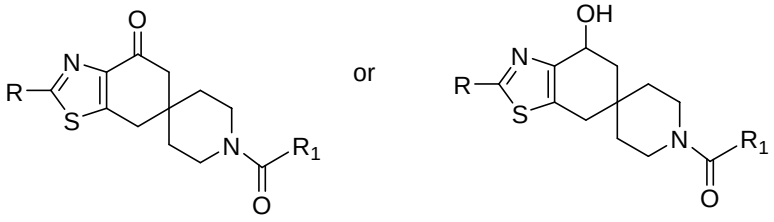
Claims

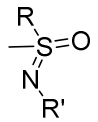
1. A compound of formula (I) having the structure:



(I)

or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt, wherein:

R is selected from the group consisting of H, C_1-C_6 alkoxy, C_1-C_6 alkyl and -$(CH_2)_m$-W, where W is C_3-C_8 cycloalkyl, bicyclo alkyl, bridged bicycloalkyl, , phenyl, , 5- or 6-membered heteroaryl or heterocyclic containing one, two or three heteroatoms selected from the group consisting of N, S and O atoms; wherein each of said alkyl, cycloalkyl, heterocyclic, phenyl, naphthyl or heteroaryl may be unsubstituted or substituted by phenyl, halo, cyano, deuterium, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, -SO_2-R', -CONR'R", NR'COR", -NR'CONR'R", -NR'CO_2R", -$(CH_2)_n$-SO_2-R', -NHSO_2-R', -NR"SO_2-R', -SO_2NR'R", NR'R" or SR' where R' and R'' are independently H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl;

R_1 is selected from the group consisting of phenyl, naphthyl, 5- or 6-membered heteroaryl or heterocyclic containing one, two, three or four heteroatoms selected from the group consisting of N, S and O atoms; and, a 9- or 10-membered bicyclic aryl, heteroaryl or heterocyclic containing one, two or three heteroatoms selected from the group consisting of N, S and O atoms; wherein each of said phenyl, naphthyl, aryl, heterocyclic, or heteroaryl may be unsubstituted or substituted by halo, cyano, deuterium, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -SO_2-R', -CONR'R", NR'COR", -NR'CONR'R", -NR'CO_2R", -$(CH_2)_n$-SO_2-R', -NHSO_2-R', -NR"SO_2-R', -SO_2NR'R", NR'R", -P(O)R'R",  or SR' where R' and R'' are independently H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl; and,

m and *n* are independently 0, 1, 2 or 3.

2. The compound of claim 1 wherein R is selected from the group consisting of H, C_1-C_6 alkyl and -$(CH_2)_m$-W, where W is C_3-C_8 cycloalkyl, wherein each of said alkyl, cycloalkyl, bicycloalkyl,

and bridged bicycloalkyl may be unsubstituted or substituted by halo, cyano, deuterium, hydroxy, C_1-C_6 alkyl and C_1-C_6 alkoxy; and,
m and *n* are independently 0, 1, 2 or 3.

3. The compound of claim 1 wherein R is t-butyl.

4. The compound according to claim 1 wherein R_1 is phenyl, pyridyl, indolyl, indazolyl, pyrrolopyridinyl, quinolinyl, isoquinolinyl or naphthyl; wherein each of said phenyl, pyridyl, indolyl, indazolyl, pyrrolopyridinyl, quinolinyl, isoquinolinyl or naphthyl may be unsubstituted or substituted by halo, cyano, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, phenyl, -CONR'R", NR'R" or SR' where R' and R'' are independently H, C_1-C_6 alkyl or C_3-C_8 cycloalkyl; and, *m* and *n* are independently 0, 1, 2 or 3.

5. The compound of claim 1 selected from the group consisting of:
2-(tert-butyl)-1'-(7-methoxy-1,3-dimethyl-1H-indazole-5-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one;
2-(tert-butyl)-1'-(7-methyl-1H-indole-5-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one;
2-(tert-butyl)-1'-(8-methyl-3-(methylamino)quinoline-6-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one;
2-(tert-butyl)-1'-(7-ethoxy-1,3-dimethyl-1H-indazole-5-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one; and,
2-(tert-butyl)-1'-(4-methyl-2-naphthoyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one;
or, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt.

6. The compound of claim 1 wherein the compound is 2-(tert-butyl)-1'-(7-methoxy-1,3-dimethyl-1H-indazole-5-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one; or, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt.

7. The compound of claim 1 wherein the compound is 2-(tert-butyl)-1'-(7-methyl-1H-indole-5-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one; or, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt.

8. The compound of claim 1 wherein the compound is 2-(tert-butyl)-1'-(8-methyl-3-(methylamino)quinoline-6-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one; or, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt.

9. The compound of claim 1 wherein the compound is 2-(tert-butyl)-1'-(7-ethoxy-1,3-dimethyl-1H-indazole-5-carbonyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one; or, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt.

10. The compound of claim 1 wherein the compound is 2-(tert-butyl)-1'-(4-methyl-2-naphthoyl)-5H-spiro[benzo[d]thiazole-6,4'-piperidin]-4(7H)-one; or, a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or pharmaceutically acceptable salt.

11. A pharmaceutical composition comprising a compound according to claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or salt, and a pharmaceutically acceptable excipient.

12. Use of a compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or salt, in the manufacture of a medicament for treating a disease or condition selected from inflammation, autoimmune disease, neuroinflammation, arthritis, rheumatoid arthritis, spondyloarthropathies, systemic lupus erythematous, lupus nephritis, osteoarthritis, gouty arthritis, pain, fever, pulmonary sarcoidosis, silicosis, cardiovascular disease, atherosclerosis, myocardial infarction, thrombosis, congestive heart failure and cardiac reperfusion injury, cardiomyopathy, stroke, ischemia, reperfusion injury, brain edema, brain trauma, neurodegeneration, liver disease, inflammatory bowel disease, Crohn’s disease, ulcerative colitis, nephritis, retinitis, retinopathy, macular degeneration, glaucoma, diabetes (type 1 and type 2), diabetic neuropathy, viral and bacterial infection, myalgia, endotoxic shock, toxic shock syndrome, osteoporosis, multiple sclerosis, endometriosis, menstrual cramps, vaginitis, candidiasis, cancer, fibrosis, obesity, muscular dystrophy, polymyositis, dermatomyositis, autoimmune hepatitis, primary biliary cirrhosis, primary sclerosing cholangitis, vitiligo, Alzheimer’s disease, skin flushing, eczema, psoriasis, atopic dermatitis, sunburn, keloid, hypertrophic scar, rheumatic diseases, urticaria, discoid lupus, cutaneous lupus, central nervous system lupus, psoriatic arthritis, asthma, allergic asthma, type I interferonopathies including Aicardi–Goutières syndrome and other mendelian diseases of overexpression of type I interferon, primary progressive multiple sclerosis, relapsing remitting multiple sclerosis, non-

alcoholic fatty liver disease, non-alcoholic steatohepatitis, scleroderma, alopecia areata, scarring alopecia, prurigo, prurigo nodularis, CPUO, lichen diseases, lichen planus, Steven’s Johnson’s syndrome, spondylopathy, myositis, vasculitis, pemphigus, lupus, major depression disorder, allergy, dry eye syndrome, transplant rejection, cancer, septic shock, cardiopulmonary dysfunction, acute respiratory disease, ankylosing spondylitis, cachexia, chronic graft-versus-host disease, acute graft-versus-host disease, Celiac Sprue, idiopathic thrombocytopenic thrombotic purpura, thrombotic thrombocytopenic purpura, myasthenia gravis, Sjogren's syndrome, epidermal hyperplasia, cartilage inflammation, bone degradation, juvenile arthritis, juvenile rheumatoid arthritis, pauciarticular juvenile rheumatoid arthritis, polyarticular juvenile rheumatoid arthritis, systemic onset juvenile rheumatoid arthritis, juvenile ankylosing spondylitis, juvenile enteropathic arthritis, juvenile Reter's Syndrome, SEA Syndrome, juvenile dermatomyositis, juvenile psoriatic arthritis, juvenile scleroderma, juvenile systemic lupus erythematosus, juvenile vasculitis, pauciarticular rheumatoid arthritis, polyarticular rheumatoid arthritis, systemic onset rheumatoid arthritis, enteropathic arthritis, reactive arthritis, Reter's Syndrome, myolitis, polymyolitis, dermatomyolitis, polyarteritis nodosa, Wegener's granulomatosis, arteritis, polymyalgia rheumatica, sarcoidosis, sclerosis, primary biliary sclerosis, sclerosing cholangitis, dermatitis, Still's disease, chronic obstructive pulmonary disease, Guillain-Barre disease, Graves' disease, Addison's disease, Raynaud's phenomenon, psoriatic epidermal hyperplasia, plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, erythrodermic psoriasis, an immune disorder associated with or arising from activity of pathogenic lymphocytes, noninfectious uveitis, Behcet’s disease and Vogt–Koyanagi–Harada syndrome.

13. The use of claim 12 wherein the compound is to be administered topically.

14. The use of claim 12, wherein the compound is to be administered as a cream, ointment, lotion, gel, solution, suspension, foam, aerosol, spray, shampoo, patch or tape.

15. Use of a compound of any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or salt, in the manufacture of a medicament for treating acne.

16. The use of claim 15 wherein the compound is to be administered topically.

17. The use of claim 15, wherein the compound is to be administered as a cream, ointment, lotion, gel, solution, suspension, foam, aerosol, spray, shampoo, patch or tape.

18. Use of a compound of any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or salt, in the manufacture of a medicament for treating inflammatory skin disease, seborrheic dermatitis, rosacea, steroid acne, papulopustular drug eruption, and hidradenitis suppurativa.

19. The use of claim 18 wherein the compound is to be administered topically.

20. The use of claim 18, wherein the compound is to be administered as a cream, ointment, lotion, gel, solution, suspension, foam, aerosol, spray, shampoo, patch or tape.

21. Use of a compound according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment of a disorder for which an ACC inhibitor is indicated.

22. Use of a compound according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment of acne.

23. A compound according to any one of claims 1 to 10 for use in the treatment of a disorder for which an ACC inhibitor is indicated.

24. A compound of any one of claims 1 to 10 or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate of said compound or salt, for use in therapy.