Claims

1. A method of purifying immunoglobulin G (IgG) from plasma or a fraction thereof using continuous affinity chromatography, the method comprising binding the IgG to an affinity chromatography resin comprising a ligand capable of specifically binding to a CH3 domain of human IgG and collecting the IgG.

2. A method of producing an immunoglobulin G (IgG) enriched preparation from plasma or a fraction thereof using continuous affinity chromatography, the method comprising binding the IgG to an affinity chromatography resin comprising a ligand capable of specifically binding to a CH3 domain of human IgG and collecting the IgG.

3. The method of claim 1 or 2:
   i) wherein:
      a) the ligand comprises a camelid-derived single domain [VHH] antibody fragment; and/or
      b) the resin comprises a matrix selected from the group consisting of a cross-linked poly(styrene-divinylbenzene) matrix and an agarose-based matrix; and/or
      c) the ligand comprises a VHH antibody fragment conjugated to a cross linked poly(styrene-divinylbenzene) matrix; and/or
   ii) the method further comprises:
      a) washing the resin with a wash buffer having a pH of between 5 and 10 and a dissociation constant (pKa) between 6.8 and 8.5 at 25°C; and/or
      b) eluting the bound IgG from the resin with an elution buffer having a pH of between 3 and 5.

4. The method of any one of claims 1 to 3, wherein the plasma or fraction thereof:
   i) contacts the resin for between 0.1 and 5 minutes; and/or
   ii) is selected from a group consisting of cryo-rich plasma, cryo-poor plasma, Supernatant I (SN I), Cohn Fraction II (Fr II), Cohn Fraction II+III (Fr II+III), Cohn Fraction I+II+III (FrI+II+III), Kistler/Nitschmann Precipitate A (KN A),

Kistler/Nitschmann Precipitate B (KN B), Kistler/Nitschmann Precipitate of Supernatant B (KN B+1), and combinations thereof; and/or

iii) is thawed at a temperature of at least 32ºC; and/or

iv) is at a temperature in the range of from 2ºC to 28ºC before the continuous affinity chromatography, optionally wherein: a) the plasma or fraction thereof is at a temperature of 21ºC before the continuous affinity chromatography; and/or the plasma or fraction thereof is at the temperature for up to 48 hrs.

5. The method of any one of claims 1 to 4, wherein:

i) the wash buffer:

a) comprises a buffering agent selected from a group consisting of sodium dihydrogen phosphate, imidazole, Tris, glycylglycine, 3-morpholinopropane-1-sulfonic acid (MOPS), piperazine-N,N′-bis(2-ethanesulfonic acid) (PIPES), 2-[(2-Hydroxy-1,1-bis(hydroxymethyl)ethyl)amino]ethanesulfonic acid (TES), bis[(2-hydroxyethyl)amino]acetic acid (Bicine), 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES), sulfurous acid, 4-(2-Hydroxyethyl)-1-piperazinepropanesulfonic acid (EPPS), N-(Hydroxyethyl)piperazine-N'-2-hydroxypropanesulfonic acid (HEPPSO), 4-(N-Morpholino)butanesulfonic acid (MOBS), Piperazine-N,N′-bis(2-hydroxypropanesulfonic acid) (POPSO), N-[Tris(hydroxymethyl)methyl]-3-amino-2-hydroxypropanesulfonic acid (TAPSO), Tricine, triethanolamine (TEA) and combinations thereof, optionally wherein the buffering agent is at a concentration of between 5 mM to 200 mM; and/or

b) further comprises sodium chloride and/or a divalent salt at a concentration of up to 1000 mM; and/or

c) comprises 20 mM sodium dihydrogen phosphate, 500 mM sodium chloride and is at a pH of 7.4; and/or

ii) the elution buffer:

a) is or comprises a phosphate buffer and/or an acetate buffer at a pH of between 3 and 5; and/or

b) contacts the resin for up to 5 minutes.

6. The method of any one of claims 1 to 5, wherein the method further comprises:
   i) equilibrating the resin with an equilibration buffer having a pH between 7 and 8, optionally wherein:
      a) the equilibration buffer comprises 20 mM sodium dihydrogen phosphate, 500 mM sodium chloride and is at a pH of 7.4; and/or
      b) the resin is equilibrated i) after stripping the resin or ii) without stripping the resin; and/or
      ii) equilibrating the resin after stripping the resin with an equilibration buffer having a pH between 7 and 8.

7. The method of any one of claims 1 to 6:
   i) wherein:
      a) the continuous affinity chromatography is selected from the group consisting of simulated moving bed (SMB) chromatography, periodic counter-current chromatography (PCC), continuous counter-current tangential chromatography (CCTC), and continuous counter-current spiral chromatography (CCSC); and/or
      b) the resin is in the form of a slurry or the resin is packed into one or more column(s), wherein each column comprises one or more zones, optionally wherein:
         A) a zone is selected from a group consisting of an equilibration zone, a binding zone, a wash zone, an elution zone or a combination thereof; and/or
         B) the columns are fluidly connected and separated by fluid conduits comprising inlet and outlet valves; and/or
         C) the resin is packed into a series of three columns, wherein each column is a separate zone; and/or
   ii) wherein:
      a) the resin is packed into a first column and one or more subsequent column(s), optionally wherein:

A) the first column is loaded with IgG at a concentration above the dynamic binding capacity (DBC) of the resin, optionally wherein the DBC of the resin is at least 5 mg IgG per mL of resin; and/or

B) the one or more subsequent column(s) are loaded with IgG at a concentration up to the DBC of the resin; and/or

C) the one or more subsequent column(s) are loaded with IgG at a concentration of up to 40 mg IgG per mL of resin.

8. The method of any one of claims 1 to 7, wherein:

i) the resin has a total bed height of at between 2 cm and 30 cm; and/or

ii) the method further comprises regenerating the resin; and/or

iii) the method further comprises sanitizing the resin; and/or

iv) the method further comprises one or more steps selected from a group consisting of ethanol precipitation, octanoic acid fractionation, ion exchange chromatography, viral inactivation, viral filtration and ultrafiltration/diafiltration, optionally wherein the ion exchange chromatography step comprises anion exchange chromatography step using a strong anion exchange resin operated in flow through mode, further optionally wherein:

a) the strong anion exchange resin comprises a matrix consisting of a poly(styrene-divinylbenzene) matrix; and/or

b) the strong anion exchange resin comprises a quaternized polyethyleneimine functional group; and/or

c) the anion exchange chromatography step comprises a post-load wash buffer selected from the group consisting of a phosphate buffer, a sodium citrate buffer, a 2-(N-morpholino)ethanesulfonic acid buffer, an acetic acid buffer, a Bis-tris buffer and a L-histidine buffer, optionally wherein:

A) the post-load wash buffer comprises a phosphate buffer at a pH in the range of 5.8 to 6.6; and/or

B) the post-load wash buffer further comprises sodium chloride at a concentration of between 0 mM and 50 mM.

9. The method of any one of claims 1 to 8, wherein:

i) at least 75% of the IgG is recovered from the plasma or fraction thereof; and/or

ii) wherein the eluted IgG has a purity of at least 95%; and/or

iii) wherein the method further comprises formulating the IgG into a pharmaceutical composition.

10. A method for purifying immunoglobulin G (IgG) from plasma or a fraction thereof using simulated moving bed (SMB) chromatography, the method comprising:

a) equilibrating an affinity chromatography resin comprising a cross-linked poly(styrene-divinylbenzene) matrix and a ligand capable of specifically binding to a CH3 domain of human IgG with a 20mM phosphate equilibration buffer having a pH of between 7 and 8;

b) binding the IgG from the plasma or fraction thereof to the resin;

c) washing the resin with a 20mM phosphate wash buffer having a pH of between 7 and 8; and

d) eluting the bound IgG with a 20mM acetate or phosphate elution buffer having a pH of between 3 and 5;

wherein steps a) to d) may be repeated on the affinity chromatography resin and wherein, the affinity chromatography resin is packed into a series of two or more fluidly-connected columns separated by fluid conduits comprising inlet and outlet valves, and optionally wherein the method does not comprise stripping the resin.

11. A pharmaceutical composition comprising IgG purified or produced by a method of any one of claims 1 to 10.

12. The pharmaceutical composition of claim 11:

i) wherein:

a) the pharmaceutical composition comprises 100 mg/mL of total human plasma protein; or

b) the pharmaceutical composition comprises 20 g/ 100 mL of total human plasma protein; and/or

ii) wherein:

a) the pharmaceutical composition comprises a purity of at least 98% immunoglobulin G (IgG); and/or

b) the pharmaceutical composition comprises a nominal osmolality of 320 mOsm/kg; and/or

c) the pharmaceutical composition comprises a pH of between 4.6 and 5.0; and/or

d) the pharmaceutical composition comprises a pH of 4.8; and/or

e) the pharmaceutical composition further comprises 250 mmol/L of L-proline; and/or

f) the pharmaceutical composition comprises a sodium content of ≤1 mmol/L; and/or

g) the pharmaceutical composition comprises an IgA content of ≤ 0.05 mg/mL; and/or

h) the pharmaceutical composition comprises a Prekallikrein activator (PKA) level of ≤ 35 IU/mL.

13. Use of IgG purified or produced by a method of any one of claims 1 to 12 in the manufacture of a medicament for treating, preventing and/or delaying progression of a condition in a subject.

14. The pharmaceutical composition of claim 11 or claim 12, for use in treating, preventing and/or delaying progression of a condition in a subject.

15. The use of claim 13 or the pharmaceutical composition of claim 14, wherein the condition is selected from a group consisting of primary immunodeficiency disease (PI), chronic inflammatory demyelinating polyneuropathy (CIDP), and chronic immune thrombocytopenic purpura (ITP).