inflammation is involved in diseases as diverse as cardiovascular diseases, cancers, allergies, obesity, diabetes, digestive system diseases, degenerative diseases, auto-immune disorders, and Alzheimer's disease.

[05] Attempts to treat chronic inflammation have met with limited success. This is due, in part, to the fact that the etiology of chronic inflammation is a complex response based in part on the various inflammation inducing molecules and the multitude of inflammation mediating and sensitizing molecules that appear to elicit inflammation via redundant mechanism. In addition, besides blocking pro-inflammatory molecules, many anti-inflammatory drugs, also inhibit regulatory loops that release endogenous anti-inflammatory molecules. For example, NSAIDs reduce inflammation by blocking the enzymatic activity of cyclooxygenase, a key enzyme that catalyzes the conversion of arachidonic acid to prostaglandins and leukotrienes. Thus, NSAIDs reduce inflammation by preventing the synthesis of all prostaglandins. However, NSAIDs not only prevents the synthesis of proinflammatory prostaglandins, these compounds also prevent the synthesis of anti-inflammatory prostaglandins. Hence, NSAIDs have limited success as they block endogenous anti-inflammatory response, which in some instances may prolong chronic inflammation. Therefore, compounds, compositions, uses, and methods preferentially inhibiting pro-inflammatory responses would be highly desirable for the treatment of chronic inflammation.

[06] The present specification discloses pharmaceutical compositions and methods for treating an individual suffering from a chronic inflammation. The pharmaceutical compositions disclosed herein are essentially a lipid delivery system that enables a therapeutic compound having anti-inflammatory activity to be delivered in a manner that more effectively inhibits a pro-inflammatory response. The end result is an improved treatment for chronic inflammation.

SUMMARY

[07] In one aspect, the present disclosure refers to a pharmaceutical composition comprising a) a therapeutic compound having an anti-inflammatory activity, wherein the therapeutic compound has a log P value of greater than 2.0; b) a pharmaceutically-acceptable solvent, wherein the solvent comprises a pharmaceutically-acceptable polyethelene glycol polymer, a pharmaceutically-acceptable alcohol or a pharmaceutically-acceptable ester of a pharmaceutically-acceptable alcohol and an acid; and c) at least 50% (v/v) of a pharmaceutically-acceptable hydrophobic lipid-adjuvant, wherein the pharmaceutically-acceptable hydrophobic lipid-adjuvant is a fatty acid having at least 12 carbons, a glycerolipid, a sphingolipid, a sterol lipid, a prenol lipid, a saccharolipid, or a polyketide, wherein the pharmaceutical composition does not comprise a pharmaceutically-acceptable emulsifying agent, and wherein the pharmaceutical composition is formulated to be solid at a temperature of 15°C or lower. Disclosed herein is a pharmaceutical composition comprising a therapeutic compound and a pharmaceutically-acceptable adjuvant. A therapeutic compound may have an anti-inflammatory activity. Other examples of the present specification disclose a pharmaceutical composition comprising a therapeutic compound disclosed herein, a pharmaceutically-acceptable solvent, and a pharmaceutically-acceptable adjuvant. In

other examples, the pharmaceutical compositions disclosed herein further comprise a pharmaceutically-acceptable stabilizing agent.

[08] In another aspect, the present disclosure refers to a method of preparing a pharmaceutical composition as defined herein, the method comprising the steps a) contacting a pharmaceutically-acceptable solvent with the therapeutic compound under conditions which allow the therapeutic compound to dissolve in the pharmaceutically-acceptable solvent, thereby forming a solution, and b) contacting the solution formed in step (a) with a pharmaceutically-acceptable hydrophobic lipid-adjuvant under conditions which allow the formation of the pharmaceutical composition. Other examples of the present specification disclose a method of preparing a pharmaceutical composition, the method comprising the step of contacting a therapeutic compound with a pharmaceutically-acceptable adjuvant under conditions which allow the formation of the pharmaceutical composition. Other examples of the present specification disclose a method of preparing a pharmaceutical composition, the method comprising the steps: a) contacting a pharmaceutically-acceptable solvent with a therapeutic compound under conditions which allow the therapeutic compound to dissolve in the pharmaceutically-acceptable solvent, thereby forming a solution, wherein the therapeutic compound has anti-inflammatory activity, and b) contacting the solution formed in step (a) with a pharmaceutically-acceptable adjuvant under conditions which allow the formation of the pharmaceutical composition. In other examples, the method of preparing disclosed herein further comprises c) removing the pharmaceutically-acceptable solvent from the pharmaceutical composition.

[09] Other examples of the present specification disclose a pharmaceutical composition, the pharmaceutical composition made according to a method comprising the step of contacting a therapeutic compound with a pharmaceutically-acceptable adjuvant under conditions which allow the formation of the pharmaceutical composition. Other examples of the present specification disclose a pharmaceutical composition, the pharmaceutical composition made according to a method comprising the steps: a) contacting a pharmaceutically-acceptable solvent with a therapeutic compound under conditions which allow the therapeutic compound to dissolve in the pharmaceutically-acceptable solvent, thereby forming a solution, wherein the therapeutic compound has anti-inflammatory activity, and b) contacting the solution formed in step (a) with a pharmaceutically-acceptable adjuvant under conditions which allow the formation of the pharmaceutical composition. In other examples, the method of making a pharmaceutical composition disclosed herein further comprises c) removing the pharmaceutically-acceptable solvent from the pharmaceutical composition.

[010] Other examples of the present specification disclose a method of treating an individual with a chronic inflammation, the method comprising the step of administering to the individual in need thereof a pharmaceutical composition disclosed herein, wherein administration results in a reduction in a symptom associated with the chronic inflammation, thereby treating the individual.

[011] Other examples of the present specification disclose a use of a pharmaceutical composition disclosed herein in the manufacture of a medicament for the treatment of a chronic

inflammation. Also disclosed herein is a use of a pharmaceutical composition as defined herein in the manufacture of a medicament for treating a chronic inflammation, wherein the use comprises that the pharmaceutical composition is to be administered to an individual in need thereof, wherein administration results in a reduction in a symptom associated with the chronic inflammation

[012] Other examples of the present specification disclose a use of a pharmaceutical composition disclosed herein for the treatment of a chronic inflammation. Also disclosed is a pharmaceutical composition as described herein for use in the treatment of a chronic inflammation.

BRIEF DESCRIPTION OF THE DRAWINGS

[013] **FIG. 1** shows the effects of a pharmaceutical composition disclosed herein on survival against Influenza A/PR/8/34 lethal challenge. Ibuprofen 335 µg = Group A; Ctrol ORAL = Group B; and ibuprofen 335 µg o/e ORAL (BC1054) = Group C.

[014] **FIG. 2** shows the effects of a pharmaceutical composition disclosed herein on in vivo levels of Th2 cytokines in the lungs of surviving mice. FIG. 2A shows a graph of the effects of a pharmaceutical composition disclosed herein on in vivo levels of IL-10, whereas FIG. 2B shows a graph of the effects of a pharmaceutical composition disclosed herein on in vivo levels of IL-4. BC1054 ORAL = Group A; Vehicle ORAL = Group B; and BC1054 Lipid ORAL = Group C.

CLAIMS

1. A pharmaceutical composition comprising:

a) a therapeutic compound having an anti-inflammatory activity, wherein the therapeutic compound has a log P value of greater than 2.0;

b) a pharmaceutically-acceptable solvent, wherein the solvent comprises a pharmaceutically-acceptable polyethelene glycol polymer, a pharmaceutically-acceptable alcohol or a pharmaceutically-acceptable ester of pharmaceutically-acceptable alcohol and an acid; and

c) at least 50% (v/v) of a pharmaceutically-acceptable hydrophobic lipid-adjuvant, wherein the pharmaceutically-acceptable hydrophobic lipid-adjuvant is a fatty acid having at least 12 carbons, a glycerolipid, a sphingolipid, a sterol lipid, a prenol lipid, a saccharolipid, or a polyketide,

wherein the pharmaceutical composition does not comprise a pharmaceutically-acceptable emulsifying agent, and

wherein the pharmaceutical composition is formulated to be solid at a temperature of 15°C or lower.

2. The pharmaceutical composition according to Claim 1, wherein the anti-inflammatory activity reduces the level of an inflammation inducing molecule, reduces the level of an inflammation inducing prostaglandin, stimulates a PPAR signaling pathway, induces apoptosis of Macrophage M1 cells, promotes differentiation of Macrophage M2 cells, or both, reduces the levels of Interferon-gamma (IFNγ), Tumor necrosis factor-alpha (TNF-α), Interleukin-12 (IL-12), or a combination thereof released from Th1 cells, increases the levels of IL-10 released from a Th2 cell, or both.

3. The pharmaceutical composition according to Claim 1 or Claim 2, wherein the therapeutic compound comprises a non-steroidal anti-inflammatory drug (NSAID), a PPARγ agonist, fibrate, and/or an ester thereof.

4. The pharmaceutical composition according to Claim 3, wherein the NSAID is a non-selective cyclo-oxygenase (COX) inhibitor, a selective cyclooxygenase 1 (COX 1) inhibitor, a selective cyclooxygenase 2 (COX 2) inhibitor or a combination thereof.

5. The pharmaceutical composition according to Claim 3, wherein the NSAID comprises a salicylate derivative NSAID, a p-amino phenol derivative NSAID, a propionic acid derivative NSAID, an acetic acid derivative NSAID, an enolic acid derivative NSAID, a fenamic acid derivative NSAID.

6. The pharmaceutical composition according to Claim 3, wherein the PPARγ agonist comprises Monascin, Irbesartan, Telmisartan, mycophenolic acid, Resveratrol, Delta(9)-tetrahydrocannabinol, a cannabidiol, Curcumin, Cilostazol, Benzbromarone, 6-shogaol, glycyrrhetinic acid, a thiazolidinedione, a NSAID, a fibrate, or a combination thereof.

7. The pharmaceutical composition according to Claim 3, wherein the fibrate comprises Bezafibrate, Ciprofibrate, Clofibrate, Gemfibrozil, Fenofibrate, or a combination thereof.

8. The pharmaceutical composition according to any one of Claims 1-7, wherein the pharmaceutically-acceptable hydrophobic lipid-adjuvant includes at least 30% of a first glycerolipid consisting of a triglyceride or an acetylated triglyceride and at least 20% of a second glycerolipid consisting of a monoglyceride or an acetylated monoglyceride.

9. The pharmaceutical composition according to Claims 1-8, wherein the pharmaceutically-acceptable solvent is from about 8% (v/v) to about 15% (v/v).

10. The pharmaceutical composition according to Claims 1-9, wherein the pharmaceutically-acceptable solvent is from about 8% (v/v) to about 12% (v/v)

11. The pharmaceutical composition according to any one of Claims 1 to 10, wherein the glycerolipid comprises a monoglyceride, a diglyceride and/or a triglyceride.

12. The pharmaceutical composition according to Claim 11, wherein the glycerolipid comprises at least 30% of a pharmaceutically-acceptable triglyceride and at least 20% of a pharmaceutically-acceptable monoglyceride.

13. A method of preparing a pharmaceutical composition as defined in any one of claims 1-12, the method comprising the steps:
a) contacting the pharmaceutically-acceptable solvent with the therapeutic compound under conditions which allow the therapeutic compound to dissolve in the pharmaceutically-acceptable solvent, thereby forming a solution, and
b) contacting the solution formed in step (a) with the pharmaceutically-acceptable hydrophobic lipid-adjuvant under conditions which allow the formation of the pharmaceutical composition.

14. The method according to Claim 13, wherein step (a) further comprises contacting a pharmaceutically-acceptable stabilizing agent with the pharmaceutically-acceptable solvent and the therapeutic compound, wherein the pharmaceutically-acceptable stabilizing agent is not an emulsifying agent.

15. Use of a pharmaceutical composition as defined in any one of Claims 1-12 in the manufacture of a medicament for the treatment of a chronic inflammation.

16. A pharmaceutical composition as defined in any one of Claims 1-12 for use in the treatment of a chronic inflammation.

17. The use according to Claim 16, wherein the chronic inflammation is associated with acne, acid reflux/heartburn, age related macular degeneration (AMD), allergy, allergic rhinitis, Alzheimer's disease, amyotrophic lateral sclerosis, anemia, appendicitis, arteritis, arthritis, asthma. atherosclerosis, autoimmune disorders, balanitis, blepharitis, bronchiolitis, bronchitis, a bullous pemphigoid, burn, bursitis, cancer, cardiac arrest, carditis, celiac disease, cellulitis, cervicitis, cholangitis, cholecystitis, chorioamnionitis, chronic obstructive pulmonary disease (COPD), cirrhosis, colitis, congestive heart failure, conjunctivitis, cyclophosphamide-induced cystitis, cystic fibrosis, cystitis, common cold, dacryoadenitis, dementia, dermatitis, dermatomyositis, diabetes, diabetic neuropathy, diabetic retinopathy, diabetic nephropathy, diabetic ulcer, digestive system disease, eczema, emphysema, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibromyalgia, fibrosis, fibrositis, gastritis, gastroenteritis, gingivitis, glomerulonephritis, glossitis, heart disease, heart valve dysfunction, hepatitis, hidradenitis suppurativa, Huntington's disease, hyperlipidemic pancreatitis, hypertension, ileitis, infection, inflammatory bowel disease, inflammatory cardiomegaly, inflammatory neuropathy, insulin resistance, interstitial cystitis, interstitial nephritis, iritis, ischemia, ischemic heart disease, keratitis, keratoconjunctivitis, laryngitis, lupus nephritis, mastitis, mastoiditis, meningitis, metabolic syndrome (syndrome X), a migraine, multiple sclerosis, myelitis, myocarditis, myositis, nephritis, non-alcoholic steatohepatitis, obesity, omphalitis, oophoritis, orchitis, osteochondritis, osteopenia, osteomyelitis, osteoporosis, osteitis, otitis, pancreatitis, Parkinson's disease, parotitis, pelvic inflammatory disease, pemphigus vularis, pericarditis, peritonitis, pharyngitis, phlebitis, pleuritis, pneumonitis, polycystic nephritis, proctitis, prostatitis, psoriasis, pulpitis, pyelonephritis, pylephlebitis, renal failure, reperfusion injury, retinitis, rheumatic fever, rhinitis, salpingitis, sarcoidosis, sialadenitis, sinusitis, spastic colon, stenosis, stomatitis, stroke, surgical complication, synovitis, tendonitis, tendinosis, tenosynovitis, thrombophlebitis, tonsillitis, trauma, traumatic brain injury, transplant rejection, trigonitis, tuberculosis, tumor, urethritis, ursitis, uveitis, vaginitis, vasculitis, or vulvitis.

18. The use according to Claim 16, wherein the chronic inflammation is a tissue inflammation or a systemic inflammation.

19. The use according to Claim 16, wherein the chronic inflammation is an auto-immune disease or a non-autoimmune disease.

20. The use according to Claim 16, wherein the chronic inflammation is associated with an arthritis, a myopathy, a vasculitis, a skin disorder, a gastrointestinal disorder, a cardiovascular disease, a cancer, a pharmacologically-induced inflammation, an infection, a tissue or organ injury, a transplant rejection, a graft-versus-host disease, a Th1-mediated inflammatory disease, a chronic neurogenic inflammation.

21. Use of a pharmaceutical composition as defined in any one of Claims 1-12 in the manufacture of a medicament for treating a chronic inflammation, wherein the use comprises that the pharmaceutical composition is to be administered to an individual in need thereof, wherein administration results in a reduction in a symptom associated with the chronic inflammation.

22. The use according to Claim 21, wherein the chronic inflammation is associated with acne, acid reflux/heartburn, age related macular degeneration (AMD), allergy, allergic rhinitis, Alzheimer's disease, amyotrophic lateral sclerosis, anemia, appendicitis, arteritis, arthritis, asthma. atherosclerosis, autoimmune disorders, balanitis, blepharitis, bronchiolitis, bronchitis, a bullous pemphigoid, burn, bursitis, cancer, cardiac arrest, carditis, celiac disease, cellulitis, cervicitis, cholangitis, cholecystitis, chorioamnionitis, chronic obstructive pulmonary disease (COPD), cirrhosis, colitis, congestive heart failure, conjunctivitis, cyclophosphamide-induced cystitis, cystic fibrosis, cystitis, common cold, dacryoadenitis, dementia, dermatitis, dermatomyositis, diabetes, diabetic neuropathy, diabetic retinopathy, diabetic nephropathy, diabetic ulcer, digestive system disease, eczema, emphysema, encephalitis, endocarditis, endometritis, enteritis, enterocolitis, epicondylitis, epididymitis, fasciitis, fibromyalgia, fibrosis, fibrositis, gastritis, gastroenteritis, gingivitis, glomerulonephritis, glossitis, heart disease, heart valve dysfunction, hepatitis, hidradenitis suppurativa, Huntington's disease, hyperlipidemic pancreatitis, hypertension, ileitis, infection, inflammatory bowel disease, inflammatory cardiomegaly, inflammatory neuropathy, insulin resistance, interstitial cystitis, interstitial nephritis, iritis, ischemia, ischemic heart disease, keratitis, keratoconjunctivitis, laryngitis, lupus nephritis, mastitis, mastoiditis, meningitis, metabolic syndrome (syndrome X), a migraine, multiple sclerosis, myelitis, myocarditis, myositis, nephritis, non-alcoholic steatohepatitis, obesity, omphalitis, oophoritis, orchitis, osteochondritis, osteopenia, osteomyelitis, osteoporosis, osteitis, otitis, pancreatitis, Parkinson's disease, parotitis, pelvic inflammatory disease, pemphigus vularis, pericarditis, peritonitis, pharyngitis, phlebitis, pleuritis, pneumonitis, polycystic nephritis, proctitis, prostatitis, psoriasis, pulpitis, pyelonephritis, pylephlebitis, renal failure, reperfusion injury, retinitis, rheumatic fever, rhinitis, salpingitis, sarcoidosis, sialadenitis, sinusitis, spastic colon, stenosis, stomatitis, stroke, surgical complication, synovitis, tendonitis, tendinosis, tenosynovitis, thrombophlebitis, tonsillitis, trauma, traumatic brain injury, transplant rejection, trigonitis, tuberculosis, tumor, urethritis, ursitis, uveitis, vaginitis, vasculitis, or vulvitis.

23. The use according to Claim 21, wherein the chronic inflammation is a tissue inflammation or a systemic inflammation.

24. The use according to Claim 21, wherein the chronic inflammation is an auto-immune disease or a non-autoimmune disease.

25. The use according to Claim 21, wherein the chronic inflammation is associated with an arthritis, a myopathy, a vasculitis, a skin disorder, a gastrointestinal disorder, a cardiovascular disease, a cancer, a pharmacologically-induced inflammation, an infection, a tissue or organ injury, a

transplant rejection, a graft-versus-host disease, a Th1-mediated inflammatory disease, a chronic neurogenic inflammation.

26. The use according to Claim 21, wherein upon administration to the individual, the pharmaceutical composition comprising the therapeutic compound results in a bio-distribution of the therapeutic compound different than a bio-distribution of the therapeutic compound included in the same pharmaceutical composition, except without the pharmaceutically-acceptable hydrophobic lipid-adjuvant.

27. The use according to Claim 21, wherein upon administration to the individual, the pharmaceutical composition reduces gastric or intestinal irritation by at least 5% when compared to the pharmaceutical composition, except without the pharmaceutically-acceptable hydrophobic lipid-adjuvant.