METHODS OF TREATING CHRONIC INFLAMMATORY DISEASES

BACKGROUND OF THE INVENTION

[0001] Chronic inflammatory disease(s) (CID) underpins the pathological condition characterized by chronic inflammation, defined as a prolonged and persistent pro-inflammatory state (1). CID includes many common and uncommon CID such as respiratory diseases (e.g., asthma, chronic obstructive pulmonary disease, pneumonitis, and pulmonary fibrosis) (2), ocular diseases (e.g., keratitis and age-related macular degeneration) (3), autoimmune diseases (4), nephropathy (5), neurodegenerative diseases (e.g., Alzheimer's disease, stroke, Parkinson's disease, and multiple sclerosis) (6), cardiovascular diseases (e.g., atherosclerosis, arteriosclerosis, and myocarditis) (7), metabolic disorders (e.g., diabetes and obesity) (8), musculoskeletal diseases (e.g., rheumatoid arthritis and osteoporosis) (9, 10), periodontal diseases (e.g., pulpitis and periodontitis) (11), digestive diseases (e.g., non-alcoholic fatty liver disease, gastroenteritis, and chronic inflammatory bowel disease) (12), and skin disorders (e.g., psoriasis and atopic dermatitis) (13, 14).

[0002] An epidemiological study showed that CID is a leading cause of death throughout the world and has been increasing over the last three decades. It has been estimated that by 2030, 171 million people will be affected by CID in the United States (15). There are various types of anti-inflammatory drugs to treat inflammation, such as aspirin, antihistamines, COX-2 inhibitors, corticosteroid, and nonsteroidal anti-inflammatory drugs (NSAIDs). However, there are limitations for long term administration of such existing drugs due to side effects and temporal efficacy.

BRIEF SUMMARY

[0002a] In one aspect of the present disclosure, there is provided a use of calcium lactate in the manufacture of a medicament for treating Alzheimer's disease, Parkinson's disease, atherosclerosis, and/or stroke, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

[0002b] In another aspect of the present disclosure, there is provided a use of calcium lactate in the manufacture of a medicament for treating multiple sclerosis, age-related macular

degeneration, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), or rheumatoid arthritis, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

[0002c] In a further aspect of the present disclosure, there is provided a use of calcium lactate in the manufacture of a medicament for treating pulpitis and/or periodontitis.

[0002d] In another aspect of the present disclosure, there is provided a use of calcium lactate in the manufacture of a medicament for treating inflammatory bowel disease (IBD), pulmonary fibrosis, liver fibrosis, ~~or~~ Crohn's disease, or ulcerative colitis, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

[0002e] In a further aspect of the present disclosure, there is provided a use of calcium lactate in the manufacture of a medicament for treating spinal cord injury, cerebral hemorrhage, myocardial infarction, keratitis, and/or diabetic retinopathy, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

[0003] Disclosed herein is a method of treating a chronic inflammatory disease, the method comprising administering to a subject in need thereof a therapeutically effective amount of calcium lactate.

[0004] Disclosed herein is a method of treating Alzheimer's disease, Parkinson's disease, atherosclerosis, and/or stroke, the method comprising administering to a subject in need thereof a therapeutically effective amount of calcium lactate.

[0005] Also disclosed is a method of treating multiple sclerosis, age-related macular degeneration, nonalcoholic fatty liver disease (NAFLD), and/or rheumatoid arthritis, the

WHAT IS CLAIMED IS

1. Use of calcium lactate in the manufacture of a medicament for treating Alzheimer's disease, Parkinson's disease, atherosclerosis, and/or stroke, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

2. Use of calcium lactate in the manufacture of a medicament for treating multiple sclerosis, age-related macular degeneration, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), or rheumatoid arthritis, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

3. Use of calcium lactate in the manufacture of a medicament for treating pulpitis and/or periodontitis.

4. Use of calcium lactate in the manufacture of a medicament for treating inflammatory bowel disease (IBD), pulmonary fibrosis, liver fibrosis, ~~or~~ Crohn's disease,p or ulcerative colitis, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

5. Use of calcium lactate in the manufacture of a medicament for treating spinal cord injury, cerebral hemorrhage, myocardial infarction, keratitis, and/or diabetic retinopathy, wherein the medicament comprises a therapeutically effective amount of calcium lactate as an active agent and a pharmaceutically acceptable a polymer and/or lipid.

6. The use of any one of claims 1-5, wherein the medicament is a pharmaceutical composition comprising a pharmaceutically acceptable carrier, excipient, or diluent.

7. The use of any one of claims 1-5, wherein the medicament is formulated into liquid, powder, aerosol, injection, fluid transfusion, patch, capsule, pill, tablet, depot, or suppository.

8. The use of any one of claims 1-~~5~~2 and 4-5, wherein the medicament further comprises a ~~therapeutically effective amount of calcium lactate as an active agent and a~~ pharmaceutically acceptable polysaccharide~~, polymer, lipid, or combinations thereof~~.

~~9. The use of claim 8, wherein the pharmaceutical composition comprises the calcium lactate and the polysaccharide.~~

~~10~~9. The use of claim ~~9~~8, wherein a weight ratio of the calcium lactate to the polysaccharide is 1:<0.2 to 1:5.

~~11. The use of any one of claims 9, wherein the pharmaceutical composition further comprises a polymer and/or lipid.~~

~~12~~10. The use of ~~claim 11~~any one of claims 1-2 and 4-5, wherein the ~~pharmaceutical composition further comprises the polymer and lipid, wherein the~~ weight ratio of the polymer to the lipid is 1:0.1 to 1:50.

~~13~~11. The use of any one of claims 8~~-12~~ or 9, wherein the medicament or pharmaceutical composition comprises the polysaccharide that is a cellulose derivative, pectin, hyaluronic acid, starch, guar gum, chitosan, gelatin, collagen, alginate, alginic acid or combinations thereof.

~~14~~12. The use of any one of claims ~~8-13~~1-2, 4-5 and 10, wherein the medicament or pharmaceutical composition comprises the polymer that is a poloxamer, polyvinylpyrrolidone, polyethylene glycol (PEG), polyglycolic lactic acid (PLGA), or combinations thereof.

~~15~~13. The use of any one of claims ~~8-14~~1-2, 4-5 and 10, wherein the medicament or pharmaceutical composition comprises the lipid that is a mono- or tri-fatty acid glycerin ester or polyethylene glycol, polyethylene glycol esters of vegetable oils, fatty acid propylene glycol

esters, sesame oil, soybean oil, castor oil, corn oil, palm oil, peanut oil, cacao oil, cottonseed oil, sunflower seed oil, safflower oil, almond oil, olive oil, hydrogenated oil, oleic acid, linolenic acid, linoleic acid, palmitic acid, palmitoleic acid, arachadonic acid, myristic acid, capric acid, caprylic acid, lauric acid, stearic acid, ethyl oleate, isopropyl palmitate, octyldodecyl myristate, cetyl palmitate, lauryl alcohol, oleyl alcohol, cetyl alcohol, stearyl alcohol, or combinations thereof.

~~16~~14. The use of any one of claims ~~8-15~~1-8, wherein the medicament or pharmaceutical composition is contained in a sterile glass or polyolefin container.

~~17~~15. The use of any one of claims 1-8, wherein the calcium lactate is coated with a pharmaceutically acceptable enteric coating.

~~18~~16. The use of claim ~~17~~15, wherein the enteric coating comprises hydroxypropyl methyl cellulose phthalate (HPMCP), cellulose acetate phthalate (CAP), polyvinyl acetate phthalate (PVAP), shellac, polymer of methacrylic acid and an ester thereof, or combinations thereof.

~~19~~17. The use of any one of claims ~~17-18~~15-16, wherein the weight ratio of the calcium lactate to the enteric coating is 10:0.5 to 1:1.5.