(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
23 March 2017 (23.03.2017)

WIPO | PCT

(10) International Publication Number
WO 2017/048860 A1

(51) International Patent Classification:
A61K 9/127 (2006.01) *A61P 37/00* (2006.01)
A61K 47/30 (2006.01) *A61P 11/00* (2006.01)
A61K 31/573 (2006.01) *A61P 37/08* (2006.01)

(21) International Application Number:
PCT/US2016/051759

(22) International Filing Date:
14 September 2016 (14.09.2016)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
62/218,558 14 September 2015 (14.09.2015) US

(71) Applicant: **VGSK TECHNOLOGIES, INC.** [US/US]; 224 Park Street, A7, Stoneham, Massachusetts 02180 (US).

(72) Inventors: **KONDURI, Kameswari**; 224 Park Street, A7, Stoneham, Massachusetts 02180 (US). **DUZGUNES, Nejat**; 508 Pixie Trail, Mill Valley, California 94941 (US). **PATTISAPU, Jogi**; 9046 Mayfair Pointe, Orlando, Florida 32827 (US). **PATTISAPU, Ram**; 103 Brook Avenue, Silverthorne, Colorado 80498 (US).

(74) Agents: **YU, Xiaozhen** et al.; Wilson Sonsini Goodrich & Rosati, 650 Page Mill Road, Palo Alto, California 94304 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report (Art. 21(3))*

WO 2017/048860 A1

(54) **Title**: A STERICALLY STABILIZED CARRIER FOR SUBCUTANEOUS, SUBLINGUAL AND ORAL THERAPEUTICS, COMPOSITIONS AND METHODS FOR TREATING A MAMMAL

(57) **Abstract**: Disclosed herein are pharmaceutical compositions and methods for oral, sublingual or subcutaneous administration comprising a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol and phosphatidylcholine. Compositions and methods for treatment of food allergy and eosinophilic esophagitis are also described.

A STERICALLY STABILIZED CARRIER FOR SUBCUTANEOUS, SUBLINGUAL AND ORAL THERAPEUTICS, COMPOSITIONS AND METHODS FOR TREATING A MAMMAL

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application No. 62/218,558, filed September 14, 2015, which application is incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

[0002] Many existing methods and compositions for delivering therapeutics and treating disease states are not entirely satisfactory. For example, a major drawback of using conventional liposomes in treating disease states is that they have a relatively short life in a mammal body. Accordingly, there is a need for new and improved methods and compositions. Compositions, methods, and kits of using a sterically stabilized liposome carrier can be used to extend the life of liposomes in a mammal body. Also, most applications of conventional liposomes are in the bloodstream. Also disclosed herein are methods of subcutaneously, sublingually, or orally administering a pharmaceutical composition, which comprises a sterically stabilized liposome carrier.

[0003] Food allergies and more specifically IgE mediated food allergies represent a growing concern among industrialized countries, and it is estimated that these allergies currently affect up to 4% of the population of westernized countries and 6–8% of young children. In contrast to the increasing number of treatments for airway allergies, the therapeutic approach for food allergy remains very limited.

STATEMENT AS TO FEDERALLY SPONSORED RESEARCH

[0004] This invention was made with government support under Grant no. 1R41HL73668-1A1 awarded by National Heart, Lung and Blood Institute. The government has certain rights in the invention.

SUMMARY OF THE INVENTION

[0005] Disclosed herein are compositions, kits, and methods of using a sterically stabilized liposome carrier for treating a condition or disorder. In one aspect, disclosed herein is a method for treating eosinophilic esophagitis (EoE), comprising: administering to a subject in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of at least

one agent suitable for treating eosinophilic esophagitis, wherein the at least one agent is encapsulated in a liposome carrier.

[0006] In some embodiments, the liposome carrier comprises phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), or any combination or derivative thereof. In some embodiments, the liposome carrier is a sterically stabilized liposome carrier. In some embodiments, the sterically stabilized liposome carrier comprises poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE), PEG-dipalmitoylphosphatidylethanolamine (DPPE), PEG-di-C:15 PE, PEG-soy PE, or PEG-egg PE. In some embodiments, the administering is performed subcutaneously, sublingually, intranasally, or orally. In some embodiments, the at least one agent comprises a proton-pump inhibitor (PPI), a corticosteroid, or any combination, or derivative thereof. In some embodiments, the proton-pump inhibitor comprises omeprazole, lansoprazole, dexlansoprazole, esomeprazole, pantoprazole, rabeprazole, ilaprazole, or any combination, or derivative thereof. In some embodiments, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

[0007] In another aspect, disclosed herein is a method for inducing tolerance to an allergen in a subject in need thereof, comprising: administering to the subject, a pharmaceutical composition comprising a therapeutically effective amount of at least one agent suitable for treating an allergy, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

[0008] In some embodiments, the allergen is a food allergen. In some embodiments, the administering to the subject is performed less than about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 times per week. In some embodiments, the pharmaceutical composition is administered to the subject about once per week. In some embodiments, the administering the pharmaceutical composition is performed orally, sublingually, buccally, by inhalation, or subcutaneously. In some embodiments, the pharmaceutical composition is provided as a lyophile. In some embodiments, the lyophile is deposited on a filter paper. In some embodiments, the lyophile is reconstituted prior to administering. In some embodiments, the lyophile is reconstituted with an aqueous diluent. In some embodiments, the aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline. In some embodiments, the pharmaceutical composition further comprises a sugar. In some embodiments, the sugar is selected from the group consisting of trehalose, glucose, sucrose, maltose, galactose, fructose, and arabinose. In some embodiments, the at least one agent comprises an allergen. In

some embodiments, the allergen is selected from the group consisting of proteins, plant products and animal products. In some embodiments, the allergen is a protein. In some embodiments, the allergen is selected from the group consisting of whole peanut, peanut powder, peanut butter, derivatives and combination thereof. In some embodiments, the allergen is derived from peanut, tree nut, egg, shellfish, soy, milk, gluten, or any combination thereof. In some embodiments, the allergen comprises a grass pollen allergen, a weed pollen allergen, an indoor allergen, a mold allergen, a tree pollen allergen, a stinging insect allergen, a food allergen, or any combination, or derivative thereof. In some embodiments, the at least one agent comprises an allergy medication. In some embodiments, the allergy medication comprises an antihistamine, a corticosteroid, a bronchodilator, a mast cell stabilizer, a leukotriene inhibitor, an anti-tuberculosis agent, a serine lung protease inhibitor, or any combination, or derivative thereof. In some embodiments, the antihistamine comprises a H_1-antihistamine, H_2-antihistamine, H_3-antihistamine, H_4-antihistamine, or any combination thereof. In some embodiments, the H_1-antihistamine comprises acrivastine, azelastine, bilastine, brompheniramine, buclizine, bromodiphenhydramine, carbinoxamine, chlorpromazine, cyclizine, chlorphenamine, chlorodiphenhydramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, dimenhydrinate, dimetindene, diphenhydramine, doxylamine, ebastine, embramine, fexofenadine, hydroxyzine, loratadine, meclozine, mirtazapine, olopatadine, orphenadrine, phenindamine, pheniramine, phenyltoloxamine, promethazine, quetiapine, rupatadine, tripelennamine, triprolidine, or any combination, or derivative thereof. In some embodiments, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof. In some embodiments, the bronchodilator comprises terbutaline, albuterol, ipatropium, pirbuterol, epinephrine, salmeterol, levalbuterol, formoterol, or any combination thereof. In some embodiments, the mast cell stabilizer comprises cromoglicic acid. In some embodiments, the leukotriene inhibitor comprises montelukast, zafirlukast, zileuton, or any combination or derivative thereof. In some embodiments, the anti-tuberculosis agent comprises isoniazid, ethambutol, pyrazinamide, rifamycin, rifampin, rifabutine, linezolid, streptomycin, clarithromycin, amikacin, kanamycin, gentamicin, capreomycin, viomycin, enviomycin, ciprofloxacin, levofloxacin, moxifloxacin, ethionamide, prothionamide, cycloserine, terizidone, or any combination, or derivative thereof. In some embodiments, the pharmaceutical composition is substantially devoid of cholesterol. In some embodiments, the at least one agent comprises azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

[0009] In another aspect, disclosed herein is a pharmaceutical composition, comprising: a therapeutically effective amount of at least one agent for treating an allergy in a subject in need thereof, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof, and wherein said pharmaceutical composition is formulated for oral administration to said subject.

[0010] In another aspect, disclosed herein is a pharmaceutical composition, comprising: a therapeutically effective amount of at least one agent for treating an allergy in a subject in need thereof, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof, and wherein said composition is formulated for subcutaneous administration to said subject.

[0011] In some embodiments, the composition comprises a lyophile. In some embodiments, the lyophile is deposited on a filter paper. In some embodiments, the lyophile is reconstituted prior to administration. In some embodiments, the lyophile is reconstituted with an aqueous diluent. In some embodiments, the aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline. In some embodiments, the pharmaceutical composition further comprises a sugar. In some embodiments, the sugar is selected from the group consisting of trehalose, glucose, sucrose, maltose, galactose, fructose, and arabinose. In some embodiments, the at least one agent comprises an allergen. In some embodiments, the allergen is selected from the group consisting of food proteins, plant products and animal products. In some embodiments, the allergen is a protein selected from the group consisting of peanut protein and tree nut protein. In some embodiments, the allergen is selected from the group consisting of whole peanut, peanut powder, peanut butter, derivatives and combinations thereof. In some embodiments, the allergen is selected from the group consisting of peanut, tree nut, egg, shellfish, soy, milk, gluten, and derivatives and combinations thereof. In some embodiments, the allergen is selected from the group consisting of indoor allergen, mold allergen, stinging insect allergen, food allergen, derivatives and combinations thereof. In some embodiments, the composition further comprises cholesterol.

[0012] In some embodiments, the at least one agent comprises an allergy medication selected from the group consisting of an antihistamine, a corticosteroid, a bronchodilator, a mast cell stabilizer, a leukotriene inhibitor, an anti-tuberculosis agent, an antibacterial agent, a serine lung protease inhibitor, and any combination and derivative thereof. In some embodiments, the antihistamine comprises a H_1-antihistamine, H_2-antihistamine, H_3-antihistamine, H_4-antihistamine, or any combination thereof. In some embodiments, the H_1-antihistamine

comprises acrivastine, azelastine, bilastine, brompheniramine, buclizine, bromodiphenhydramine, carbinoxamine, chlorpromazine, cyclizine, chlorphenamine, chlorodiphenhydramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, dimenhydrinate, dimetindene, diphenhydramine, doxylamine, ebastine, embramine, fexofenadine, hydroxyzine, loratadine, meclozine, mirtazapine, olopatadine, orphenadrine, phenindamine, pheniramine, phenyltoloxamine, promethazine, quetiapine, rupatadine, tripelennamine, triprolidine, or any combination or derivative thereof. In some embodiments, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof. In some embodiments, the bronchodilator comprises terbutaline, albuterol, ipatropium, pirbuterol, epinephrine, salmeterol, levalbuterol, formoterol, or any combination or derivative thereof. In some embodiments, the mast cell stabilizer comprises cromoglicic acid. In some embodiments, the leukotriene inhibitor comprises montelukast, zafirlukast, zileuton, or any combination or derivative thereof. In some embodiments, the anti-tuberculosis agent comprises isoniazid, ethambutol, pyrazinamide, rifamycin, rifampin, rifabutine, linezolid, streptomycin, clarithromycin, amikacin, kanamycin, gentamicin, capreomycin, viomycin, enviomycin, ciprofloxacin, levofloxacin, moxifloxacin, ethionamide, prothionamide, cycloserine, terizidone, or any combination or derivative thereof. In some embodiments, the composition is substantially devoid of cholesterol.

[0013] In another aspect, disclosed herein is a pharmaceutical composition, comprising: a therapeutically effective amount of at least one agent suitable for treating eosinophilic esophagitis (EoE) in a subject in need thereof, wherein the at least one agent is encapsulated in a liposome carrier.

[0014] In some embodiments, the liposome carrier comprises phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), or any combination or derivative thereof. In some embodiments, the liposome carrier is a sterically stabilized liposome carrier. In some embodiments, the sterically stabilized liposome carrier comprises poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE), PEG-dipalmitoylphosphatidylethanolamine (DPPE), PEG-di-C:15 PE, PEG-soy PE, or PEG-egg PE. In some embodiments, the composition comprises a lyophile. In some embodiments, the lyophile is deposited on a filter paper. In some embodiments, the lyophile is reconstituted prior to administration. In some embodiments, the lyophile is reconstituted with an aqueous diluent. In some embodiments, the aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline. In some embodiments, the pharmaceutical composition is suitable for subcutaneous, sublingual, or oral

administration. In some embodiments, the at least one agent comprises a proton-pump inhibitor (PPI), a corticosteroid, or any combination or derivative thereof. In some embodiments, the proton-pump inhibitor comprises omeprazole, lansoprazole, dexlansoprazole, esomeprazole, pantoprazole, rabeprazole, ilaprazole, or any combination or derivative thereof. In some embodiments, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof. In some embodiments, the at least one agent comprises azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

[0015] In another aspect, disclosed herein is a pharmaceutical composition, comprising: a therapeutically effective amount of at least one agent suitable for treating tuberculosis, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

[0016] In some embodiments, the composition comprises a lyophile. In some embodiments, the lyophile is deposited on a filter paper. In some embodiments, the lyophile is reconstituted prior to administration. In some embodiments, the lyophile is reconstituted with an aqueous diluent. In some embodiments, the aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline. In some embodiments, the pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration. In some embodiments, the at least one agent comprises isoniazid, rifampin, gangamycin, pyrazinamide, ethambutol, rifabutin, kanamycin, amikacin, capreomycin, streptomycin, levofloxacin, levofloxacin, ofloxacin, para–aminosalicylic acid, cycloserine, terizidone, ethionamide, protionamide, clofazimine, linezolid, amoxicillin/clavulanate, thioacetazone, imipenem/cilastatin, high dose isoniazid, clarithromycin, or any combination or derivative thereof.

[0017] In some embodiments, the at least one agent comprises an antibody, derivative or fragment thereof. In some embodiments, the antibody is an anti-IgE antibody. In some embodiments, the at least one agent comprises a monophosphoryl lipid A (MPL). In some embodiments, the at least one agent is released from the liposome carrier in a pH sensitive manner upon administration. In some embodiments, the at least one agent is released from the liposome carrier in a pH independent manner upon administration. In some embodiments, the sterically stabilized liposome carrier comprises a membrane portion, and wherein at least about 50%, about 60%, about 70% or about 75% of the at least one agent is displaced within the

membrane portion of the liposome carrier at the time of said administration. In some embodiments, the sterically stabilized liposome carrier comprises an internal portion encompassed by a membrane portion, and wherein at least about 25%, about 50%, about 60%, about 75%, or about 80% of the at least one agent is in the internal portion of the liposome carrier. In some embodiments, the pharmaceutical composition comprises at least about 60% phosphatidylglycerol, at least about 60% phosphatidylcholine, or at least about 60% combination of phosphatidylglycerol and phosphatidylcholine. In some embodiments, the pharmaceutical composition contains about 60% to about 99% phosphatidylcholine, phosphatidylglycerol, or combination thereof. In some embodiments, the pharmaceutical composition contains about 1% to about 5% PEG-DSPE. In some embodiments, the pharmaceutical composition contains about 1% to about 33% of the at least one agent. In some embodiments, the sterically stabilized liposome carrier is stable at about pH 3 to about pH 7 or at about pH 7 to about pH 10. In some embodiments, the sterically stabilized liposome carrier has a gel-liquid crystalline phase transition temperature in a range from about -20°C to about 44°C.

[0018] In another aspect, disclosed herein is a kit, comprising the pharmaceutical composition described herein. In some embodiments, the kit further comprises instructions for use of the pharmaceutical composition.

[0019] In another aspect, disclosed herein is a method for treating a subject in need thereof, comprising: administering the pharmaceutical composition described herein. In some embodiments, the administering the pharmaceutical composition is performed subcutaneously, sublingually, or orally. In some embodiments, the subject has a non-asthmatic allergy. In some embodiments, the subject has a food allergy. In some embodiments, the subject has eosinophilic esophagitis. In some embodiments, the pharmaceutical composition is administered to the subject less than about 7 times per week. In some embodiments, the pharmaceutical composition is administered to the subject about once per week.

[0020] In another aspect, disclosed herein is a method for treating tuberculosis, comprising: administering to a subject in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of at least one agent suitable for treating tuberculosis, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

[0021] In some embodiments, the composition comprises a lyophile. In some embodiments, the lyophile is deposited on a filter paper. In some embodiments, the lyophile is reconstituted prior to administration. In some embodiments, the lyophile is reconstituted with an aqueous diluent. In some embodiments, the aqueous diluent is selected from the group consisting of: distilled water,

deionized water; sterile water; bacteriostatic water; and normal saline. In some embodiments, the administering the pharmaceutical composition is performed subcutaneously, sublingually, or orally. In some embodiments, the at least one agent comprises isoniazid, rifampin, gangamycin, pyrazinamide, ethambutol, rifabutin, kanamycin, amikacin, capreomycin, streptomycin, levofloxacin, levofloxacin, ofloxacin, para–aminosalicylic acid, cycloserine, terizidone, ethionamide, protionamide, clofazimine, linezolid, amoxicillin/clavulanate, thioacetazone, imipenem/cilastatin, high dose isoniazid, clarithromycin, or any combination or derivative thereof.

[0022] In some embodiments, the at least one agent comprises an antibody, derivative or fragment thereof. In some embodiments, the antibody is an anti-IgE antibody. In some embodiments, the at least one agent comprises a monophosphoryl lipid A (MPL). In some embodiments, the pharmaceutical composition is in powder, liquid, tablet, or capsule form. In some embodiments, the pharmaceutical composition is suspended in a solvent before administration. In some embodiments, at least about 75% of the at least one agent is in a membrane portion of the liposome carrier. In some embodiments, at least about 75% of the at least one agent is in an internal portion of the liposome carrier. In some embodiments, the pharmaceutical composition contains at least about 60% phosphatidylglycerol, phosphatidylcholine, or a combination thereof. In some embodiments, the pharmaceutical composition contains about 60% to about 99% phosphatidylglycerol, phosphatidylcholine, or a combination thereof. In some embodiments, the pharmaceutical composition contains at least about 1% PEG-DSPE. In some embodiments, the pharmaceutical composition contains about 1% to about 5% PEG-DSPE. In some embodiments, the pharmaceutical composition comprises at least about 1% of the at least one agent. In some embodiments, the pharmaceutical composition contains about 1% to about 33% of the at least one agent. In some embodiments, the sterically stabilized liposome carrier is stable at about pH 7 to about pH 10. In some embodiments, the sterically stabilized liposome carrier is stable at about pH 3 to about 7. In some embodiments, the sterically stabilized liposome carrier has a gel-liquid crystalline phase transition temperature in a range from about -20°C to about 44°C. In some embodiments, the pharmaceutical composition is administered to the subject less than about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 times per week. In some embodiments, the pharmaceutical composition is administered to the subject about once per week.

[0023] In another aspect, disclosed herein is a method for treating inflammation in a subject in need thereof, comprising: administering subcutaneously, sublingually, or orally to said subject, an effective amount of a pharmaceutical composition comprising a sterically stabilized liposome

comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

[0024] In some embodiments, the composition comprises a lyophile. In some embodiments, the lyophile is deposited on a filter paper. In some embodiments, the lyophile is reconstituted prior to administration. In some embodiments, the lyophile is reconstituted with an aqueous diluent. In some embodiments, the aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline. In some embodiments, the inflammation is associated with an allergy or a disease. In some embodiments, the sterically stabilized liposome carrier is stable at about pH 7 to about 10. In some embodiments, the sterically stabilized liposome carrier is stable at about pH 3 to about 7. In some embodiments, the sterically stabilized liposome carrier has a gel-liquid crystalline phase transition temperature in a range from -20°C to 44°C. In some embodiments, the pharmaceutical composition is administered to the subject less than about 7 times per week. In some embodiments, the pharmaceutical composition is administered to the subject about once or about two times per week. In some embodiments, the pharmaceutical composition further comprises a therapeutically effective amount of at least one agent suitable for treating said allergy or disease. In some embodiments, the at least one agent is a corticosteroid. In some embodiments, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination thereof.

[0025] In some embodiments, the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered concurrently. In some embodiments, the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered sequentially. In some embodiments, the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered sequentially, and wherein the sterically stabilized liposome is administered first. In some embodiments, the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered sequentially, and wherein the at least one agent suitable for treating said allergy or disease is administered first.

INCORPORATION BY REFERENCE

[0026] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0027] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0028] FIG. 1 depicts a structure of a sterically stabilized liposome carrier having at least a membrane portion and an interior portion.

[0029] FIG. 2 shows a comparison of PB eosinophil levels in mice, among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Sensitized, Untreated mice), Daily Bud group (daily oral administration of 20μg of budesonide without a sterically stabilized liposome carrier), Wk-S-Bud group (20μg of a composition described herein, budesonide in a sterically stabilized liposome carrier administered orally once a week), Wk-Empty-S group (Buffer loaded empty sterically stabilized liposome carrier without drug given once a week), Wk-C-Bud group (20μg of budesonide encapsulated in Conventional Carrier administered once a week), and Wk-Bud group (20μg of budesonide without a carrier described herein administered once a week).

[0030] FIG. 3 shows a comparison of IgE levels in mice among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Sensitized, Untreated mice), Daily Bud group (20μg of budesonide without carrier administered orally daily-Standard therapy), Wk-S-Bud group (20μg of budesonide in a sterically stabilized liposome carrier described herein, administered orally once a week), Wk-Empty-S group (Buffer loaded empty sterically stabilized liposome carrier described herein, administered orally once a week), Wk-C-Bud group (20μg of budesonide encapsulated in Conventional Carrier given once a week), and Wk-Bud group (20μg of budesonide without any carrier given once a week).

[0031] FIG. 4 shows a comparison of PB eosinophil levels among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (sensitized, Untreated mice), Daily Bud group (20μg of budesonide without a carrier given daily-Standard therapy), Wk-S-Bud group (20μg of budesonide in sterically stabilized liposome carrier described herein given orally once a week), Wk-Empty-S group (Buffer loaded empty sterically stabilized liposome carrier described herein without drug given orally once a week), Wk-Bud group (20μg of budesonide without carrier given orally once a week), and Wk-Bud & ES group (Wk- Empty-S and Wk-Bud without encapsulation in a carrier, given orally once a week).

[0032] FIG. 5 shows a comparison of IgE levels in mice among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Senstitized, Untreated mice), Daily Bud group (20μg of budesonide without Carrier given daily-Standard therapy), Wk-S-Bud group (20μg of budesonide in sterically stabilized liposome carrier given orally once a week), Wk-

Empty-S group (Buffer loaded empty sterically stabilized liposome carrier without drug given orally once a week), Wk-Bud group (20μg of budesonide without any carrier given once a week), and Wk-Bud & ES group (Wk-Empty-S and Wk-Bud without encapsulation in the carrier, given once a week).

[0033] FIG. 6 shows a comparison of PB eosinophil levels among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Sensitized, Untreated mice), Daily Bud group (20μg of budesonide without a carrier given daily-Standard therapy), Wk-S-Bud + group (20μg of budesonide in the sterically stabilized liposome carrier with cholesterol given orally once a week), Wk-S-Bud - group (20μg of budesonide in the sterically stabilized liposome carrier without cholesterol given orally once a week),Wk-Empty-S group (Buffer loaded empty carrier without drug or cholesterol given once a week), and Wk-Bud group (20μg of budesonide without Carrier given once a week).

[0034] FIG. 7 shows a comparison of IgE levels among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Sensitized, Untreated mice), Daily Bud group (20μg of budesonide without Carrier given daily-Standard therapy), Wk-S-Bud + group (20μg of budesonide in the sterically stabilized liposome carrier with Cholesterol given orally once a week), Wk-S-Bud - group (20μg of budesonide in the sterically stabilized liposome carrier without Cholesterol given orally once a week), Wk-Empty-S group (Buffer loaded empty sterically stabilized liposome carrier without drug or cholesterol given once a week), and Wk-Bud group (20μg of budesonide without carrier given once a week).

[0035] FIG. 8 shows a comparison of IgE levels among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Sensitized, Untreated mice), Daily Bud group (20μg of budesonide without carrier given daily-Standard therapy), Wk-S-Bud + group (20μg of budesonide in the sterically stabilized liposome carrier with Monophosphoryl lipid A (MPL), given once a week), Wk-S-Bud-group (20μg of budesonide in the sterically stabilized liposome carrier without MPL given once a week), Wk-Empty-S group (Buffer loaded empty sterically stabilized liposome carrier without drug or MPL given orally once a week), and Wk-Bud group (20μg of budesonide without a carrier given once a week).

[0036] FIG. 9 shows a comparison of IgE levels among: NORMAL group (Unsensitized, Untreated Normal mice), Sens group (Sensitized, Untreated mice), Daily Bud group (20μg of budesonide without carrier given daily-Standard therapy), Wk-S-Bud group (20μg of budesonide in the sterically stabilized liposome carrier given once a week), Wk-S-Tri-20μg group (20μg of triamcinolone in the sterically stabilized liposome carrier given orally once a week), Wk-S-Tri-40μg group (40μg of triamcinolone in the sterically stabilized liposome carrier given orally once

a week), and Wk-Empty-S group (Buffer loaded empty sterically stabilized liposome carrier without drug or MPL given orally once a week).

[0037] FIG. 10 shows that once a week administration of the empty sterically stabilized drug delivery system (WK-ES) and once a week oral administration of Budesonide encapsulated in the sterically stabilized liposome carrier significantly decreased levels of the pro-inflammatory cytokine IL-4.

[0038] FIG. 11 shows that once a week oral administration of the empty sterically stabilized drug delivery system (WK-ES) and once a week oral administration of Budesonide encapsulated in the sterically stabilized liposome carrier significantly decreased levels of the pro-inflammatory cytokine IL-5.

[0039] FIG. 12 shows that once a week oral administration of the empty sterically stabilized drug delivery system/carrier (WK-ES) and once a week oral administration of Budesonide encapsulated in the sterically stabilized liposome carrier significantly increased levels of the anti-inflammatory cytokine IL-10.

[0040] Fig. 13 shows hematoxylin and eosin stained slides of skin. Top two frames show Empty sterically stabilized liposome carrier administered orally once a week to a sensitized mouse with allergic inflammation (10X magnification-top left and 40X magnification-top right). Bottom two frames show untreated sensitized mice at 40X magnification.

[0041] Fig. 14 shows hematoxylin and eosin stained slides of gastrointestinal tract. Top left is empty sterically stabilized liposome carrier delivered orally once a week to a sensitized mouse with allergic inflammation. Top right depicts once a week budesonide encapsulated in the sterically stabilized liposome carrier given orally once a week to a sensitized mouse with allergic inflammation. Bottom left is an example of a Normal untreated mouse. Right bottom is an example of inflammation in an untreated, sensitized mouse with allergic inflammation.

DETAILED DESCRIPTION OF THE INVENTION

[0042] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of the ordinary skill in the art to which this invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of the formulations or unit doses herein, some methods and materials are now described. Unless mentioned otherwise, the techniques employed or contemplated herein are standard methodologies. The materials, methods and examples are illustrative only and not limiting.

[0043] The details of one or more inventive embodiments are set forth in the accompanying drawings, the claims, and the description herein. Other features, objects, and advantages of the

inventive embodiments disclosed and contemplated herein can be combined with any other embodiment unless explicitly excluded.

[0044] Unless otherwise indicated, open terms for example "contain," "containing," "include," "including," and the like mean comprising.

[0045] The singular forms "a", "an", and "the" are used herein to include plural references unless the context clearly dictates otherwise. Accordingly, unless the contrary is indicated, the numerical parameters set forth in this application are approximations that may vary depending upon the desired properties sought to be obtained by the present invention.

[0046] Unless otherwise indicated, some embodiments herein contemplate numerical ranges. When a numerical range is provided, unless otherwise indicated, the range includes the range endpoints. Unless otherwise indicated, numerical ranges include all values and subranges therein as if explicitly written out.

[0047] The term "about" and its grammatical equivalents in relation to a reference numerical value and its grammatical equivalents as used herein can include a range of values plus or minus 10% from that value. For example, the amount "about 10" includes amounts from 9 to 11. The term "about" in relation to a reference numerical value can also include a range of values plus or minus 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2%, or 1% from that value.

[0048] Unless otherwise indicated, the ratios used herein are expressed as molar ratios. Unless otherwise indicated, the percentages used herein are expressed as molar percentages.

Overview

[0049] Disclosed herein are compositions, kits, and methods of using a sterically stabilized liposome carrier for treating a condition or disorder. In some cases, the condition is an allergy, for instance a food allergy. As such, in some embodiments are provided compositions and methods for the treatment of Immunoglobulin E (IgE)-mediated food allergy. In some embodiments, the food allergy is not characterized by airway inflammations.

[0050] In some cases, are provided compositions and methods for treating an inflammatory condition in a subject, wherein the inflammatory condition is not an airway inflammation. In some cases, the inflammatory condition is caused by eosinophilic esophagitis (EoE) or tuberculosis (TB). In some cases, the compositions, kits, and methods described herein can be used for treating more than one condition. The compositions, kits, and methods can be used to treat an inflammatory disorder and an allergy. The compositions, kits, and methods can be used to treat eosinophilic esophagitis and an allergy.

Subject

[0051] A "subject", as used herein, can be a mammal, preferably human. The subject can be diagnosed with a condition. In some cases, the condition is an allergy. In some cases, the condition is an inflammatory disorder. In some cases, the condition is eosinophilic esophagitis (EoE). In some cases, the condition is tuberculosis (TB). In some cases, the condition is not asthma. In some cases, the condition is not allergic asthma.

[0052] The subject can be a male or a female. The subject can be patients of any age. The subject can be an adult, child, or newborn. For example, the subject may be a patient of at least about 1, 5, 10, 20, 30, 40, 50, 60, 70, 80, 90, or 100 years old. For example, the subject can be a patient of less than about 10 years old. Often, the subject is a patient or other individual undergoing a treatment regimen, or being evaluated for a treatment regimen (*e.g.*, allergen immunotherapy). However, in some instances, the subject is not undergoing a treatment regimen.

Compositions

[0053] Disclosed herein are pharmaceutical compositions particularly suitable for oral, subcutaneous, sublingual or buccal administration, comprising a sterically stabilized liposome carrier. Compositions described herein can provide sustained slow release of an agent formulated with a sterically stabilized liposome carrier described herein, and in certain embodiments can be administered orally, subcutaneously or sublingually about once a week. In some embodiments, the sterically stabilized liposome carrier can be spherical vesicles having at least one lipid bilayer. The sterically stabilized liposome carrier can comprise phospholipids and can encapsulate a variety of drugs, therapeutic agents and/or allergens in amounts specifically suited for oral, subcutaneous or sublingual delivery. In certain embodiments, the sterically stabilized liposome carrier can also be used to encapsulate allergens to treat allergy, for instance food allergy.

[0054] In certain embodiments, sterically stabilized liposome carriers described herein can have various interactions with cells upon administration to a subject. In some cases, the sterically stabilized liposome carrier can exchange materials, such as lipids, lipids and proteins with cell membranes. In some cases, the sterically stabilized liposome carrier can transfer encapsulated therapeutic agents to the cell. In some cases, the sterically stabilized liposome carrier can be absorbed to cells. In some cases, the sterically stabilized liposome carrier can bind to cells. In some cases, the sterically stabilized liposome carrier can be internalized by cells via endocytosis or phagocytosis once bound to the cells. In some cases, the sterically stabilized liposome carrier can fuse to cell membranes once bound.

[0055] The sterically stabilized liposome carrier described herein can be used to extend the life of conventional liposomes in a mammalian body. Conventional liposomes are composed of naturally-occurring phospholipids, such as phosphatidylglycerol and phosphatidylcholine. Conventional liposomes can be recognized in vivo by the cells of the reticuloendothelial system and can be cleared rapidly from the circulation. In addition, incorporation of certain therapeutic agents, such as triamcinolone (TRJ) or beclomethasone, into conventional liposomes can result in their rapid redistribution and leakage from liposomes into the medium. In contrast to conventional liposomes, the sterically stabilized liposomes described herein can exhibit increased stability in plasma and decreased uptake by the reticuloendothelial system.

[0056] In certain embodiments, sterically stabilized liposome carrier described herein can retain drugs, therapeutic agents or allergens for a predetermined period of time. In some cases the predetermined period of time is 1, 2, 3, 4, 5, 6, 7 or 8 days. In some cases, the composition of the sterically stabilized liposome carrier can facilitate the encapsulation of a drug, therapeutic agent or allergen within the bilayer or inside the carrier. In some cases, the presence of sufficient amounts of PEGylated (PEG refers to poly(ethylene glycol)) lipids in the sterically stabilized liposome carrier can stabilize and protect the liposome from disruption upon exposure to biological milieu. In some cases, the composition comprises an amount of PEGylated lipid in the sterically stabilized liposome carrier, wherein the amount is sufficient to enable the drug, allergen or therapeutic agent to remain liposome-associated for a desired period of time. In some embodiments, the desired period of time is up to about one week.

[0057] In certain embodiments, sterically stabilized liposome carriers described herein can comprise poly(ethylene glycol) (PEG), phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), or any combination thereof. In some cases, the sterically stabilized liposome carrier can comprise poly(ethylene glycol) and phosphatidylglycerol. In some cases, the sterically stabilized liposome carrier can comprise poly(ethylene glycol) and phosphatidylcholine. In some cases, the sterically stabilized liposome carrier can comprise poly(ethylene glycol), phosphatidylglycerol, and/or phosphatidylcholine. The PEG component of the sterically stabilized liposome carrier can be poly(ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE), PEG-dipalmitoylphosphatidylethanolamine (DPPE), PEG-di-C:15 PE, PEG-soy PE, or PEG-egg PE. In certain embodiments, the pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration. In some cases, the pharmaceutical composition is comprised in a lyophilized powder. In some cases, the pharmaceutical composition is deposited on a filter paper. In some cases, the pharmaceutical composition (e.g., lyophilized powder deposited on a filter paper) is reconstituted with a solvent, *e.g.*, water, saline (e.g., 5% saline), or glycerol.

Sterically stabilized liposome carrier

[0058] The PEG (*e.g.*, PEG-DSPE), PG, or PC component of the sterically stabilized liposome carrier can have a molecular weight ranges from about 300 to about 6000 Daltons. For example, the PEG (*e.g.*, PEG-DSPE), PG, or PC component of the sterically stabilized liposome carrier can have a molecular weight ranges from about 300 to about 500 Daltons, from about 300 to about 1000 Daltons, from about 300 to about 1500 Daltons, from about 300 to about 2000 Daltons, from about 300 to about 2500 Daltons, from about 300 to about 3000 Daltons, from about 300 to about 3500 Daltons, from about 300 to about 4000 Daltons, from about 300 to about 4500 Daltons, from about 300 to about 5000 Daltons, from about 300 to about 5500 Daltons, from about 300 to about 6000 Daltons, from about 400 to about 500 Daltons, from about 400 to about 1000 Daltons, from about 400 to about 1500 Daltons, from about 400 to about 2000 Daltons, from about 400 to about 2500 Daltons, from about 400 to about 3000 Daltons, from about 400 to about 3500 Daltons, from about 400 to about 4000 Daltons, from about 400 to about 4500 Daltons, from about 400 to about 5000 Daltons, from about 400 to about 5500 Daltons, from about 400 to about 6000 Daltons, from about 500 to about 1000 Daltons, from about 500 to about 1500 Daltons, from about 500 to about 2000 Daltons, from about 500 to about 2500 Daltons, from about 500 to about 3000 Daltons, from about 500 to about 3500 Daltons, from about 500 to about 4000 Daltons, from about 500 to about 4500 Daltons, from about 500 to about 5000 Daltons, from about 500 to about 5500 Daltons, from about 500 to about 6000 Daltons, from about 1000 to about 1500 Daltons, from about 1000 to about 2000 Daltons, from about 1000 to about 2500 Daltons, from about 1000 to about 3000 Daltons, from about 1000 to about 3500 Daltons, from about 1000 to about 4000 Daltons, from about 1000 to about 4500 Daltons, from about 1000 to about 5000 Daltons, from about 1000 to about 5500 Daltons, from about 1000 to about 6000 Daltons, from about 1500 to about 2000 Daltons, from about 1500 to about 2500 Daltons, from about 1500 to about 3000 Daltons, from about 1500 to about 3500 Daltons, from about 1500 to about 4000 Daltons, from about 1500 to about 4500 Daltons, from about 1500 to about 5000 Daltons, from about 1500 to about 5500 Daltons, from about 1500 to about 6000 Daltons, from about 2000 to about 2500 Daltons, from about 2000 to about 3000 Daltons, from about 2000 to about 3500 Daltons, from about 2000 to about 4000 Daltons, from about 2000 to about 4500 Daltons, from about 2000 to about 5000 Daltons, from about 2000 to about 5500 Daltons, from about 2000 to about 6000 Daltons, from about 2500 to about 3000 Daltons, from about 2500 to about 3500 Daltons, from about 2500 to about 4000 Daltons, from about 2500 to about 4500 Daltons, from about 2500 to about 5000 Daltons, from about 2500 to about 5500 Daltons, from about 2500 to about 6000 Daltons, from about 3000 to about 3500 Daltons,

from about 3000 to about 4000 Daltons, from about 3000 to about 4500 Daltons, from about 3000 to about 5000 Daltons, from about 3000 to about 5500 Daltons, from about 3000 to about 6000 Daltons, from about 3500 to about 4000 Daltons, from about 3500 to about 4500 Daltons, from about 3500 to about 5000 Daltons, from about 3500 to about 5500 Daltons, from about 3500 to about 6000 Daltons, from about 4000 to about 4500 Daltons, from about 4000 to about 5000 Daltons, from about 4000 to about 5500 Daltons, from about 4000 to about 6000 Daltons, from about 4500 to about 5000 Daltons, from about 4500 to about 5500 Daltons, from about 4500 to about 6000 Daltons, from about 5000 to about 5500 Daltons, from about 5000 to about 6000 Daltons, or from about 5500 to about 6000 Daltons. In one example, the molecular weight of the PEG component is from about 851 to about 5802 Daltons. In another example, the molecular weight of the PEG component is from about 1019 to about 3775 Daltons. In another example, the molecular weight of the PEG component is from about 2749 to about 2806 Daltons. In another example, the molecular weight of the PC component is from about 509 to about 791 Daltons. In another example, the molecular weight of the PC component is from about 677 to about 791 Daltons. In another example, the molecular weight of the PC component is from about 734 to about 791 Daltons. In another example, the molecular weight of the PG component is from about 520 to about 802 Daltons. In another example, the molecular weight of the PG component is from about 688 to about 802 Daltons. In another example, the molecular weight of the PG component is from about 744 to about 802 Daltons.

[0059] The PEG component (*e.g.*, PEG-DSPE), PG component, or PC component of the sterically stabilized liposome carrier can have a molecular weight of at least about 300 Daltons. For example, the PEG component (*e.g.*, PEG-DSPE), PG component, or PC component of the sterically stabilized liposome carrier can have a molecular weight of at least about 300 Daltons, at least about 400 Daltons, at least about 500 Daltons, at least about 600 Daltons, at least about 700 Daltons, at least about 800 Daltons, at least about 900 Daltons, at least about 1000 Daltons, at least about 1500 Daltons, at least about 2000 Daltons, at least about 2500 Daltons, at least about 3000 Daltons, at least about 3500 Daltons, at least about 4000 Daltons, at least about 4500 Daltons, at least about 5000 Daltons, at least about 5500 Daltons, or at least about 6000 Daltons.

[0060] The head groups (phosphatidylcholine and phosphatidylglycerol) or the poly(ethylene glycol) (*e.g.*, PEG-DSPE), may be attached to acyl groups containing from about 8 to about 24 carbon atoms. For example, the acyl group can comprise from about 8 to about 10 carbon atoms, from about 8 to about 12 carbon atoms, from about 8 to about 14 carbon atoms, from about 8 to about 16 carbon atoms, from about 8 to about 18 carbon atoms, from about 8 to about 20 carbon atoms, from about 8 to about 22 carbon atoms, from about 8 to about 24 carbon atoms, from about 10 to about 12 carbon atoms, from about 10 to about 14 carbon atoms, from about 10 to

about 16 carbon atoms, from about 10 to about 18 carbon atoms, from about 10 to about 20 carbon atoms, from about 10 to about 22 carbon atoms, from about 10 to about 24 carbon atoms, from about 12 to about 14 carbon atoms, from about 12 to about 16 carbon atoms, from about 12 to about 18 carbon atoms, from about 12 to about 20 carbon atoms, from about 12 to about 22 carbon atoms, from about 12 to about 24 carbon atoms, from about 14 to about 16 carbon atoms, from about 14 to about 18 carbon atoms, from about 14 to about 20 carbon atoms, from about 14 to about 22 carbon atoms, from about 14 to about 24 carbon atoms, from about 16 to about 18 carbon atoms, from about 16 to about 20 carbon atoms, from about 16 to about 22 carbon atoms, from about 16 to about 24 carbon atoms, from about 18 to about 20 carbon atoms, from about 18 to about 22 carbon atoms, from about 18 to about 24 carbon atoms, from about 20 to about 22 carbon atoms, from about 20 to about 24 carbon atoms, or from about 22 to about 24 carbon atoms. The acyl group can comprise distearoyl, stearoyl oleoyl, stearoyl palmitoyl, dipalmitoyl, dioleoyl, palmitoyl oleoyl, or dipalmitoleoyl. The phosphatidylcholine and/or phosphatidylglycerol can be synthetically derived or derived from eggs (*e.g.*, chicken eggs) or soybeans. The phosphatidylcholine and/or phosphatidylglycerol derived from chicken eggs can contain acyl groups having varying numbers of carbon atoms, depending on the variety and diet of the chicken that produces the eggs.

[0061] The head groups (phosphatidylcholine and phosphatidylglycerol) or the poly(ethylene glycol) (*e.g.*, PEG-DSPE), may be attached to acyl groups containing at least about 8 carbon atoms. For example, the acyl group can comprise at least about 8, at least about 10, at least about 12, at least about 14, at least about 16, at least about 18, at least about 20, at least about 22, or at least about 24 carbon atoms.

Active Pharmaceutical Agents such as MPL

[0062] A pharmaceutical composition described herein can comprise at least one agent, wherein the at least one agent comprises a monophosphoryl lipid A (MPL). The pharmaceutical composition can also be substantially devoid of a MPL.

[0063] In some embodiments, the pharmaceutical composition can comprise a therapeutically effective amount of at least one agent which is a therapeutic or pharmaceutical agent. In some cases, the at least one agent comprises two or more therapeutic agents for treating the same condition. In some cases, the at least one agent comprises two or more agents, wherein a first agent of the two or more agent is for treating a first condition, and wherein a second agent of the two or more agents is for treating a second condition that is different from the first condition.

[0064] In some embodiments, the at least one agent is for treating an allergy in a subject in need thereof. In some embodiments, the allergy is a food allergy, which may be a non-asthmatic food

allergy. In some cases, the at least one agent is for treating an inflammatory disorder in a subject in need thereof, wherein said inflammatory disorder is not an airway inflammation. In some cases, the at least one agent is for treating eosinophilic esophagitis in a subject in need thereof. In some cases, the at least one agent is for treating tuberculosis (TB) in a subject in need thereof.

[0065] The pharmaceutical composition can comprise cholesterol. The pharmaceutical composition can also be substantially devoid of cholesterol.

[0066] The pharmaceutical composition can comprise about 0% to about 99.9% of any component of the composition, including the at least one agent, cholesterol, monophosphoryl lipid A (MPL), PEG (*e.g.*, PEG-DSPE), PG, and PC. For example, the pharmaceutical composition can comprise about 0% to about 0.1%, about 0% to about 0.5%, about 0% to about 1%, about 0% to about 2%, about 0% to about 3%, about 0% to about 4%, about 0% to about 5%, about 0% to about 10%, about 0% to about 15%, about 0% to about 20%, about 0% to about 25%, about 0% to about 30%, about 0% to about 40%, about 0% to about 50%, about 0% to about 60%, about 0% to about 70%, about 0% to about 80%, about 0% to about 90%, about 0% to about 95%, about 0% to about 98%, about 0% to about 99%, about 0% to about 99.5%, about 0% to about 99.9%, about 0.1% to about 0.5%, about 0.1% to about 1%, about 0.1% to about 2%, about 0.1% to about 3%, about 0.1% to about 4%, about 0.1% to about 5%, about 0.1% to about 10%, about 0.1% to about 15%, about 0.1% to about 20%, about 0.1% to about 25%, about 0.1% to about 30%, about 0.1% to about 40%, about 0.1% to about 50%, about 0.1% to about 60%, about 0.1% to about 70%, about 0.1% to about 80%, about 0.1% to about 90%, about 0.1% to about 95%, about 0.1% to about 98%, about 0.1% to about 99%, about 0.1% to about 99.5%, about 0.1% to about 99.9%, about 0.5% to about 1%, about 0.5% to about 2%, about 0.5% to about 3%, about 0.5% to about 4%, about 0.5% to about 5%, about 0.5% to about 10%, about 0.5% to about 15%, about 0.5% to about 20%, about 0.5% to about 25%, about 0.5% to about 30%, about 0.5% to about 40%, about 0.5% to about 50%, about 0.5% to about 60%, about 0.5% to about 70%, about 0.5% to about 80%, about 0.5% to about 90%, about 0.5% to about 95%, about 0.5% to about 98%, about 0.5% to about 99%, about 0.5% to about 99.5%, about 0.5% to about 99.9%, about 1% to about 2%, about 1% to about 3%, about 1% to about 4%, about 1% to about 5%, about 1% to about 10%, about 1% to about 15%, about 1% to about 20%, about 1% to about 25%, about 1% to about 30%, about 1% to about 40%, about 1% to about 50%, about 1% to about 60%, about 1% to about 70%, about 1% to about 80%, about 1% to about 90%, about 1% to about 95%, about 1% to about 98%, about 1% to about 99%, about 1% to about 99.5%, about 1% to about 99.9%, about 2% to about 3%, about 2% to about 4%, about 2% to about 5%, about 2% to about 10%, about 2% to about 15%, about 2% to about 20%, about 2% to about 25%, about 2% to about 30%, about 2% to about 40%, about 2% to about 50%, about 2% to

about 60%, about 2% to about 70%, about 2% to about 80%, about 2% to about 90%, about 2% to about 95%, about 2% to about 98%, about 2% to about 99%, about 2% to about 99.5%, about 2% to about 99.9%, about 3% to about 4%, about 3% to about 5%, about 3% to about 10%, about 3% to about 15%, about 3% to about 20%, about 3% to about 25%, about 3% to about 30%, about 3% to about 40%, about 3% to about 50%, about 3% to about 60%, about 3% to about 70%, about 3% to about 80%, about 3% to about 90%, about 3% to about 95%, about 3% to about 98%, about 3% to about 99%, about 3% to about 99.5%, about 3% to about 99.9%, about 4% to about 5%, about 4% to about 10%, about 4% to about 15%, about 4% to about 20%, about 4% to about 25%, about 4% to about 30%, about 4% to about 40%, about 4% to about 50%, about 4% to about 60%, about 4% to about 70%, about 4% to about 80%, about 4% to about 90%, about 4% to about 95%, about 4% to about 98%, about 4% to about 99%, about 4% to about 99.5%, about 4% to about 99.9%, about 5% to about 10%, about 5% to about 15%, about 5% to about 20%, about 5% to about 25%, about 5% to about 30%, about 5% to about 40%, about 5% to about 50%, about 5% to about 60%, about 5% to about 70%, about 5% to about 80%, about 5% to about 90%, about 5% to about 95%, about 5% to about 98%, about 5% to about 99%, about 5% to about 99.5%, about 5% to about 99.9%, about 10% to about 15%, about 10% to about 20%, about 10% to about 25%, about 10% to about 30%, about 10% to about 40%, about 10% to about 50%, about 10% to about 60%, about 10% to about 70%, about 10% to about 80%, about 10% to about 90%, about 10% to about 95%, about 10% to about 98%, about 10% to about 99%, about 10% to about 99.5%, about 10% to about 99.9%, about 15% to about 20%, about 15% to about 25%, about 15% to about 30%, about 15% to about 40%, about 15% to about 50%, about 15% to about 60%, about 15% to about 70%, about 15% to about 80%, about 15% to about 90%, about 15% to about 95%, about 15% to about 98%, about 15% to about 99%, about 15% to about 99.5%, about 15% to about 99.9%, about 20% to about 25%, about 20% to about 30%, about 20% to about 40%, about 20% to about 50%, about 20% to about 60%, about 20% to about 70%, about 20% to about 80%, about 20% to about 90%, about 20% to about 95%, about 20% to about 98%, about 20% to about 99%, about 20% to about 99.5%, about 20% to about 99.9%, about 25% to about 30%, about 25% to about 40%, about 25% to about 50%, about 25% to about 60%, about 25% to about 70%, about 25% to about 80%, about 25% to about 90%, about 25% to about 95%, about 25% to about 98%, about 25% to about 99%, about 25% to about 99.5%, about 25% to about 99.9%, about 30% to about 40%, about 30% to about 50%, about 30% to about 60%, about 30% to about 70%, about 30% to about 80%, about 30% to about 90%, about 30% to about 95%, about 30% to about 98%, about 30% to about 99%, about 30% to about 99.5%, about 30% to about 99.9%, about 40% to about 50%, about 40% to about 60%, about 40% to about 70%, about 40% to about 80%, about 40% to about 90%, about 40% to about 95%,

about 40% to about 98%, about 40% to about 99%, about 40% to about 99.5%, about 40% to about 99.9%, about 50% to about 60%, about 50% to about 70%, about 50% to about 80%, about 50% to about 90%, about 50% to about 95%, about 50% to about 98%, about 50% to about 99%, about 50% to about 99.5%, about 50% to about 99.9%, about 60% to about 70%, about 60% to about 80%, about 60% to about 90%, about 60% to about 95%, about 60% to about 98%, about 60% to about 99%, about 60% to about 99.5%, about 60% to about 99.9%, about 70% to about 80%, about 70% to about 90%, about 70% to about 95%, about 70% to about 98%, about 70% to about 99%, about 70% to about 99.5%, about 70% to about 99.9%, about 80% to about 90%, about 80% to about 95%, about 80% to about 98%, about 80% to about 99%, about 80% to about 99.5%, about 80% to about 99.9%, about 90% to about 95%, about 90% to about 98%, about 90% to about 99%, about 90% to about 99.5%, about 90% to about 99.9%, about 95% to about 98%, about 95% to about 99%, about 95% to about 99.5%, about 95% to about 99.9%, about 98% to about 99%, about 98% to about 99.5%, about 98% to about 99.9%, about 99% to about 99.5%, about 99% to about 99.9%, or about 99.5% to about 99.9% of any component of the composition, including the at least one agent, cholesterol, MPL, PEG (*e.g.*, PEG-DSPE), PG, and PC. In some cases, the pharmaceutical composition can comprise about 0% to about 99.4% of the PC. In some cases, the pharmaceutical composition can comprise about 60% to about 90% of the PC. In some cases, the pharmaceutical composition can comprise about 70% to about 80% of the PC. In some cases, the pharmaceutical composition can comprise about 0% to about 98.5% of the PC. In some cases, the pharmaceutical composition can comprise about 0.1% to about 99.4% of the PC. In some cases, the pharmaceutical composition can comprise about 0% to about 99.4% of the PG. In some cases, the pharmaceutical composition can comprise about 10% to about 40% of the PG. In some cases, the pharmaceutical composition can comprise about 20% to about 30% of the PG. In some cases, the pharmaceutical composition can comprise about 0% to about 98.5% of the PG. In some cases, the pharmaceutical composition can comprise about 0.1% to about 99.4% of the PG. In some cases, the pharmaceutical composition can comprise about 0.5% to about 10% of the PEG (*e.g.*, PEG-DSPE). In some cases, the pharmaceutical composition can comprise about 1% to about 5% of the PEG (*e.g.*, PEG-DSPE). In some cases, the pharmaceutical composition can comprise about 2% to about 5% of the PEG (*e.g.*, PEG-DSPE). In some cases, the pharmaceutical composition can comprise about 0% to about 33% of the cholesterol. In some cases, the pharmaceutical composition can comprise about 0.1% to about 33% of the cholesterol. In some cases, the pharmaceutical composition can comprise about 0.1% to about 20% of the cholesterol. In some cases, the pharmaceutical composition can comprise about 0.1% to about 10% of the cholesterol. In some cases, the pharmaceutical composition can comprise about 0% to

about 33% of the at least one agent. In some cases, the pharmaceutical composition can comprise about 1% to about 33% of the at least one agent.

[0067] Table 1: Some suitable sterically stabilized liposome carrier composition ranges useful in compositions claimed herein are shown below:

Carrier 1		
PC (mole %)	PG (mole %)	PEG-PE (mole %)
0-99.4	0-99.4	0.5-10
60-90	10-40	1-5
70-80	20-30	2-5

Carrier 2			
PC (mole %)	PG (mole %)	PEG-PE (mole %)	CHOL (mole %)
0-99.4	0-99.4	0.5-10	0.5-33
Preferred 60-90	10-40	1-5	0.5-20
70-80	20-30	2-5	0.5-10

Composition 1			
PC (mole %)	PG (mole %)	PEG-PE* (mole %)	therapeutic agents (mole %)
0-98.5	0-98.5	0.5-10	1-33
60-90	10-40	1-5	1-33
70-80	20-30	2-5	1-33

* The molecular weight of the PEG is limited to 350.

Composition 2				
PC (mole %)	PG (mole %)	PEG-PE* (mole %)	CHOL (mole %)	therapeutic agents (mole %)
0.1-99.4	0.1-99.4	0.5-10	0.1-33	1-33
60-90	10-40	1-5	0.1-20	1-33
70-80	20-30	2-5	0.1-10	1-33

* The molecular weight of the PEG is limited to 350.

[0068] A pharmaceutical composition described herein can comprise at least about 0.1% of any component of the composition, including the at least one agent, cholesterol, MPL, PEG (*e.g.*, PEG-DSPE), PG, and PC. For example, the pharmaceutical composition can comprise at least about 0.1%, at least about 0.2%, at least about 0.3%, at least about 0.4%, at least about 0.5%, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, at least about 99%, at least about 99.5%, or at

least about 99.5% of any component of the composition, including the at least one agent, cholesterol, MPL, PEG (*e.g.*, PEG-DSPE), PG, and PC.

[0069] A pharmaceutical composition described herein can comprise an effective amount of at least one agent which is a therapeutic agent, allergen, or pharmaceutical agent, and at least one of cholesterol, MPL, PEG (*e.g.*, PEG-DSPE), PG, or PC in an oral, subcutaneous or sublingual formulation. In some cases, the ratio of the at least one agent to cholesterol, MPL, PEG, PG, or PC is about 1:0.01, about 1:0.02, about 1:0.03, about 1:0.04, about 1:0.05, about 1:0.1, about 1:0.2, about 1:0.3, about 1:0.4, about 1:0.5, about 1:0.6, about 1:0.7, about 1:0.8, about 1:0.9, about 1:1, about 1:1.5, about 1:2, about 1:2.5, about 1:3, about 1:3.5, about 1:4, about 1:4.5, about 1:5, about 1:5.5, about 1:6, about 1:6.5, about 1:7, about 1:7.5, about 1:8, about 1:8.5, about 1:9, about 1:9.5, about 1:10, about 1:20, about 1:30, about 1:40, about 1:50, about 1:60, about 1:70, about 1:80, about 1:90, or about 1:100. In some cases, the ratio of cholesterol to the at least one agent, MPL, PEG, PG, or PC is about 1:0.01, about 1:0.02, about 1:0.03, about 1:0.04, about 1:0.05, about 1:0.1, about 1:0.2, about 1:0.3, about 1:0.4, about 1:0.5, about 1:0.6, about 1:0.7, about 1:0.8, about 1:0.9, about 1:1, about 1:1.5, about 1:2, about 1:2.5, about 1:3, about 1:3.5, about 1:4, about 1:4.5, about 1:5, about 1:5.5, about 1:6, about 1:6.5, about 1:7, about 1:7.5, about 1:8, about 1:8.5, about 1:9, about 1:9.5, about 1:10, about 1:20, about 1:30, about 1:40, about 1:50, about 1:60, about 1:70, about 1:80, about 1:90, or about 1:100. In some cases, the ratio of MPL to the at least one agent, cholesterol, PEG, PG, or PC is about 1:0.01, about 1:0.02, about 1:0.03, about 1:0.04, about 1:0.05, about 1:0.1, about 1:0.2, about 1:0.3, about 1:0.4, about 1:0.5, about 1:0.6, about 1:0.7, about 1:0.8, about 1:0.9, about 1:1, about 1:1.5, about 1:2, about 1:2.5, about 1:3, about 1:3.5, about 1:4, about 1:4.5, about 1:5, about 1:5.5, about 1:6, about 1:6.5, about 1:7, about 1:7.5, about 1:8, about 1:8.5, about 1:9, about 1:9.5, about 1:10, about 1:20, about 1:30, about 1:40, about 1:50, about 1:60, about 1:70, about 1:80, about 1:90, or about 1:100. In some cases, the ratio of PEG to the at least one agent, cholesterol, MPL, PG, or PC is about 1:0.01, about 1:0.02, about 1:0.03, about 1:0.04, about 1:0.05, about 1:0.1, about 1:0.2, about 1:0.3, about 1:0.4, about 1:0.5, about 1:0.6, about 1:0.7, about 1:0.8, about 1:0.9, about 1:1, about 1:1.5, about 1:2, about 1:2.5, about 1:3, about 1:3.5, about 1:4, about 1:4.5, about 1:5, about 1:5.5, about 1:6, about 1:6.5, about 1:7, about 1:7.5, about 1:8, about 1:8.5, about 1:9, about 1:9.5, about 1:10, about 1:20, about 1:30, about 1:40, about 1:50, about 1:60, about 1:70, about 1:80, about 1:90, or about 1:100. In some cases, the ratio of PG to the at least one agent, cholesterol, MPL, PEG, or PC is about 1:0.01, about 1:0.02, about 1:0.03, about 1:0.04, about 1:0.05, about 1:0.1, about 1:0.2, about 1:0.3, about 1:0.4, about 1:0.5, about 1:0.6, about 1:0.7, about 1:0.8, about 1:0.9, about 1:1, about 1:1.5, about 1:2, about 1:2.5, about 1:3, about 1:3.5, about 1:4, about 1:4.5, about 1:5, about 1:5.5, about 1:6, about 1:6.5, about 1:7,

about 1:7.5, about 1:8, about 1:8.5, about 1:9, about 1:9.5, about 1:10, about 1:20, about 1:30, about 1:40, about 1:50, about 1:60, about 1:70, about 1:80, about 1:90, or about 1:100. In some cases, the ratio of PC to the at least one agent, cholesterol, MPL, PEG, or PG is about 1:0.01, about 1:0.02, about 1:0.03, about 1:0.04, about 1:0.05, about 1:0.1, about 1:0.2, about 1:0.3, about 1:0.4, about 1:0.5, about 1:0.6, about 1:0.7, about 1:0.8, about 1:0.9, about 1:1, about 1:1.5, about 1:2, about 1:2.5, about 1:3, about 1:3.5, about 1:4, about 1:4.5, about 1:5, about 1:5.5, about 1:6, about 1:6.5, about 1:7, about 1:7.5, about 1:8, about 1:8.5, about 1:9, about 1:9.5, about 1:10, about 1:20, about 1:30, about 1:40, about 1:50, about 1:60, about 1:70, about 1:80, about 1:90, or about 1:100.

[0070] The poly(ethylene glycol)-lipid can be exchanged into biological milieu when shorter chains (*e.g.*, palmitoyl, dimyristoyl, didodecanoyl, didecanoyl or dioctanoyl) are used. In some cases, the sterically stabilized liposome carrier can be better partitioned into the mucosal lining of a target organ after sustained shedding or sustained exchanging its poly(ethylene glycol) moiety.

[0071] The sterically stabilized liposome carrier can comprise lipids conjugated to hydrophilic steric coating molecules safe for *in vivo* use. For example, the hydrophilic steric coating molecule can be lipid conjugated polyoxyethylene or lipid conjugated polysorbate.

[0072] The sterically stabilized liposome carrier can comprise dipalmitoylphosphatidylcholine (DPPC). In some cases, the sterically stabilized liposome carrier can comprise dipalmitoylphosphatidylglycol (DPPG). For example, the sterically stabilized liposome carrier can comprise DPPC, DPPG, and PEG-DSPE, wherein the ratio of DPPC:DPPG:PEG-DSPE is 80:15:5. In another example, the sterically stabilized liposome carrier can c comprise DPPC, DPPG, and PEG-DSPE, wherein the ratio of DPPC:DPPG:PEG-DSPE is 78:18:4.

Gel-liquid crystalline phase transition temperature

[0073] In compositions described herein, the sterically stabilized liposome carrier can have a gel-liquid crystalline phase transition temperature in a range from about -20°C to about 44°C. For example, the sterically stabilized liposome carrier can have a gel-liquid crystalline phase transition temperature in a range from about -20°C to about -10°C, from about -20°C to about 0°C, from about -20°C to about 10°C, from about -20°C to about 20°C, from about -20°C to about 30°C, from about -20°C to about 37°C, from about -20°C to about 40°C, from about -20°C to about 42°C, from about -20°C to about 44°C, from about -10°C to about 0°C, from about -10°C to about 10°C, from about -10°C to about 20°C, from about -10°C to about 30°C, from about -10°C to about 37°C, from about -10°C to about 40°C, from about -10°C to about 42°C, from about -10°C to about 44°C, from about 0°C to about 10°C, from about 0°C to about 20°C, from about 0°C to about 30°C, from about 0°C to about 37°C, from about 0°C to about 40°C,

from about 0°C to about 42°C, from about 0°C to about 44°C, from about 10°C to about 20°C, from about 10°C to about 30°C, from about 10°C to about 37°C, from about 10°C to about 40°C, from about 10°C to about 42°C, from about 10°C to about 44°C, from about 20°C to about 30°C, from about 20°C to about 37°C, from about 20°C to about 40°C, from about 20°C to about 42°C, from about 20°C to about 44°C, from about 30°C to about 37°C, from about 30°C to about 40°C, from about 30°C to about 42°C, from about 30°C to about 44°C, from about 37°C to about 40°C, from about 37°C to about 42°C, from about 37°C to about 44°C, from about 40°C to about 42°C, from about 40°C to about 44°C, or from about 42°C to about 44°C. In some cases, the sterically stabilized liposome carrier can have a gel-liquid crystalline phase transition temperature in a range from about -10°C to about 42°C. In some cases, the composition is substantially devoid of cholesterol. In some cases, the composition comprises an amount of cholesterol, wherein the amount of cholesterol is sufficient for the transition range of the sterically stabilized liposome carrier containing cholesterol to be broadened compared to that of sterically stabilized liposome carriers substantially devoid of cholesterol. In some cases, are provided stabilized liposome carriers with sufficient cholesterol to enable a relatively high transition temperature (*e.g.*, in the gel phase at 37° C.) to have a substantial portion of the membrane in the fluid or liquid crystalline phase at body temperature.

[0074] The sterically stabilized liposome carrier can have a gel-liquid crystalline phase transition temperature of at least about -20°C. For example, the sterically stabilized liposome carrier can have a gel-liquid crystalline phase transition temperature of at least about -20°C, at least about -10°C, at least about 0°C, at least about 10°C, at least about 20°C, at least about 30°C, at least about 37°C, at least about 40°C, at least about 42°C, or at least about 44°C.

Vesicle sizes

[0075] In certain embodiments, pharmaceutical compositions for oral, subcutaneous or sublingual administration as described herein, can comprise vesicles (*e.g.*, unilamellar or multilamellar) having an average diameter of about 0.01 to about 50 microns. For example, the pharmaceutical composition can comprise vesicles (*e.g.*, unilamellar or multilamellar) having an average diameter of about 0.01 to about 0.02 microns, about 0.01 to about 0.05 microns, about 0.01 to about 0.1 microns, about 0.01 to about 0.5 microns, about 0.01 to about 1 microns, about 0.01 to about 1.5 microns, about 0.01 to about 2 microns, about 0.01 to about 2.5 microns, about 0.01 to about 3 microns, about 0.01 to about 4 microns, about 0.01 to about 5 microns, about 0.01 to about 10 microns, about 0.01 to about 20 microns, about 0.01 to about 30 microns, about 0.01 to about 40 microns, about 0.01 to about 50 microns, about 0.02 to about 0.05 microns, about

0.02 to about 0.1 microns, about 0.02 to about 0.5 microns, about 0.02 to about 1 microns, about 0.02 to about 1.5 microns, about 0.02 to about 2 microns, about 0.02 to about 2.5 microns, about 0.02 to about 3 microns, about 0.02 to about 4 microns, about 0.02 to about 5 microns, about 0.02 to about 10 microns, about 0.02 to about 20 microns, about 0.02 to about 30 microns, about 0.02 to about 40 microns, about 0.02 to about 50 microns, about 0.05 to about 0.1 microns, about 0.05 to about 0.5 microns, about 0.05 to about 1 microns, about 0.05 to about 1.5 microns, about 0.05 to about 2 microns, about 0.05 to about 2.5 microns, about 0.05 to about 3 microns, about 0.05 to about 4 microns, about 0.05 to about 5 microns, about 0.05 to about 10 microns, about 0.05 to about 20 microns, about 0.05 to about 30 microns, about 0.05 to about 40 microns, about 0.05 to about 50 microns, about 0.1 to about 0.5 microns, about 0.1 to about 1 microns, about 0.1 to about 1.5 microns, about 0.1 to about 2 microns, about 0.1 to about 2.5 microns, about 0.1 to about 3 microns, about 0.1 to about 4 microns, about 0.1 to about 5 microns, about 0.1 to about 10 microns, about 0.1 to about 20 microns, about 0.1 to about 30 microns, about 0.1 to about 40 microns, about 0.1 to about 50 microns, about 0.5 to about 1 microns, about 0.5 to about 1.5 microns, about 0.5 to about 2 microns, about 0.5 to about 2.5 microns, about 0.5 to about 3 microns, about 0.5 to about 4 microns, about 0.5 to about 5 microns, about 0.5 to about 10 microns, about 0.5 to about 20 microns, about 0.5 to about 30 microns, about 0.5 to about 40 microns, about 0.5 to about 50 microns, about 1 to about 1.5 microns, about 1 to about 2 microns, about 1 to about 2.5 microns, about 1 to about 3 microns, about 1 to about 4 microns, about 1 to about 5 microns, about 1 to about 10 microns, about 1 to about 20 microns, about 1 to about 30 microns, about 1 to about 40 microns, about 1 to about 50 microns, about 1.5 to about 2 microns, about 1.5 to about 2.5 microns, about 1.5 to about 3 microns, about 1.5 to about 4 microns, about 1.5 to about 5 microns, about 1.5 to about 10 microns, about 1.5 to about 20 microns, about 1.5 to about 30 microns, about 1.5 to about 40 microns, about 1.5 to about 50 microns, about 2 to about 2.5 microns, about 2 to about 3 microns, about 2 to about 4 microns, about 2 to about 5 microns, about 2 to about 10 microns, about 2 to about 20 microns, about 2 to about 30 microns, about 2 to about 40 microns, about 2 to about 50 microns, about 2.5 to about 3 microns, about 2.5 to about 4 microns, about 2.5 to about 5 microns, about 2.5 to about 10 microns, about 2.5 to about 20 microns, about 2.5 to about 30 microns, about 2.5 to about 40 microns, about 2.5 to about 50 microns, about 3 to about 4 microns, about 3 to about 5 microns, about 3 to about 10 microns, about 3 to about 20 microns, about 3 to about 30 microns, about 3 to about 40 microns, about 3 to about 50 microns, about 4 to about 5 microns, about 4 to about 10 microns, about 4 to about 20 microns, about 4 to about 30 microns, about 4 to about 40 microns, about 4 to about 50 microns, about 5 to about 10 microns, about 5 to about 20 microns, about 5 to about 30 microns, about 5 to about 40 microns, about 5 to about 50 microns, about 10 to about 20 microns, about 10 to about

30 microns, about 10 to about 40 microns, about 10 to about 50 microns, about 20 to about 30 microns, about 20 to about 40 microns, about 20 to about 50 microns, about 30 to about 40 microns, about 30 to about 50 microns, or about 40 to about 50 microns. In some cases, the pharmaceutical composition can comprise vesicles (*e.g.*, unilamellar or multilamellar) having an average diameter of about 0.02 to about 2.5 microns. In some cases, the pharmaceutical composition can comprise vesicles (*e.g.*, unilamellar or multilamellar) having an average diameter of about 0.05 to about 5 microns. In some cases, the desired sizes of vesicles can be obtained from extrusion of the pharmaceutical composition through polycarbonate membranes having pores of selected sizes, *e.g.* from about 0.05 to about 5 microns.

[0076] In certain embodiments, pharmaceutical compositions for oral, subcutaneous or sublingual administration as described herein can comprise vesicles (*e.g.*, unilamellar or multilamellar) having an average diameter of at least about 0.01 microns. For example, the pharmaceutical composition can comprise vesicles (*e.g.*, unilamellar or multilamellar) having an average diameter of at least about 0.01 microns, at least about 0.02 microns, at least about 0.05 microns, at least about 0.1 microns, at least about 0.5 microns, at least about 1 microns, at least about 1.5 microns, at least about 2 microns, at least about 2.5 microns, at least about 3 microns, at least about 4 microns, at least about 5 microns, at least about 10 microns, at least about 20 microns, at least about 30 microns, at least about 40 microns, or at least about 50 microns.

Antibodies

[0077] In certain embodiments, pharmaceutical compositions for oral, subcutaneous or sublingual administration as described herein can comprise at least one agent, wherein the at least one agent comprises an antibody, derivative or fragment thereof. In some cases, the antibody is an anti-IgE antibody, derivative or fragment thereof. In some embodiments, the anti-IgE antibody can be, for example, recombinant, fully human, humanized, camelid, diabody or a chimeric antibody.

[0078] In some embodiments is provided a pharmaceutical composition for oral, subcutaneous or sublingual administration as described herein, comprising an antibody and sterically stabilized liposome carrier described herein, wherein the antibody can be an antibody against a molecule or target recognized to have a role in modulating an allergic response to food in a subject, *e.g.*, in a human. In some embodiments, the pharmaceutical composition can be orally co-administered or sequentially administered with an allergen. In some embodiments, an allergen can be included in the pharmaceutical composition. For example, an anti-IgE antibody can be loaded into a sterically stabilized liposome carrier described herein along with a peanut derivative or peanut extract such as peanut protein, peanut powder or peanut butter for administration as part of an

allergy treatment. The administration can be subcutaneous, sublingual, or oral, and in some embodiments provided about once a week. The pharmaceutical composition can also be substantially devoid of an antibody.

Locations of agents and/or allergens in sterically stabilized liposome carriers

[0079] As shown in **FIG. 1**, liposomes can have at least a membrane portion and an interior portion. A sterically stabilized liposome carrier includes an anti-IgE antibody (**105**) located in a membrane of the sterically stabilized liposome carrier and an allergen (**110**) located in a hydrophilic core (interior portion) of the sterically stabilized liposome.

[0080] The interior portion can be largely aqueous, having a different environment from the phospholipid bilayer of the membrane portion. Further, in some liposomes, multilamellar liposomes (not shown), there can be multiple membranes per liposome with interior portions between the membranes.

[0081] In some cases, one or more agent can be loaded into separate portions of the liposomes. For example, MPL can be loaded into (*e.g.*, embedded in) the membrane portion, while the therapeutic agent or allergen is located in the interior portion. In another example, the therapeutic agent can be loaded in both the interior and membrane portions of the liposome. A wide variety of combinations are possible, according to the thermodynamics and kinetics of the partitioning of various agents between the interior (aqueous) and membrane (hydrophobic/amphipathic) portions of the liposome, as well as on the manner of formation of liposome and loading of the therapeutic agent. In some cases, MPL is loaded into the membrane. In some cases, an anti-IgE antibody or fragment or derivative thereof is loaded into the membrane portion of the liposome, while an allergen or derivative thereof (*e.g.*, peanut protein, peanut powder, peanut butter) is loaded into the interior portion of the liposome. In some cases, anti-IgE antibody or fragment or derivative thereof is placed (at least in part) in the interior of the liposome, permitting a controlled release of the antibody from the liposome. In some cases, a drug or therapeutic or pharmaceutical agent (*e.g.*, steroid) is added to the liposome, in addition to the protein (*e.g.*, peanut protein). Compositions comprising the sterically stabilized liposome carrier described herein can then be administered subcutaneously, sublingually, or orally to a subject in need of thereof.

[0082] In some cases, one or more pharmaceutical or therapeutic agent is not loaded exclusively into a single liposome compartment, but rather can be predominately loaded into the compartment, *e.g.*, more than about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, or 99% of the one or more agent is loaded into a specified portion (interior or membrane) of the liposome.

[0083] A sterically stabilized liposome carrier described herein can comprise a population of individual liposomes, such that the carrier can be said to have an interior portion (meaning, for example, the collective interior portions of the constituent liposomes) and a membrane portion (meaning, for example, the collective membrane portions of the constituent liposomes).

[0084] The pharmaceutical composition can comprise at least one agent, wherein said agent is at least one of a therapeutic agent and an allergen, wherein about 1% to about 99% of the at least one agent is in a membrane or internal portion of the liposome carrier. For example, about 1% to about 2%, about 1% to about 3%, about 1% to about 4%, about 1% to about 5%, about 1% to about 10%, about 1% to about 15%, about 1% to about 20%, about 1% to about 25%, about 1% to about 30%, about 1% to about 40%, about 1% to about 50%, about 1% to about 60%, about 1% to about 70%, about 1% to about 80%, about 1% to about 90%, about 1% to about 95%, about 1% to about 98%, about 1% to about 99%, about 2% to about 3%, about 2% to about 4%, about 2% to about 5%, about 2% to about 10%, about 2% to about 15%, about 2% to about 20%, about 2% to about 25%, about 2% to about 30%, about 2% to about 40%, about 2% to about 50%, about 2% to about 60%, about 2% to about 70%, about 2% to about 80%, about 2% to about 90%, about 2% to about 95%, about 2% to about 98%, about 2% to about 99%, about 3% to about 4%, about 3% to about 5%, about 3% to about 10%, about 3% to about 15%, about 3% to about 20%, about 3% to about 25%, about 3% to about 30%, about 3% to about 40%, about 3% to about 50%, about 3% to about 60%, about 3% to about 70%, about 3% to about 80%, about 3% to about 90%, about 3% to about 95%, about 3% to about 98%, about 3% to about 99%, about 4% to about 5%, about 4% to about 10%, about 4% to about 15%, about 4% to about 20%, about 4% to about 25%, about 4% to about 30%, about 4% to about 40%, about 4% to about 50%, about 4% to about 60%, about 4% to about 70%, about 4% to about 80%, about 4% to about 90%, about 4% to about 95%, about 4% to about 98%, about 4% to about 99%, about 5% to about 10%, about 5% to about 15%, about 5% to about 20%, about 5% to about 25%, about 5% to about 30%, about 5% to about 40%, about 5% to about 50%, about 5% to about 60%, about 5% to about 70%, about 5% to about 80%, about 5% to about 90%, about 5% to about 95%, about 5% to about 98%, about 5% to about 99%, about 10% to about 15%, about 10% to about 20%, about 10% to about 25%, about 10% to about 30%, about 10% to about 40%, about 10% to about 50%, about 10% to about 60%, about 10% to about 70%, about 10% to about 80%, about 10% to about 90%, about 10% to about 95%, about 10% to about 98%, about 10% to about 99%, about 15% to about 20%, about 15% to about 25%, about 15% to about 30%, about 15% to about 40%, about 15% to about 50%, about 15% to about 60%, about 15% to about 70%, about 15% to about 80%, about 15% to about 90%, about 15% to about 95%, about 15% to about 98%, about 15% to about 99%, about 20% to about 25%, about 20% to about 30%, about 20% to

about 40%, about 20% to about 50%, about 20% to about 60%, about 20% to about 70%, about 20% to about 80%, about 20% to about 90%, about 20% to about 95%, about 20% to about 98%, about 20% to about 99%, about 25% to about 30%, about 25% to about 40%, about 25% to about 50%, about 25% to about 60%, about 25% to about 70%, about 25% to about 80%, about 25% to about 90%, about 25% to about 95%, about 25% to about 98%, about 25% to about 99%, about 30% to about 40%, about 30% to about 50%, about 30% to about 60%, about 30% to about 70%, about 30% to about 80%, about 30% to about 90%, about 30% to about 95%, about 30% to about 98%, about 30% to about 99%, about 40% to about 50%, about 40% to about 60%, about 40% to about 70%, about 40% to about 80%, about 40% to about 90%, about 40% to about 95%, about 40% to about 98%, about 40% to about 99%, about 50% to about 60%, about 50% to about 70%, about 50% to about 80%, about 50% to about 90%, about 50% to about 95%, about 50% to about 98%, about 50% to about 99%, about 60% to about 60%, about 60% to about 70%, about 60% to about 80%, about 60% to about 90%, about 60% to about 95%, about 60% to about 98%, about 60% to about 99%, about 70% to about 80%, about 70% to about 90%, about 70% to about 95%, about 70% to about 98%, about 70% to about 99%, about 80% to about 90%, about 80% to about 95%, about 80% to about 98%, about 80% to about 99%, about 90% to about 95%, about 90% to about 98%, about 90% to about 99%, about 95% to about 98%, about 95% to about 99%, or about 98% to about 99% of the at least one agent is in a membrane or internal portion of the liposome carrier.

[0085] The pharmaceutical composition can comprise at least one agent, wherein at least about 1% of the at least one agent is in a membrane or internal portion of the liposome carrier. For example, at least about 1%, at least about 2%, at least about 3%, at least about 4%, at least about 5%, at least about 6%, at least about 7%, at least about 8%, at least about 9%, at least about 10%, at least about 15%, at least about 20%, at least about 25%, at least about 30%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 55%, at least about 60%, at least about 65%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95%, at least about 98%, or at least about 99% of the at least one agent is in a membrane or internal portion of the liposome carrier.

Controlled Release of agents from liposomes by tuning pH-stability

[0086] The release of the one or more agents from the sterically stabilized liposome carrier can be controlled by tuning pH-stability to adjust to various body compartments with different pH profiles. Therefore, the sterically stabilized liposome carrier can be stable in one pH range and not in another. For example, the sterically stabilized liposome carrier can be selected to be stable in the stomach but not in the small intestine, or vice versa, thereby. For example, the sterically

stabilized liposome carrier can be tuned to be stable above about pH 3, 4, 5, 6, 7, 8, 9, and 10; or below about pH 10, 9, 8, 7, 6, 5, 4, or 3. In some cases, two populations of sterically stabilized liposome carriers can be used: a first population of sterically stabilized liposome carrier is stable in acid and passes through the stomach with contents inside, but which is not stable in the small intestine, where its liposomal contents are released; a second population is not stable in the stomach and releases its contents there. In this manner, the pharmaceutical composition described herein can be used to control the release of multiple agents in different body compartments. In some cases, the pharmaceutical composition and/or the sterically stabilized liposome carrier can comprise cholesteryl hemisuccinate. In some cases, the pharmaceutical composition and/or the sterically stabilized liposome carrier can be substantially devoid of cholesteryl hemisuccinate.

[0087] A pH sensitive component of the pharmaceutical composition and/or the sterically stabilized liposome carrier can comprise a phospholipid, an acylated amino acid, a fatty acid, a cholesterol or cholesterol derivative, a double chain amphiphile, or any combination thereof. For example, the pH sensitive component can be N-palmitoyl homocysteine (PHC).

[0088] The pharmaceutical composition and/or the sterically stabilized liposome carrier can be stable or can release its content at about pH 1 to about pH 14. For example, the pharmaceutical composition and/or the sterically stabilized liposome carrier can be stable at about pH 1 to about pH 2, about pH 1 to about pH 3, about pH 1 to about pH 4, about pH 1 to about pH 5, about pH 1 to about pH 6, about pH 1 to about pH 7, about pH 1 to about pH 8, about pH 1 to about pH 9, about pH 1 to about pH 10, about pH 1 to about pH 11, about pH 1 to about pH 12, about pH 1 to about pH 13, about pH 1 to about pH 14, about pH 2 to about pH 3, about pH 2 to about pH 4, about pH 2 to about pH 5, about pH 2 to about pH 6, about pH 2 to about pH 7, about pH 2 to about pH 8, about pH 2 to about pH 9, about pH 2 to about pH 10, about pH 2 to about pH 11, about pH 2 to about pH 12, about pH 2 to about pH 13, about pH 2 to about pH 14, about pH 3 to about pH 4, about pH 3 to about pH 5, about pH 3 to about pH 6, about pH 3 to about pH 7, about pH 3 to about pH 8, about pH 3 to about pH 9, about pH 3 to about pH 10, about pH 3 to about pH 11, about pH 3 to about pH 12, about pH 3 to about pH 13, about pH 3 to about pH 14, about pH 4 to about pH 5, about pH 4 to about pH 6, about pH 4 to about pH 7, about pH 4 to about pH 8, about pH 4 to about pH 9, about pH 4 to about pH 10, about pH 4 to about pH 11, about pH 4 to about pH 12, about pH 4 to about pH 13, about pH 4 to about pH 14, about pH 5 to about pH 6, about pH 5 to about pH 7, about pH 5 to about pH 8, about pH 5 to about pH 9, about pH 5 to about pH 10, about pH 5 to about pH 11, about pH 5 to about pH 12, about pH 5 to about pH 13, about pH 5 to about pH 14, about pH 6 to about pH 7, about pH 6 to about pH 8, about pH 6 to about pH 9, about pH 6 to about pH 10, about pH 6 to about pH 11, about pH 6 to

about pH 12, about pH 6 to about pH 13, about pH 6 to about pH 14, about pH 7 to about pH 8, about pH 7 to about pH 9, about pH 7 to about pH 10, about pH 7 to about pH 11, about pH 7 to about pH 12, about pH 7 to about pH 13, about pH 7 to about pH 14, about pH 8 to about pH 9, about pH 8 to about pH 10, about pH 8 to about pH 11, about pH 8 to about pH 12, about pH 8 to about pH 13, about pH 8 to about pH 14, about pH 9 to about pH 10, about pH 9 to about pH 11, about pH 9 to about pH 12, about pH 9 to about pH 13, about pH 9 to about pH 14, about pH 10 to about pH 11, about pH 10 to about pH 12, about pH 10 to about pH 13, about pH 10 to about pH 14, about pH 11 to about pH 12, about pH 11 to about pH 13, about pH 11 to about pH 14, about pH 12 to about pH 13, about pH 12 to about pH 14, or about pH 13 to about pH 14. In some cases, the at least one agent can be released from the liposome carrier in a pH sensitive manner, for example, the at least one agent can be released from the liposome carrier in one of the above pH ranges. In some cases, the at least one agent can be released from the liposome carrier in a pH independent manner.

[0089] The pharmaceutical composition and/or the sterically stabilized liposome carrier can remain stable in the presence of serum and/or in the extra-cellular environment. In some cases, the stability of the sterically stabilized liposome carrier in combination with the encapsulated therapeutic agent is more pronounced than currently available drug therapies. In some cases, the stability of the sterically stabilized liposome carrier can allow a therapeutic agent, such as a corticosteroid, to be administered only once every one to two weeks. The dosage used in these treatments is typically the same or similar to that used on a daily basis. The therapeutic agent may thus be administered at two, three, four, five, six or seven days or longer intervals. In some instances, the effective life may be up to two weeks or longer. The term "effective life" as used herein means a period during which the therapeutic agent effect is continued.

Multiple populations of liposomes

[0090] In some embodiments, more than one population of liposome (*e.g.*, differing in one or more characteristics, such as agents contained, phospholipid composition, presence absence of anti-IgE antibody, cholesterol, or steroid) are administered to a subject in need thereof.

Formulations

[0091] The pharmaceutical compositions can be formulated as a formulation for oral, subcutaneous, sublingual or buccal administration. The formulation can comprise nontoxic therapeutically acceptable carriers, adjuvants, and/or vehicles as desired. The formulation can be in dosage unit as desired.

[0092] Formulation of therapeutic agents is discussed in, for example, Hoover, John E., Remington's Pharmaceutical Sciences, Mack Publishing Co., Easton, Pa. (1975), and Liberman, H. A. and Lachman, L., Eds., Pharmaceutical Dosage Forms, Marcel Decker, New York, N.Y. (1980).

[0093] The pharmaceutical compositions may be administered *per se* or in the form of a formulation wherein the active compound(s) is in admixture or mixture with one or more therapeutically acceptable carriers, excipients or diluents. Pharmaceutical compositions may be formulated in conventional manner using one or more therapeutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used therapeutically. Proper formulation is dependent upon the route of administration chosen.

[0094] Compositions described herein can be provided as lyophiles. A lyophilized formulation described here in can be further formulated for oral delivery for instance, in tablet or capsule form. Lyophile compositions described herein can be deposited on a filter paper for oral delivery to a subject. Specific lyophile compositions described herein can comprise additional excipients or stabilizers which in some cases can be useful to stabilize the liposomes in lyophilized form. In some embodiments, lyophile compositions described herein can comprise a sugar, in some cases in an amount sufficient to stabilize the liposomes in lyophilized form. In some embodiments, the sugar can selected from the group consisting of trehalose, glucose, sucrose, maltose, galactose, fructose, and arabinose. In specific embodiments are provided compositions described herein, further comprising an amount of trehalose.

[0095] In some cases, lyophile composition described herein can be stable for a period of up to about 3 months. In some cases, lyophile compositions described herein can be stable for a period of up to about 6 months, about 9 months, about 1 year, about 1.5 years, about 2 years, about 2.5 years, about 3 years, about 3.5 years, about 4 years, about 4.5 years or about 5 years. In some cases, after about 6 months, the lyophile composition retains about 100% efficacy. In some cases, after 6 months, the lyophile composition retains about 99%, 97%, 95%, 90%, 85%, 80%, 75% or 70% efficacy.

[0096] In some cases, a lyophile compositions described herein is reconstituted prior to administration. In some cases, the administration is oral, subcutaneous or sublingual. In some cases, the administration is intranasal. In some cases, the composition is reconstituted with an appropriate diluent. In some embodiments, the diluent comprises a solvent or co-solvent selected from tert-butyl alcohol, n-butanol, ethanol, iso-propyl alcohol, dimethyl sulfone, chlorobutanol, Sterile Water for Injection, 0.9% sodium chloride solution, 5% dextrose solution, or mixtures thereof. In some cases, the composition is reconstituted with an aqueous diluent. In some

embodiments, the aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

[0097] Examples of suitable coating materials include, but are not limited to, cellulose polymers such as cellulose acetate phthalate, hydroxypropyl cellulose, hydroxypropyl methylcellulose, hydroxypropyl methylcellulose phthalate and hydroxypropyl methylcellulose acetate succinate; polyvinyl acetate phthalate, acrylic acid polymers and copolymers, and methacrylic resins that are commercially available under the trade name Eudragit® (Roth Pharma, Westerstadt, Germany), zein, shellac, and polysaccharides.

[0098] Additionally, the coating material may contain conventional carriers such as plasticizers, pigments, colorants, glidants, stabilization agents, pore formers and surfactants.

[0099] Therapeutically acceptable excipients present in the drug-containing tablets, beads, granules or particles include, but are not limited to, diluents, binders, lubricants, disintegrants, colorants, stabilizers, and surfactants. Diluents, also referred to as "fillers," are typically necessary to increase the bulk of a solid dosage form so that a practical size is provided for compression of tablets or formation of beads and granules. Suitable diluents include, but are not limited to, dicalcium phosphate dihydrate, calcium sulfate, lactose, sucrose, mannitol, sorbitol, cellulose, microcrystalline cellulose, kaolin, sodium chloride, dry starch, hydrolyzed starches, pregelatinized starch, silicon dioxide, titanium oxide, magnesium aluminum silicate and powdered sugar.

[00100] Binders are used to impart cohesive qualities to a solid dosage formulation, and thus ensure that a tablet or bead or granule remains intact after the formation of the dosage forms. Suitable binder materials include, but are not limited to, starch, pregelatinized starch, gelatin, sugars (including sucrose, glucose, dextrose, lactose and sorbitol), polyethylene glycol, waxes, natural and synthetic gums such as acacia, tragacanth, sodium alginate, cellulose, including hydroxypropylmethylcellulose, hydroxypropylcellulose, ethylcellulose, and veegum, and synthetic polymers such as acrylic acid and methacrylic acid copolymers, methacrylic acid copolymers, methyl methacrylate copolymers, aminoalkyl methacrylate copolymers, polyacrylic acid/polymethacrylic acid and polyvinylpyrrolidone.

[00101] Lubricants are used to facilitate tablet manufacture. Examples of suitable lubricants include, but are not limited to, magnesium stearate, calcium stearate, stearic acid, glycerol behenate, polyethylene glycol, talc, and mineral oil.

[00102] Disintegrants are used to facilitate dosage form disintegration or "breakup" after administration, and generally include, but are not limited to, starch, sodium starch glycolate, sodium carboxymethyl starch, sodium carboxymethylcellulose, hydroxypropyl cellulose,

pregelatinized starch, clays, cellulose, alginine, gums or cross linked polymers, such as cross-linked PVP (Polyplasdone XL from GAF Chemical Corp).

[00103] Stabilizers are used to inhibit or retard drug decomposition reactions which include, by way of example, oxidative reactions.

[00104] Surfactants may be anionic, cationic, amphoteric or nonionic surface active agents. Suitable anionic surfactants include, but are not limited to, those containing carboxylate, sulfonate and sulfate ions. Examples of anionic surfactants include sodium, potassium, ammonium of long chain alkyl sulfonates and alkyl aryl sulfonates such as sodium dodecylbenzene sulfonate; dialkyl sodium sulfosuccinates, such as sodium dodecylbenzene sulfonate; dialkyl sodium sulfosuccinates, such as sodium bis-(2-ethylthioxyl)-sulfosuccinate; and alkyl sulfates such as sodium lauryl sulfate. Cationic surfactants include, but are not limited to, quaternary ammonium compounds such as benzalkonium chloride, benzethonium chloride, cetrimonium bromide, stearyl dimethylbenzyl ammonium chloride, polyoxyethylene and coconut amine. Examples of nonionic surfactants include ethylene glycol monostearate, propylene glycol myristate, glyceryl monostearate, glyceryl stearate, polyglyceryl-4-oleate, sorbitan acylate, sucrose acylate, PEG-150 laurate, PEG-400 monolaurate, polyoxyethylene monolaurate, polysorbates, polyoxyethylene octylphenylether, PEG-1000 cetyl ether, polyoxyethylene tridecyl ether, polypropylene glycol butyl ether, Poloxamer® 401, stearoyl monoisopropanolamide, and polyoxyethylene hydrogenated tallow amide. Examples of amphoteric surfactants include sodium N-dodecyl-β-alanine, sodium N-lauryl-β-iminodipropionate, myristoamphoacetate, lauryl betaine and lauryl sulfobetaine.

[00105] If desired, the tablets, beads, granules, or particles may also contain minor amount of nontoxic auxiliary substances such as wetting or emulsifying agents, dyes, pH buffering agents, or preservatives.

[00106] The compounds may be complexed with other agents as part of their being therapeutically formulated. The pharmaceutical compositions may take the form of, for example, tablets or capsules prepared by conventional means with therapeutically acceptable excipients such as binding agents (*e.g.*, acacia, methylcellulose, sodium carboxymethylcellulose, polyvinylpyrrolidone (Povidone), hydroxypropyl methylcellulose, sucrose, starch, and ethylcellulose); fillers (*e.g.*, corn starch, gelatin, lactose, acacia, sucrose, microcrystalline cellulose, kaolin, mannitol, dicalcium phosphate, calcium carbonate, sodium chloride, or alginic acid); lubricants (*e.g.* magnesium stearates, stearic acid, silicone fluid, talc, waxes, oils, and colloidal silica); and disintegrators (*e.g.* micro-crystalline cellulose, corn starch, sodium starch glycolate and alginic acid. If water-soluble, such formulated complex then may be formulated in an appropriate buffer, for example, phosphate buffered saline or other physiologically compatible

solutions. Alternatively, if the resulting complex has poor solubility in aqueous solvents, then it may be formulated with a non-ionic surfactant such as TWEEN™, or polyethylene glycol. Thus, the compounds and their physiologically acceptable solvates may be formulated for administration.

[00107] Liquid formulations (*e.g.* for oral administration) prepared in water or other aqueous vehicles may contain various suspending agents such as methylcellulose, alginates, tragacanth, pectin, kelgin, carrageenan, acacia, polyvinylpyrrolidone, and polyvinyl alcohol. The liquid formulations may also include solutions, emulsions, syrups and elixirs containing, together with the active compound(s), wetting agents, sweeteners, and coloring and flavoring agents. Various liquid and powder formulations can be prepared by conventional methods for inhalation by the patient.

[00108] Delayed release and extended release compositions (*e.g.*, for buccal administration) can be prepared. The delayed release/extended release pharmaceutical compositions can be obtained by complexing therapeutic agent with a therapeutically acceptable ion-exchange resin and coating such complexes. The formulations are coated with a substance that will act as a barrier to control the diffusion of the therapeutic agent from its core complex into the gastrointestinal fluids. Optionally, the formulation is coated with a film of a polymer which is insoluble in the acid environment of the stomach, and soluble in the basic environment of lower GI tract in order to obtain a final dosage form that releases less than 10% of the therapeutic agent dose within the stomach.

[00109] In addition, combinations of immediate release compositions and delayed release/extended release compositions may be formulated together.

Lyophilization Methods

[00110] Lyophilization is the technical name for a process often referred to as "freeze-drying." In this process, an aqueous mixture or suspension is frozen into a solid, then it is generally subjected to a vacuum for a substantial period of time. The vacuum causes the water molecules to sublimate.

[00111] The methods described herein include the step of lyophilizing the composition comprising a sterically stabilized liposome carrier as described herein . In one embodiment, lyophilization occurs after sterilization. In one embodiment, during the lyophilization process, the solvent system used, such as by way of example only, tert-butyl alcohol and Sterile Water for Injection is substantially removed by sublimation. In another embodiment, less than about 5% residual solvent remains after lyophilization; in other embodiments, less than about 3% remains;

in yet other embodiments, less than about 2% remains; in further embodiments, less than about 1% or about 0.1% remains.

[00112] In one embodiment, the lyophilization process comprises the steps of (1) placing the sample to be lyophilized (composition comprising sterically stabilized liposome carrier and optionally an active agent) in a suitable vial and placing the vial into a lyophilization chamber and lowering the shelf temperature to about −30° C. to about −50° C. at atmospheric pressure; (2) holding the shelf temperature at the temperature range described above until the temperature of the sample is about −30° C. to about −50° C.; (3) raising the temperature to about −10° C. to about −20° C. to anneal the lyophile for about 1 to 2 hours; (4) lowering the shelf temperature to about −30° C. to about −50° C. and reducing the pressure of the system to about 50 mTorr to about 100 mTorr; and holding until sublimation of the solvent system is substantially complete. The temperature of the product should be below about −25° C. to about −28° C. to avoid cake collapse; (5) increasing the temperature to about 30° C. to about 50° C.; and (6) allowing the samples to reach a temperature of about 20° C. to about 30° C. for an amount of time to remove bound water or solvent levels; (7) back-filling vials with nitrogen or appropriate gas after which the vials are aseptically sealed. Table 7 describes, in one embodiment, the lyophilization cycle for lyophilizing a bulk solution comprising fluticasone or salmeterol or their pharmaceutically acceptable salts or a combination thereof. In one embodiment, the process requires a step-wise lowering or increasing of the temperature of the system, such as, at a rate of 0.5° C. per minute up to about 1° C. per minute to ensure proper and substantially complete sublimation. The lyophilization step provides a composition comprising sterically stabilized liposome carrier and optionally an active agent, such as for example, an allergen or a steroid or a combination thereof, that can be stored at room temperature for extended periods of time. Additionally, the lyophilized compositions (also referred to as lyophiles) described herein are stable for a period of at least 4 weeks at a temperature of about 0° C. to about 50° C. In some embodiments, the lyophilized compositions are stable from at least about 3 months to at least about 5 years at a temperature of about 0° C. to about 50° C. In certain embodiments, the lyophilized compositions are stable for a period of at least about 4 months to at least about 4 years at a temperature of about 0° C. to about 50° C. In still further or additional embodiments, the lyophilized compositions are stable for a period of at least about 6 months to at least about 2 years at a temperature of about 0° C. to about 50° C. In some embodiments, the lyophilized compositions are stable for at least about 3 months, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, or at least about 5 years at a temperature of about 0° C. to about 50° C. In other embodiments, the lyophiles described herein are in the form of a cake or free flowing powder. In other embodiment, the lyophilized composition is a cake.

Reconstitution

[00113] In some embodiments, the lyophiles described herein readily reconstitute once contacted with a sufficient amount of a pharmaceutically acceptable carrier or diluent. For example, in some embodiments, the lyophile is mixed in the vial it is contained in, e.g., shaken for about 1 to about 3 minutes, with a pharmaceutically acceptable carrier, such as, Sterile Water for Injection, 0.9% sodium chloride solution, or 5% dextrose solution to provide a reconstituted composition suitable for subcutaneous injection. In one embodiment, the lyophile is reconstituted in a relatively short period of time, such as for example, less than 1 minute, less than 30 seconds, and in other embodiments, about 20 seconds. In certain embodiments, the lyophiles reconstitute in a time of less than 2, 3, 4, or 5 minutes. These short reconstitution times provide an advantage in that the therapeutic agent has not decomposed from exposure in a solution for an extended period of time prior to administration. In one embodiment, the reconstituted composition is suitable for subcutaneous administration, such as for example, subcutaneous injection. In another embodiment, the reconstituted form is a non-suspension. In a further embodiment, the reconstituted form is a clear solution and remains substantially clear prior to administration.

[00114] A feature of the subject matter described herein is a lyophilized composition is formulated with a minimal amount of trehalose, that is manufactured as a lyophile, and that is amenable to full reconstitution with a carrier or diluents in a short period of time.

Route of administration

[00115] Compositions described herein can be administered orally, sublingually, buccally, subcutaneously, intramuscularly, rectally, intradermally, transdermally, by inhalation, or topically. In some cases, the compositions can be administered via subcutaneous injection, or infusion techniques. In some cases, the pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration, but not inhalation or pulmonary delivery. In some cases, the composition is administered orally. In some cases, the composition is administered subcutaneously. In some cases, the composition is administered sublingually. In some cases, the composition is administered buccally.

Schedule of administration

[00116] Provided are pharmaceutical compositions suitable for sustained slow release of an active agent upon oral, sublingual or subcutaneous administration to a subject. The pharmaceutical composition and/or sterically stabilized liposome carrier can be administered to a subject in need thereof three times daily, twice daily, once daily, seven times weekly, six times

weekly, five times weekly, four times weekly, three times weekly, twice weekly, once weekly, every other week, or monthly.

[00117] The pharmaceutical composition and/or sterically stabilized liposome carrier can be administered to a subject in need thereof with a dosage schedule less frequent. In some cases, the pharmaceutical composition is administered subcutaneously, sublingually, or orally. In some cases, the pharmaceutical composition and/or sterically stabilized liposome carrier can be administered to a subject in need thereof with a dosage schedule about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50%, about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, or about 95% less frequent than a comparable composition with a different carrier (*e.g.*, conventional carrier that is not a sterically stabilized liposome carrier) or a comparable composition with different route of administration (*e.g.*, IV).

Compositions and Methods for treating an allergy

[00118] Disclosed herein are methods and compositions for treating an allergy or inducing tolerance to an allergen, comprising administering a pharmaceutical composition described herein to a subject in need thereof. In specific embodiments, the allergy is a food allergy, for instance an IgE mediated food allergy. In some embodiments, the allergy does not result in an airway inflammation. The pharmaceutical composition can comprise a therapeutically effective amount of at least one agent for treating an allergy or inducing tolerance to an allergen. In some cases, the allergy is not allergic asthma. In some cases, administration of a composition described herein to a subject in need thereof, can result in decreasing inflammation, anaphylaxis, gastrointestinal inflammation/reaction, skin rashes/urticaria/angioedema, or any combination thereof. In some embodiments, the subject is at risk for developing a food allergy (*e.g.*, IgE mediated food allergy). For example, the subject has a family history of developing a food allergy (*e.g.*, IgE mediated food allergy). In some embodiments, the subject is at risk for developing a gastrointestinal allergy. For example, the subject has a family history of developing a gastrointestinal allergy. In some embodiments, the subject has an elevated antibody level (*e.g.*, IgE) to an allergen (*e.g.*, food allergen). The methods and compositions described herein can be used to reset the IgE antibody production in the subject to the allergen, and thereby can allow an individual to tolerate exposure to that allergen without a reaction.

[00119] In certain embodiments is provided a composition suitable for oral, sublingual or subcutaneous administration comprising at least one agent at least one agent for treating an allergy or inducing tolerance to an allergen, and a sterically stabilized liposome carrier as described herein. In some embodiments, the at least one agent can comprise an allergen. Without

limitation, an allergen can be included in the liposome, optionally in addition to any other contents, such as those listed above. It should be appreciated that a wide variety of food allergens can be used. Examples of allergens are substances capable of inducing an allergic response in a mammal, *e.g.*, a human. Examples of allergens include for instance, proteins (whole or fragments), peptides, polypeptides, recombinant peptides. Some allergens can be derived from, or related to food substances (*e.g.*, peanut, tree nut, egg, shellfish, soy, milk, gluten). Still other allergens come from medicines, including small molecule medicines, *e.g.*, penicillin, sulfa drugs. Yet other allergens are contact allergens, *e.g.*, poison ivy (urushiol). Peanut allergens that can be used in compositions for oral, subcutaneous or sublingual administration as described herein, include, for instance, without limitation Ara h 1, Ara h2, Ara h3, and Ara h8. Additional allergen that can be provided as part of, or in conjunction with a composition suitable for oral, sublingual or subcutaneous administration described herein, are listed in the tables below.

[00120] Table 2: Major Class II Food Allergens, including the following:

Plant Allergen	**Protein**	**Food**	**Food Allergen**
Latex-fruit cross	Class I chitinases	Avocado, chestnut,	
reactivity		banana	
	Thaumatin-like	Cherry	Pru A2
		Apple	Mal d2
Birch	Bet vl homologues = pathogen-related proteins 10	Apple	Mal d 1
		Cherry	Pru a 1
		Pear	Pyr a 1
		Celery	Api g 1
		Carrot	Dau c 1
		Potato	
Celery-mugwort spice syndrome	Bet v2 homologues = Profilin	Latex	Hev b 8
		Celery	Api g 4
		Potato	
		Cherry	Pru av 4
		Pear	Pyr c 4
		Peanut	Ara h 5
		Soybean	Gly m 3
		Apple, tomato, and carrot	
	Lipid-transfer proteins	Peach	Pru p
		Apple	Mal d3
		Soy	
Seed Storage Proteins	2S albumin	Mustard	Sin a 1
		English walnut	Jug r 1
		Rapeseed and Brazil nut	
	Vicilin	Peanut	Ara h 1
		Walnut	Jug r 1
	Conglutin	Peanut	Ara h2
	Glycinin	Peanut	Ara h3
		Soy	
	β-Glycinin	Soy	

[00121] Table 3: Major Class 1 Food Allergens, including the following:

Foods	Examples of Proteins	Examples of Food Allergens
Cow's milk	Caseins αs1-Casein αs2-Casein β-Casein κ-Casein	Bos d 8
	Whey β-Lactoglobulin α-Lactalbumin Bos d 4 Serum albumin	 Bos d 5 Bos d 4 Bos d 6
Chicken egg white	Ovalbumin Ovomucoid Ovotransferrin	Gal d 1 Gal d 2 Gal d 3
Wheat	Globulin Glutenin	
Peanut	Vicilin Conglutin Glycinin	Ara h 1 Ara h 2 Ara h 3
Soybean	Glycinin G1 acidic chain Profilin	Gly m 3
Fish	Codfish-Parvalbumin	Gad c 1
	Salmon	Sal s 1
Shrimp	Tropomyosin	Pen a 1

[00122] Table 4: Food Allergen Protein Families of Animal Origin, including the following:

Allergen Family	Examples of Source and Allergen
Tropomyosins	Brown shrimp (Pen a 1), Crab (Cha f 1), Oyster (Cra g 1, Cra g)
Parvalbumin	Salmon (Sal s 1.01), Tuna (Thu o 1.01), Carp (Cyp c 1.01), Frog (Ran e 1)
Caseins	Cow (Bas d 8)

[00123] Table 5: Food Allergen Protein Families of Plant Origin, including the following:

Allergen Family	Examples of Source and Allergen
11 S (legumin like) globulins	Peanut (Ara h3, Ara h4), Soy (Glycinin), Buckwheat (Fag e 1), Cashew (Ana o 2)
Bet v 1 superfamily	Apple (Mal d 1), Cherry (Pm av 1), Pear (Pyr c 1), Carrot (Dau c 1)
Nonspecific lipid transfer proteins	Apricot (Pru ar 3), Cherry (Pm av 3), Peach (Pm p 3), Strawberry (Fra a 3), Grape (Vit v 1), Walnut (Jug r 3), Lettuce (Lac s 1),

	Corn (Zea m 14)
Chitinases	Avocado (Pers a 1), Banana (Mus xp Chitinase)
Profilins	Pear (Pyr c 4), Cherry (Pm av 4), Celery (Api g 4), Latex (Hev b 8)

[00124] In some embodiments are provided compositions described herein, suited for oral, subcutaneous or sublingual administration, comprising non-food allergens, sources of which allergens can include, without limitation, the following:

[00125] Table 6: Grass Pollen Allergens, including components of the following species:

Scientific Name	**Examples of Component allergens**
Paspalum notatum	Pas n 1, 13
Cynodon dactylon	Cyn d 1-14
Sorghum ha/epense	Sor h 1-14
Phleum pratense	Phl p 1-14
Lolium perenne	Lol p 1-14
Poa pratensis	Poa p 1-14

[00126] Table 7: Weed Pollen Allergens, including components of the following species:

Scientific Name	**Examples of Component allergens**
Ambrosia artemisiifolia	Amb a 1-10 profilin, and cystatin
Artemisia vulgaris	Art v 1-3 and profilin
Parietaria spp.	Par o 1 and 2

[00127] Table 8: Indoor Allergens, including components of following species of dust mites, storage mites, animals, and insects:

Scientific Name	**Examples of Component allergens**
Dermatophagoides farinae	Der f 1,2,3,7,10,11,14,15-17,18w
Dermatophagoides pteronyssinus	Der p 1-11, 14, 20
Euroglyphus maynei	Eur m 2,14
Blomia tropicalis	Blo t 1-9, 13, 21
Lepidoglyphus destructor	Lep d 2,5,7,10,13
Glycyphagus domesticus	Glyd 2
Tyrophagus putrescentia	Tyr p 2,13
Canis familiaris	Can f 1-4
Felis domesticus	Fel d 1-4, 5w-7w
Equus caballus	Equ ca 1-5
Cavia porcellus	Cav p 1,2
Mus musculus	Mus m 1
Rattus norvegius	Rat n 1
Blattella germanica	Bla g 1-6
Periplaneta americana	Per a 1,3,7

[00128] Table 9: Mold Allergens, including components of the following species:

Scientific Name	**Examples of Component allergens**

Alternaria alternata	Alt a 1-12
Cladosporium herbarum	Cla h 1-12
Aspergillus fumigates	Asp f 1-22
Penicillium chrysogenum	Pen ch 13,18,20

[00129] Table 10: Tree Pollen Allergens, including components of the following species:

Scientific Name	Examples of Component allergens
Fraxinus	Fra a 1
Betulaceae	Bet v 1-7
Juniperus	Jun a 1-3
Quercus	Que a 1
Oleaceae	Ole e 1-8
Platanus	Pia a 1

[00130] Table 11: Stinging Insect Allergens, including components of the following:

Subfamily Name	Examples of Component allergens
Honeybee	Api m 1 (Phospholipase A2)
	Api m 2 (Hyaluronidase)
	Api m 3 (Acid phosphatase)
	Api m 4 (Melittin)
Bumblebee	Born p 1 (Phospholipase A2)
	Born p 4 (Protease)
Vespinae and Polistinae	Grp 1 (Phospholipase A 1)
	Grp 2 (Hyaluronidase)
	Grp 3 (Acid phosphatase)
	Grp 4 (Protease)
	Grp 5 (Antigen 5)
Fire ants	Sol i 1 (Phospholipase A 1)
	Sol i 2 (Unknown protein)
	Sol i 3 (Antigen 5 protein family)
	Sol i 4

[00131] As an example, a peanut derivative such as peanut powder, butter or protein can be loaded into a sterically stabilized liposome carrier for administration as part of an allergy treatment. As another example, multiple allergens can be loaded into a single liposome. Optionally, MPL is loaded in the liposome in combination with the allergen. The administration can be subcutaneous, sublingual, or oral.

[00132] The methods disclosed herein can comprise administering compositions comprising an allergy medication for instance selected from the group consisting of an antihistamine, a corticosteroid, a bronchodilator, a mast cell stabilizer, a leukotriene inhibitor, an anti-tuberculosis agent, a serine lung protease inhibitor, and any combination and derivative thereof which may optionally be administered concurrently or subsequently with an allergen which may be administered separately or as part of the same composition.

[00133] In some cases, the antihistamine comprises a H_1-antihistamine, H_2-antihistamine, H_3-antihistamine, H_4-antihistamine, or any combination thereof. In some cases, the H_1-antihistamine comprises acrivastine, azelastine, bilastine, brompheniramine, buclizine, bromodiphenhydramine, carbinoxamine, chlorpromazine, cyclizine, chlorphenamine, chlorodiphenhydramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, dimenhydrinate, dimetindene, diphenhydramine, doxylamine, ebastine, embramine, fexofenadine, hydroxyzine, loratadine, meclozine, mirtazapine, olopatadine, orphenadrine, phenindamine, pheniramine, phenyltoloxamine, promethazine, quetiapine, rupatadine, tripelennamine, triprolidine, cetirizine, desloratadine, pyrilamine, or any combination or derivative thereof. In some cases, the H_2-antihistamine comprises cimetidine, famotidine, lafutidine, nizatidine, ranitidine, roxatidine, tiotidine, or any combination or derivative thereof. In some cases, the H_3-antihistamine comprises clobenpropit, ABT-239, ciproxifan, conessine, A-349,821, thioperamide, or any combination or derivative thereof. In some cases, the H_3-antihistamine comprises thioperamide, JNJ 7777120, VUF-6002, or any combination or derivative thereof.

[00134] In some cases, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

[00135] In some cases, the bronchodilator comprises terbutaline, albuterol, ipatropium, pirbuterol, epinephrine, salmeterol, levalbuterol, formoterol, or any combination or derivative thereof.

[00136] In some cases, the mast cell stabilizer comprises β2-adrenergic agonists, cromoglicic acid, ketotifen, methylxanthines, olopatadine, omalizumab, pemirolast, quercetin, or any combination or derivative thereof.

[00137] In some cases, the leukotriene inhibitor comprises montelukast, zafirlukast, zileuton, or any combination or derivative thereof.

[00138] In some cases, the anti-tuberculosis agent comprises isoniazid, ethambutol, pyrazinamide, rifamycin, rifampin, streptomycin, clarithromycin, or any combination or derivative thereof.

[00139] In some cases, the at least one agent comprises gangamycin, azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

[00140] Oral desensitization can be used for treating an allergy or inducing tolerance to an allergen, such as peanut allergy. Oral desensitization can be the administration of measured amounts of an allergen (*e.g.*, peanut powder, butter or protein) to an allergic individual, in an incremental manner till the individual can ingest the allergen without having a reaction. In some

cases, a daily, weekly, biweekly, monthly, quarterly, biennial or annual dose of the allergen may continue for years, or even for a lifetime.

[00141] Allergy, for instance food allergy, can include a number of conditions caused by hypersensitivity of the immune system to a particular allergen. It can be defined by an elevated Immunoglobulin E (IgE) antibody level to the particular allergen. Tolerance is a process that resets the IgE antibody production, and thereby can allow an individual to tolerate exposure to that allergen without a reaction. In some cases, a certain level of bacterial endotoxin (PAMP-lipid mediators) is needed for antigen presenting cells (*e.g.*, dendritic cells) to present to T lymphocyte regulatory cells (T reg cells) to turn off signals so sensitization does not occur. If the level of lipid mediators is below or inadequate, it can result in a loss of regulation of the immune system, mainly the T lymphocyte regulatory cells (T reg cells). This loss of regulation can allow B lymphocytes producing IgE specific to an allergen, such as peanut, to be unregulated, thereby allowing for sensitization to that allergen. In some cases, the level of bacterial antigens or endotoxin, such as a lipid mediator, may play a role in resetting the T regulatory system. One such example of a lipid mediator is Lipid A, which is a bacterial endotoxin. In some cases, the Lipid A can be Monophosphoryl Lipid A (MPL), which is a Toll-like receptor TLR-4 agonist. TLR-4 can play a role in the innate immune system, for example, with dendritic cells. TLR-4 can also have an impact on the T regulatory system therefore playing a role in resetting the balance of the immune system. These immunomodulating lipids can decrease the pro-inflammatory cytokines such as IL-4 and IL-5 which drive the inflammatory cascade. In addition, these immunomodulating lipids can also increase IL-10 which is a cytokine that supports the innate system and/or drives T-regulatory lymphocytes.

[00142] Also disclosed are methods for treating allergic inflammations which are non-airway inflammations by administering orally, sublingually or subcutaneously a pharmaceutical composition described herein. In some cases, the treatment is with allergen desensitization to the food (immunotherapy). In some cases, the methods comprise administering an allergen (*e.g.*, in incremental doses) via injections administered subcutaneously (SCIT), *e.g.* "allergy shots". In some cases, the methods comprise administering an allergen (*e.g.*, in incremental doses) under the tongue (sublingual immunotherapy-SLIT). In some cases, the methods comprise administering an allergen (*e.g.*, in incremental doses) orally.

Compositions and Methods of treating an inflammatory disorder

[00143] The compositions and methods disclosed herein can be used for treating an inflammatory disorder. For example, the inflammatory disorder can be an undesired gut or esophagus

inflammatory response (*e.g.* eosinophilic esophagitis). The pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration.

[00144] The compositions can comprise or be co-administered with one or more agent for treating another condition (*e.g.* an allergy). For example, the compositions can be administered with one or more food allergen. The sterically stabilized liposome carrier can have an inherent calming property to the gut, and/or can be used for reducing inflammation (*e.g.* in the gut). One or more agent, such as allergen, corticosteroid, anti-IgE antibody, MPL, or any combination thereof, can be formulated with or co-administered or sequentially administered with a sterically stabilized liposome carrier to treat the inflammatory disorder.

[00145] In some cases, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

[00146] In some cases, the at least one agent comprises azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

[00147] A composition described herein, comprising sterically stabilized liposome carrier can be administered orally, sublingually or subcutaneously for treating an inflammatory disorder which is not an airway inflammation. In some cases, the composition can further comprise one or more agent for treating the inflammatory disorder. In some cases, the composition can further comprise one or more agent for treating another condition (*e.g.*, a food allergy).

Methods of treating eosinophilic esophagitis (EoE)

[00148] Eosinophilic esophagitis (EoE) is a chronic immune system disease. In EoE, a type of white blood cell (eosinophil) can build up in the lining of the tube that connects mouth to stomach (esophagus). This buildup, which can be a reaction to foods and/or allergens, can inflame or injure the esophageal tissue. Damaged esophageal tissue can lead to difficulty swallowing or cause food to get caught when you swallow.

[00149] Disclosed herein are compositions, kits, and methods relating to oral, sublingual or subcutaneous administration of a sterically stabilized liposome carrier for treating EoE. In some cases, the pharmaceutical compositions comprise a therapeutically effective amount of at least one agent for treating EoE. In some cases, the pharmaceutical composition can comprise MPL and/or steroids such as budesonide and triamcinolone. In some cases, immunomodulating lipids can also play a role in decreasing inflammation, and thus be used in treating the inflammatory disorder.

[00150] Disclosed herein are methods of administering a pharmaceutical composition comprising a therapeutically effective amount of at least one agent for treating eosinophilic esophagitis. The pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration. The at least one agent can comprises a proton-pump inhibitor (PPI), a corticosteroid, or any combination or derivative thereof. In some cases, the proton-pump inhibitor comprises omeprazole, lansoprazole, dexlansoprazole, esomeprazole, pantoprazole, rabeprazole, ilaprazole, or any combination or derivative thereof. In some cases, the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof. In some cases, the at least one agent comprises azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

[00151] The compositions can be co-administered with one or more agent for treating another condition (*e.g.* an allergy). For example, the compositions can be administered with one or more allergen. The sterically stabilized liposome carrier can have an inherent calming property to the gut, and/or can be used for reducing inflammation (*e.g.* in the gut). One or more agent, such as allergen, steroid, anti-IgE antibody, MPL, and any combination thereof, can be co-administered with the sterically stabilized liposome carrier to treat eosinophilic esophagitis.

Methods of treating tuberculosis

[00152] Tuberculosis (TB) is an infectious disease caused by the bacterium *Mycobacterium tuberculosis* (MTB). Tuberculosis can affect the lungs. Tuberculosis can also affect other parts of the body. MPL can play a role in the interaction of macrophages and dendritic cells, both cell types which can have important role in controlling the TB infection by the body. Anti-TB agents can have sustained effect as a once a week therapy.

[00153] Disclosed herein are compositions, kits, and methods of using a sterically stabilized liposome carrier for treating TB. In some cases, a pharmaceutical composition comprising a therapeutically effective amount of at least one agent for treating TB can be used. In some cases, the pharmaceutical composition can comprise MPL and/or steroids such as Isoniazid, Gangamycin, and Streptomycin.

[00154] Disclosed herein are methods of administering a pharmaceutical composition comprising a therapeutically effective amount of at least one agent for treating TB. The pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration. The at least one agent can comprises isoniazid, rifampin (rifadin, rimactane), ethambutol (myambutol), pyrazinamide, fluoroquinolone, amikacin, kanamycin, capreomycin, gangamycin, streptomycin,

bedaquiline, linezolid, or any combination or derivative thereof. In some cases, the at least one agent comprises isoniazid. In some cases, the at least one agent comprises gangamycin. In some cases, the at least one agent comprises streptomycin. The pharmaceutical composition further comprises MPL.

Kits

[00155] A kit according to the invention can include at least one dosage forms, *e.g.*, one or more dosage forms. In some cases, the kit includes sufficient doses for a period of time. In particular cases, the kit includes a sufficient dose of the pharmaceutical composition for a day, a week, 14 days, 28 days, 30 days, 90 days, 180 days, a year, etc. In some specific cases, the each dose is physically separated into a compartment, in which each dose is segregated from the others.

[00156] In some cases, the kit can contain one or more pharmaceutical composition, in a form that requires further processing. For example, the one or more pharmaceutical composition can be in powder form (*e.g.*, table and capsule) and the kit can contain a solution that is used to recombine the power with the solution, *e.g.*, 0.9% NaCl solution. In some case, this reconstituted powder solution can be administered at various locations. In some cases, the powder is contained into a container that can be used as an applicator.

[00157] In particular cases, the kit may advantageously be a blister pack. Blister packs are known in the art, and generally include a clear side having compartments (blisters or bubbles), which separately hold the various doses, and a backing, such as a paper, foil, paper-foil or other backing, which is easily removed so that each dose may be separately extracted from the blister pack without disturbing the other doses. In some cases, the kit may be a blister pack in which each day's dose of the pharmaceutical composition. In some cases, the kit may be a blister pack in which each week's dose of the pharmaceutical composition. In some cases, the kit may be a blister pack in which each month's dose of the pharmaceutical composition. In some such cases, the blister pack may have perforations, which allow each daily, weekly, or monthly dose to be separated from the others by tearing it away from the rest of the blister pack. The separate dosage forms may be contained within separate blisters. Segregation of the two pharmaceutical compositions into separate blisters can be advantageous in that it prevents separate dosage forms (*e.g.* tablet and capsule) from contacting and damaging one another during shipping and handling. Additionally, the separate dosage forms can be accessed and/or labeled for administration to the patient at different times.

[00158] In other cases, the kit may be box having separate compartments with separate lids. For example, a kit may comprise a box having seven compartments, each for a separate day of the week, and each compartment marked to indicate which day of the week it corresponds to. In

some specific cases, each compartment is further subdivided to permit segregation of one pharmaceutical composition from another. As stated above, such segregation is advantageous in that it prevents damage to the dosage forms and permits dosing at different times and labeling to that effect.

[00159] In some cases, the kit may contain written instructions, in any language, directing a subject or a physician to use the contents of the kits in a way to effectively treat a condition disclosed herein.

EXAMPLES

Example 1 – Materials and Methods

[00160] *Animals*

[00161] Six week-old male C57 black 6 mice were purchased from Charles River Laboratories, Inc., Wilmington, MA. The animals were provided with an ovalbumin-free diet and water ad libitum and were housed in an environment-controlled, pathogen-free animal facility. All animal protocols were approved by the Animal Care Committee of the University of Illinois at Chicago, the Medical College of Wisconsin and the Zablocki Veterans Administration Medical Center, and were in agreement with the National Institute of Health's guidelines for the care and use of laboratory animals.

[00162] *Ovalbumin Sensitization*

[00163] The animals were sensitized with ovalbumin (OVA). On day 0, each mouse was anesthetized with methoxyflurane given by inhalation. A fragmented heat-coagulated OVA implant was inserted subcutaneously on the dorsal aspect of the cervical region.

[00164] For a ten-day period (days 14-24), each mouse was given a 30-minute aerosolization of a 6% OVA solution on alternate days. This method of sensitization led to significant elevations in eosinophil peroxidase (EPO), peripheral blood (PB) eosinophils, and serum IgE levels, along with inflammation as seen on histopathology by day 24.

[00165] Each of the doses was given at a volume of 1 milliliter for 2 minutes through use of a chamber. The mouse had skin and whole body exposure and were allowed to breathe freely. All treatment groups were compared with either sensitized untreated (SENS) or unsensitized (Normal) mice.

[00166] *Drugs and Reagents*

[00167] BUD for daily therapy was diluted from premixed vials (0.25 mg/ml) commercially available from AstraZeneca Pharmaceutical, Wayne, PA. BUD for encapsulation and N-2-hydroxethylpiperzine-N'-2-ethanesulfonic acid (HEPES) was purchased from Sigma Chemical, St. Louis, MO. Phosphatidylcholine (PC), phosphatidylglycerol (PG), and poly (ethylene

glycol)-distearoylphosphatidylethanolamine (PEG-DSPE) were obtained from Avanti Polar Lipids, Alabaster, AL. Cholesterol was purchased from Calbiochem, La Jolla, CA. NaCl and KCl were purchased from Fisher Scientific, Pittsburgh, PA.

[00168] *Liposome Preparation*

[00169] Budesonide (BUD) was encapsulated into either sterically stabilized (phosphatidylglycerol-phosphotidylcholine-poly(ethylene glycol)-cholesterol: distearoylphosphatidylethanolamine):(phosphatidyl glycerol[PG]: phosphatidylcholine [PC]: cholesterol: poly(ethylene glycerol)[PEG] distearoylphosphatidylethanolamine [DSPE] - [PG:PC:Cholesterol:PEG-DSPE] (2:8:5:0.5) sterically stabilized liposomes or conventional (phosphatidylglycerol-phosphatidylcholine-cholesterol) (2:8:5) as a carrier through use of a modified protocol derived from the protocol described by Gangadharam, et al., Antimicrob Agents Chemother, 1995:39:725-730.

[00170] Triamcinolone (TRI) was encapsulated into either sterically stabilized (phosphatidylglycerol-phosphatidylcholine-poly (ethylene glycol)-cholesterol: distearoylphosphatidylethanolamine):(phosphatidyl glycerol[PG]: phosphatidylcholine [PC]: cholesterol: poly(ethylene glycerol)[PEG] distearoylphosphatidylethanolamine [DSPE] - [PG:PC:Cholesterol:PEG-DSPE] (2:8:5:0.5) sterically stabilized liposomes.

[00171] A portion of the cholesterol used in control liposomes was replaced by BUD or TRI dissolved in chloroform-methanol (2:1) during the preparation of the lipid mixture. The resulting composition was PG:PC:Cholesterol:PEG-DSPE:BUD (2:8:3:0.5:2). Lipids were dried onto the sides of a round-bottomed glass flask or glass tube by rotary evaporation. The dried film was then hydrated by adding sterile 140 mmol/L, NaCl and 10 mmol/L HEPES (pH 7.4) and vortexing.

[00172] The resulting multilamellar liposome preparations were extruded 21 times through polycarbonate membranes (either 0.2 or 0.8 μm in pore diameter), (Nuclepore, Pleasanton, CA) through use of an Avestin extrusion apparatus, Toronto, Canada. The control carriers were prepared the same way and of the same composition except that no BUD was added. The resulting multilamellar liposome preparation contained about 96.8 weight percent water and was diluted to suitable concentration (20 μg /ml) for administration.

[00173] Liposomes without cholesterol were prepared in a similar manner, except that the molar ratio of the lipids were PG:PC:PEG-DSPE (2:8:0.5) .

[00174] Liposomes containing MPL were prepared in a similar manner, except that the molar ratio of the lipids were PG:PC:MPL:PEG-DSPE (2:8:0.1:0.5). Liposomes containing both MPL and budesonide were also prepared, in the ratio PG:PC:BUD:MPL:PEG-DSPE (2:8:2:0.1:0.5).

Both liposomes were extruded 21 times through polycarbonate membranes with a pore diameter of 0.8 μm.

[00175] The amounts of lipid used for the Wk-Empty-S group were based on the amount of lipid nebulized for each of the BUD-encapsulated liposomes (1.39 μmol for the sterically stabilized liposomes and 3.19 μmol for the conventional liposomes).

[00176] The dose of BUD chosen was based on preliminary dose-response studies with 5 to 50μg of BUD as follows.

[00177] Each day, 5, 10, 15, 20 or 50μg of BUD was administered to groups of sensitized mice, and the dose-dependent effects on the inflammatory parameters were evaluated. These data were compared with data for either a group of sensitized untreated mice (SENS group) or a group of unsensitized mice (Normal group). A 20μg/ml dose of BUD was shown on histopathologic examination to effectively decrease, PB eosinophils and inflammation of tissues, along with other inflammatory parameters, without evidence of toxicity to the spleen, liver, bone morrow or gastrointestinal tract. In addition, there were no granulomas or abnormalities in any of the tissues evaluated.

[00178] *Histopathology Observations*

[00179] Histopathological examinations performed were as follows:

[00180] The tissues were removed and fixed with 10% phosphate buffered formalin. Tissue samples were taken from the skin, spleen, liver, gastrointestinal tract, and kidney. The tissues were embedded in paraffin, sectioned at 5μm thickness and stained with hematoxylin and eosin and analyzed using light microscopy.

[00181] Coded slides were examined by a pathologist in a blinded fashion for evidence of inflammatory changes, including epithelial hyperplasia and perivascular edema and accumulation of eosinophils, neutrophils, and mononuclear inflammatory cells. Each of the parameters evaluated was given an individual number score. Objective measurements of histopathological changes include aggregation of eosinophils around blood vessels (perivascular), accumulation of other inflammatory cells, presence of desquamation and hyperplasia of the epithelium, and infiltration of inflammatory cells.

[00182] The percentages of eosinophils were obtained by counting the number of eosinophils in 100 white blood cells under a high-power field scope (x100) from the PB smears stained with Wright-Giemsa stain.

[00183] *Total Serum IgE*

[00184] Ninety-six well flat bottom plates (Fisher Scientific) were coated with 100μL per well of 2μg/ml rat antimouse IgE monoclonal antibody (BD, PharMingen, San Diego, CA), and incubated overnight at 4°C. Serum was added at a dilution of 1:50 and incubated overnight at

4°C. Purified mouse IgE (k isotype, small b allo-type anti-TNP:BD PharMingen) was used as the standard for total IgE. The samples were incubated for one hour with biotin-conjugated rate antimouse IgE (detection antibody purchased from Southern Biotechnology, Birmingham, AL).

[00185] *Study Groups*

[00186] Therapy was initiated on day 25, the day after the OVA sensitization was completed. Sensitized animals received treatments for four weeks. Each study group consisted of 20 mice and was followed for a four-week period. Five animals from each treatment group and from each of the two control groups, sensitized and unsensitized, were euthanized by means of an overdose of methoxyflurane inhaled 24 hours after the first treatments were given and then at weekly intervals for four weeks. At each time point, measurements of PB eosinophils, and total serum IgE levels were obtained and histopathologic examination of the tissues was performed.

[00187] *Data Analysis*

[00188] Serum Total IgE levels and peripheral blood eosinophil count analyses were performed using the Student t test. Over the Study period, there were no significant increases or decreases in inflammation within each group according to weekly measurements for all of the inflammatory parameters being evaluated. Therefore all the weekly measurements are presented as Cumulative data. A $p<0.05$ was considered to be statistically significant for all of the above statistical comparisons.

Example 2 – BUD 1: Comparison of BUD in the Carrier with Conventional Liposomes

BUD 1: TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice
SENS	Sensitized, Untreated mice
Daily BUD	20µg of budesonide without Carrier given daily-Standard therapy
WK-S-BUD	20µg of budesonide in the Carrier given once a week
WK-C-BUD	20µg of budesonide encapsulated in Conventional Carrier given once a week
WK-ES	Buffer loaded empty Carrier without drug given once a week
WK-BUD	20µg of budesonide without Carrier given once a week

BUD 1: RESULTS

	PB Eos *(Fig. 2)*	IgE levels *(Fig. 3)*
NORMAL	--	--
SENS	↑	↑
Daily BUD	↓	↓
WK-S-BUD	↓	↓
WK-C-BUD	∅	∅
WK-ES	∅	∅
WK-BUD	∅	∅

Legend	↑	∅	↓	--
	Moderate-Severe inflammation	No significant reduction in inflammation	Significant reduction in inflammation	No inflammation

[00189] In the set of data given for BUD 1, it was demonstrated that one dose of budesonide (BUD) encapsulated in the carrier given once a week (WK-S-BUD), reduced inflammation as effectively as the same dosage of BUD given once a day (Daily BUD) when compared to the Sensitized Untreated group (SENS) and was comparable to the NORMAL group. Weekly treatments with free BUD without Carrier (WK-BUD), BUD encapsulated in Conventional Carrier (WK-C-BUD) and Empty Carrier (WK-ES) did not have comparable effects.

Example 3 - BUD 2: Comparison of BUD in the Carrier with Free drug/Free Carrier administered simultaneously

BUD 2: TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice
SENS	Sensitized, Untreated mice
Daily BUD	20µg of budesonide without the Carrier given daily-Standard therapy
WK-S-BUD	20µg of budesonide in the Carrier given once a week
WK-ES	Buffer loaded Empty Carrier without drug given once a week
WK-BUD	20µg of budesonide without the Carrier given once a week
WK-BUD & ES	WK-ES and WK-BUD without encapsulation in the Carrier, given once a week

BUD 2: RESULTS

	PB Eos ***(Fig. 4)***	**IgE levels** ***(Fig. 5)***
NORMAL	--	--
SENS	↑	↑
Daily BUD	↓	↓
WK-S-BUD	↓	↓
WK-ES	∅	∅
WK-BUD	∅	∅
WK-BUD & ES	∅	∅

[00190] In the set of data given for BUD 2, it was demonstrated that one dose of budesonide (BUD) encapsulated in the Carrier given once a week (WK-S-BUD), reduced inflammation as effectively as the same dosage of BUD given once a day (Daily BUD) when compared to the Sensitized Untreated group (SENS) and was comparable to the NORMAL group. Weekly treatments with only free BUD without Carrier (WK-BUD), Empty Carrier (WK-ES), or free

BUD (WK-BUD) and Empty Carrier (WK-ES) given simultaneously did not have comparable effects.

Example 4 - BUD 3: Comparison of BUD Encapsulated in the Carrier With and Without Cholesterol

BUD 3: TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice
SENS	Sensitized, Untreated mice
Daily BUD	20µg of budesonide without the Carrier given daily-Standard therapy
WK-S-BUD + (plus Chol)	20µg of budesonide in the Carrier With Cholesterol given once a week
WK-S-BUD -- (minus Chol)	20µg of budesonide in the Carrier Without Cholesterol given once a week
WK-ES--	Buffer loaded empty Carrier without cholesterol or drug given once a week
WK-BUD	20µg of budesonide without the Carrier given once a week

BUD 3: RESULTS

	PB Eos *(Figs 2, 4 & 6)*	**IgE levels** *(Figs 3, 5 & 7)*
NORMAL	--	--
SENS	↑	↑
Daily BUD	↓	↓
WK-S-BUD +	↓	↓
WK-S-BUD --	↓	↓
WK-ES --	∅	∅
WK-BUD	∅	∅

[00191] In the set of data given for BUD 3, it was demonstrated that BUD encapsulated in the Carrier with (WK-S-BUD+) or without Cholesterol (WK-S-BUD--) given once a week, reduced inflammation as effectively as the same dosage of BUD given once a day (Daily BUD), when compared to the Sensitized Untreated group (SENS) and, was comparable to the NORMAL group. Only the WK-S-BUD + and WK-S-BUD-- treated groups significantly reduced the BUD in the Carrier without Cholesterol (WK-S-Bud--) was equally effective as BUD encapsulated in the Carrier with Cholesterol (WK-S-BUD+). Weekly treatments with only free BUD without Carrier (WK-BUD) and Empty Carrier without cholesterol (WK-ES--) did not have comparable effects on inflammation as the WK-S-BUD+ and WK-S-BUD-- treated groups.

Example 5 - BUD 4: Comparison of BUD in the Carrier With and Without MPL

BUD 4: TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice

SENS	Sensitized, Untreated mice
Daily BUD	20µg of budesonide without the Carrier given daily-Standard therapy
WK-S-BUD -- (minus MPL)	20µg of budesonide in the Carrier Without MPL given once a week
WK-S-BUD + (plus MPL)	20µg of budesonide in the Carrier With MPL given once a week
WK-ES --	Buffer loaded empty Carrier without drug or MPL given once a week
WK-ES-MPL	Buffer loaded empty Carrier without drug, With MPL given once a week

BUD 4: RESULTS

	IgE levels ***(Fig. 8)***
NORMAL	--
SENS	↑
Daily BUD	↓
WK-S-BUD +	↓
WK-S-BUD --	↓
WK-ES --	∅
WK-ES-MPL	∅

[00192] In the set of data given for BUD 4, it was demonstrated that BUD encapsulated in the Carrier with (WK-S-BUD+) or without MPL (WK-S-BUD--) given once a week, reduced inflammation as effectively as the same dosage of BUD given once a day (Daily BUD) when compared to the Sensitized Untreated group (SENS) and was comparable to the NORMAL group. Only the WK-S-BUD+, WK-S-BUD--, and the weekly Empty Carrier with MPL (WK-ES-MPL) treatment groups significantly reduced the inflammation. BUD in the Carrier with MPL (WK-S-Bud+) was equally as effective as BUD encapsulated in the Carrier without MPL (WK-S-BUD--). Weekly treatments with Empty Carrier without MPL (WK-ES--) did not have comparable effects as the WK-S-BUD+, WK-S-BUD--, or Empty Carrier with MPL (WK-ES-MPL) treated groups.

Example 6 - BUD 5: Comparison of BUD with TRI in the Carrier

BUD 5: TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice
SENS	Sensitized, Untreated mice
Daily BUD	20µg of budesonide without the Carrier given daily-Standard therapy
WK-S-BUD	20µg of budesonide in the Carrier given once a week
WK-S-TRI-20µg	20µg of triamcinolone in the Carrier given once a week
WK-S-TRI-40µg	40µg of triamcinolone in the Carrier given once a week

WK-ES	Buffer loaded empty Carrier without drug given once a week

BUD 5: RESULTS

	IgE levels ***(Fig. 9)***
NORMAL	--
SENS	↑
Daily BUD	↓
WK-S-BUD	↓
WK-S-TRI-20µg	↓
WK-S-TRI-40µg	↓
WK-ES	∅

[00193] In the set of data given for BUD 5, it was demonstrated that 20 µg of Triamcinolone (TRI) encapsulated in the Carrier (WK-S-TRI-20 µg) or 40 µg of TRI encapsulated in the Carrier (WK-S-TRI-40 µg) given once a week, reduced inflammation as effectively as 20 µg of Budesonide (BUD) encapsulated in the Carrier with (WK-S-BUD) or BUD given once a day (Daily BUD) when compared to the Sensitized Untreated group (SENS) and was comparable to the NORMAL group. WK-S-TRI-20 µg, WK-S-TRI-40 µg, WK-S-BUD, and Daily BUD all reduced the inflammation.

Example 7 - Pro-Inflammatory Cytokines Levels

TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice
SENS	Sensitized, Untreated mice
D-Bud	20µg of budesonide without the Carrier given daily-Standard therapy
WK-BUD	20µg of budesonide in the Carrier given once a week
WK-ES	Buffer loaded empty Carrier without drug given once a week

RESULTS

[00194] As shown in Figs. 10 and 11, once a week administration of the empty sterically stabilized drug delivery system (WK-ES) and once a week administration of Budesonide encapsulated in the sterically stabilized drug delivery system significantly decreased levels of the pro-inflammatory cytokines IL-4 and IL-5.

Example 8 - Anti-Inflammatory Cytokines Levels

TREATMENT GROUPS

NORMAL	Unsensitized, Untreated Normal mice
SENS	Sensitized, Untreated mice
D-Bud	20µg of budesonide without the Carrier given daily-Standard therapy

WK-BUD	20µg of budesonide in the Carrier given once a week
WK-ES	Buffer loaded empty Carrier without drug given once a week

RESULTS

[00195] As shown in Fig. 12, once a week administration of the Empty sterically stabilized drug delivery system (WK-ES) and once a week administration of Budesonide encapsulated in the sterically stabilized drug delivery system significantly increased levels of the anti-inflammatory cytokine IL-10.

Example 9 - Stained Slides of Skin

[00196] Fig. 13 illustrated hematoxylin and eosin stained slides of skin. Top two frames show Empty delivery system administered once a week to a sensitized mouse with allergic inflammation (10X magnification-top left and 40X magnification-top right). Bottom two frames show untreated sensitized mice at 40X magnification. There was a significant decrease in inflammation in the treated group when compared to the untreated, sensitized group.

Example 10 - Stained Slides of Gastrointestinal Tract

[00197] Fig. 14 illustrated hematoxylin and eosin stained slides of gastrointestinal tract. Top left is empty delivery system delivered once a week to a sensitized mouse with allergic inflammation. Top right depicts once a week budesonide encapsulated in the delivery system given once a week to a sensitized mouse with allergic inflammation. Bottom left is an example of a Normal untreated mouse. Right bottom is an example of inflammation in an untreated, sensitized mouse with allergic inflammation. There was a significant decrease in inflammation in the treated groups when compared to the untreated and normal groups.

Example 11 – Oral application of Budesonide for treating EoE

[00198] The safety and efficacy of the oral steroid for EoE will be accessed with four groups for a period of 6 weeks. Each group will consist of 10 patients per group. Group 1 will be the untreated group. Group 2 will be treated with conventional treatment. Group 3 will be administered 100 or 200 micrograms of budesonide encapsulated in the delivery system daily via oral administration. Group 4 will be administered 100 or 200 micrograms of budesonide encapsulated in the delivery system once a week via oral administration.

[00199] The liposome preparation will be similar to the procedures used in Example 1. Specifically, the conventional treatment will using 100 or 200 micrograms of budesonide encapsulated in a conventional carrier of phosphatidylglycerol:phosphatidylcholine:cholesterol at 2:8:5. In one example, the delivery systems used in Groups 3 and 4 will be

PG:PC:Cholesterol:PEG-DSPE at 2:8:5:0.5. In another example, the delivery systems will be PG:PC:PEG-DSPE at 2:8:0.5.

Example 12 – Oral application of peanut allergen

[00200] The safety and efficacy of oral application of peanut allergen will be accessed with two sets of experiments, each with four groups, as shown below.

	Group 1	Group 2	Group 3	Group 4
Set 1	Untreated group	Conventional Treatment	pH sensitive delivery system given with encapsulated peanut peptides	pH sensitive delivery system given with peanut powder
Set 2	Untreated group	Conventional Treatment	pH resistant delivery system given with encapsulated peanut peptides	pH resistant delivery system given with peanut powder

[00201] The liposome preparation will be similar to the procedures used in Example 1. Specifically, the conventional treatment will use peanut peptides encapsulated in a conventional carrier of phosphatidylglycerol:phosphatidylcholine:cholesterol at 2:8:5. In one example, the delivery systems will use PG:PC:Cholesterol:PEG-DSPE at 2:8:5:0.5. In another example, the delivery systems will be PG:PC:PEG-DSPE at 2:8:0.5. The pH sensitive delivery system will have an additional pH sensitive component, *e.g.* N-palmitoyl homocysteine (PHC), with the same molar amount as PEG-DSPE.

Example 13 – Immunotherapy using subcutaneous and sublingual administrations

[00202] SCIT therapy: Allergy shots will be given in multiple dilutions (usually five bottles) which will be built up slowly over 8 to 10 months. They will be given once a week and after 8 months the patient will be switched to every other week and eventually every three to four weeks.

[00203] SLIT: diluted solutions from the allergy extracts will be created for allergy shots. The dilution will be made into 2 bottles with droppers. One less concentrated and one more concentrated.

[00204] Allergens (*e.g.*, pollen peptides) encapsulated in the liposome preparation for SCIT and SLIT will be given once a week. Therapy will follow similar dosing regimens as conventional allergy shots. The liposome preparation will be similar to the procedures used in Example 1. In addition, comparison studies will be performed evaluated delivering single allergen versus multiple allergen therapy at one time with the delivery system.

SCIT	Conventional Treatment	Delivery system given with encapsulated with a single pollen peptide	Delivery system encapsulated with several pollen/allergen peptides given at the same time

SLIT	Convention al Treatment	Delivery system given with encapsulated with a single pollen peptide	Delivery system encapsulated with several encapsulated pollen/allergen peptides given at the same time

[00205] Bloodwork evaluating total IgE, skin testing to allergens, and IgG subclass will be monitored as markers to evaluate the response for therapy. SLIT therapy protocols will be comparable to conventional therapy such as allowing the patient to take the doses at home.

Example 14 – Treating tuberculosis

[00206] Four groups of experiments will be compared to evaluation the safety and efficacy of the pharmaceutical formulation in treating TB: untreated, placebo group, pH sensitive formulation (with Isoniazid, Gangamycin, or Streptomycin), and pH resistance formulation (with Isoniazid, Gangamycin, or Streptomycin).

Untreated group	Placebo control to receive solution of similar volume once a week	pH sensitive formulation with Isoniazid given orally once a week	pH resistant formulation with Isoniazid given orally once a week
Untreated group	Placebo control to receive solution of similar volume once a week	pH sensitive formulation with Gangamycin given orally once a week	pH resistant formulation with Gangamycin given orally once a week
Untreated group	Placebo control to receive solution of similar volume once a week	pH sensitive formulation with Streptomycin given orally once a week	pH resistant formulation with Streptomycin given orally once a week

[00207] The liposome preparation will be similar to the procedures used in Example 1. Dosage will administer per the standard dosing protocol for that particular drug. The drug will be encapsulated in the liposome carrier to be dosed once a week for a period of 6 weeks. Symptom scores will be recorded. Patients will be followed once a week to monitor them for urine and blood tests as well as examination.

[00208] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1. A method for treating eosinophilic esophagitis (EoE), comprising: administering to a subject in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of at least one agent suitable for treating eosinophilic esophagitis, wherein the at least one agent is encapsulated in a liposome carrier.

2. The method of claim 1, wherein the liposome carrier comprises phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), or any combination or derivative thereof.

3. The method of claim 1 or 2, wherein the liposome carrier is a sterically stabilized liposome carrier.

4. The method of claim 3, wherein the sterically stabilized liposome carrier comprises poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE), PEG-dipalmitoylphosphatidylethanolamine (DPPE), PEG-di-C:15 PE, PEG-soy PE, or PEG-egg PE.

5. The method of any one of claims 1-4, wherein the administering is performed subcutaneously, sublingually, intranasally, or orally.

6. The method of any one of claims 1-5, wherein the at least one agent comprises a proton-pump inhibitor (PPI), a corticosteroid, or any combination, or derivative thereof.

7. The method of claim 6, wherein the proton-pump inhibitor comprises omeprazole, lansoprazole, dexlansoprazole, esomeprazole, pantoprazole, rabeprazole, ilaprazole, or any combination, or derivative thereof.

8. The method of claim 6, wherein the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

9. A method for inducing tolerance to an allergen in a subject in need thereof, comprising: administering to the subject, a pharmaceutical composition comprising a therapeutically effective amount of at least one agent suitable for treating an allergy, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

10. The method of claim 9, wherein the allergen is a food allergen.

11. The method of any one of claims 1-10, wherein said administering to the subject is performed less than about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 times per week.

12. The method of any one of claims 1-11, wherein the pharmaceutical composition is administered to the subject about once per week.

13. The method of any one of claims 1-12, wherein the administering the pharmaceutical composition is performed orally, sublingually, buccally, by inhalation, or subcutaneously.

14. The method of any one of claims 1-13, wherein the pharmaceutical composition is provided as a lyophile.

15. The method of claim 14, wherein said lyophile is deposited on a filter paper.

16. The method of claim 14 or 15, wherein the lyophile is reconstituted prior to administering.

17. The method of claim 16, wherein the lyophile is reconstituted with an aqueous diluent.

18. The method of claim 17, wherein said aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

19. The method of any of claims 1-18, wherein said pharmaceutical composition further comprises a sugar.

20. The method of claim 19, wherein said sugar is selected from the group consisting of trehalose, glucose, sucrose, maltose, galactose, fructose, and arabinose.

21. The method of any one of claims 1-20, wherein the at least one agent comprises an allergen.

22. The method of claim 21, wherein the allergen is selected from the group consisting of proteins, plant products and animal products.

23. The method of claim 21 or 22, wherein the allergen is a protein.

24. The method of any one of claims 21-23, wherein the allergen is selected from the group consisting of whole peanut, peanut powder, peanut butter, derivatives and combinations thereof.

25. The method of any one of claims 21-24, wherein the allergen is derived from peanut, tree nut, egg, shellfish, soy, milk, gluten, or any combination thereof.

26. The method of any one of claims 21-25, wherein the allergen comprises a grass pollen allergen, a weed pollen allergen, an indoor allergen, a mold allergen, a tree pollen allergen, a stinging insect allergen, a food allergen, or any combination or derivative thereof.

27. The method of any one of claims 1-26, wherein the at least one agent comprises an allergy medication.

28. The method of claim 27, wherein the allergy medication comprises an antihistamine, a corticosteroid, a bronchodilator, a mast cell stabilizer, a leukotriene inhibitor, an anti-tuberculosis agent, a serine lung protease inhibitor, or any combination or derivative thereof.

29. The method of claim 28, wherein the antihistamine comprises a H_1-antihistamine, H_2-antihistamine, H_3-antihistamine, H_4-antihistamine, or any combination thereof.

30. The method of claim 29, wherein the H_1-antihistamine comprises acrivastine, azelastine, bilastine, brompheniramine, buclizine, bromodiphenhydramine, carbinoxamine, chlorpromazine, cyclizine, chlorphenamine, chlorodiphenhydramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, dimenhydrinate, dimetindene, diphenhydramine, doxylamine, ebastine, embramine, fexofenadine, hydroxyzine, loratadine, meclozine, mirtazapine, olopatadine, orphenadrine, phenindamine, pheniramine, phenyltoloxamine, promethazine, quetiapine, rupatadine, tripelennamine, triprolidine, or any combination, or derivative thereof.

31. The method of claim 28, wherein the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

32. The method of claim 28, wherein the bronchodilator comprises terbutaline, albuterol, ipatropium, pirbuterol, epinephrine, salmeterol, levalbuterol, formoterol, or any combination thereof.

33. The method of claim 28, wherein the mast cell stabilizer comprises cromoglicic acid.

34. The method of claim 28, wherein the leukotriene inhibitor comprises montelukast, zafirlukast, zileuton, or any combination or derivative thereof.

35. The method of claim 28, wherein the anti-tuberculosis agent comprises isoniazid, ethambutol, pyrazinamide, rifamycin, rifampin, rifabutine, linezolid, streptomycin, clarithromycin, amikacin, kanamycin, gentamicin, capreomycin, viomycin, enviomycin, ciprofloxacin, levofloxacin, moxifloxacin, ethionamide, prothionamide, cycloserine, terizidone, or any combination, or derivative thereof.

36. The method of any one of claims 1-35, wherein the pharmaceutical composition is substantially devoid of cholesterol.

37. The method of any one of claims 1-36, wherein the at least one agent comprises azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

38. A pharmaceutical composition comprising: a therapeutically effective amount of at least one agent for treating an allergy in a subject in need thereof, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof, and wherein said pharmaceutical composition is formulated for oral administration to said subject.

39. A pharmaceutical composition comprising: a therapeutically effective amount of at least one agent for treating an allergy in a subject in need thereof, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof, and wherein said composition is formulated for subcutaneous administration to said subject.

40. The pharmaceutical composition of claim 38 or 39, wherein said composition comprises a lyophile.

41. The pharmaceutical composition of claim 40, wherein said lyophile is deposited on a filter paper.

42. The pharmaceutical composition of claim 40, wherein the lyophile is reconstituted prior to administration.

43. The pharmaceutical composition of claim 42, wherein the lyophile is reconstituted with an aqueous diluent.

44. The pharmaceutical composition of claim 43, wherein said aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

45. The pharmaceutical composition of any of claims 38-44, further comprising a sugar.

46. The pharmaceutical composition of claim 45, wherein said sugar is selected from the group consisting of trehalose, glucose, sucrose, maltose, galactose, fructose, and arabinose.

47. The pharmaceutical composition of any of claims 38-46, wherein the at least one agent comprises an allergen.

48. The pharmaceutical composition of claim 47, wherein the allergen is selected from the group consisting of food proteins, plant products and animal products.

49. The pharmaceutical composition of claim 47 or 48, wherein the allergen is a protein selected from the group consisting of peanut protein and tree nut protein.

50. The pharmaceutical composition of any of claims 47-49, wherein the allergen is selected from the group consisting of whole peanut, peanut powder, peanut butter, derivatives and combinations thereof.

51. The pharmaceutical composition of any of claims 47-50, wherein the allergen is selected from the group consisting of peanut, tree nut, egg, shellfish, soy, milk, gluten, and derivatives and combinations thereof.

52. The pharmaceutical composition of any of claims 47-51, wherein the allergen is selected from the group consisting of indoor allergen, mold allergen, stinging insect allergen, food allergen, derivatives and combinations thereof.

53. The pharmaceutical composition of any one of claims 38-52, wherein the composition further comprises cholesterol.

54. The pharmaceutical composition of any one of claims 38-53, wherein the at least one agent comprises an allergy medication selected from the group consisting of an antihistamine, a corticosteroid, a bronchodilator, a mast cell stabilizer, a leukotriene inhibitor, an anti-tuberculosis agent, an antibacterial agent, a serine lung protease inhibitor, and any combination and derivative thereof.

55. The pharmaceutical composition of claim 54, wherein the antihistamine comprises a H_1-antihistamine, H_2-antihistamine, H_3-antihistamine, H_4-antihistamine, or any combination thereof.

56. The pharmaceutical composition of claim 55, wherein the H_1-antihistamine comprises acrivastine, azelastine, bilastine, brompheniramine, buclizine, bromodiphenhydramine, carbinoxamine, chlorpromazine, cyclizine, chlorphenamine, chlorodiphenhydramine, clemastine, cyproheptadine, dexbrompheniramine, dexchlorpheniramine, dimenhydrinate, dimetindene, diphenhydramine, doxylamine, ebastine, embramine, fexofenadine, hydroxyzine, loratadine, meclozine, mirtazapine, olopatadine, orphenadrine, phenindamine, pheniramine, phenyltoloxamine, promethazine, quetiapine, rupatadine, tripelennamine, triprolidine, or any combination or derivative thereof.

57. The pharmaceutical composition of claim 54, wherein the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

58. The pharmaceutical composition of claim 54, wherein the bronchodilator comprises terbutaline, albuterol, ipatropium, pirbuterol, epinephrine, salmeterol, levalbuterol, formoterol, or any combination or derivative thereof.

59. The pharmaceutical composition of claim 54, wherein the mast cell stabilizer comprises cromoglicic acid.

60. The pharmaceutical composition of claim 54, wherein the leukotriene inhibitor comprises montelukast, zafirlukast, zileuton, or any combination or derivative thereof.

61. The pharmaceutical composition of claim 54, wherein the anti-tuberculosis agent comprises isoniazid, ethambutol, pyrazinamide, rifamycin, rifampin, rifabutine, linezolid, streptomycin, clarithromycin, amikacin, kanamycin, gentamicin, capreomycin, viomycin, enviomycin, ciprofloxacin, levofloxacin, moxifloxacin, ethionamide, prothionamide, cycloserine, terizidone, or any combination or derivative thereof.

62. The pharmaceutical composition of any of claims 38-61, wherein the composition is substantially devoid of cholesterol.

63. A pharmaceutical composition, comprising: a therapeutically effective amount of at least one agent suitable for treating eosinophilic esophagitis (EoE) in a subject in need thereof, wherein the at least one agent is encapsulated in a liposome carrier.

64. The pharmaceutical composition of claim 63, wherein the liposome carrier comprises phosphatidylglycerol (PG), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI), or any combination or derivative thereof.

65. The pharmaceutical composition of claim 63 or 64, wherein the liposome carrier is a sterically stabilized liposome carrier.

66. The pharmaceutical composition of claim 65, wherein the sterically stabilized liposome carrier comprises poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE), PEG-dipalmitoylphosphatidylethanolamine (DPPE), PEG-di-C:15 PE, PEG-soy PE, or PEG-egg PE.

67. The pharmaceutical composition of any one of claims 63-66, wherein said composition comprises a lyophile.

68. The pharmaceutical composition of claim 67, wherein said lyophile is deposited on a filter paper.

69. The pharmaceutical composition of claim 67, wherein the lyophile is reconstituted prior to administration.

70. The pharmaceutical composition of claim 69, wherein the lyophile is reconstituted with an aqueous diluent.

71. The pharmaceutical composition of claim 70, wherein said aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

72. The pharmaceutical composition of any of claims 63-71, wherein the pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration.

73. The pharmaceutical composition of any of claims 63-72, wherein the at least one agent comprises a proton-pump inhibitor (PPI), a corticosteroid, or any combination or derivative thereof.

74. The pharmaceutical composition of claim 73, wherein the proton-pump inhibitor comprises omeprazole, lansoprazole, dexlansoprazole, esomeprazole, pantoprazole, rabeprazole, ilaprazole, or any combination or derivative thereof.

75. The pharmaceutical composition of claim 73, wherein the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination or derivative thereof.

76. The pharmaceutical composition of any of claims 63-75, wherein the at least one agent comprises azelastine, theophylline, amikacin, gentamicin, tobramycin, rifabutin, rifapentine, sparfioxacin, ciprofloxacin, quinolones, azithromycin, erythromycin, or any combination or derivative thereof.

77. A pharmaceutical composition, comprising: a therapeutically effective amount of at least one agent suitable for treating tuberculosis, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

78. The pharmaceutical composition of claim 77, wherein said composition comprises a lyophile.

79. The pharmaceutical composition of claim 78, wherein said lyophile is deposited on a filter paper.

80. The pharmaceutical composition of claim 78 or 79, wherein the lyophile is reconstituted prior to administration.

81. The pharmaceutical composition of claim 80, wherein the lyophile is reconstituted with an aqueous diluent.

82. The pharmaceutical composition of claim 81, wherein said aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

83. The pharmaceutical composition of any one of claims 77-82, wherein the pharmaceutical composition is suitable for subcutaneous, sublingual, or oral administration.

84. The pharmaceutical composition of any one of claims 77-83, wherein the at least one agent comprises isoniazid, rifampin, gangamycin, pyrazinamide, ethambutol, rifabutin, kanamycin, amikacin, capreomycin, streptomycin, levofloxacin, levofloxacin, ofloxacin, para–aminosalicylic acid, cycloserine, terizidone, ethionamide, protionamide, clofazimine, linezolid, amoxicillin/clavulanate, thioacetazone, imipenem/cilastatin, high dose isoniazid, clarithromycin, or any combination or derivative thereof.

85. The pharmaceutical composition of any one of claims 38-84, wherein the at least one agent comprises an antibody, derivative or fragment thereof.

86. The pharmaceutical composition of claim 85, wherein the antibody is an anti-IgE antibody.

87. The pharmaceutical composition of any one of claims 38-86, wherein the at least one agent comprises a monophosphoryl lipid A (MPL).

88. The pharmaceutical composition of any one of claims 38-87, wherein upon administration, the at least one agent is released from the liposome carrier in a pH sensitive manner.

89. The pharmaceutical composition of any one of claims 38-87, wherein upon administration, the at least one agent is released from the liposome carrier in a pH independent manner.

90. The pharmaceutical composition of any one of claims 38-89, wherein said sterically stabilized liposome carrier comprises a membrane portion, and wherein at least about 50%, about 60%, about 70% or about 75% of the at least one agent is displaced within the membrane portion of the liposome carrier at the time of said administration.

91. The pharmaceutical composition of any one of claims 38-90, wherein said sterically stabilized liposome carrier comprises an internal portion encompassed by a membrane portion, and wherein at least about 25%, about 50%, about 60%, about 75%, or about 80% of the at least one agent is in the internal portion of the liposome carrier.

92. The pharmaceutical composition of any one of claims 38-91,comprising at least about 60% phosphatidylglycerol, at least about 60% phosphatidylcholine, or at least about 60% combination of phosphatidylglycerol and phosphatidylcholine.

93. The pharmaceutical composition of any one of claims 38-92, wherein the pharmaceutical composition contains about 60% to about 99% phosphatidylcholine, phosphatidylglycerol, or combination thereof.

94. The pharmaceutical composition of any one of claims 38-93, wherein the pharmaceutical composition contains about 1% to about 5% PEG-DSPE.

95. The pharmaceutical composition of any one of claims 38-94, wherein the pharmaceutical composition contains about 1% to about 33% of the at least one agent.

96. The pharmaceutical composition of any one of claims 38-95, wherein the sterically stabilized liposome carrier is stable at about pH 3 to about pH 7 or at about pH 7 to about pH 10.

97. The pharmaceutical composition of any one of claims 38-96, wherein the sterically stabilized liposome carrier has a gel-liquid crystalline phase transition temperature in a range from about -20°C to about 44°C.

98. A kit, comprising the pharmaceutical composition of any one of claims 38-97.

99. The kit of claim 98, further comprising instructions for use of the pharmaceutical composition.

100. A method for treating a subject in need thereof, comprising: administering the pharmaceutical composition of any one of claims 38-97 to the subject.

101. The method of claim 100, wherein the administering the pharmaceutical composition is performed subcutaneously, sublingually, or orally.

102. The method of claim 100 or 101, wherein the subject has a non-asthmatic allergy.

103. The method of any one of claims 100-102, wherein the subject has a food allergy.

104. The method of any one of claims 100-103, wherein the subject has eosinophilic esophagitis.

105. The method of any one of claims 100-104, wherein the pharmaceutical composition is administered to the subject less than about 7 times per week.

106. The method of any one of claims 100-105, wherein the pharmaceutical composition is administered to the subject about once per week.

107. A method for treating tuberculosis, comprising: administering to a subject in need thereof, a pharmaceutical composition comprising a therapeutically effective amount of at least one agent suitable for treating tuberculosis, wherein the at least one agent is encapsulated in a sterically stabilized liposome carrier comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

108. The method of any one of claims 100-107, wherein said composition comprises a lyophile.

109. The method of claim 108, wherein said lyophile is deposited on a filter paper.

110. The method of claim 108, wherein the lyophile is reconstituted prior to administration.

111. The method of claim 110, wherein the lyophile is reconstituted with an aqueous diluent.

112. The method of claim 111, wherein said aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

113. The method of any one of claims 107-112, wherein the administering the pharmaceutical composition is performed subcutaneously, sublingually, or orally.

114. The method of any one of claims 107-113, wherein the at least one agent comprises isoniazid, rifampin, gangamycin, pyrazinamide, ethambutol, rifabutin, kanamycin, amikacin, capreomycin, streptomycin, levofloxacin, levofloxacin, ofloxacin, para–aminosalicylic acid, cycloserine, terizidone, ethionamide, protionamide, clofazimine, linezolid, amoxicillin/clavulanate, thioacetazone, imipenem/cilastatin, high dose isoniazid, clarithromycin, or any combination or derivative thereof.

115. The method of any one of claims 100-114, wherein the at least one agent comprises an antibody, derivative or fragment thereof.

116. The method of claim 115, wherein the antibody is an anti-IgE antibody.

117. The method of any one of claims 100-116, wherein the at least one agent comprises a monophosphoryl lipid A (MPL).

118. The method of any one of claims 100-117, wherein the pharmaceutical composition is in powder, liquid, tablet, or capsule form.

119. The method of any one of claims 100-118, wherein the pharmaceutical composition is suspended in a solvent before administration.

120. The method of any one of claims 100-119, wherein at least about 75% of the at least one agent is in a membrane portion of the liposome carrier.

121. The method of any one of claims 100-120, wherein at least about 75% of the at least one agent is in an internal portion of the liposome carrier.

122. The method of any one of claims 100-121, wherein the pharmaceutical composition contains at least about 60% phosphatidylglycerol, phosphatidylcholine, or a combination thereof.

123. The method of any one of claims 100-122, wherein the pharmaceutical composition contains about 60% to about 99% phosphatidylglycerol, phosphatidylcholine, or a combination thereof.

124. The method of any one of claims 100-123, wherein the pharmaceutical composition contains at least about 1% PEG-DSPE.

125. The method of any one of claims 100-124, wherein the pharmaceutical composition contains about 1% to about 5% PEG-DSPE.

126. The method of any one of claims 100-125, wherein the pharmaceutical composition comprises at least about 1% of the at least one agent.

127. The method of any one of claims 100-126, wherein the pharmaceutical composition contains about 1% to about 33% of the at least one agent.

128. The method of any one of claims 100-127, wherein the sterically stabilized liposome carrier is stable at about pH 7 to about pH 10.

129. The method of any one of claims 100-128, wherein the sterically stabilized liposome carrier is stable at about pH 3 to about 7.

130. The method of any one of claims 100-129, wherein the sterically stabilized liposome carrier has a gel-liquid crystalline phase transition temperature in a range from about -20°C to about 44°C.

131. The method of any one of claims 100-130, wherein the pharmaceutical composition is administered to the subject less than about 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13 or 14 times per week.

132. The method of any one of claims 100-131, wherein the pharmaceutical composition is administered to the subject about once per week.

133. A method for treating inflammation in a subject in need thereof, comprising: administering subcutaneously, sublingually, or orally to said subject, an effective amount of a pharmaceutical composition comprising a sterically stabilized liposome comprising: i) poly (ethylene glycol) distearoylphosphatidylethanolamine (PEG-DSPE); and ii) at least one of phosphatidylglycerol, phosphatidylcholine, or any combination or derivative thereof.

134. The method of claim 133, wherein said composition comprises a lyophile.

135. The method of claim 134, wherein said lyophile is deposited on a filter paper.

136. The method of claim 134 or 135, wherein the lyophile is reconstituted prior to administration.

137. The method of any claim 136, wherein the lyophile is reconstituted with an aqueous diluent.

138. The method of claim 137, wherein said aqueous diluent is selected from the group consisting of: distilled water, deionized water; sterile water; bacteriostatic water; and normal saline.

139. The method of any one of claims 133-138, wherein the inflammation is associated with an allergy or a disease.

140. The method of any one of claims 133-139, wherein the sterically stabilized liposome carrier is stable at about pH 7 to about 10.

141. The method of any one of claims 133-140, wherein the sterically stabilized liposome carrier is stable at about pH 3 to about 7.

142. The method of any one of claims 133-141, wherein the sterically stabilized liposome carrier has a gel-liquid crystalline phase transition temperature in a range from -20°C to 44°C.

143. The method of any one of claims 133-142, wherein the pharmaceutical composition is administered to the subject less than about 7 times per week.

144. The method of any one of claims 133-143, wherein the pharmaceutical composition is administered to the subject about once or about two times per week.

145. The method of any one of claims 133-144, wherein the pharmaceutical composition further comprises a therapeutically effective amount of at least one agent suitable for treating said allergy or disease.

146. The method of claim 145, wherein the at least one agent is a corticosteroid.

147. The method of claim 146, wherein the corticosteroid comprises budesonide, flunisolide, triamcinolone, beclomethasone, fluticasone, mometasone, dexamethasone, hydrocortisone, methylprednisolone, prednisone, cortisone, betamethasone, or any combination thereof.

148. The method of any one of claims 145-147, wherein the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered concurrently.

149. The method of any one of claims 145-147, wherein the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered sequentially.

150. The method of claim 149, wherein the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered sequentially, and wherein the sterically stabilized liposome is administered first.

151. The method of claim 149, wherein the sterically stabilized liposome and the at least one agent suitable for treating said allergy or disease are administered sequentially, and wherein the at least one agent suitable for treating said allergy or disease is administered first.

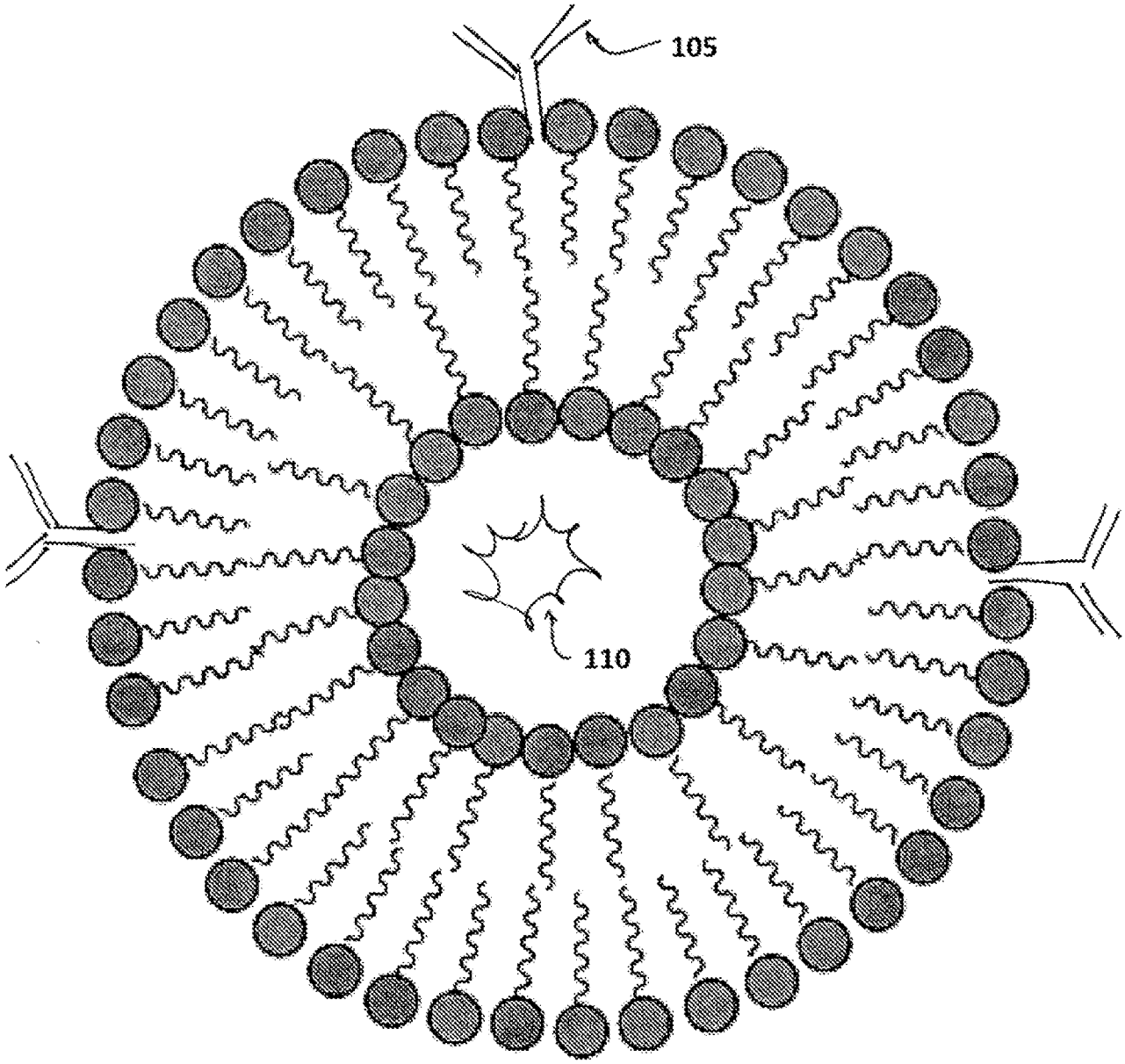


Figure 1

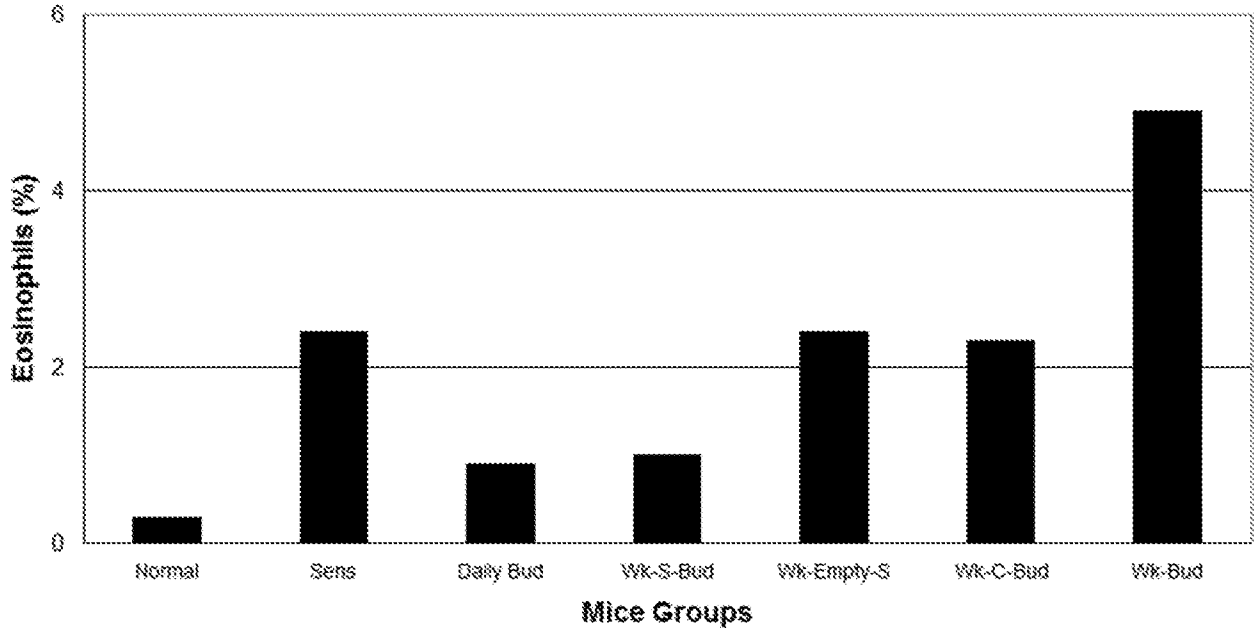

6
4
2
0
Eosinophils (%)
Normal
Sens
Daily Bud
Wk-S-Bud
Wk-Empty-S
Wk-C-Bud
Wk-Bud
Mice Groups

Figure 2

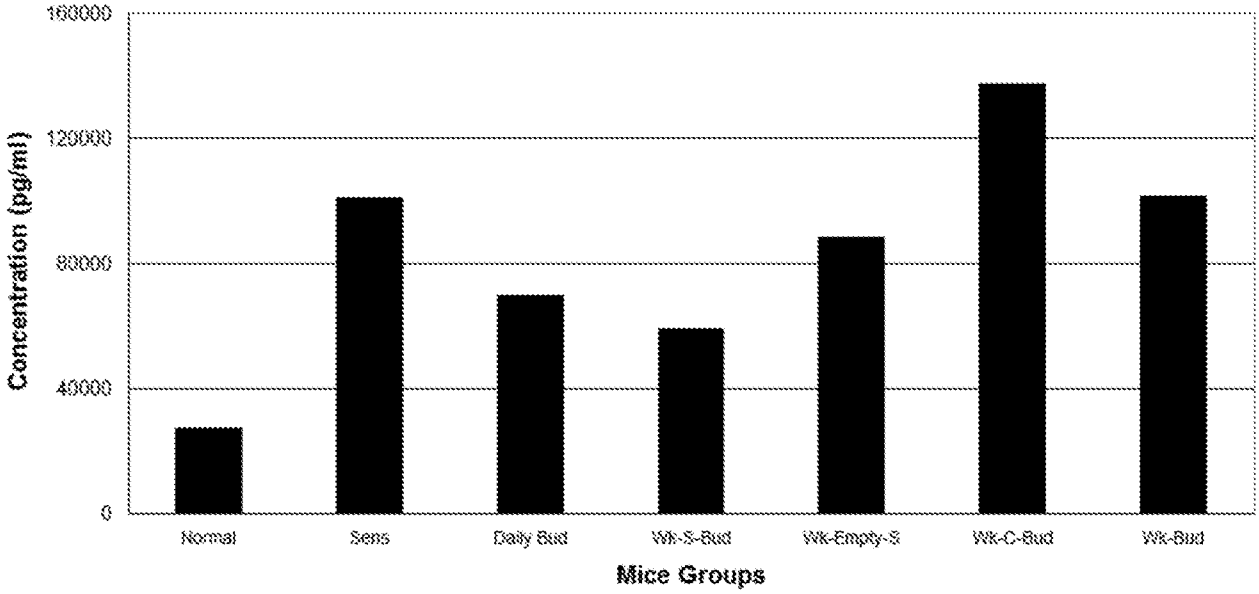

160000
120000
80000
40000
0
Concentration (pg/ml)
Normal
Sens
Daily Bud
Wk-S-Bud
Wk-Empty-S
Wk-C-Bud
Wk-Bud
Mice Groups

Figure 3

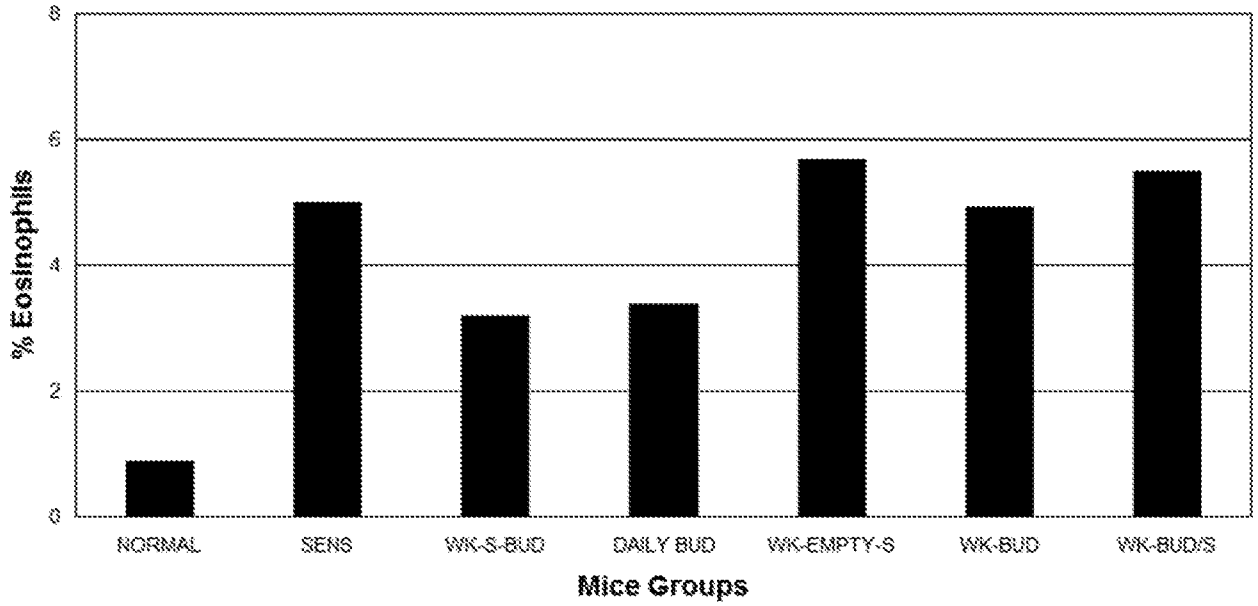

% Eosinophils
0
2
4
6
8
NORMAL
SENS
WK-S-BUD
DAILY BUD
WK-EMPTY-S
WK-BUD
WK-BUD/S
Mice Groups

Figure 4

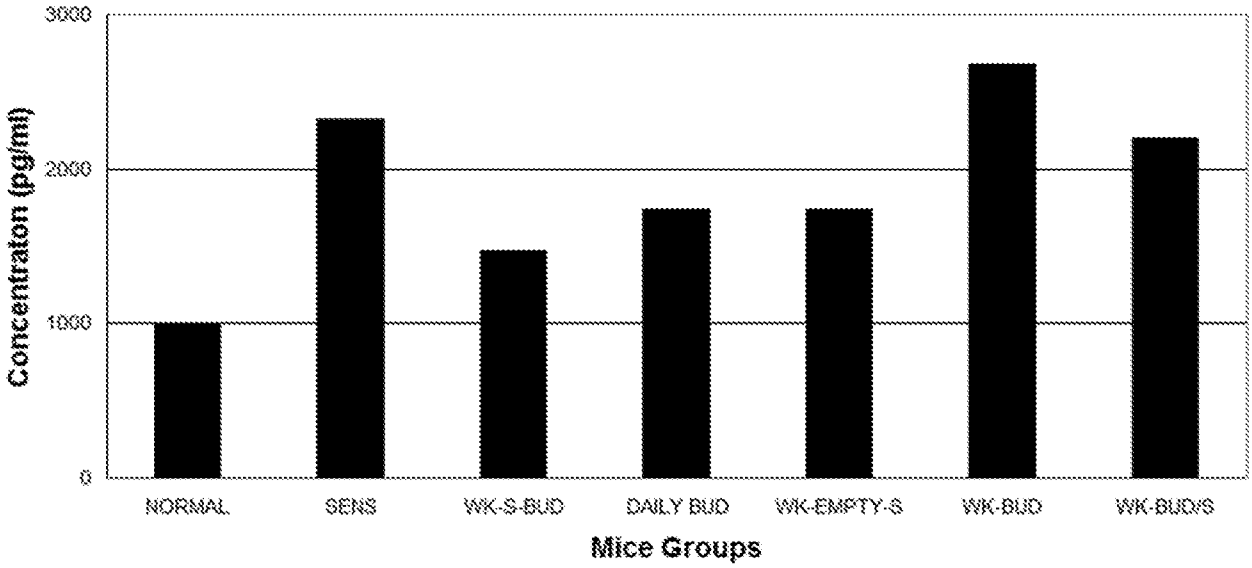

3000
2000
1000
0
Concentraton (pg/ml)
NORMAL
SENS
WK-S-BUD
DAILY BUD
WK-EMPTY-S
WK-BUD
WK-BUD/S
Mice Groups

Figure 5

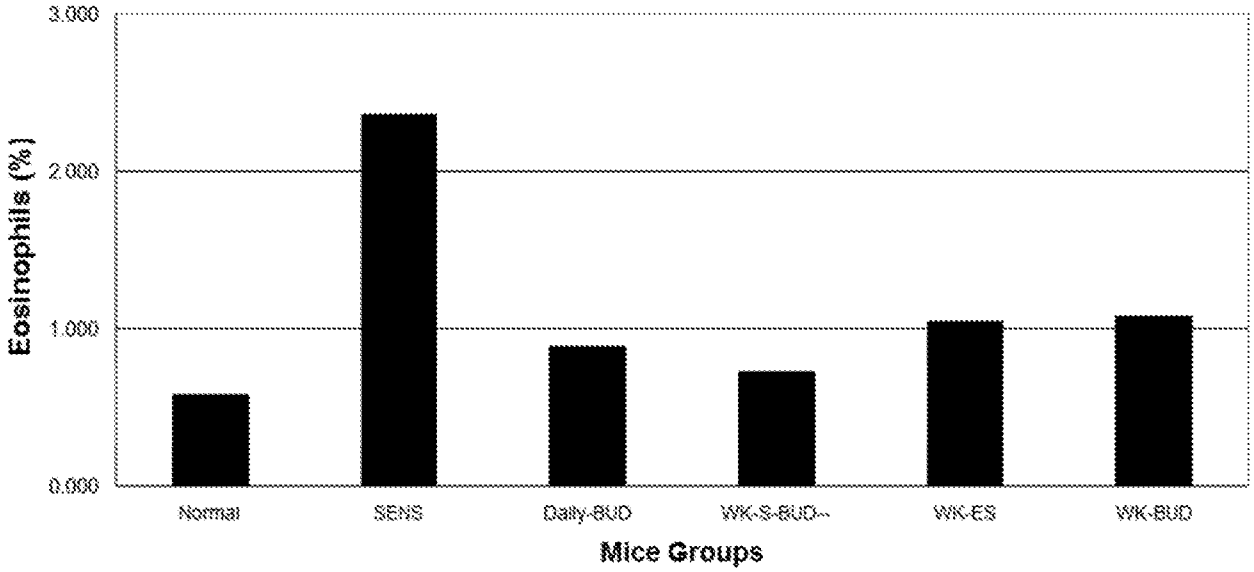

3.000
2.000
1.000
0.000
Eosinophils (%)
Normal
SENS
Daily-BUD
WK-S-BUD--
WK-ES
WK-BUD
Mice Groups

Figure 6

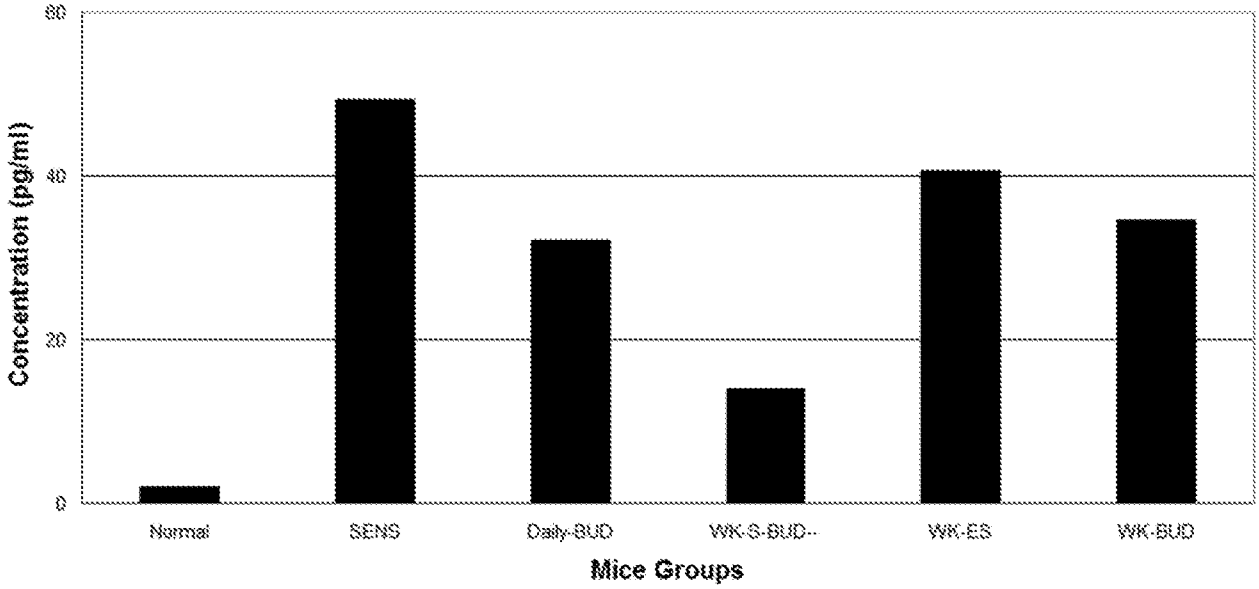

60
40
20
0
Concentration (pg/ml)
Normal
SENS
Daily-BUD
WK-S-BUD--
WK-ES
WK-BUD
Mice Groups

Figure 7

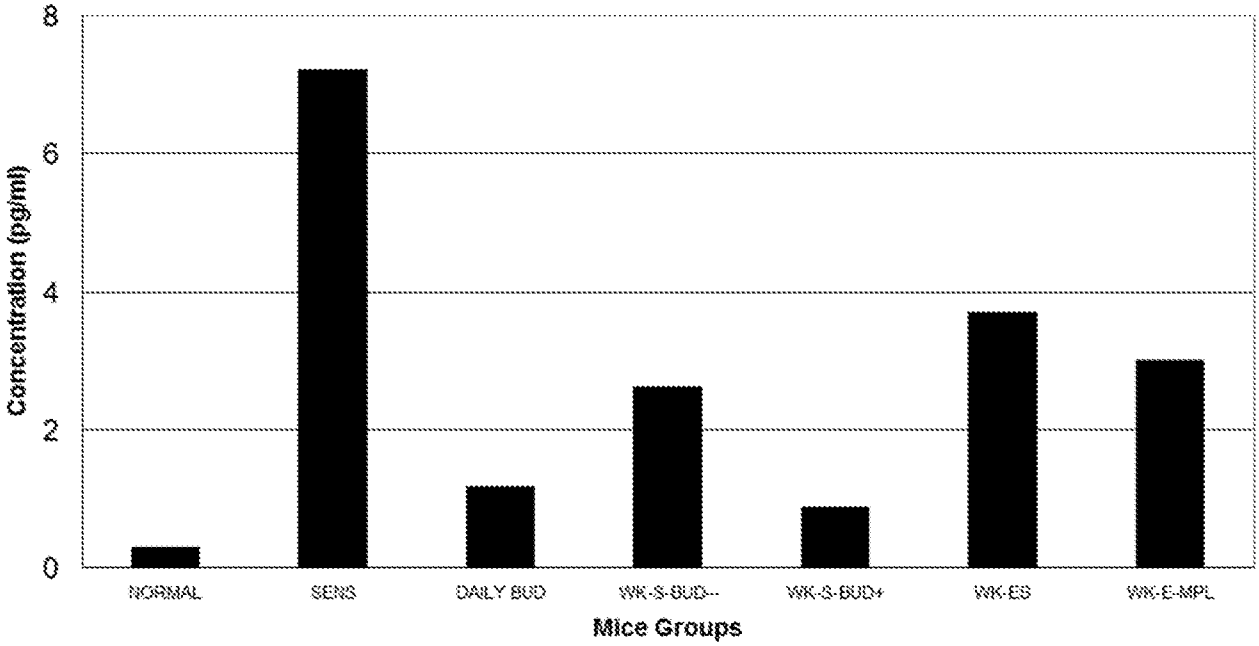

8
6
4
2
0
Concentration (pg/ml)
NORMAL
SENS
DAILY BUD
WK-S-BUD--
WK-S-BUD+
WK-ES
WK-E-MPL
Mice Groups

Figure 8

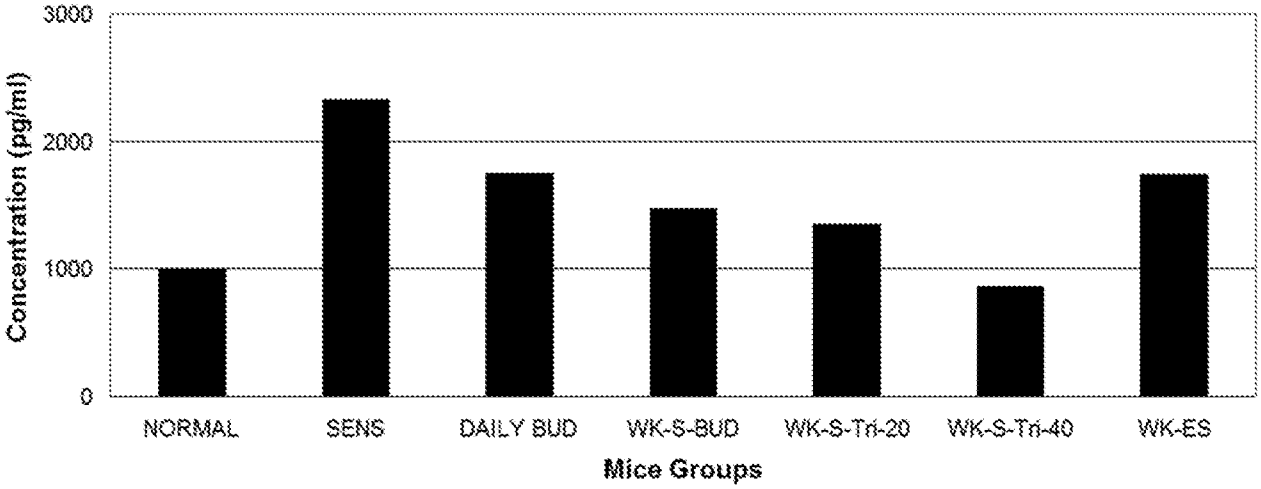

3000
2000
1000
0
Concentration (pg/ml)
NORMAL
SENS
DAILY BUD
WK-S-BUD
WK-S-Tri-20
WK-S-Tri-40
WK-ES
Mice Groups

Figure 9

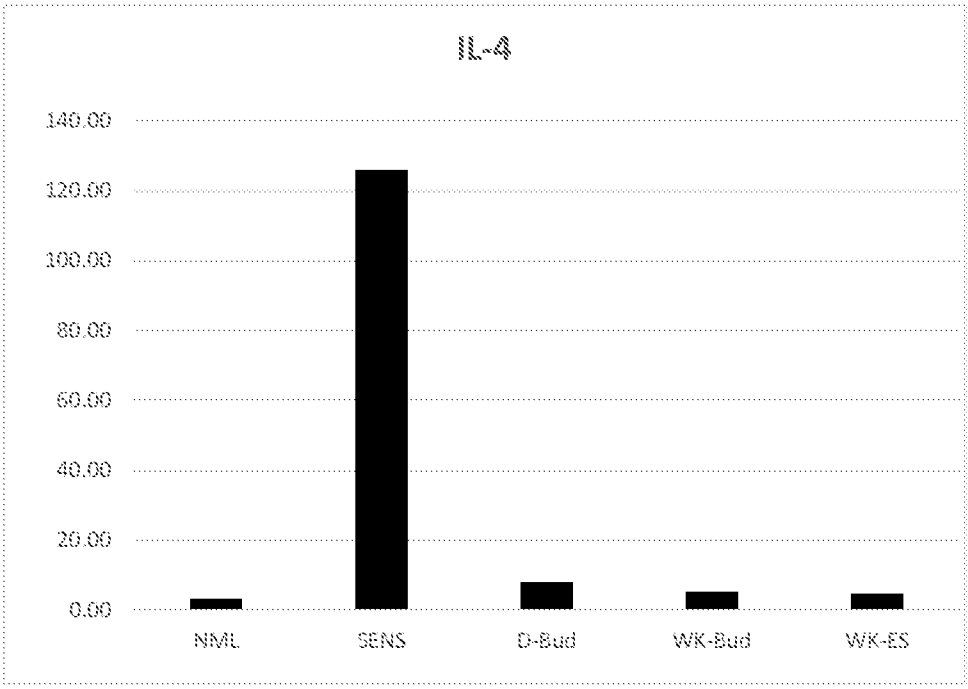

IL-4
140.00
120.00
100.00
80.00
60.00
40.00
20.00
0.00
NML
SENS
D-Bud
WK-Bud
WK-ES

Figure 10

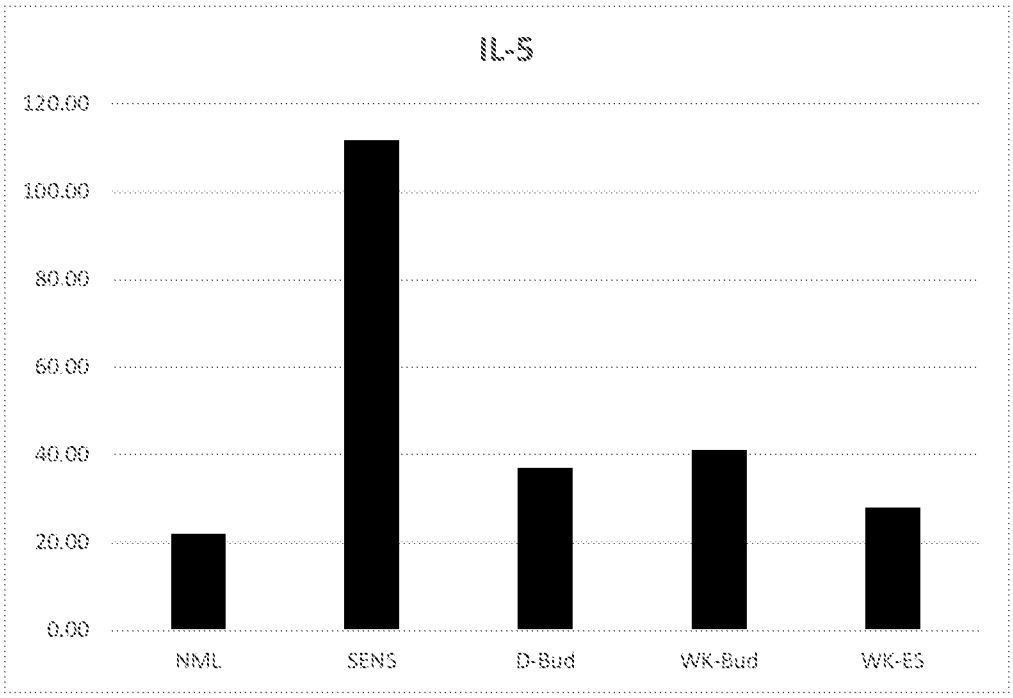

IL-5
120.00
100.00
80.00
60.00
40.00
20.00
0.00
NML
SENS
D-Bud
WK-Bud
WK-ES

Figure 11

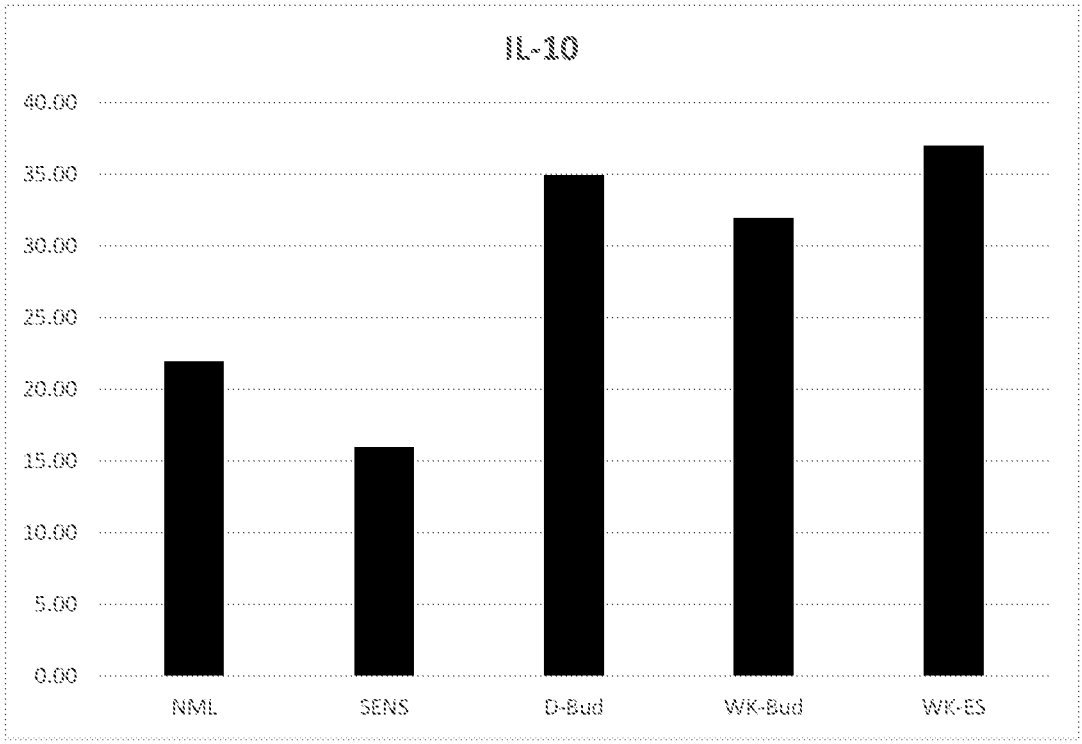

IL-10
40.00
35.00
30.00
25.00
20.00
15.00
10.00
5.00
0.00
NML
SENS
D-Bud
WK-Bud
WK-ES

Figure 12

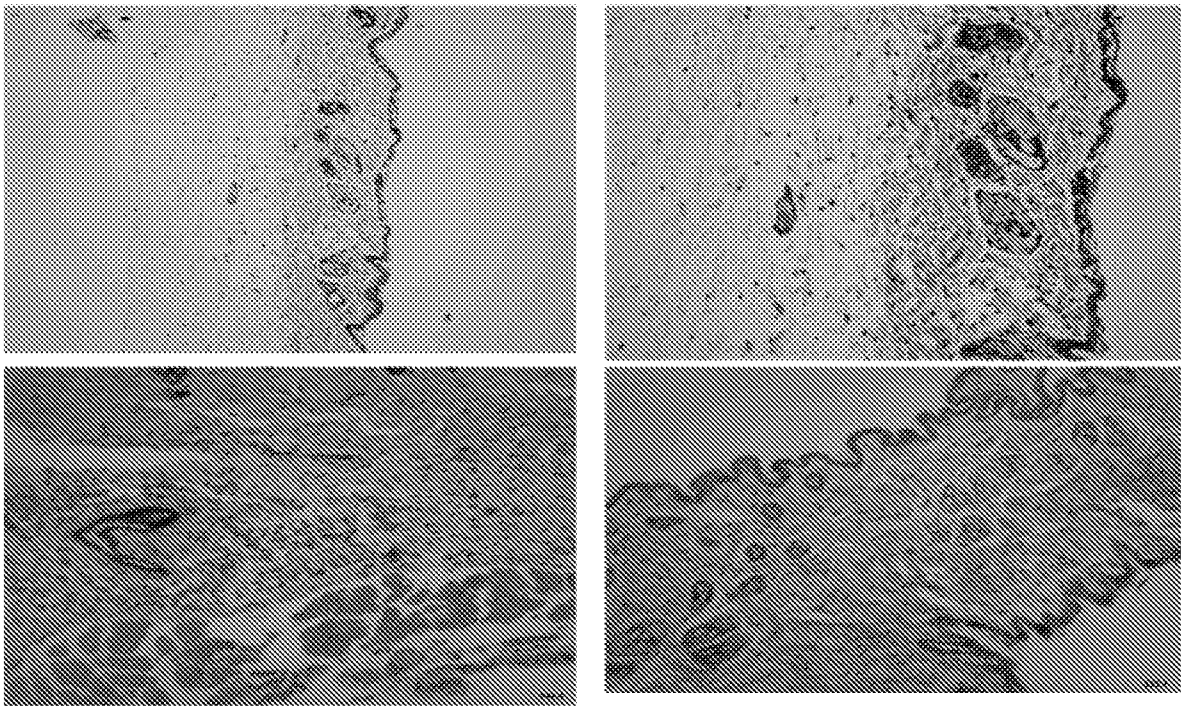


Figure 13

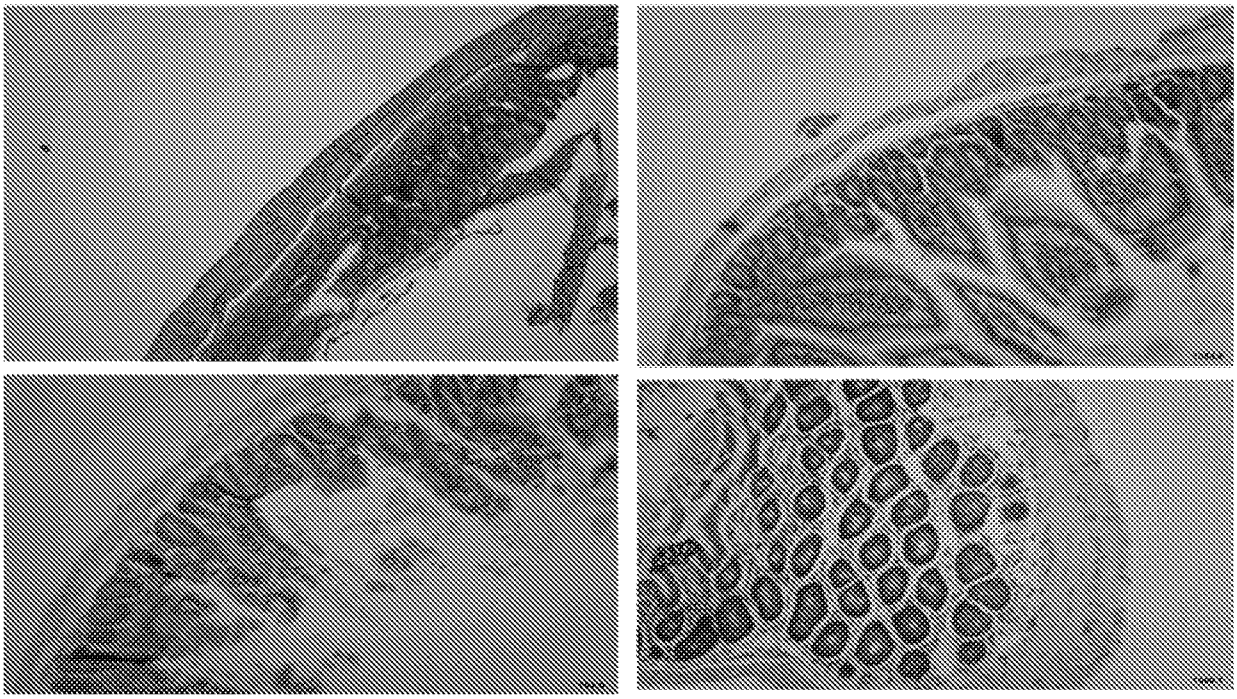


Figure 14

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/051759

A. CLASSIFICATION OF SUBJECT MATTER

A61K 9/127 (2006.01) A61K 47/30 (2006.01) A61K 31/573 (2006.01) A61P 37/00 (2006.01) A61P 11/00 (2006.01) A61P 37/08 (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

WPIAP, EPODOC, MEDLINE, CAPLUS & Keywords: sterically stabilised liposome, phosphatidylcholine, phosphatidylglycerol, PEG-DSPE, inflammation, allergy, eosinophillic eosophagitis, tuberculosis and like terms

PatentScope, PubMed: VGSK Technologies, Duzgunes, Konduri, Pattisapu

Applicant/inventor names searched in internal databases

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	

[X] Further documents are listed in the continuation of Box C

[X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 November 2016	30 November 2016
Name and mailing address of the ISA/AU	**Authorised officer**
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustralia.gov.au	Nathalie Tochon-Danguy AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. 0262833101

INTERNATIONAL SEARCH REPORT C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		International application No. **PCT/US2016/051759**
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2015/0071988 A1 (VGSK TECHNOLOGIES INC.) 12 March 2015 Abstract, [0031]-[0035], [0041], [0043], [0048]-[0052], [0058]-[0066], Examples, Figures 1-32, claims	1-148
A	US 6197333 B1 (ONYUKSEL H. et al.) 06 March 2001 Abstract, columns 8-10, 14 and 16, examples	1-151
A	GASPAR M.M. et al., " Rifabutin encapsulated in liposomes exhibits increased therapeutic activity in a model of disseminated tuberculosis", INTERNATIONAL JOURNAL OF ANTIMICROBIAL AGENTS, 2008, vol. 31, pages 37-45. whole document	1-151
A	ALMIÑANA N. et al., "Biodistribution Study of Doxorubicin Encapsulated in Liposomes: Influence of Peptide Coating and Lipid Composition", PREPARATIVE BIOCHEMISTRY & BIOTECHNOLOGY, 2004, vol. 34, no.1, pages 77-96. whole document	1-151
A	ICHIKAWA K. et al., "Suppression of immune response by antigen-modified liposomes encapsulating model agents: A novel strategy for the treatment of allergy", JOURNAL OF CONTROLLED RELEASE, 2013, vol. 167, pages 284-289. whole document	1-151
A	ZHU G. et al., "Secretory phospholipase A_2 responsive liposomes", JOURNAL OF PHARMACEUTICAL SCIENCES, 2011, vol. 100, no-8, pages 3146-3159. whole document	1-151
A	IMMORDINO M. L. et al., "Stealth liposomes: review of the basic science, rationale, and clinical applications, existing and potential", INTERNATIONAL JOURNAL OF NANOMEDICINE, 2006, vol. 1, no. 3, pages 297-315. whole document	1-151

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/US2016/051759**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
US 2015/0071988 A1	12 March 2015	US 2015071988 A1	12 Mar 2015
		US 8846079 B1	30 Sep 2014
		US 2006115523 A1	01 Jun 2006
		US 2006251711 A1	09 Nov 2006
		WO 2006060759 A2	08 Jun 2006
		WO 2006060759 B1	21 Feb 2008
US 6197333 B1	06 March 2001	US 6197333 B1	06 Mar 2001
		AU 733212 B2	10 May 2001
		AU 2426197 A	17 Oct 1997
		AU 2549297 A	17 Oct 1997
		AU 2002359511 A1	10 Jun 2003
		CA 2250219 A1	02 Oct 1997
		EP 0914094 A1	12 May 1999
		JP 2001521486 A	06 Nov 2001
		US 6348214 B1	19 Feb 2002
		US 2002114829 A1	22 Aug 2002
		WO 9735560 A1	02 Oct 1997
		WO 9735561 A1	02 Oct 1997
		WO 03046145 A2	05 Jun 2003

End of Annex

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.