[0005]
Disclosed herein is a dry vaccine powder formulation comprising: one or more antigens, one or more saccharides, one or more buffers; and microcrystalline cellulose. An antigen in a vaccine powder formulation described herein can be a viral antigen. A viral antigen can be live attenuated virus, whole inactivated virus, split-inactivated virus, subunit antigens, virosome, or cold-adapted live influenza virus. A viral antigen can be influenza virus; for example, an antigen could H1N1; or H5N1; or a mixture of H1N1, H3N2 and Influenza type B. An antigen in a vaccine powder formulation described herein can be a bacterial antigen. A bacterial antigen can be killed whole bacteria, attenuated bacteria, toxoids, purified surface protein, or purified recombinant surface protein. A bacterial antigen can be tetanus toxoid or diphtheria toxoid. An antigen in the dry vaccine powder formulation can also be a protist. An antigen could also be protein. The saccharide used can be trehalose, mannitol, or lactose. The saccharide used can be trehalose. The buffer used can be a phosphate buffer. A vaccine powder formulation described herein can be stable at room temperature and 60% relative humidity for at least 12 months.
[0006]
Also provided herein is an intranasal dry vaccine powder formulation comprising:
a. one or more antigens;
b. one or more saccharides; and
c. microcrystalline cellulose, wherein said microcrystalline cellulose has a mean particle diameter of between 10 micro m and 100 micro m,
wherein the intranasal dry vaccine powder formulation, when administered intranasally, stimulates a higher sIgA and IgG response in a subject than a corresponding liquid formulation, when administered intranasally.
[0006a]
Also provided herein is a method for generating an intranasal dry vaccine powder formulation comprising:
a. preparing a liquid formulation comprising one or more antigens and one or more saccharides;
b. quick freezing said liquid formulation, wherein the quick freezing does not comprise spray freezing; and,
c. blending the freeze-dried sample with to generate the intranasal dry vaccine powder formulation, wherein the one or more excipients comprise a microcrystalline cellulose.
[0006b]
Also provided herein is a method for generating a dry vaccine powder formulation comprising: preparing a liquid formulation comprising an antigen; quick freezing said liquid formulation, wherein the quick freezing does not comprise spray freezing; blending the freeze-dried sample with one or more excipients to generate the dry vaccine powder formulation. A viral antigen can be live attenuated virus, whole inactivated virus, split-inactivated virus, subunit antigens, virosome, or cold-adapted live influenza virus. A viral antigen can be influenza virus; for example, an antigen could H1N1; or H5N1; or a mixture of H1N1, H3N2 and Influenza type B. An antigen in a vaccine powder formulation described herein can be a bacterial antigen. A bacterial antigen can be killed whole bacteria, attenuated bacteria, toxoids, purified surface protein, or purified recombinant surface protein. A bacterial antigen can be tetanus

toxoid or diphtheria toxoid. An antigen in the dry vaccine powder formulation can also be a protist. An antigen could also be protein. The preparation of a liquid formulation can comprise addition of a saccharide, for example trehalose, mannitol, or lactose. Preparation of a liquid formulation can also comprise addition of a buffer, such as a phosphate buffer. The powder can comprise fine particles. The powder can be stable at room temperature and 60% relative humidity for at least 12 months. Excipients useful in methods described herein can comprise one or more nasal carriers, such as microcrystalline cellulose and tribasic calcium phosphate. An excipient can improve flowability of the powder and/or reduce hygroscopicity of the powder. Some vaccine powders produced by a method herein do not comprise an adjuvant. Quick freezing can comprise the use of liquid nitrogen.

[0007]

Another method provided herein is a method of stimulating an sIgA response in a subject to an antigen comprising administering a dry vaccine powder formulation to a subject, wherein the dry powder formulation comprises the antigen and wherein the dry powder formulation is generated by quick freezing a liquid vaccine formulation, wherein the quick freezing does not comprise spray-freezing. In some instances, an IgG response is also stimulated. sIgA production can be stimulated at the site of administration and/or at a mucosal site other than the site of administration.

CLAIMS

1. An intranasal dry vaccine powder formulation comprising:
a. one or more antigens;
b. one or more saccharides; and
c. microcrystalline cellulose, wherein said microcrystalline cellulose has a mean particle diameter of between 10 micro m and 100 micro m,
wherein the intranasal dry vaccine powder formulation, when administered intranasally, stimulates a higher sIgA and IgG response in a subject than a corresponding liquid formulation, when administered intranasally.

2. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is viral antigen.

3. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is influenza viral antigen.

4. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is live attenuated virus, whole inactivated virus, split virus, subunit antigen, virosome, or cold-adapted live influenza virus.

5. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is whole inactive virus.

6. The intanasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is split-inactive virus.

7. The intanasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is H1N1 influenza virus.

8. The intanasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is H5N1 influenza virus.

9. The intranasal dry vaccine powder formulation of claim 1, wherein said one or more antigens comprises H1N1 influenza virus, H3N2 influenza virus, and Influenza B virus.

10. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is a bacterial antigen.

11. The intanasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is killed whole bacteria, attenuated bacteria, toxoids, purified surface protein, or purified recombinant surface protein.

12. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is tetanus toxoid.

13. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is diphtheria toxoid.

14. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more antigens is a protist antigen.

15. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of

said one or more antigens is a protein.

16. The intranasal dry vaccine powder formulation of claim 1, wherein at least one of said one or more saccharides is trehalose, mannitol, or lactose.

17. The intranasal dry vaccine powder formulation of claim 16, wherein at least one of said one or more saccharides is trehalose.

18. The intranasal dry vaccine powder formulation of claim 1, wherein said microcrystalline cellulose has a specific surface area between 1.3 m^2/g and 20 m^2/g.

19. The intranasal dry vaccine powder formulation of claim 1, wherein said microcrystalline cellulose has a bulk density between 0.1 g/cm^3 and 1.0 g/cm^3.

20. The intranasal dry vaccine powder formulation of claim 1, further comprising one or more buffers.

21. The intranasal dry vaccine powder formulation of claim 20, wherein at least one of said one or more buffers is a phosphate buffer.

22. The intranasal vaccine powder formulation of claim 1, wherein said intranasal dry vaccine powder formulation is stable at room temperature and 60% relative humidity for at least 12 months.

23. A method for generating an intranasal dry vaccine powder formulation comprising:
a. preparing a liquid formulation comprising one or more antigens and one or more saccharides;
b. quick freezing said liquid formulation, wherein the quick freezing does not comprise spray freezing; and,
c. blending the freeze-dried sample with one or more excipients to generate the intranasal dry vaccine powder formulation, wherein the one or more excipients comprise a microcrystalline cellulose.

24. The method of claim 23, wherein at least one of said one or more antigens is viral antigen.

25. The method of claim 23, wherein at least one of said one or more antigens is influenza virus.

26. The method of claim 23, wherein at least one of said one or more antigens is H1N1 influenza virus.

27. The method of claim 23, wherein at least one of said one or more antigens is H5N1 influenza virus.

28. The method of claim 23, wherein said one or more antigens comprises H1N1 influenza virus, H3N2 influenza virus, and Influenza B virus.

29. The method of claim 23, wherein at least one of said one or more

antigens is live attenuated virus, whole inactivated virus, split virus, subunit antigen, virosome, or cold-adapted live influenza virus.

30. The method of claim 23, wherein at least one of said one or more antigens is a bacterial antigen.

31. The method of claim 23, wherein at least one of said one or more antigens is killed whole bacteria, attenuated bacteria, toxoids, purified surface protein, or purified recombinant surface protein.

32. The method of claim 23, wherein at least one of said one or more antigens is tetanus toxoid.

33. The method of claim 23, wherein at least one of said one or more antigens is diphtheria toxoid.

34. The method of claim 23, wherein at least one of said one or more antigens is a protist antigen.

35. The method of claim 23, wherein at least one of said one or more antigens is a protein.

36. The method of claim 23, wherein at least one of said one or more saccharides is lactose.

37. The method of claim 23, wherein at least one of said one or more saccharides is trehalose.

38. The method of claim 23, wherein at least one of said one or more saccharides is mannitol.

39. The method of claim 23, wherein preparing said liquid formulation further comprises addition of one or more buffers.

40. The method of claim 39, wherein at least one of said one or more buffers is a phosphate buffer.

41. The method of claim 23, wherein said powder has a mean particle diameter between 10 micro m and 100 micro m.

42. The method of claim 23, wherein said powder is stable at room temperature and 60% relative humidity for at least 12 months.

43. The method of claim 23, wherein said one or more excipients comprise one or more nasal carriers.

44. The method of claim 23, wherein said one or more nasal carriers comprise tribasic calcium phosphate (TCP).

45. The method of claim 43, wherein said nasal carrier has a mean particle diameter of between 10 micro m and 100 micro m.

46. The method of claim 43, wherein said nasal carrier has a specific surface area between 1.3 m^2/g and 20 m^2/g.

47. The method of claim 43, wherein said nasal carrier has a bulk density between 0.1 g/cm^3 and 1.0 g/cm^3.

48. The method of claim 23, wherein said one or more excipients improves flowability.

49. The method of claim 23, wherein said one or more excipients reduces hygroscopicity.

50. The method of claim 23, wherein said vaccine powder formulation does not comprise adjuvant.

51. The method of claim 23, wherein said quick freezing comprises using liquid nitrogen.

52. Use of an intranasal dry vaccine powder formulation in the manufacture of a medicament for stimulating an sIgA response in a subject, wherein the dry powder formulation comprises one or more antigens and wherein the dry powder formulation is generated by quick freezing a liquid vaccine formulation, wherein the quick freezing does not comprise spray-freezing.

53. The use of claim 52, wherein an IgG response is also stimulated.

54. The use of claim 52, wherein said vaccine dry powder formulation can induce sIgA production at a mucosal site other than the site of administration.

55. The use of claim 52, wherein said administration is intranasal.

56. The use of claim 52, wherein the vaccine powder formulation does not comprise adjuvant.

57. The use of claim 52, wherein said quick freezing comprising using liquid nitrogen.

58. The use of claim 52, wherein at least one of said one or more antigens is viral antigen.

59. The use of claim 52, wherein at least one of said one or more antigens is live attenuated virus, whole inactivated virus, split virus, subunit antigen, virosome, or cold-adapted live influenza virus.

60. The use of claim 52, wherein at least one of said one or more antigens is influenza virus.

61. The use of claim 52, wherein at least one of said one or more antigens is H1N1 influenza virus.

62. The use of claim 52, wherein at least one of said one or more antigens is H5N1 influenza virus.

63. The use of claim 52, wherein said one or more antigens comprises H1N1 influenza virus, H3N2 influenza virus, and Influenza B virus.

64. The use of claim 52, wherein at least one of said one or more antigens is a bacterial antigen.

65. The use of claim 52, wherein at least one of said one or more antigens is killed whole bacteria, attenuated bacteria, toxoids, purified surface protein, or purified recombinant surface protein.

66. The use of claim 52, wherein at least one of said one or more antigens is tetanus toxoid.

67. The use of claim 52, wherein at least one of said one or more antigens is diphtheria toxoid.

68. The use of claim 52, wherein at least one of said one or more antigens is a protist antigen.

69. The use of claim 52, wherein at least one of said one or more antigens is a protein.

70. The use of claim 52, wherein said liquid formulation comprises one or more saccharides.

71. The use of claim 70, wherein at least one of said one or more saccharides is lactose.

72. The use of claim 70, wherein at least one of said one or more saccharides is trehalose.

73. The use of claim 70, wherein at least one of said one or more saccharides is mannitol.

74. The use of claim 52, wherein said liquid formulation comprises one or more buffers.

75. The use of claim 74, wherein at least one of said one or more buffers is a phosphate buffer.

76. The use of claim 52, wherein said powder has a mean particle diameter between 10 micro m and 100 micro m.

77. The use of claim 52, wherein said powder is stable at room temperature and 60% relative humidity for at least 12 months.

78. The use of claim 52, wherein said dry vaccine powder formulation comprises one or more excipients.

79. The use of claim 78, wherein said one or more excipients comprise one or more nasal carriers.

80. The use of claim 79, wherein said one or more nasal carriers comprise microcrystalline cellulose or tribasic calcium phosphate (TCP).

81. The use of claim 79, wherein said nasal carrier has a mean particle diameter of between 10micro m and 100 micro m.

82. The use of claim 79, wherein said nasal carrier has a specific surface area between 1.3 m^2/g and 20 m^2/g.

83. The use of claim 79, wherein said nasal carrier has a bulk density between 0.1 g/cm^3 and 1.0 g/cm^3.

84. The use of claim 78, wherein said one or more excipients reduces hygroscopicity.

85. A device for administration of an intransal dry vaccine powder formulation comprising the vaccine powder formulation generated by the method of claim 23.

86. The device of claim 85, wherein the device is configured for a single use.