COMPOSITIONS AND METHODS FOR TREATING ALLERGIC CONDITIONS

FIELD

[0001] The present disclosure relates generally to compositions and methods treating allergic condition with an adjuvant, optionally with one or more allergens.

BACKGROUND

[0002] The prevalence of allergic conditions, such as asthma, rhinitis, and rhinoconjunctivitis, has steadily increased over the past decades. Asthma has become the most common chronic disease among children and is one of the major causes of hospitalization among those younger than 15. European Environment and Health Information System, World Health Organization Fact Sheet No. 3.1, May 2007.

[0003] Many scientists also believe that the number of people with food allergies is rising, as is the number of foods to which they are allergic. One survey estimated that about 4% of the U.S. population are allergic to peanuts, tree nuts, fish or shellfish. EMBO Rep. 2006 November; 7(11): 1080–1083.

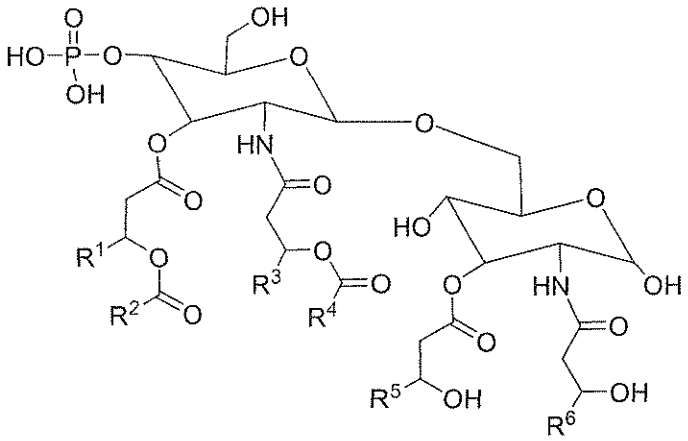
[0004] Symptoms of allergy are frequently caused by an Immunoglobulin E-mediated, type I hypersensitivity reaction. This type of response is mediated by Th2 cells and is an inappropriate immunological response to the allergen. Current treatment of allergic conditions is typically focused on avoiding the allergen, e.g. avoiding intake of food allergens, or treatment of the symptoms and sequelae, such as antihistamines or decongestants to treat rhinitis, or bronchodilators to treat airway constriction.

SUMMARY ~~OF THE INVENTION~~

~~In one aspect, t~~The present disclosure provides methods and compositions for treating allergic conditions, by non-parenteral administration of an effective amount of a composition comprising an adjuvant, such as GLA of formula I or Ia or Ib, or DSLP of Formula I or Ia, or a TLR4 agonist. In certain embodiments, the composition comprising an adjuvant, such as GLA of formula I or Ia or Ib, or DSLP of Formula I or Ia, or a TLR4 agonist, comprises an allergen. Thus, in certain embodiments, the present disclosure provides compositions comprising an adjuvant, such as GLA of formula I or Ia or Ib, or DSLP of Formula I or Ia, or

a TLR4 agonist in combination with an allergen. In another embodiment, the present disclosure provides compositions comprising an adjuvant, such as GLA of formula I or Ia or Ib, or DSLP of Formula I or Ia, or a TLR4 agonist in combination with an allergen for treating food allergies or seasonal allergies.

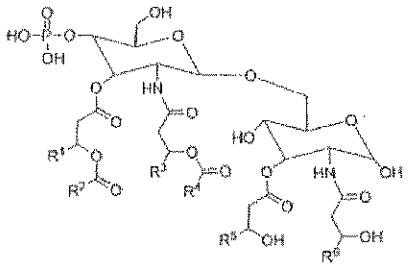
[0005] In any of the embodiments herein, the adjuvant is GLA of formula (Ia):



or a pharmaceutically acceptable salt thereof, where: R1, R3, R5 and R6 are C11-C20 alkyl; and R2 and R4 are C12-C20 alkyl; in a more specific embodiment, the GLA has the formula (Ia) set forth above wherein R1, R3, R5 and R6 are C11-14 alkyl; and R2 and R4 are C12-15 alkyl. In a further more specific embodiment, the GLA has the formula (Ia) set forth above wherein R1, R3, R5 and R6 are C11 alkyl, or undecyl; and R2 and R4 are C13 alkyl, or tridecyl. In yet a further specific embodiment, the GLA has the formula (Ia) set forth above wherein R1, R3, R5 and R6 are undecyl and R2 and R4 are tridecyl.

[0006] Exemplary amounts of GLA for dosing humans, including adult humans, include 0.1-10 μg, or 0.1-20 μg, or 1-20 μg or 0.2-5 μg, or 0.5-2.5 μg, or 0.5-8 μg or 0.5-15 μg per dose.

[0007a] In one aspect of the present disclosure, there is provided a composition comprising (a) GLA of the formula (Ia):



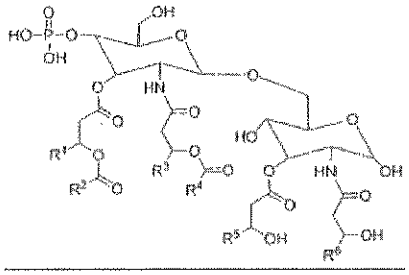
or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, for use in a method of treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months.

[0007b] In another aspect of the present disclosure, there is provided a composition comprising (a) GLA of the formula (Ia):



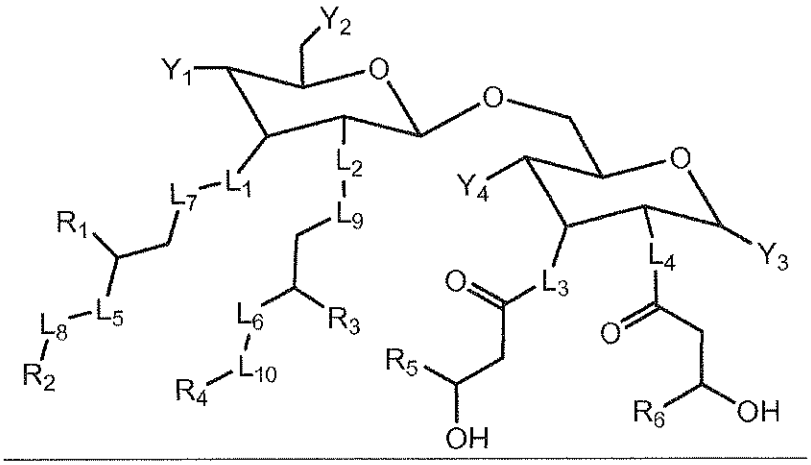
or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, for use in treating a mammal who suffers from an allergic condition, wherein at least two doses of an effective amount of a composition comprising GLA are administered, and wherein the time period between said two doses is at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months.

[0007c] In a further aspect of the present disclosure, there is provided a composition comprising (a) GLA of the formula (Ib):

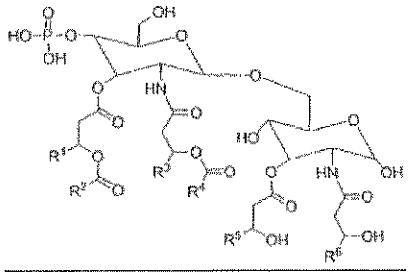


or a pharmaceutically acceptable salt thereof;

wherein: L1, L2, L3, L4, L5 and L6 are the same or different and are independently selected from O , NH , and (CH2) ; L7, L8, L9 and L10 are the same or different, and at any occurrence may be either absent or C(=O) ; Y1 is an acid functional group; Y2 and Y3 are the same or different and are each independently selected from OH, SH, and an acid functional group; Y4 is OH or SH; R1, R3, R5 and R6 are the same or different and are each independently selected from the group of C8-C13 alkyl; and R2 and R4 are the same or different and are each independently selected from the group of C6-C11 alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, for use in treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months.

[0007d] In another aspect of the present disclosure, there is provided a composition comprising (a) GLA of the formula (Ia):



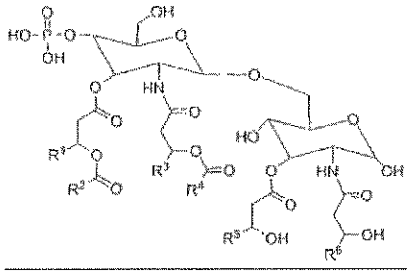
or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, for use in treating a mammal who suffers from an allergic condition, wherein an effective amount of a composition comprising GLA is administered by non-parenteral delivery, optionally wherein the composition is an aqueous formulation.

[0007e] In a further aspect of the present disclosure, there is provided a use of a composition comprising (a) GLA of the formula (Ia):



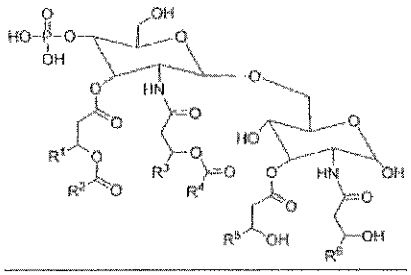
or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are to be administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months.

[0007f] In another aspect of the present disclosure, there is provided a use of a composition comprising (a) GLA of the formula (Ia):



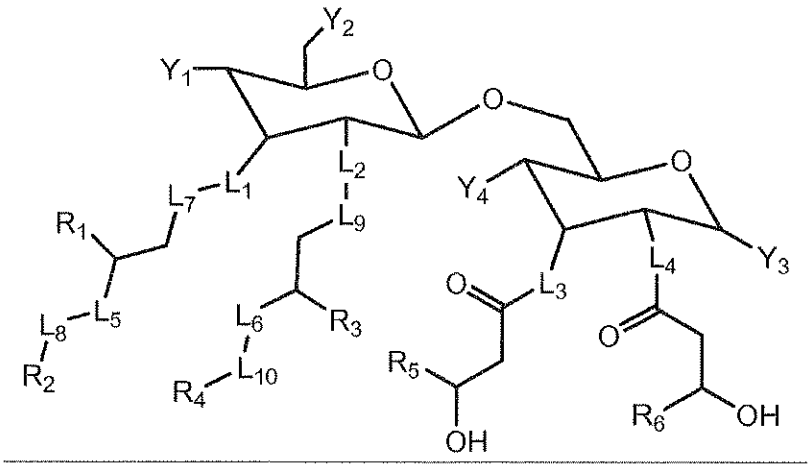
or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein at least two doses of an effective amount of a composition comprising GLA are to be administered, and wherein the time period between said two doses is at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months.

[0007g] In a further aspect of the present disclosure, there is provided a use of a composition comprising (a) GLA of the formula (Ib):



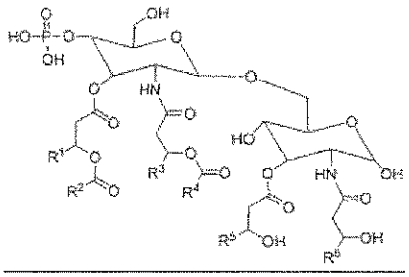
or a pharmaceutically acceptable salt thereof;

wherein: L1, L2, L3, L4, L5 and L6 are the same or different and are independently selected from O , NH , and (CH2) ; L7, L8, L9 and L10 are the same or different, and at any occurrence may be either absent or C(=O) ; Y1 is an acid functional group; Y2 and Y3 are the same or different and are each independently selected from OH, SH, and an acid functional group; Y4 is OH or SH; R1, R3, R5 and R6 are the same or different and are each independently selected from the group of C8-C13 alkyl; and R2 and R4 are the same or different and are each independently selected from the group of C6-C11 alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are to be administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a

maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months.

[0007h] In another aspect of the present disclosure, there is provided a use of a composition comprising (a) GLA of the formula (Ia):



or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein an effective amount of a composition comprising GLA is to be administered by non-parenteral delivery, optionally wherein the composition is an aqueous formulation.

[0007] ~~According to this first aspect, n~~Non-parenteral administration can include delivery routes such as oral, sublingual, intranasal, intratracheal, intrapulmonary or mucosal delivery. Examples include administration via intranasal instillation, intratracheal instillation, intranasal inhalation or oral inhalation.

[0008] ~~In a second aspect, t~~The present disclosure also provides methods and compositions for treating allergic conditions wherein the time period between doses of GLA, e.g. between maintenance doses, or between active treatment periods (between induction phases), is at least 1 month or longer. Thus, the disclosure provides a method of treating a mammal who

suffers from an allergic condition, comprising administering at least two doses of an effective amount of a composition comprising an adjuvant, preferably GLA of the formula above, and wherein the time period between said two doses is at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months. In general, time periods between doses ranges from, e.g. about 1 week to 4 months, or about 1 week to 6 months, or about 1 week to 12 months. For example, methods include (a) administering multiple doses of a composition comprising GLA, optionally administered once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose, during a second treatment period, of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months, preferably at least 4-8 weeks, or 1-4 months, or 1-6 months, or 1-2 months, or 2-4 months, or 2-6 months, or 2-9 months or 1-12 months or 2-12 months or 4-12 months. Examples of the first treatment period include 2 weeks, 3 weeks, 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 or 2 months.

[0010] ~~Another aspect of t~~The present disclosure ~~invention~~ also provides methods and compositions for treating allergic conditions wherein doses of GLA, are administered over long periods of time, e.g., at least 1 month or longer. Thus, the disclosure provides a method of treating a mammal who suffers from an allergic condition, comprising administering at least two doses of an effective amount of a composition comprising an adjuvant, preferably GLA of the formula above, over a time period of at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months. In general, time periods between doses ranges from, e.g. about 1 week to 4 months, or about 1 week to 6 months, or about 1 week to 12 months. For example, methods include (a) administering multiple doses of a composition comprising GLA, optionally administered once weekly, for a period of at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months, at least 4-8 weeks, or 1-4 months, or 1-6 months, or 1-2 months, or 2-4 months, or 2-6 months, or 2-9 months or 1-12 months or 2-12 months or 4-12 months.

[0011] ~~According to the second aspect, b~~Both parenteral and non-parenteral administration is contemplated. Examples of parenteral administration include, e.g. by intramuscular, subcutaneous or intradermal injection, or by needle-free injection. Other examples of routes

of administration that are contemplated include, but are not limited to, oral, oral inhalation, sublingual, nasal, nasal inhalation, and buccal.

[0012] ~~In any of the aspects of the invention, t~~The adjuvant may be administered as part of an aqueous formulation or a non-aqueous formulation, such as a stable emulsion containing oil. Examples include liquid formulation or aerosolized formulation (liquid aerosol or powder aerosol). The adjuvant compositions may include one or more pharmaceutically acceptable carriers or excipients.

[0013] ~~In any of the aspects of the invention, t~~The adjuvant composition may be substantially devoid of an antigen or allergen, or may include one or more allergens. Example doses of allergen for humans, including adult humans, include, e.g., about 1-20 ug or higher, or about 1-50 ug or higher, or about 1-100 ug or higher, about 0.1ug to 100ug or higher, or about 500 to 2000 allergy units (AU) or bioequivalent allergy units (BAU) or higher, or about 100 to 3000 AU or BAU or higher, or about 100 to 4000 AU or BAU or higher, or about 1000 to 4000 AU or BAU or higher, or about 3000 to 5000 protein nitrogen units (PNU) or higher, or about 1000 to 5000 PNU or higher, or about 300 to 6000 standard units (SU) or higher, or about 300-4000 standard units (SU) or higher. Compositions including allergens may be used as part of allergen immunotherapy.

[0014] ~~In any of the aspects of the invention, t~~The mammal, e.g. human, may have previously suffered or may suffer from any allergic condition including but not limited to allergic rhinitis or asthma, including one or more episodes of acute bronchial asthma. In certain embodiments, the allergic condition is not a seasonal allergy condition. In one embodiment of the present disclosure~~invention~~, the condition is a food allergy. In a further embodiment, the condition is a grass allergy, such as allergy to timothy grass.

[0015] ~~In any of the aspects of the invention, t~~The mammal, e.g. human, may be administered a second therapeutic agent.

[0016] It is understood that uses corresponding to the methods described herein are equally contemplated, such as: use of the adjuvants described herein in preparation of a medicament for use in the methods described herein; or, adjuvants such as are described herein for use in the therapeutic methods described herein.

[0017] The present disclosure ~~invention~~ thus provides, ~~in one aspect,~~ a composition comprising GLA of the formula (I) or (Ia) or (Ib) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, for use in a method of treatment of an allergic condition

in a mammal, wherein said treatment comprises non-parenteral delivery of the composition to the mammal.

[0018] The present disclosure~~invention~~ also provides~~, in a second aspect,~~ a composition comprising GLA of the formula (I) or (Ia) or (Ib) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, for use in a method of treatment of an allergic condition in a mammal, wherein said treatment comprises the administration of at least two doses (or treatment periods) of the composition, said doses (or treatment periods) being administered at least 4 weeks apart.

[0019] The present disclosure ~~invention~~ also provides ~~in another aspect,~~ a composition comprising GLA of the formula (I) or (Ia) or (Ib) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or excipient, for use in a method of treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months. In certain embodiments, the allergic condition is not a seasonal allergic condition. In other embodiments, the human suffers from a food allergy. In one embodiment, the rest period between step (a) and (b) is at least 5 or 6 weeks.

[0020] Thus, the composition for treatment of an allergic condition may be characterized by a first treatment period of administration of said composition, wherein said first treatment period comprises multiple doses of said composition, followed by a rest period of at least 4 weeks, then a second treatment period comprising at least one maintenance dose of said composition.

[0021] The present disclosure ~~invention of the second aspect~~ also provides a composition comprising GLA of the formula (I) or (Ia) or (Ib) or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, as a maintenance dose, for use in a method of treatment of an allergic condition in a mammal, wherein said mammal has previously received said composition for a first treatment period, which first treatment period ceased at least 4 weeks prior to administration of the maintenance dose.

[0022] ~~In such aspects, f~~For example, the composition for use includes compositions wherein the first treatment period ceased from 4 to 52 weeks prior to administration of the maintenance dose (or prior to said second treatment period).

[0023] Further, ~~in such aspects,~~ said first treatment period may comprise the administration of at least four doses of the composition, e.g., once weekly, or twice weekly, or daily.

[0024] As used herein and in the appended claims, the singular forms "a," "and," and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "an antigen" includes a plurality of such antigens, and reference to "a cell" or "the cell" includes reference to one or more cells and equivalents thereof (e.g., plurality of cells) known to those skilled in the art, and so forth. Similarly, reference to "a compound" or "a composition" includes a plurality of such compounds or compositions, and refers to one or more compounds or compositions, respectively, unless the context clearly dictates otherwise. When steps of a method are described or claimed, and the steps are described as occurring in a particular order, the description of a first step occurring (or being performed) "prior to" (i.e., before) a second step has the same meaning if rewritten to state that the second step occurs (or is performed) "subsequent" to the first step. The term "about" when referring to a number or a numerical range means that the number or numerical range referred to is an approximation within experimental variability (or within statistical experimental error), and thus the number or numerical range may vary between 1% and 15% of the stated number or numerical range. The term "comprising" (and related terms such as "comprise" or "comprises" or "having" or "including") is not intended to exclude that in other certain embodiments, for example, an embodiment of any composition of matter, composition, method, or process, or the like, described herein, may "consist of" or "consist essentially of" the described features.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] **Figure 1A** depicts the area under the curve (AUC) of the graph of airway resistance in response to aerosolized methacholine challenge (percent change of airway resistance from baseline, plotted against concentration of methacholine, mg/ml); the three bars show airway resistance for (a) mice challenged with saline, (b) mice challenged with OVA and treated with vehicle, and (c) mice challenged with OVA and treated with GLA-AF (2 ug). **Figure 1B** depicts the area under the curve (AUC) of the graph of dynamic lung compliance in response to aerosolized methacholine challenge (percent change of dynamic lung compliance

months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months.

16. The composition of claim 15 wherein the composition further comprises one or more allergens.

17. The composition of claim 15, wherein the composition further comprises a food allergen.

18. The composition of claim 17 wherein the food allergen is a milk allergen, an egg allergen, a peanut allergen, a fish allergen or a shellfish allergen.

19. The ~~method~~ composition according to claim 15 wherein the composition is administered parenterally, e.g. by intramuscular, subcutaneous or intradermal injection, or by needle-free injection.

20. The composition ~~method~~ according to claim 15 wherein the composition is administered by oral, sublingual, intranasal or intrapulmonary delivery.

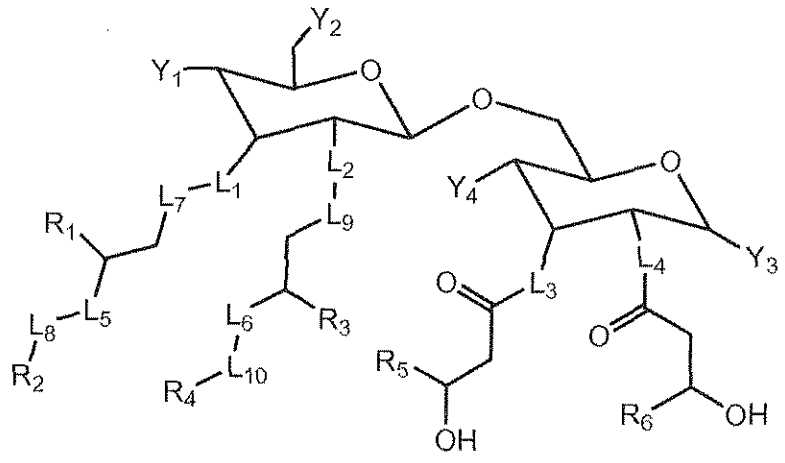
21. The composition of any one of claims 16-20 wherein the human suffers from a food allergy.

22. The composition of any one of claims 16-20 wherein the human has suffered one or more episodes of acute bronchial asthma.

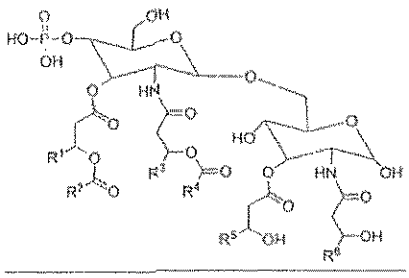
23. The composition of any one of claims 16-20 wherein the amount of GLA is about 1-20 μg.

24. The composition of any one of claims 16-20 wherein the human is administered a second therapeutic agent.

25. A composition comprising (a) GLA of the formula (Ib):



28. Use of a composition comprising (a) GLA of the formula (Ia):



or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are to be administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months.

29. The use of claim 28 wherein R^1, R^3, R^5 and R^6 are undecyl and R^2 and R^4 are tridecyl.

30. The use of claim 28 wherein the allergic condition is not a seasonal allergic condition.

31. The use of claim 28 wherein the human suffers from a food allergy.

32. The use of claim 28 wherein the rest period between step (a) and (b) is at least 5 weeks.

33. The use of claim 28 wherein the rest period between step (a) and (b) is at least 6 weeks.

34. The use of any one of claims 28-33 wherein the composition is to be administered by oral, oral inhalation, sublingual, intranasal, intranasal inhalation, intrapulmonary, intratracheal instillation, or mucosal delivery.

35. The use of any one of claims 28-33 wherein the mammal is a human.

36. The use of claim 28 wherein the composition is administered via liquid formulation, aerosol, or nebulizer, optionally liquid or powder.

37. The use of any one of claims 28-33 wherein the amount of GLA is about 1-20 µg.

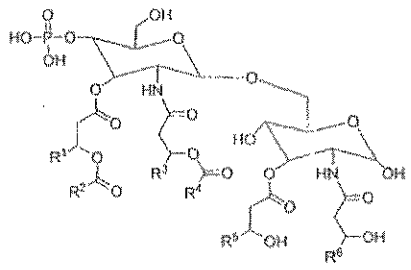
38. The use of any one of claims 28-33 wherein the composition further comprises one or more allergens.

39. The use of claim 38, wherein the one or more allergens is a food allergen.

40. The use of claim 39 wherein the food allergen is a milk allergen, an egg allergen, a peanut allergen, a fish allergen or a shellfish allergen.

41. The use of any one of claims 28-33 wherein the mammal is to be administered a second therapeutic agent.

42. Use of a composition comprising (a) GLA of the formula (Ia):



or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein at least two doses of an effective amount of a composition comprising GLA are to be administered, and wherein the time period between said two doses is at least 4 weeks, 5 weeks, 6 weeks, 7 weeks, 8 weeks, or 1 month, 2 months, 3 months, 4 months, 5 months, 6 months, 7 months, 8 months, 9 months, 11 months or 12 months.

43. The use of claim 42 wherein the composition further comprises one or more allergens.

44. The use of claim 42, wherein the composition further comprises a food allergen.

45. The use of claim 44 wherein the food allergen is a milk allergen, an egg allergen, a peanut allergen, a fish allergen or a shellfish allergen.

46. The use according to claim 42 wherein the composition is to be administered parenterally, e.g. by intramuscular, subcutaneous or intradermal injection, or by needle-free injection.

47. The use according to claim 42 wherein the composition is to be administered by oral, sublingual, intranasal or intrapulmonary delivery.

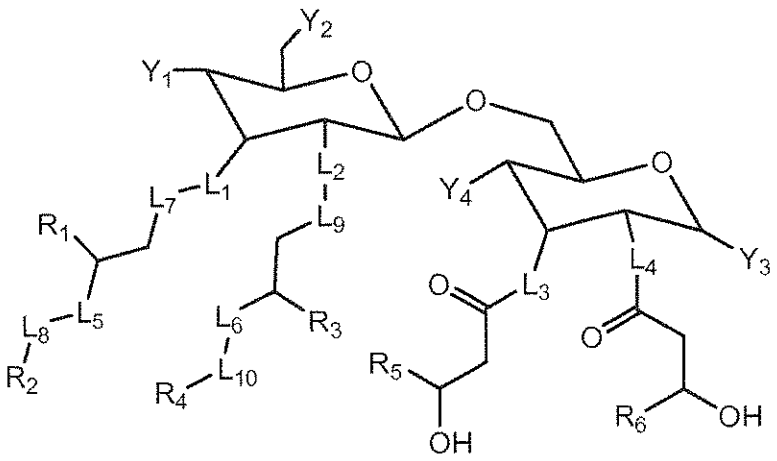
48. The use of any one of claims 43-47 wherein the human suffers from a food allergy.

49. The use of any one of claims 43-47 wherein the human has suffered one or more episodes of acute bronchial asthma.

50. The use of any one of claims 43-47 wherein the amount of GLA is about 1-20 µg.

51. The use of any one of claims 43-47 wherein the human is to be administered a second therapeutic agent.

52. Use of a composition comprising (a) GLA of the formula (Ib):



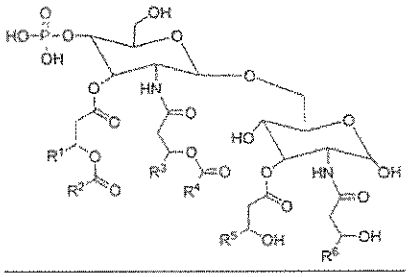
or a pharmaceutically acceptable salt thereof;

wherein: L1, L2, L3, L4, L5 and L6 are the same or different and are independently selected from O , NH , and (CH2) ; L7, L8, L9 and L10 are the same or different, and at any occurrence may be either absent or C(=O) ; Y1 is an acid functional group; Y2 and Y3 are the same or different and are each independently selected from OH, SH, and an acid

functional group; Y4 is OH or SH; R1, R3, R5 and R6 are the same or different and are each independently selected from the group of C8-C13 alkyl; and R2 and R4 are the same or different and are each independently selected from the group of C6-C11 alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein one, two, three or four doses of a composition comprising GLA are to be administered, optionally once weekly, for a first treatment period, followed by a rest period, followed by (b) administering a maintenance dose of an effective amount of a composition comprising GLA, and wherein the rest period between step (a) and (b) is between at least 4 weeks and 12 months.

53. Use of a composition comprising (a) GLA of the formula (Ia):



or a pharmaceutically acceptable salt thereof, where:

R^1, R^3, R^5 and R^6 are C_{11}-C_{20} alkyl; and

R^2 and R^4 are C_{12}-C_{20} alkyl; and

(b) a pharmaceutically acceptable carrier or excipient, in the manufacture of a medicament for treating a mammal who suffers from an allergic condition, wherein an effective amount of a composition comprising GLA is to be administered by non-parenteral delivery, optionally wherein the composition is an aqueous formulation.

54. The use of claim 53 wherein R^1, R^3, R^5 and R^6 are undecyl and R^2 and R^4 are tridecyl.