

CLAIMS

WHAT IS CLAIMED:

1. A composition comprising: an effective amount of heparin having an average molecular weight from about 20 kDa to about 40 kDa, wherein at least 50% of heparin chains in the heparin have a molecular weight of at least 20 kDa; and a pharmaceutically acceptable excipient.
2. The composition of claim 1, wherein the heparin comprises an average molecular weight of at least 20 kDa.
3. The composition of claim 2, wherein the heparin comprises an average molecular weight of at least 30 kDa.
4. The composition of claim 3, wherein the heparin comprises an average molecular weight of at least 40 kDa.
5. The composition of claim 1, wherein at least 60% of heparin chains in the heparin have a molecular weight of at least 20 kDa.
6. The composition of claim 5, wherein at least 70% of heparin chains in the heparin have a molecular weight of at least 20 kDa.
7. The composition of claim 1, wherein the effective amount of heparin is about 3 mg.
8. The composition of claim 7, wherein the effective amount of heparin is about 1 mg.
9. The composition of claim 8, wherein the effective amount of heparin is about 0.5 mg.
10. The composition of claim 1, wherein the heparin is configured to bind to one or more eosinophil granule proteins.
11. The composition of claim 10, wherein the binding affinity of the heparin for the one or more eosinophil granule proteins is greater than the binding affinity of a low molecular weight heparin for the one or more eosinophil granule proteins.

12. The composition of claim 10, wherein the one or more eosinophil granule proteins comprise one or more of major basic protein 1 (MBP-1), major basic protein 2 (MBP-2), eosinophil derived neurotoxin (EDN), eosinophil cationic protein (ECP), and eosinophil peroxidase (EPO).

13. The composition of claim 1, wherein the composition is configured to be administered orally.

14. The composition of claim 1, wherein the composition is therapeutically effective to treat eosinophilic esophagitis.

15. The composition of claim 1, further comprising a therapeutic agent conjugated to the heparin.

16. The composition of claim 15, wherein the therapeutic agent is a glucocorticoid.

17. The composition of claim 1, further comprising a radiolabeled contrast agent conjugated to the heparin.

18. The composition of claim 18, wherein the radiolabeled contrast agent is ^{99m}Tc .

19. A method of treating a tissue exhibiting eosinophil-related inflammation in a subject, the method comprising: administering to the subject a composition comprising a therapeutically effective dose of heparin having an average molecular weight from about 20 kDa to about 40 kDa, wherein at least 50% of heparin chains in the heparin have a molecular weight of at least 20 kDa, and a pharmaceutically acceptable excipient, wherein the heparin binds to one or more eosinophil granule proteins in the tissue to reduce the eosinophil-related inflammation.

20. A method of reducing eosinophil-related inflammation in a tissue, the method comprising: administering to a subject a composition comprising a therapeutically effective dose of heparin having an average molecular weight from about 20 kDa to about 40 kDa, wherein at least 50% of heparin chains in the heparin have a molecular weight of at least 20 kDa, and a pharmaceutically acceptable excipient, wherein the heparin binds to one or more eosinophil granule proteins in the tissue to reduce the eosinophil-related inflammation.

21. The method of claim 19 or 20, wherein the heparin comprises an average molecular weight of at least 20 kDa.

22. The method of claim 21, wherein the heparin comprises an average molecular weight of at least 30 kDa.

23. The method of claim 22, wherein the heparin comprises an average molecular weight of at least 40 kDa.

24. The method of claim 19 or 20, wherein at least 60% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

25. The method of claim 24, wherein at least 70% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

26. The method of claim 19 or 20, wherein the therapeutically effective dose of heparin is about 3 mg.

27. The method of claim 26, wherein the therapeutically effective dose of heparin is about 1 mg.

28. The method of claim 27, wherein the therapeutically effective dose of heparin is about 0.5 mg.

29. The method of claim 19 or 20, wherein the binding affinity of the heparin for the one or more eosinophil granule proteins is greater than the binding affinity of a low molecular weight heparin for the one or more eosinophil granule proteins.

30. The method of claim 19 or 20, wherein the one or more eosinophil granule proteins comprise one or more of major basic protein 1 (MBP-1), major basic protein 2 (MBP-2), eosinophil derived neurotoxin (EDN), eosinophil cationic protein (ECP), and eosinophil peroxidase (EPO).

31. The method of claim 19 or 20, wherein the composition is configured to be administered orally.

32. The method of claim 19 or 20, wherein the composition is therapeutically effective to treat eosinophilic esophagitis.

33. The method of claim 19 or 20, further comprising a therapeutic agent conjugated to the heparin.

34. The method of claim 33, wherein the therapeutic agent is a glucocorticoid.

35. The method of claim 19 or 20, further comprising a radiolabeled contrast agent conjugated to the heparin.

36. The method of claim 35, wherein the radiolabeled contrast agent is ^{99m}Tc .

37. A method of producing a medical image of an organ in a subject, the method comprising:

detecting an eosinophil granule protein in the mucosal tissue of the organ in a subject, comprising administering to a subject radiolabeled heparin under conditions wherein the radiolabeled heparin binds to an eosinophil granule protein to form a radiolabeled heparin/eosinophil granule protein complex, and

detecting the radiolabeled heparin/eosinophil granule protein complex in the mucosal tissue of the organ, whereby detecting the radiolabeled heparin/eosinophil granule protein complex in the mucosal tissue of the organ produces a medical image of the organ in the subject.

38. A method of diagnosing eosinophilic esophagitis in a subject, the method comprising:

detecting an eosinophil granule protein in the mucosal tissue of the esophagus in a subject, comprising administering to a subject radiolabeled heparin under conditions wherein the radiolabeled heparin binds to an eosinophil granule protein to form a radiolabeled heparin/eosinophil granule protein complex, and

detecting the radiolabeled heparin/eosinophil granule protein complex in the mucosal tissue of the esophagus, whereby detecting the radiolabeled heparin/eosinophil granule protein complex in the mucosal tissue of the esophagus diagnoses eosinophilic esophagitis in the subject.

39. A method of detecting a change in eosinophilic esophagitis in a subject diagnosed with eosinophilic esophagitis, the method comprising:

a) producing a first medical image of the esophagus in a subject diagnosed with eosinophilic esophagitis according to the method of claim 37;

b) producing a second medical image of the esophagus in the subject of step (a), according to the method of claim 37; and

c) comparing the medical image of step (b) with the medical image of step (a), whereby detecting a change in the medical image of step (b) compared to the medical image of step (a) detects a change in eosinophilic esophagitis in the subject.

40. A method of detecting eosinophil degranulation in a subject, the method comprising:

detecting an eosinophil granule protein in a subject, comprising administering to a subject radiolabeled heparin under conditions wherein the radiolabeled heparin binds to an eosinophil granule protein to form a radiolabeled heparin/eosinophil granule protein complex, and

detecting the radiolabeled heparin/eosinophil granule protein complex, whereby detecting the radiolabeled heparin/eosinophil granule protein complex detects eosinophil degranulation in the subject.

41. A method of delivering a therapeutic agent to a diseased organ, the method comprising, administering a therapeutically effective amount of a composition comprising heparin conjugated to a therapeutic agent to a subject.

42. The method of any one of claims 37-41, wherein the heparin has an average molecular weight from about 20 kDa to about 40 kDa, and wherein at least 50% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

43. A method of treating eosinophilic-related inflammation in a subject, the method comprising, administering a therapeutically effective amount of a composition comprising an effective amount of heparin having an average molecular weight from about 20 kDa to about 40 kDa, wherein at least 50% of heparin chains in the heparin have a molecular weight of at least 20 kDa; and a pharmaceutically acceptable excipient to the subject.

44. The method of claim 42 or 43, wherein the heparin comprises an average molecular weight of at least 20 kDa.

45. The method of claim 44, wherein the heparin comprises an average molecular weight of at least 30 kDa.

46. The method of claim 45, wherein the heparin comprises an average molecular weight of at least 40 kDa.

47. The method of claim 42 or 43, wherein at least 60% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

48. The method of claim 47, wherein at least 70% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

49. The method of claim 41 or 43, wherein the therapeutically effective dose of heparin is about 3 mg.

50. The method of claim 49, wherein the therapeutically effective dose of heparin is about 1 mg.

51. The method of claim 50, wherein the therapeutically effective dose of heparin is about 0.5 mg.

52. The method of claim 42 or 43, wherein the heparin is configured to bind to one or more eosinophil granule proteins.

53. The method of claim 52, wherein the binding affinity of the heparin for the one or more eosinophil granule proteins is greater than the binding affinity of a low molecular weight heparin for the one or more eosinophil granule proteins.

54. A method of treating eosinophilic-related inflammation in a subject, the method comprising, administering a therapeutically effective amount of a composition comprising heparin conjugated to a therapeutic agent to a subject.

55. The method of claim 37 or 41, wherein the organ is an ovary, a breast, a brain, a muscle, a heart, a lung, a stomach, a proximal large intestine, a distal large intestine, a small intestine, a pancreas, a thyroid, skin, an eye, a testicle, a thymus, a gallbladder, a uterus, an esophagus or a major blood organ.

56. The method of claim 55, wherein the major blood organ is the liver, spleen, kidneys, or bladder.

57. The method of any of claims 37-40 and 52-53, wherein the eosinophil granule protein is major basic protein 1 (MBP-1), major basic protein 2 (MBP-2), eosinophil derived neurotoxin (EDN), eosinophil cationic protein (ECP), or eosinophil peroxidase (EPO).

58. The method of claim 57, wherein the eosinophil granule protein is MBP-1.

59. The method of any of claims 37-40 or 55-57, wherein the radiolabel of the radiolabeled heparin is ^{99m}Tc.

60. The method of any of claims 37-40 or 55-58, wherein the radiolabeled heparin is administered to the subject orally.

61. The method of claim 60, wherein the subject swallows the radiolabeled heparin through one or more swallows.

62. The method of claim 61, wherein the radiolabeled heparin is administered orally to the subject in 1 ml aliquots over 15 minutes.

63. The method of any of claims 37-40 or 55-62, further comprising a washing step.

64. The method of claim 63, wherein the washing step comprises the subject swallowing a liquid after the one or more swallows of the radiolabeled heparin.

65. The method of claim 64, wherein the liquid is water.

66. The method of claim 64, wherein the washing step is performed before, during or after the production of a medical image.

67. The method of claim 62, wherein the administration of the liquid comprises the subject swallowing the liquid through one or more swallows.

68. The method of any of claims 64-67, wherein the liquid is administered in a volume of 1 to 100 ml.

69. The method of any of the preceding claims, wherein the heparin or heparin portion of the radiolabeled heparin is high molecular weight heparin, low molecular weight heparin or unfractionated heparin.

70. The method of claim 69, wherein the heparin or heparin portion of the radiolabeled heparin is high molecular weight heparin.

71. The method of claim 70, wherein the high molecular weight heparin is administered in an amount less than 1 mg.

72. The method of claim 70, wherein the high molecular weight heparin is administered in an amount ranging from 0.1 mg to 1 mg.

73. The method of any of the preceding claims, wherein the radiolabel of the radiolabeled heparin is administered in an amount ranging from 0.3 mCi to 3 mCi.

74. The method of any of the preceding claims, wherein the subject is a human.

75. The method of any of claims 37-40 or 55-74, wherein the radiolabeled heparin/eosinophil granule protein complex is detected using one or more of single-photon emission computed tomography (SPECT), positron emission tomography (PET) scans, X-ray, conventional or computed tomography (CT), a combination of SPECT and CT, or magnetic resonance imaging (MRI).

76. The method of any of claims 37-40 or 55-74, wherein the medical image is three-dimensional.

77. The method of any of claims 37-40 or 55-74, wherein the medical image is two-dimensional.

78. The method of any of claims 41-56, wherein the therapeutic agent is a glucocorticoid.

79. The method of claim 78, wherein the glucocorticoid is mometasone, fluticasone, budesonide, prednisone or solumedrol.

80. The method of any of claims 41-56 or 78-79, further comprising identifying the subject in need thereof.

81. The method of claim 80, wherein the subject in need thereof is identified by any one of the methods of claims 37-40, 43 and 54.

82. The method of any of claims 41-56 or 78-81, wherein the composition is administered to the subject orally, intravenously, optically or topically.