,8,11-tetraoxatridecan-2-yl 4-dodecyl-3-fluoro-1H-pyrrole-2-carboxylate

Ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

3-Fluoro-4-tridecyl-1H-pyrrole-2-carboxylic acid

Methyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

Isopropyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

Tert-butyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

Cyclohexyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

Benzyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2,2,2-Trifluoroethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2-(2,5-Dioxopyrrolidin-1-yl)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2-(2-Oxopyrrolidin-1-yl)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

(5-Methyl-2-oxo-1,3-dioxol-4-yl)methyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2-((2-Ethoxy-2-oxoethyl)(methyl)amino)-2-oxoethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2-Hydroxyethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

3-Hydroxypropyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

4-Hydroxybutyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

5-Hydroxypentyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

6-Hydroxyhexyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

7-Hydroxyheptyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

8-Hydroxyoctyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

9-Hydroxynonyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2,3-Dihydroxypropyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1,3-Dihydroxypropan-2-yl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2-(2-(2-(2-Hydroxyethoxy)ethoxy)ethoxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

2-(2-Ethoxyethoxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-((Isopropoxycarbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-((Tert-butoxycarbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-(((Nonyloxy)carbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-(((Cyclohexyloxy)carbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-(((Benzyloxy)carbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-(((2-Methoxyethoxy)carbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

1-(((3-Hydroxypropoxy)carbonyl)oxy)ethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

4-Oxo-3,5,8,11-tetraoxatridecan-2-yl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate

3-Fluoro-4-tetradecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-pentadecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-heptadecyl-1H-pyrrole-2-carboxylic acid

5-Dodecyl-3-fluoro-1H-pyrrole-2-carboxylic acid

3-Chloro-4-decyl-1H-pyrrole-2-carboxylic acid

3-Chloro-4-undecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-4-dodecyl-1H-pyrrole-2-carboxylic acid

9-Hydroxynonyl 3-chloro-4-dodecyl-1H-pyrrole-2-carboxylate

2-(2,5-dioxopyrrolidin-1-yl)ethyl 3-chloro-4-dodecyl-1H-pyrrole-2-carboxylate

3-Chloro-4-tridecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-4-pentadecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-4-hexadecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-5-undecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-5-dodecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-5-tridecyl-1H-pyrrole-2-carboxylic acid

3-chloro-5-tetradecyl-1H-pyrrole-2-carboxylic acid

3-Bromo-4-tridecyl-1H-pyrrole-2-carboxylic acid

1-Butyl-3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-1-isopropyl-4-tridecyl-1H-pyrrole-2-carboxylic acid

4-(Decyloxy)-3-fluoro-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylic acid

4-(Dodecyloxy)-3-fluoro-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-(tridecyloxy)-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-(tetradecyloxy)-1H-pyrrole-2-carboxylic acid

4-(Dodecylthio)-3-fluoro-1H-pyrrole-2-carboxylic acid

3-Chloro-4-(nonyloxy)-1H-pyrrole-2-carboxylic acid

3-Chloro-4-(decyloxy)-1H-pyrrole-2-carboxylic acid

3-chloro-4-(undecyloxy)-1H-pyrrole-2-carboxylic acid

3-Chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylic acid

2,2,2-trifluoroethyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

9-hydroxynonyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2-(2-ethoxyethoxy)ethyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

2,3-Dihydroxypropyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

1-((isopropoxycarbonyl)oxy)ethyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

4-Oxo-3,5,8,11-tetraoxatridecan-2-yl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

1-(((3-hydroxypropoxy)carbonyl)oxy)ethyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl 3-chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylate

3-Chloro-4-(tridecyloxy)-1H-pyrrole-2-carboxylic acid

3-Chloro-4-(tetradecyloxy)-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-pentadecanoyl-1H-pyrrole-2-carboxylic acid

4-(12-Ethoxydodecyl)-3-fluoro-1H-pyrrole-2-carboxylic acid

3-fluoro-4-(2-fluorotridecyl)-1H-pyrrole-2-carboxylic acid

4-(2,2-Difluorotridecyl)-3-fluoro-1H-pyrrole-2-carboxylic acid

4-(3,3-dimethyldodecyl)-3-fluoro-1H-pyrrole-2-carboxylic acid

4-((2,2-dimethyltridecyl)oxy)-3-fluoro-1H-pyrrole-2-carboxylic acid

4-((2,2-difluorotetradecyl)oxy)-3-fluoro-1H-pyrrole-2-carboxylic acid

4-((2,2-difluoroundecyl)oxy)-3-fluoro-1H-pyrrole-2-carboxylic acid

3-chloro-4-((2-fluorotetradecyl)oxy)-1H-pyrrole-2-carboxylic acid

3-chloro-4-((9-ethoxynonyl)oxy)-1H-pyrrole-2-carboxylic acid

3-Methyl-4-tridecyl-1H-pyrrole-2-carboxylic acid

4-(2,2-Dimethyldodecyl)-3-fluoro-1H-pyrrole-2-carboxylic acid

2,2,2-Trifluoroethyl 3-fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylate

2-(2-Ethoxyethoxy)ethyl 3-fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylate

1-((Isopropoxycarbonyl)oxy)ethyl 3-fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylate

1-(((2-Methoxyethoxy)carbonyl)oxy)ethyl 3-fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylate

4-Oxo-3,5,8,11-tetraoxatridecan-2-yl 3-fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylate

2,2,2-Trifluoroethyl 3-chloro-4-tridecyl-1H-pyrrole-2-carboxylate

2-(2-Ethoxyethoxy)ethyl 3-chloro-4-tridecyl-1H-pyrrole-2-carboxylate

1-((Isopropoxycarbonyl)oxy)ethyl 3-chloro-4-tridecyl-1H-pyrrole-2-carboxylate

1-(((2-methoxyethoxy)carbonyl)oxy)ethyl 3-chloro-4-tridecyl-1H-pyrrole-2-carboxylate

4-Oxo-3,5,8,11-tetraoxatridecan-2-yl 3-chloro-4-tridecyl-1H-pyrrole-2-carboxylate

2,2,2-trifluoroethyl 3-chloro-5-dodecyl-1H-pyrrole-2-carboxylate

2-(2-ethoxyethoxy)ethyl 3-chloro-5-dodecyl-1H-pyrrole-2-carboxylate

1-((isopropoxycarbonyl)oxy)ethyl 3-chloro-5-dodecyl-1H-pyrrole-2-carboxylate

1-(((2-methoxyethoxy)carbonyl)oxy)ethyl 3-chloro-5-dodecyl-1H-pyrrole-2-carboxylate

4-oxo-3,5,8,11-tetraoxatridecan-2-yl 3-chloro-5-dodecyl-1H-pyrrole-2-carboxylate

2,3-dihydroxypropyl 3-chloro-5-dodecyl-1H-pyrrole-2-carboxylate

3-Fluoro-5-undecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-tridecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-tetradecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-pentadecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-hexadecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-heptadecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-octadecyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-octadecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-5-(2,2-dimethyldodecyl)-1H-pyrrole-2-carboxylic acid

3-Chloro-5-(3,3-difluorododecyl)-1H-pyrrole-2-carboxylic acid

3-Cyano-5-dodecyl-1H-pyrrole-2-carboxylic acid

3-Chloro-5-dodecyl-1-methyl-1H-pyrrole-2-carboxylic acid

3-Fluoro-5-(14-fluorotetradecyl)-1H-pyrrole-2-carboxylic acid

3-Fluoro-4-hexadecyl-1H-pyrrole-2-carboxylic acid

or a pharmaceutically acceptable salt, or solvate, or N-oxide, or stereoisomer, or tautomer, or isotopically labelled derivative thereof.

14. A pyrrole derivative according to claim 1 which is 3-Fluoro-4-tridecyl-1H-pyrrole-2-carboxylic acid, or a pharmaceutically acceptable salt, or solvate, or N-oxide, or stereoisomer, or tautomer, or isotopically labelled derivative thereof.

15. A pyrrole derivative according to claim 1 which is 2,2,2-Trifluoroethyl 3-fluoro-4-tridecyl-1H-pyrrole-2-carboxylate, or a pharmaceutically acceptable salt, or solvate, or N-oxide, or stereoisomer, or tautomer, or isotopically labelled derivative thereof

16. A pyrrole derivative according to claim 1 which is 3-Fluoro-4-(undecyloxy)-1H-pyrrole-2-carboxylic acid, or a pharmaceutically acceptable salt, or solvate, or N-oxide, or stereoisomer, or tautomer, or isotopically labelled derivative thereof

17. A pyrrole derivative according to claim 1 which is 3-Chloro-4-(dodecyloxy)-1H-pyrrole-2-carboxylic acid, or a pharmaceutically acceptable salt, or solvate, or N-oxide, or stereoisomer, or tautomer, or isotopically labelled derivative thereof

18. A pyrrole derivative as defined in any one of claims 1 to 17, for use in the treatment of a pathological condition or disease susceptible to amelioration by inhibition of Acetyl-CoA carboxylase.

19. Use of a pyrrole derivative as defined in any one of claims 1 to 17 in the manufacture of a medicament for treating a pathological condition or disease susceptible to amelioration by inhibition of Acetyl-CoA carboxylase.

20. Use of a pyrrole derivative according to any one of claims 1 to 17 in the manufacture of a medicament for treating a pathological condition or disease selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, rosacea, Rhinophyma-type rosacea, seborrhea, seborrheic dermatitis, sebaceous gland hyperplasia, Meibomian gland dysfunction of facial rosacea, mitogenic alopecia, oily skin, plaque psoriasis, guttate psoriasis, inverse psoriasis,

erythrodermic psoriasis, scalp psoriasis, nail psoriasis, postular psoriasis and palmoplantar pustulosis.

21. Use of a pyrrole derivative according to any one of claims 1 to 17 in the manufacture of a medicament for treating a pathological condition or disease selected from acne vulgaris, acne conglobata, inflammatory acne, choracne, plaque psoriasis, guttate psoriasis, inverse psoriasis, erythrodermic psoriasis, scalp psoriasis, nail psoriasis and postular psoriasis.

22. A pharmaceutical composition comprising a pyrrole derivative as defined in any one of claims 1 to 17 in association with a pharmaceutically acceptable diluent or carrier.

23. A combination product comprising (i) at least one pyrrole derivative as defined in any one of claims 1 to 17, and (ii) one or more active ingredients selected from:

a) Corticoids and glucocorticoids ;
b) Dihydrofolate reductase inhibitors ;
c) Dihydroorotate dehydrogenase (DHODH) inhibitors ;
d) Purine antagonists ;
e) Antimalarials ;
f) Calcineurin inhibitors ;
g) Inosine-monophosphate dehydrogenase (IMPDH) inhibitors ;
h) Fumaric acid esters ;
i) Vitamine D3 derivatives ;
j) Retinoids ;
k) Anti-tumor necrosis factor-alpha (Anti-TNF-alpha) monoclonal antibodies ;
l) Soluble Tumor necrosis factor-alpha (TNF-alpha) receptors ;
m) Anti-Interleukin 6 Receptor (IL-6R) antibody ;
n) Anti-Interleukin 12 (IL-12) / Interleukin 23 (IL-23) antibody ;
o) Anti-Interleukin 17 Receptor (IL-17R) antibody ;
p) Anti-CD20 (B lymphocyte protein) antibody ;
q) Anti-Interleukin 5 (IL-5) antibody ;
r) Anti-Interleukin 5 Receptor (IL-5R) antibody ;

s) Anti-Interleukin 13 (IL-13) antibody ;
t) Anti-Interleukin 4 Receptor (IL-4R) / Interleukin 13 Receptor (IL-13R) antibody ;
u) Anti-Interleukin 17 (IL-17) antibody ;
v) An anti-IL-23 antibody ;
w) Anti-Interleukin 1 Receptor (IL-1R) antibody;
x) Anti-Inmunoglobuline E (IgE) antibody ;
y) Anti-B-cell activating factor (BAFF) ;
z) Anti-CD19 (B lymphocyte protein) monoclonal antibody ;
aa) Kappa opioid agonists ;
bb) Neurokinin receptor 1 antagonists ;
cc) Dihydropteroate synthase inhibitors ;
dd) Histamine 1 (H1) receptor antagonists ;
ee) Cysteinyl leukotriene (CysLT) receptor antagonists ;
ff) Chemoattractant receptor homologous molecule expressed on TH2 cells (CRTh2) antagonists ;
gg) Topical anti-septics ;
hh) Antibiotics ;
ii) Azelaic acid;
jj) α-hydroxy acids ;
kk) β-hydroxy acids ; and
ll) A PDE4 inhibitor .

24. A combination product according to claim 23, wherein
Corticoid or glucocorticoid is beclomethasone, betamethasone, betamethasone dipropionate, budesonide, dexamethasone, fluticasone furoate, fluticasone propionate, hydrocortisone, methylprednisolone, mometasone furoate, prednicarbate, prednisolone or prednisone;
Dihydrofolate reductase inhibitor is methotrexate or pralatrexate;
Dihydroorotate dehydrogenase (DHODH) inhibitor is leflunomide, teriflunomide or ASLAN-003 or LAS186323;
Purine antagonist is azathioprine, mercaptopurine or tioguanine;
Antimalarial is hydroxichloroquine, chloroquine or quinacrine;
Calcineurin inhibitor is cyclosporine A, tacrolimus, pimecrolimus or voclosporin;

Inosine-monophosphate dehydrogenase (IMPDH) inhibitor is mycophenolate mophetyl, ribavirin or mizoribine;
Fumaric acid ester is dimethyl fumarate;
Vitamine D3 derivative is calcipotriol, calcitriol or tacalcitol;
Retinoid is tazarotene, alitretinoin, acitretin or isotretinoin;
Anti-tumor necrosis factor-alpha (Anti-TNF-alpha) monoclonal antibody is infliximab, adalimumab, certolizumab pegol or golimumab;
Soluble Tumor necrosis factor-alpha (TNF-alpha) receptor is etanercept or CC-11050;
Anti-Interleukin 6 Receptor (IL-6R) antibody is tocilizumab, sarilumab, SA-237 or ALX-0061;
Anti-Interleukin 12 Receptor (IL-12R) / Interleukin 23 Receptor (IL-23R) antibody is ustekinumab;
Anti-Interleukin 17 Receptor (IL-17R) antibody is brodalumab;
Anti-CD20 (B lymphocyte protein) antibody is rituximab, ofatumumab, obinutuzumab, ocrelizumab, ublituximab, veltuzumab, or ocaratuzumab;
Anti-Interleukin 5 (IL-5) antibody is mepolizumab;
Anti-Interleukin 5 Receptor (IL-5R) antibody is benralizumab;
Anti-Interleukin 13 (IL-13) antibody is lebrikizumab or tralokinumab;
Anti-Interleukin 4 Receptor (IL-4R) / Interleukin 13 Receptor (IL-13R) antibody is dupilumab;
Anti-Interleukin 17 (IL-17) antibody is secukinumab, ixekizumab or bimekizumab;
An anti-IL-23 antibody is tildrakizumab, guselkumab or risankizumab;
Anti-Inmunoglobuline E (IgE) antibody is omalizumab or quilizumab;
Anti-B-cell activating factor (BAFF) is belimumab or atacicept;
Anti-CD19 (B lymphocyte protein) monoclonal antibody is blinatumomab, MEDI-551 or MOR-208;
Kappa opioid agonist is nalfurafine, nalbuphine, asimadoline or CR-845;
Neurokinin receptor 1 antagonist is aprepitant, fosaprepitant, rolapitant, orvepitant, tradipitant or serlopitant;
Dihydropteroate synthase inhibitor is dapsone or sulfadoxine;
Histamine 1 (H1) receptor antagonist is azelastine, ebastine, desloratadine, promethazine, mizolastine or cetirizine;
Cysteinyl leukotriene (CysLT) receptor antagonist is montelukast, zafirlukast, tipelukast, or masilukast;
Chemoattractant receptor homologous molecule expressed on TH2 cells (CRTH2) inhibitor is OC-459, AZD-1981, ADC-3680, ARRY-502 or setipripant;

Topical anti-septics is triclosan, chlorhexidine, crystal violet 0.3% or sodium hypochlorite water-baths;
Antibiotics is tetracyclines, macrolides or clindamycin;
α-hydroxy acids is glycolic acid or lactic acid;
β-hydroxy acids is salycilic acid; and
A PDE4 inhibitor is apremilast.

25. A combination product according to claim 24, wherein Tetracyclines is doxycycline, minocycline and tetracycline; and Macrolides is azithromycin, clarithromycin or erythromycin.