matrix; and (b) washing the chromatography matrix with a sodium caprylate wash buffer comprising 150-500 mM sodium caprylate.

**[005]** In an example, the sodium caprylate wash buffer comprises 150-350 mM sodium caprylate. In an example, the sodium caprylate wash buffer comprises 200-350 mM sodium caprylate. In an example, the sodium caprylate wash buffer comprises about 300 mM sodium caprylate. In an example, the sodium caprylate wash buffer comprises about 50 mM Tris. In an example, the sodium caprylate wash buffer comprises 0.5-1.5 M NaCl. In an example, the sodium caprylate wash buffer comprises about 1M NaCl. In an example, the sodium caprylate wash buffer has a pH of 7-9. In an example, the sodium caprylate wash buffer has a pH of about 8.

**[006]** In an example, the method further comprises washing the chromatography matrix with a NaCl wash buffer comprising 0.5-1.5 M NaCl. In an example, the NaCl wash buffer comprises about 1M NaCl. In an example, the NaCl wash buffer comprises about 50 mM Tris. In an example, the NaCl wash buffer has a pH of 7-9. In an example, the NaCl wash buffer has a pH of about 8.

**[007]** In an example, the chromatography column is washed with the NaCl wash buffer prior to being washed with the sodium caprylate wash buffer. In an example, the chromatography column is washed with the sodium caprylate wash buffer prior to being washed with the NaCl wash buffer.

**[008]** In an example, the chromatography matrix is equilibrated with a Tris buffer at a pH of 7-9 between step (a) and step (b). In an example, the Tris buffer comprises 10-100 mM Tris. In an example, the Tris buffer comprises about 50 mM Tris. In an example, the Tris buffer has a pH of about 8.0.

**[009]** In an example, the chromatography matrix is washed with 2-10 column volumes of the sodium caprylate wash buffer. In an example, the chromatography matrix is washed with about 2 column volumes of the sodium caprylate wash buffer. In an example, the chromatography matrix is washed with 2-10 column volumes of the NaCl wash buffer. In an example, the chromatography matrix is washed with about 5 column volumes of the NaCl wash buffer.

**[0010]** In an example, the chromatography matrix is sequentially washed with: about 5 column volumes of a NaCl wash buffer comprising about 50 mM Tris and about 1 M NaCl, with

a pH of about 8; and about 2 column volumes of a sodium caprylate wash buffer comprising about 50 mM Tris and about 300 mM sodium caprylate, with a pH of about 8.

**[0011]** In an example, the chromatography matrix is washed with the NaCl wash buffer at a flow rate of 300 ± 30 cm/hr. In an example, the chromatography matrix is washed with the sodium caprylate wash buffer at a flow rate of 300 ± 30 cm/hr.

**[0012]** In an example, the method further comprises washing the chromatography matrix with a Tris buffer comprising 10-100 mM Tris, optionally the Tris buffer comprises about 50 mM Tris at a pH of 8.0.

**[0013]** In an example, the method further comprises contacting the chromatography matrix with an elution buffer to produce an eluate containing dulaglutide. In an example, the elution buffer has a pH of 2.5-4. In an example, the elution buffer has a pH of about 3. In an example, the elution buffer comprises sodium citrate. In an example, the elution buffer comprises 5-25 mM sodium citrate. In an example, the elution buffer comprises about 10 mM sodium citrate.

**[0014]** In an example, the eluate is monitored by absorbance using a spectrophotometer. In an example, the eluate comprises at least about 70% of the dulaglutide present in the mixture prior to performing the method.

**[0015]** In an example, the chromatography column has a diameter of 50-150 cm. In an example, the chromatography column has a diameter of 75-150 cm. In an example, the chromatography column has a diameter of about 100 cm. In an example, the Protein A chromatography matrix has an average particle size of 80-90 µm. In an example, the Protein A chromatography matrix has an average particle size of about 85 µm. In an example, the Protein A chromatography matrix has an average particle size of 50-70 µm. In an example, the Protein A chromatography matrix has an average particle size of about 60 µm.

**[0016]** In an example, the protein A chromatography matrix is stable in alkali.

**[0017]** In an example, the one or more HCP is a protease selected from the group consisting of serine protease, aspartic protease, cysteine protease, metalloprotease, and aminopeptidase, or a combination thereof. In an example, the one or more HCP is cathepsin D.

**[0018]** In an example, the eluate comprises a reduced amount of the one or more HCP compared to the mixture. In an example, the eluate comprises no more than 100 ng/mg of

HCPs. In an example, the amount of one or more HCP is measured by mass spectrometry or ELISA.

**[0019]** In an example, the eluate comprises a reduced amount of cathepsin D compared to the mixture. In an example, the eluate comprises no more than 100 ng/mg cathepsin D. In an example, the amount of cathepsin D is measured by mass spectrometry or ELISA. In an example, the amount of cathepsin D is measured by an enzymatic assay. In an example, the amount of cathepsin D is measured by an enzymatic assay wherein a fluorescent substrate of Cathepsin D is added to the sample and its cleavage product is measure by HPLC with Fluorescent detection.

**[0020]** In an example, the mass spectrometry is LC-MS.

**[0021]** In an example, the eluate comprises less than 300 μU/mL cathepsin D activity.

**[0022]** In an aspect, provided herein is dulaglutide produced by any one of the methods disclosed herein.

**[0022a]** In an aspect, provided herein is a composition comprising dulaglutide produced by any one of the methods disclosed herein.

*Statements of the present disclosure are described below:*

1. A method of purifying an Fc-containing protein from a mixture comprising the Fc-containing protein and one or more host cell protein (HCP), the method comprising the steps of:

(a) applying the mixture to a chromatography column comprising a Protein A chromatography matrix, under conditions whereby the Fc-containing protein binds to the chromatography matrix; and

(b) washing the chromatography matrix with a sodium caprylate wash buffer comprising 150-500 mM sodium caprylate.

2. The method of statement 1, wherein the sodium caprylate wash buffer comprises 200-500 mM or 150-350 mM sodium caprylate.

3. The method of statement 1 or 2, wherein the sodium caprylate wash buffer comprises 200-350 mM sodium caprylate.

4. The method of any one of statements 1-3, wherein the sodium caprylate wash buffer comprises about 300 mM sodium caprylate.

5. The method of any one of statements 1-4, wherein the sodium caprylate wash buffer comprises about 50 mM Tris and about 300 mM sodium caprylate.

6. The method of any one of statements 1-5, wherein the sodium caprylate wash buffer comprises 0.5-1.5 M NaCl.

7. The method of any one of statements 1-6, wherein the sodium caprylate wash buffer comprises about 1M NaCl.

8. The method of any one of statements 1-7, wherein the sodium caprylate wash buffer has a pH of 7-9.

9. The method of any one of statements 1-8, wherein the sodium caprylate wash buffer has a pH of about 8.

10. The method of statement 1, further comprising washing the chromatography matrix with a NaCl wash buffer comprising 0.5-1.5 M NaCl.

11. The method of statement 10, wherein the NaCl wash buffer comprises about 1M NaCl.

12. The method of statement 10 or 11, wherein the NaCl wash buffer comprises about 50 mM Tris and about 1M NaCl.

13. The method of any one of statements 10-12, wherein the NaCl wash buffer has a pH of 7-9.

14. The method of any one of statements 10-13, wherein the NaCl wash buffer has a pH of about 8.

15. The method of any one of statements 10-14, wherein the chromatography column is washed with the NaCl wash buffer prior to being washed with sodium caprylate wash buffer.

16. The method of any one of statements 10-14, wherein the chromatography column is washed with the sodium caprylate wash buffer prior to being washed with NaCl wash buffer.

17. The method of any one of statements 1-16, wherein the chromatography matrix is equilibrated with a Tris buffer at a pH of 7-9 between step (a) and step (b).

18. The method of statement 17, wherein the Tris buffer comprises 10-100 mM Tris.

19. The method of statement 17 or 18, wherein the Tris buffer comprises about 50 mM Tris.

20. The method of any one of statements 17-19, wherein the Tris buffer has a pH of about 8.0.

21. The method of any one of statements 1-20, wherein the chromatography matrix is washed with 2-10 column volumes of the sodium caprylate wash buffer.

22. The method of any one of statements 1-21, wherein the chromatography matrix is washed with about 2 column volumes of the sodium caprylate wash buffer.

23. The method of any one of statements 10-22, wherein the chromatography matrix is washed with 2-10 column volumes of the NaCl wash buffer.

24. The method of any one of statements 10-23, wherein the chromatography matrix is washed with about 2 or about 5 column volumes of the NaCl wash buffer.

25. The method of statement 1, wherein the chromatography matrix is sequentially washed with:

(a) about 2 column volumes of a NaCl wash buffer comprising about 50 mM Tris and about 1 M NaCl, with a pH of about 8; and

(b) about 2 column volumes of a sodium caprylate wash buffer comprising about 50 mM Tris and about 300 mM sodium caprylate, with a pH of about 8.

26. The method of any one of statements 10-25, wherein the chromatography matrix is washed with the NaCl wash buffer at a flow rate of 300 ± 30 cm/hr.

27. The method of any one of statements 1-26, wherein the chromatography matrix is washed with the sodium caprylate wash buffer at a flow rate of 300 ± 30 cm/hr.

28. The method of any one of statements 1-27, further comprising washing the chromatography matrix with a Tris buffer comprising 10-100 mM Tris, optionally wherein the Tris buffer comprises about 50 mM Tris at a pH of about 8.0.

29. The method of any one of statements 1-28, further comprising contacting the chromatography matrix with an elution buffer to produce an eluate containing the Fc-containing protein.

30. The method of statement 29, wherein the elution buffer has a pH of 2.5-4.

31. The method of statement 29 or 30, wherein the elution buffer has a pH of about 3.

32. The method of any one of statements 29-31, wherein the elution buffer comprises sodium citrate.

33. The method of any one of statements 29-32, wherein the elution buffer comprises 5-25 mM sodium citrate.

34. The method of any one of statements 29-33, wherein the elution buffer comprises about 10 mM sodium citrate.

35. The method of any one of statements 29-34, wherein the eluate is monitored by absorbance using a spectrophotometer.

36. The method of any one of statements 29-35, wherein the eluate comprises at least 70% of the Fc-containing protein present in the mixture.

37. The method of any one of statements 1-36, wherein the chromatography column has a diameter of 75-150 cm.

38. The method of any one of statements 1-37, wherein the chromatography column has a diameter of about 100 cm.

39. The method of any one of statements 1-38, wherein the Protein A chromatography matrix has an average particle size of 80-90 µm.

40. The method of any one of statements 1-39, wherein the Protein A chromatography matrix has an average particle size of about 85 µm.

41. The method of any one of statements 1-40, wherein the protein A chromatography matrix is stable in alkali.

42. The method of any one of statements 1-41, wherein the one or more HCP is a protease selected from the group consisting of serine protease, aspartic protease, cysteine protease, metalloprotease, and aminopeptidase, or a combination thereof.

43. The method of statement 1-42, wherein the one or more HCP is cathepsin D.

44. The method of any one of statements 29-43, wherein the eluate comprises a reduced amount of the one or more HCP compared to the mixture.

45. The method of any one of statements 29-44, wherein the eluate comprises no more than 100 ng/mg of HCPs.

46. The method of statement 43 or 44, wherein the one or more HCP is measured by mass spectrometry or ELISA.

47. The method of any one of statements 29-46, wherein the eluate comprises a reduced amount of cathepsin D compared to the mixture.

48. The method of any one of statements 29-47, wherein the eluate comprises no more than 100 ng/mg cathepsin D.

49. The method of statement 47 or 48, wherein the amount of cathepsin D is measured by mass spectrometry or ELISA.

50. The method of statement 46 or 49, wherein the mass spectrometry is LC-MS.

51. The method of any one of statements 29-50, wherein the eluate comprises less than 300 µU/mL cathepsin D activity.

52. The method of any one of statements 1-51, wherein the Fc-containing protein is not an antibody.

53. The method of any one of statements 1-52, wherein the Fc-containing protein comprises a glucagon-like peptide 1 (GLP-1) analog comprising one or more modifications compared to a wild type GLP-1 amino acid sequence (SEQ ID NO: 1).

54. The method of any one of statements 1-53, wherein the Fc-containing protein comprises a GLP-1 analog comprising the amino acid sequence of SEQ ID NO: 2.

55. The method of any one of statements 1-54, wherein the Fc-containing protein comprises a peptide linker.

56. The method of statement 55, wherein the peptide linker comprises 1-10 $G_4S$ units (SEQ ID NO: 3).

57. The method of any one of statements 1-56, wherein the Fc-containing protein comprises:

(a) a GLP-1 analog comprising the amino acid sequence of SEQ ID NO: 2;

(b) a peptide linker comprising the amino acid sequence of SEQ ID NO: 3; and

c) an Fc portion of an immunoglobulin.

58. The method of statement 57, wherein the N-terminal residue of the peptide linker is directly fused to the C-terminal residue of the GLP-1 analog, and the C-terminal residue of the peptide linker is directly fused to the N-terminal residue of the Fc portion.

59. The method of any one of statements 1-58, wherein the Fc-containing protein comprises the amino acid sequence of SEQ ID NO: 4.

60. The method of any one of statements 1-59, wherein the wherein the Fc-containing protein is a homodimer comprising two identical amino acid chains each comprising the amino acid sequence of SEQ ID NO: 4.

61. The method of any one of statements 1-60, wherein the Fc-containing protein is dulaglutide.

62. An Fc-containing protein produced by the method of any one of the preceding statements.

## BRIEF DESCRIPTION OF DRAWINGS

**[0023]** **FIG. 1** is a UV chromatogram of flow throughs from washes with the indicated buffer solutions on a Protein A chromatography column. The Protein A column was pre-loaded with a mixture comprising dulaglutide and host cell proteins prior to the wash steps.