CLAIMS

1. An oral adjuvant, for use in a pharmaceutical composition comprising an immunogen, wherein the adjuvant comprises a lipid and an alcohol, and stimulates uptake of the immunogen by dendritic cells and/or macrophages such that they modulate immunomodulatory cytokines, and wherein the immunomodulatory activity of the immunogen in the presence of the adjuvant is greater than its immunomodulatory activity in the absence of the adjuvant.

2. An adjuvant according to claim 1, wherein the adjuvant comprises at least about 10%, 20%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95% or at least about 99% (w/w) lipid.

3. An adjuvant according to either claim 1 or 2, wherein the adjuvant comprises between about 35% and 99% (w/w) lipid, or between about 45% and 99% (w/w) lipid, or between about 50% and 99% (w/w) lipid, or between about 60% and 98% (w/w) lipid, or between about 70% and 97% (w/w) lipid, or between about 80% and 96% (w/w) lipid, or between about 85% and 95% (w/w) lipid, or between about 85% and 95% (w/w) lipid, or between about 88% and 94% (w/w) lipid, or between about 89% and 93% (w/w) lipid.

4. An adjuvant according to any preceding claim, wherein the adjuvant comprises a natural oil or a vegetable oil.

5. An adjuvant according to claim 4, wherein the natural oil is selected from a group consisting of linseed oil; soyabean oil; fractionated coconut oil; mineral oil; triacetin; ethyl oleate; a hydrogenated natural oil; or a mixture thereof. Examples of suitable vegetable oils may be selected from a group consisting of rapeseed oil; olive oil; peanut oil; soybean oil; corn oil; safflower oil; arachis oil; sunflower oil; canola oil; walnut oil; almond oil; avocado oil; castor oil; coconut oil; corn oil; cottonseed oil; rice bran oil; sesame oil; and refined palm oil; or a mixture thereof.

6. An adjuvant according to any preceding claim, wherein the lipid comprises linseed oil.

7. An adjuvant according to any preceding claim, wherein the adjuvant comprises less than about 90%, 80%, 70%, 65%, 60%, 55%, 50%, 45%, 40%, 35%, 30%, 25%, 20%, 15%, 10%, 5%, or less than about 1% (w/w) alcohol.

8. An adjuvant according to any preceding claim, wherein the adjuvant comprises between about 1% and 90% alcohol (w/w), or between about 1% and 70% (w/w) alcohol, or between about 1% and 60% (w/w) alcohol, or between about 1% and 50% (w/w) alcohol, or between about 2% and 40% (w/w) alcohol, or between about 4% and 30% (w/w) alcohol, or between about 6% and 20% (w/w) alcohol, or between about 8% and 15% (w/w) alcohol.

9. An adjuvant according to any preceding claim, wherein the alcohol is an aliphatic alcohol, for example a C_{1-20} alcohol, a C_{1-15} alcohol, a C_{1-10} alcohol, a C_{1-5} alcohol, or a C_{2-4} alcohol.

10. An adjuvant according to any preceding claim, wherein the alcohol is ethanol, propanol or butanol, preferably ethanol.

11. An adjuvant according to any one of claims 1-9, wherein the alcohol is menthol, or a sugar alcohol, such as glycerol, sorbitol, erythritol, xylitol, mannitol, isomalt or maltitol.

12. An adjuvant according to any preceding claim, wherein the adjuvant is anhydrous.

13. An adjuvant according to any preceding claim, wherein the adjuvant does not comprise a hydrophilic surfactant.

14. An adjuvant according to any preceding claim, wherein the immunomodulatory cytokine which is modulated is selected from a group of cytokines including IL-10; IL4; TNF-α; and IFN-γ.

15. An adjuvant according to any preceding claim, wherein the adjuvant stimulates the dendritic cells and/or macrophages in the subject to produce or increase production of an immunological cytokine, for example IL-10 and/or TNF- α and/or IL-4.

16. An adjuvant according to any preceding claim, wherein the adjuvant stimulates the dendritic cells and/or macrophages in the subject to stop or decrease production of an immunological cytokine, for example IFN-γ.

17. An adjuvant according to any preceding claim, wherein the immunogen present in the composition is a pharmaceutically active agent having a log P value of greater than 2.0 and/or a polar surface area of between about 25 Å^2 and 70 Å^2.

18. An adjuvant according to any preceding claim, wherein the immunogen is a small molecule having a molecular weight of less than 1000 Da.

19. An adjuvant according to any preceding claim, wherein the immunogen has a log P value which is greater than 3.0, 4.0, 5.0 or 6.0.

20. An adjuvant according to any preceding claim, wherein the immunogen has a polar surface area of between 35 Å^2 and 65 Å^2, or between 40 Å^2 and 60 Å^2, or between 45 Å^2 and 55 Å^2.

21. An adjuvant according to any preceding claim, wherein the immunogen comprises a peroxidase proliferator-activator receptor gamma (PPAR-γ) agonist.

22. An adjuvant according to claim 21, wherein the PPAR-γ agonist is a compound selected from Table 1.

23. An adjuvant according to either claim 21 or 22, wherein the PPAR-γ agonist is a fibrate, which is selected from the group of fibrates consisting of bezafibrate; ciprofibrate; clofibrate; gemfibrozil; and fenofibrate.

24. An adjuvant according to either claim 21 or 22, wherein the PPAR-γ agonist is selected from the group of agonists including Monascin; Irbesartan; Telmisartan; Mycophenolic acid; Resveratrol; Delta(9)-tetrahydrocannabinol; Cannabidiol; Curcumin; Cilostazol; Benzbromarone; 6-shogaol; and Glycyrrhetinic acid.

25. An adjuvant according to any one of claims 1-22, wherein the immunogen is a non-steroidal anti-inflammatory drug (NSAID), for example ibuprofen.

26. A pharmaceutical composition comprising an immunogen and the adjuvant according to any preceding claim.

27. A pharmaceutical composition according to claim 26, for use in therapy.

28. A pharmaceutical composition according to claim 26, for use in treating Th1-mediated disease, cancer, or a bacterial or viral infection.

29. A method of eliciting, in a subject, an effective immune response, the method comprising administering, to a subject, an effective amount of the pharmaceutical composition of claim 26.

30. A pharmaceutical composition comprising a therapeutically effective amount of a compound which is capable of increasing interleukin-10 (IL-10) production, and a pharmaceutically acceptable vehicle comprising a lipid and an alcohol, for use in treating a Th1-mediated disease, wherein the IL-10 is endogenously produced by Th2 cells, dendritic cells and/or macrophages.

31. A composition according to claim 30, wherein the compound, which is capable of increasing endogenous IL-10 production, is recognised by dendritic cells and/or macrophages.

32. A composition according to either claim 30 or 31, wherein the Th1-mediated disease is a Th1-mediated inflammatory disease, preferably systemic inflammatory disease.

33. A composition according to any one of claims 30-32, wherein the disease is selected from a group of Th1-mediated diseases consisting of rheumatoid arthritis (RA); psoriatic arthritis; psoriasis; inflammatory bowel syndrome (IBD); Crohn's disease; ulcerative colitis; multiple sclerosis (MS); flu, including pandemic flu; respiratory disorders, for example those caused by viruses, such as respiratory syncytial virus (RSV); cystic fibrosis (CF); herpes, including genital herpes; asthma and allergies; sepsis and septic shock; bacterial pneumonia; bacterial meningitis; dengue hemorrhagic fever; diabetes Type I; endometriosis; prostatitis; uveitis; uterine ripening; and age-related macular degeneration.

34. A composition according to any one of claims 30-33, wherein the Th1-mediated disease is virally, bacterially or chemically (e.g. environmentally) induced.

35. A composition according to any one of claims 30-34, wherein the Th1-mediated disease is systemic inflammatory disease, for example inflammatory bowel syndrome (IBD), rheumatoid arthritis (RA) or cystic fibrosis (CF).

36. A composition according to any one of claims 30-35, wherein the compound is used to increase endogenous IL-10 production in a paracrine manner.

37. A composition according to any one of claims 30-36, wherein the compound modulates Th1 cytokine concentration, such as IFNγ, TNF-α and IL-12.

38. A composition according to any one of claims 30-37, wherein the compound, which is capable of inducing endogenous production of interleukin-10 (IL-10) by Th2 cells, dendritic cells and/or macrophages, is a non-steroidal anti-inflammatory drug (NSAID).

39. A composition according to claim 38, wherein the NSAID is a propionic acid derivative, an acetic acid derivative, an enolic acid derivative, a fenamic acid derivative, or a selective- or non-selective cyclo-oxygenase (COX) inhibitor.

40. A composition according to any one of claims 30-39, wherein the compound is selected from a group consisting of: Alminoprofen; Benoxaprofen; Dexketoprofen; Flurbiprofen; Ibuprofen; Indoprofen; Ketoprofen; Loxoprofen; Pranoprofen; Protizinic acid; Suprofen; Aceclofenac; Acemetacin; Actarit; Alcofenac; Amfenac; Clometacin; Diclofenac; Etodolac; Felbinac; Fenclofenac; Indometacin; Ketorolac; Metiazinic acid; Mofezolac; Naproxen; Oxametacin; Sulindac; Zomepirac; Celecoxib; Etoricoxib; Lumiracoxib; Meloxicam; Rofecoxib; Valdecoxib; Aloxipirin; Aminophenazone; Antraphenine; Aspirin; Azapropazone; Benorilate; Benzydamine; Butibufen; Chlorthenoxacin; Choline Salicylate; Diflunisal; Emorfazone; Epirizole; Feclobuzone; Fenbufen; Glafenine; Hydroxylethyl salicylate; Lactyl phenetidin; Mefenamic acid; Metamizole; Mofebutazone; Nabumetone; Nifenazone; Niflumic acid; Phenacetin; Pipebuzone; Propyphenazone; Proquazone; Salicylamide; Salsalate; Tiaramide; Tinoridine; and Tolfenamic acid.

41. A composition according to any one of claims 30-40, wherein the compound is Alminoprofen, Benoxaprofen, Dexketoprofen, Flurbiprofen, Ibuprofen, Indoprofen, Ketoprofen, Loxoprofen, Pranoprofen protizininic acid, or Suprofen.

42. A composition according to any one of claims 30-41, wherein the compound is Ibuprofen.

43. A composition according to any one of claims 38 to 42, wherein the composition comprises the R- or S-enantiomer of the NSAID.

44. A composition according to claim 43, wherein the composition comprises R-ibuprofen.

45. A composition according to claim 43, wherein the composition comprises S-ibuprofen.

46. A composition according to any one of claims 30-45, wherein the lipid component of the vehicle is as defined in any one of claims 2-6.

47. A composition according to any one of claims 30-46, wherein the lipid component of the pharmaceutical vehicle comprises a fatty acid comprising between 8 and 24 carbon atoms, between 10 and 22 carbon atoms, between 14 and 20 atoms, or between 16 and 20 atoms.

48. A composition according to any one of claims 30-47, wherein the lipid comprises a fatty acid selected from a group consisting of myristic acid (C 14:0); palmitic acid (C 16:0); palmitoleic acid (C 16:1); stearic acid (C 18:0); oleic acid (C 18:1); linoleic acid (C 18:2); linolenic acid (C 18:3) and arachidic acid (C 20:0); or a mixture thereof.

49. A composition according to any one of claims 30-48, wherein the alcohol component of the vehicle is as defined in any one of claims 7-11.

50. A composition according to any one of claims 30-49, wherein the vehicle comprises between approximately 80% and 95% (w/w) linseed oil, and between approximately 5% and 20% (w/w) ethanol, and optionally water.

51. A composition according to any preceding claim, wherein the composition is orally administrable.

52. A composition according to any preceding claim, wherein the vehicle does not comprise a hydrophilic surfactant.

53. A drug delivery device comprising:-

(i) a pharmaceutical composition comprising a therapeutically effective amount of a compound which is capable of increasing endogenous interleukin-10 (IL-10) production by Th2 cells, dendritic cells and/or macrophages, and a pharmaceutically acceptable vehicle comprising a lipid and an alcohol; and

(ii) a support matrix.

54. A drug delivery device according to claim 53, wherein the device comprises the pharmaceutical composition defined in any one of claims 30 to 52.

55. A drug delivery device according to either claim 53 or claim 54, wherein the device is a pessary, a vaginal ring, or the like.

56. A drug delivery device according to any one of claims 53 to 55, wherein the device is worn by a subject requiring treatment of a Th1-mediated condition.

57. A drug delivery device according to any one of claims 53 to 56, wherein the delivery device is used by pregnant women to prevent or delay premature labour.

58. A drug delivery device according to any one of claims 53 to 57, wherein the support matrix comprises a material capable of melting at, or around, body temperature, such that, over time, the matrix dissolves thereby releasing the composition, which is absorbed by the subject.

59. A drug delivery device according to any one of claims 54 to 58, wherein the support matrix is a gel or wax, for example glycerol/gelatin, glyco-gelatin, macrogol (e.g. polyethylene glycol), natural, synthetic or semi-synthetic hard fat, or fractionated palm kernel oil.

60. A method of preventing, treating and/or ameliorating a Th1-mediated disease, the method comprising administering, to a subject in need of such treatment, a pharmaceutical composition comprising a therapeutically effective amount of a compound which is capable of increasing interleukin-10 (IL-10) production, and a pharmaceutically acceptable vehicle comprising a lipid and an alcohol, wherein the IL-10 is endogenously produced by Th2 cells, dendritic cells and/or macrophages.

CLAIMS

1. Use of an oral adjuvant in the manufacture of a medicament comprising an immunogen for the treatment of a Th-1-mediated inflammatory disease,

   wherein the adjuvant comprises at least 50% (w/w) of a lipid and between 2% and 40% (w/w) of an alcohol,

   wherein the immunogen comprises a Non-Steroidal Anti-Inflammatory Drug (NSAID) or a peroxidase proliferator-activator receptor gamma (PPAR-γ) agonist,

   wherein the adjuvant stimulates uptake of the immunogen by dendritic cells and/or macrophages such that the immunogen modulates immunomodulatory cytokines, and

   wherein the immunomodulatory activity of the immunogen in the presence of the adjuvant is greater than its immunomodulatory activity in the absence of the adjuvant,

   wherein the medicament is a solution that does not comprise a surfactant, and

   wherein the Th-1-mediated inflammatory disease is not a respiratory disorder.

2. Use of a composition in the manufacture of an oral medicament for the treatment of a Th-1-mediated inflammatory disease, the composition comprising an immunogen and an adjuvant,

   wherein the adjuvant comprises at least 50% (w/w) of a lipid and between 2% and 40% (w/w) of an alcohol,

   wherein the immunogen comprises a Non-Steroidal Anti-Inflammatory Drug (NSAID) or a peroxidase proliferator-activator receptor gamma (PPAR-γ) agonist,

   wherein the adjuvant stimulates uptake of the immunogen by dendritic cells and/or macrophages such that the immunogen modulates immunomodulatory cytokines,

wherein the immunomodulatory activity of the immunogen in the presence of the adjuvant is greater than its immunomodulatory activity in the absence of the adjuvant,

wherein the medicament is a solution that does not comprise a surfactant, and

wherein the Th-1-mediated inflammatory disease is not a respiratory disorder.

3. The use according to claim 1 or claim 2, wherein the adjuvant comprises at least about at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or 95 (w/w) lipid.

4. The use according to claim 1 or claim 2, wherein the adjuvant between 50% and 99% (w/w) lipid, or between 60% and 98% (w/w) lipid, or between 70% and 97% (w/w) lipid, or between-80% and 96% (w/w) lipid, or between 85% and 95% (w/w) lipid, or between 85% and 95% (w/w) lipid, or between 88% and 94% (w/w) lipid, or between 89% and 93% (w/w) lipid.

5. The use according to any one of claims 1-4, wherein the lipid is an oil or oil-based liquid, a liquid fat, a fatty acid, a fatty acid ester, a fatty alcohol, a glyceride, a glycol ester, a sucrose ester, or a mixture thereof.

6. The use according to claim 5, wherein the fatty acid is myristic acid, oleic acid, stearic acid, palmitic acid, palmitoleic acid, linoleic acid, linolenic acid, or arachidic acid, or a mixture thereof.

7. The use according to claim 5, wherein the glyceride is a mono-glyceride, a di-glyceride, or a tri-glyceride.

8. The use according to claim 5, wherein the oil is a natural oil or a vegetable oil.

9. The use according to claim 8, wherein the natural oil comprises linseed oil, soyabean oil, fractionated coconut oil, mineral oil, triacetin, ethyl oleate, a hydrogenated natural oil, or a mixture thereof

10. The use according to claim 8, wherein the vegetable oil is selected from a group consisting of olive oil, rapeseed oil, peanut oil, soybean oil, corn oil, safflower oil, arachis oil, sunflower oil, canola oil, walnut oil, almond oil, avocado oil, castor oil, coconut oil, corn oil, cottonseed oil, rice bran oil,

sesame oil, or refined palm oil, or a mixture thereof.

11. The use according to any one of claims 1-10, wherein the adjuvant comprises less than less than 40%, less than 35%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, or less than 5 (w/w) alcohol.

12. The use according to any one of claims 1-10, wherein the adjuvant comprises between 4% and 30% (w/w) alcohol, or between 6% and 20% (w/w) alcohol, or between 8% and 15% (w/w) alcohol.

13. The use according to any one of claims 1-12, wherein the alcohol is an aliphatic alcohol, for example a C1-20 alcohol, a C1-15 alcohol, a C1-10 alcohol, a C1-5 alcohol, or a C2-4 alcohol.

14. The use according to any one of claims 1-13, wherein the alcohol is ethanol, propanol or butanol, preferably ethanol.

15. The use according to any one of claims 1-14, wherein the alcohol is menthol, or a sugar alcohol, such as glycerol, sorbitol, erythritol, xylitol, mannitol, isomalt or maltitol.

16. The use according to any one of claims 1-15, wherein the adjuvant is anhydrous.

17. The use according to any one of claims 1-16, wherein the adjuvant is selected from the following ranges: between 80% (w/w) and 95% (w/w) lipid and between 5% (w/w) and 20% (w/w) ethanol or between 88% and 92% (w/w) lipid and between 8% (w/w) and 12% (w/w) ethanol.

18. The use according to any one of claims 1-17, wherein the NSAID is a nonselective COX inhibitor or a COX-2-selective inhibitor.

19. The use according to claim 18, wherein the nonselective COX inhibitor or the COX-2-selective inhibitor is a propionic acid NSAID, an acetic acid NSAID, an enolic acid NSAID, a fenamic acid NSAID.

20. The use according to claim 18, wherein the nonselective COX inhibitor or the COX-2-selective inhibitor is a propionic acid NSAID.

21. The use according to claim 20, wherein the propionic acid NSAID is Ibuprofen.

22. The use according to any one of claims 1-21, wherein the non-steroidal anti-inflammatory drug is Alminoprofen, Benoxaprofen, Dexketoprofen, Flurbiprofen, Ibuprofen, Indoprofen, Ketoprofen, Loxoprofen, Pranoprofen, Protizinic acid, Suprofen, Aceclofenac, Acemetacin, Actarit, Alcofenac, Amfenac, Clometacin, Diclofenac, Etodolac, Felbinac, Fenclofenac, Indometacin, Ketorolac, Metiazinic acid, Mofezolac, Naproxen, Oxametacin, Sulindac, Zomepirac, Celecoxib, Etoricoxib, Lumiracoxib, Meloxicam, Rofecoxib, Valdecoxib, Aloxipirin, Aminophenazone, Antraphenine, Aspirin, Azapropazone, Benorilate, Benzydamine, Butibufen, Chlorthenoxacin, Choline Salicylate, Diflunisal, Emorfazone, Epirizole, Feclobuzone, Fenbufen, Glafenine, Hydroxylethyl salicylate, Lactyl phenetidin, Mefenamic acid, Metamizole, Mofebutazone, Nabumetone, Nifenazone, Niflumic acid, Phenacetin, Pipebuzone, Propyphenazone, Proquazone, Salicylamide, Salsalate, Tiaramide, Tinoridine, or Tolfenamic acid.

23. The use according to any one of claims 1-22, wherein the PPAR-γ agonist is a fibrate.

24. The use according to claim 23, wherein the fibrate is bezafibrate, ciprofibrate, clofibrate, gemfibrozil, or fenofibrate.

25. The use according to any one of claims 1-22, wherein the PPAR-γ agonist is Monascin, Irbesartan, Telmisartan, Mycophenolic acid, Resveratrol, Delta(9)-tetrahydrocannabinol, Cannabidiol, Curcumin, Cilostazol, Benzbromarone, 6-shogaol, or Glycyrrhetinic acid.

26. The use according to any one of claims 1-25, wherein the immunomodulatory cytokine which is modulated includes IL-10, IL4, TNF-α, or IFN-γ.

27. The use according to any one of claims 1-26, wherein the medicament stimulates the dendritic cells and/or macrophages in the subject to produce or increase production of an immunological cytokine.

28. The use according to claim 27, wherein the immunological cytokine includes IL-10 and/or TNF- α and/or IL-4.

29. The use according to any one of claims 1-28, wherein the medicament stimulates the dendritic cells and/or macrophages in the subject to stop or decrease production of an immunological cytokine.

30. The use according to claim 29, wherein the immunological cytokine includes IFN-γ

31. The use according to any one of claims 1-30, wherein the Th1-mediated inflammatory disease is a systemic inflammatory disease.

32. The use according to any one of claims 1-31, wherein the Th1-mediated inflammatory disease is a cancer, a rheumatoid arthritis, a psoriatic arthritis, a psoriasis, an inflammatory bowel syndrome, a Crohn's disease, an ulcerative colitis, a multiple sclerosis, an asthma, an allergy, a sepsis, a septic shock, a diabetes Type I, an endometriosis, a prostatitis, an uveitis, an uterine ripening, an alopecia areata, an ankylosing spondylitis, a coeliac disease, a dermatomyositis, a diabetes mellitus Type 1, a Goodpasture's syndrome, a Graves' disease, a Guillain-Barré syndrome, a juvenile idiopathic arthritis, a Hashimoto's thyroiditis, an idiopathic thrombocytopenic purpura, a Lupus erythematosus, a mixed connective tissue disease, a myasthenia gravis, a narcolepsy, an osteoarthritis, a pemphigus vulgaris, a pernicious an anaemia, a polymyositis, a primary biliary cirrhosis, a relapsing polychondritis, a Sjögren's syndrome, a temporal arteritis, a vasculitis, a Wegener's granulumatosis, or an age-related macular degeneration.