equal incidence in the proximal, distal, or both portions of the esophagus being affected within cohorts, but such infiltrate varies in each individual with many demonstrating a less intense infiltrate proximally. EoE also affects the luminal structure of the esophagus. The areas of inflammation are not evenly distributed throughout an affected esophagus, as the disease often presents in patches or select segments of the 25-30 cm long adult esophagus. Pronounced rings or furrows can develop into strictures that close off the esophagus, resulting in odynophagia, dysphagia, food impaction, and emergency hospital visits. Accordingly, expeditious treatment of EoE is important to alleviate symptoms before they exacerbate and restrict the esophageal lumen.

[0006] Although EoE can be diagnosed by esophagogastroduodenoscopy (EGD), some cases may never present as a "ringed-esophagus" during EGD and may be difficult to diagnose by this method. A conclusive means currently available to clinicians to positively identify EoE is to detect the presence of eosinophils in biopsy specimens. Tissue samples may be collected during EGD and then examined with traditional histological analysis to confirm or reject a case of EoE. However, the patchy nature of the disease complicates collection of tissue samples for biopsy. When clinical suspicion for EoE is high, consensus practice requires sampling at 4 to 5 sites throughout the esophagus and this still might result in under diagnosis of EoE if mucosal eosinophilia is particularly patchy. Accordingly, there is a need for more accessible methods of diagnosis and monitoring.

[0007] Despite the rapidly growing incidence of EoE, state-of-the-art diagnostic techniques remain inadequate to fully characterize this disease. Further, available treatments are not able to adequately target and localize to eosinophil-related inflammation. As such, there exists a need to develop a non-invasive, precise, and comprehensive technique to image, diagnose, monitor, and treat eosinophil-related inflammation and conditions such as EoE.

SUMMARY

[0008] This summary is provided to comply with 37 C.F.R. § 1.73. It is submitted with the understanding that it will not be used to interpret or limit the scope or meaning of the present disclosure.

[0008a] In an aspect, there is provide a composition comprising: an effective amount of heparin having an average molecular weight from 20 kDa to 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.

[0009] In an example, there is provided a composition comprising an effective amount of high molecular weight 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.

[0010] Disclosed herein are methods 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.

[0010a] In another aspect, there is provided a use of a composition comprising a therapeutically effective dose of heparin having an average molecular weight from 20 kDa to 40 kDa, and a pharmaceutically acceptable excipient in the manufacture of a medicament for treating a tissue exhibiting eosinophil-related inflammation in a subject, wherein the heparin binds to one or more eosinophil granule proteins in the tissue to reduce the eosinophil-related inflammation.

[0011] Disclosed herein are methods of reducing eosinophil-related inflammation in a tissue, the methods 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.

[0011a] In another aspect, there is provided a use of a composition comprising a therapeutically effective dose of heparin having an average molecular weight from 20 kDa to 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 in the manufacture of a medicament for reducing eosinophil-related inflammation in a tissue wherein the heparin binds to one or more eosinophil granule proteins in the tissue to reduce the eosinophil-related inflammation.

[0012] In another example, there is provided a method of producing a medical image of an organ in a subject, the methods 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. In some examples, the radiolabeled heparin

comprises 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.

[0013] In another example, there is provided a method of diagnosing eosinophilic esophagitis in a subject, the methods 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. In some examples, the radiolabeled heparin

comprises 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.

[0013a] In another example, there is provided 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 as defined above;

b) producing a second medical image of the esophagus in the subject of step (a), according to the method as defined above; 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.

[0014] In another example, there is provided a method of detecting eosinophil degranulation in a subject, the methods 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. In some examples, the radiolabeled heparin comprises 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.

[0015] In another example, there is provided a method of delivering a therapeutic agent to a diseased organ, the methods comprising, administering a therapeutically effective amount of a composition comprising heparin conjugated to a therapeutic agent to a subject. In some examples, the heparin has 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.

[0016] Disclosed herein are methods of treating eosinophilic-related inflammation in a subject, the methods 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.

[0016a] In another aspect, there is provided a use of a therapeutically effective amount of a composition comprising an effective amount of heparin having an average molecular weight from 20 kDa to 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 in the manufacture of a medicament for treating eosinophilic-related inflammation in a subject.

[0017] Disclosed herein are methods of treating eosinophilic-related inflammation in a subject, the methods comprising, administering a therapeutically effective amount of a composition comprising heparin conjugated to a therapeutic agent to a subject. In some aspects, the heparin has 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.

CLAIMS

WHAT IS CLAIMED:

1. A composition comprising: an effective amount of heparin having an average molecular weight from 20 kDa to 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 1, wherein the heparin comprises an average molecular weight of at least 30 kDa.

4. The composition of claim 2, 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 4, 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 6, wherein the effective amount of heparin is about 1 mg.

9. The composition of claim 7, 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 one or more of 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 17, wherein the radiolabeled contrast agent is 99mTc.

19. A use of a composition comprising a therapeutically effective dose of heparin having an average molecular weight from 20 kDa to 40 kDa, and a pharmaceutically acceptable excipient in the manufacture of a medicament for treating a tissue exhibiting eosinophil-related inflammation in a subject, wherein the heparin binds to one or more eosinophil granule proteins in the tissue to reduce the eosinophil-related inflammation.

20. A use of a composition comprising a therapeutically effective dose of heparin having an average molecular weight from 20 kDa to 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 in the manufacture of a medicament for reducing eosinophil-related inflammation in a tissue, wherein the heparin binds to one or more eosinophil granule proteins in the tissue to reduce the eosinophil-related inflammation.

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

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

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

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

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

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

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

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

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

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

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

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

36. The use of claim 33, wherein the radiolabeled contrast agent is 99mTc.

37. Use of a therapeutically effective amount of a composition comprising an effective amount of heparin having an average molecular weight from 20 kDa to 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 in the manufacture of a medicament for treating eosinophilic-related inflammation in a subject.

38. The use of claim 37, wherein the heparin comprises an average molecular weight of at least 20 kDa.

39. The use of claim 38, wherein the heparin comprises an average molecular weight of at least 30 kDa.

40. The use of claim 39, wherein the heparin comprises an average molecular weight of at least 40 kDa.

41. The use of claim 39, wherein at least 60% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

42. The use of claim 41, wherein at least 70% of heparin chains in the heparin have a molecular weight of at least 20 kDa.

43. The use of claim 37, wherein the therapeutically effective dose of heparin is about 3 mg.

44. The use of claim 43, wherein the therapeutically effective dose of heparin is about 1 mg.

45. The use of claim 44, wherein the therapeutically effective dose of heparin is about 0.5 mg.

46. The use of claim 37, wherein the heparin is configured to bind to one or more eosinophil granule proteins.

47. The use of claim 42, 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.

48. The use of any of claims 46-47, 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).

49. The use of claim 48, wherein the eosinophil granule protein is MBP-1.

50. The use of claim 48, wherein the radiolabel of the radiolabeled heparin is ^{99m}Tc.

51. The use of any of claims 48-49, wherein the radiolabeled heparin is to be administered to the subject orally.

52. The use 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.

53. The use of claim 52, wherein the heparin or heparin portion of the radiolabeled heparin is high molecular weight heparin.

54. The use of claim 53, wherein the high molecular weight heparin is to be administered in an amount less than 1 mg.

55. The use of claim 53, wherein the high molecular weight heparin is to be administered in an amount ranging from 0.1 mg to 1 mg.

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

57. The use of any of the preceding claims, wherein the subject is a human.

58. The use of any of claims 48-57, 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).

59. The use of any of claims 48-57, wherein the medical image is three-dimensional.

60. The use of any of claims 48-57, wherein the medical image is two-dimensional.

61. The use of any of claims 37-47, wherein the therapeutic agent is a glucocorticoid.

62. The use of claim 61, wherein the glucocorticoid is mometasone, fluticasone, budesonide, prednisone or solumedrol.

63. The use of any of claims 37-47 or 61-62, further comprising identifying the subject in need thereof.

64. The use of claim 63, wherein the subject in need thereof is identified by any one of the uses of claims 37.

65. The use of any of claims 37-47 or 61-64, wherein the composition is to be administered to the subject orally.