WHAT IS CLAIMED IS:

1. A method of enhancing efficiency of downstream chromatography steps for purification of proteins comprising:

a. passing a composition comprising a polypeptide of interest and various contaminants through an ion exchange membrane, wherein the polypeptide and the membrane have opposite charge, at operating conditions comprised of a buffer having a pH sufficiently distinct from the pI of the polypeptide to enhance the charge of the polypeptide and a low ionic strength effective to prevent the shielding of charges by buffer ions, which cause the membrane to bind the polypeptide and at least one contaminant;

b. overloading the ion exchange membrane such that at least one contaminant remains bound to the membrane while the polypeptide of interest is primarily in the effluent;

c. collecting the effluent from the ion exchange membrane comprising the polypeptide of interest;

d. subjecting the membrane effluent comprising the polypeptide of interest to a ion exchange chromatography step of similar charge as the previous membrane , and

e. recovering the purified polypeptide from the effluent of the charged ion exchange chromatography step.

2. The method of claim 1 wherein the ion exchange membrane has a pore size of 0.1 to 100 μm.

3. The method of claim 1 wherein the ion exchange membrane is replaced by a monolith or depth filter.

4. A method of enhancing efficiency of downstream chromatography steps for purification of proteins comprising:

a. passing a composition comprising a polypeptide of interest and various contaminants through a cation exchange membrane, wherein the polypeptide and the membrane have opposite charge, at operating conditions comprised of a buffer having a pH of about 1 to about 5 pH units below the pI of the polypeptide and a conductivity of ≤ about 40 mS/cm, which cause the membrane to bind the polypeptide and at least one contaminant,

b. overloading the cation exchange membrane such that at least one contaminant remains bound to the membrane while the polypeptide of interest is primarily in the effluent;

c. collecting the effluent from the cation exchange membrane comprising the polypeptide

of interest;

d. subjecting the membrane effluent comprising the polypeptide of interest to a cation exchange chromatography purification step, and

e. recovering the purified polypeptide from the effluent of the cation exchange chromatography purification step.

5. The method of claim 4 wherein the pH is about 1 to about 4 pH units below the pI of the polypeptide.

6. The method of claim 4 wherein the pH is about 1 to about 3 pH units below the pI of the polypeptide.

7. The method of claim 4 wherein the pH is about 1 to about 2 pH units below the pI of the polypeptide.

8. The method of claim 4 wherein the pH is about 1 pH unit below the pI of the polypeptide.

9. The method of claim 4 wherein the conductivity is ≤ about 20 mS/cm.

10. The method of claim 4 wherein the conductivity is ≤ about 10 mS/cm.

11. The method of claim claim 4 wherein the cation exchange membrane is a cation exchange monolith or depth filter.

12. A method of enhancing efficiency of downstream chromatography steps for purification of proteins comprising:

a. passing a composition comprising a polypeptide of interest and various contaminants through an anion exchange membrane, wherein the polypeptide and the membrane have opposite charge, at operating conditions comprised of a buffer having a pH of about 1 to about 5 pH units above the pI of the polypeptide and a conductivity of ≤ about 40 mS/cm, which cause the membrane to bind the polypeptide and the at least one contaminant,

b. overloading the anion exchange membrane such that at least one contaminant remains bound to the membrane while the polypeptide of interest is primarily in the effluent;

c. collecting the effluent from the anion exchange membrane comprising the polypeptide of interest;

d. subjecting the membrane effluent comprising the polypeptide of interest to a anion exchange chromatography purification step, and

e. recovering the purified polypeptide from the effluent of the anion exchange

chromatography purification step.

13. The method of claim 12 wherein the pH is about 1 to about 4 pH units above the pI of the polypeptide.

14. The method of claim 12 wherein the pH is about 1 to about 3 pH units above the pI of the polypeptide.

15. The method of claim 12 wherein the pH is about 1 to about 2 pH units above the pI of the polypeptide.

16. The method of claim 12 wherein the pH is about 1 pH unit above the pI of the polypeptide.

17. The method of claim 12 wherein the conductivity is ≤ about 20 mS/cm.

18. The method of claim 12 wherein the conductivity is ≤ about 10 mS/cm.

19. The method of claim 12 wherein the anion exchange membrane is replaced with an anion exchange monolith or depth filter

20. The method of any of claims 1 to 19 wherein the membrane is a mixed mode adsorber.

21. The method of any of claims 1 to 20 wherein the contaminant is a host cell protein

22. The method of claim 21 wherein the host cell protein is a Chinese Hamster Ovary Protein (CHOP).

23. The method of claim 21 wherein the host cell protein is an *E.coli* protein (ECP).

24. The method of any of claims 1 to 20 wherein the contaminant is an aminoglycoside antibiotic.

25. The method of claim 24 wherein the aminoglycoside antibiotic is gentamicin.

26. The method of any of claims 1 to 20 wherein the contaminant is an ionic polymer

27. The method of claim 26 wherein the ionic polymer is polyethyleneimine (PEI).

28. The method of any of claims 1 to 20 wherein the polypeptide comprises a CH2/CH3 region.

29. The method of claim 28 wherein the polypeptide is an antibody.

30. The method of claim 29 wherein the antibody is a monoclonal antibody.

31. The method of any of claims 1 to 30 wherein the further purification step(s) comprises ion exchange chromatography.

32. The method of any of claims 1 to 30 wherein the further purification step(s) run continuously during steps a through e, said purification step being ion exchange chromatography.

33. The method of claim 31 or 32, wherein the ion exchange chromatography comprises a cation exchange column.

34. The method of claim 31 or 32, wherein the ion exchange chromatography comprises an anion exchange column.

35. The method of any of claims 1 to 34 further comprising preparing a pharmaceutical composition by combining the purified polypeptide with a pharmaceutically acceptable carrier.

Claims:

1. A method of enhancing efficiency of downstream chromatography steps for purification of antibodies comprising:

a. passing a composition comprising an antibody of interest and various contaminants through an ion exchange membrane, wherein the antibody and the membrane have opposite charge, at operating conditions comprised of a buffer having a pH sufficiently distinct from the pI of the antibody to enhance the charge of the antibody and a low ionic strength effective to prevent the shielding of charges by buffer ions, which cause the membrane to bind the antibody and at least one contaminant;

b. overloading the ion exchange membrane to a load density of 1000-5000 g/L such that at least one contaminant remains bound to the membrane while the antibody of interest is primarily in the effluent;

c. collecting the effluent from the ion exchange membrane comprising the antibody of interest;

d. subjecting the membrane effluent comprising the antibody of interest to a ion exchange chromatography step of similar charge as the previous membrane , and

e. recovering the purified antibody from the effluent of the charged ion exchange chromatography step.

2. The method of claim 1 wherein the ion exchange membrane has a pore size of 0.1 to 100 μm.

3. The method of claim 1 wherein the ion exchange membrane is replaced by a monolith or depth filter.

4. A method of enhancing efficiency of downstream chromatography steps for purification of antibodies comprising:

a. passing a composition comprising an antibody of interest and various contaminants through a cation exchange membrane, wherein the antibody and the membrane have opposite charge, at operating conditions comprised of a buffer having a pH of about 1 to about 5 pH units below the pI of the antibody and a conductivity of < about 40 mS/cm, which cause the membrane to bind the antibody and at least one contaminant,

b. overloading the cation exchange membrane such that at least one contaminant remains bound to the membrane while the antibody of interest is primarily in the effluent;

c. collecting the effluent from the cation exchange membrane comprising the antibody of interest;

d. subjecting the membrane effluent comprising the antibody of interest to a cation exchange chromatography purification step, and

e. recovering the purified antibody from the effluent of the cation exchange chromatography purification step.

5. The method of claim 4 wherein the pH is about 1 to about 4 pH units below the pI of the antibody.

6. The method of claim 4 wherein the pH is about 1 to about 3 pH units below the pI of the antibody.

7. The method of claim 4 wherein the pH is about 1 to about 2 pH units below the pI of the antibody.

8. The method of claim 4 wherein the pH is about 1 pH unit below the pI of the antibody.

9. The method of claim 4 wherein the conductivity is < about 20 mS/cm.

10. The method of claim 4 wherein the conductivity is < about 10 mS/cm.

11. The method of claim 4 wherein the cation exchange membrane is a cation exchange monolith or depth filter.

12. A method of enhancing efficiency of downstream chromatography steps for purification of antibodies comprising:

a. passing a composition comprising an antibody of interest and various contaminants through an anion exchange membrane, wherein the antibody and the membrane have opposite charge, at operating conditions comprised of a buffer having a pH of about 1 to about 5 pH units above the pI of the antibody and a conductivity of < about 40 mS/cm, which cause the membrane to bind the antibody and the at least one contaminant,

b. overloading the anion exchange membrane such that at least one contaminant remains bound to the membrane while the antibody of interest is primarily in the effluent;

c. collecting the effluent from the anion exchange membrane comprising the antibody of interest;

d. subjecting the membrane effluent comprising the antibody of interest to a anion exchange chromatography purification step, and

e. recovering the purified antibody from the effluent of the anion exchange chromatography purification step.

13. The method of claim 12 wherein the pH is about 1 to about 4 pH units above the pI of the antibody.

14. The method of claim 12 wherein the pH is about 1 to about 3 pH units above the pI of the antibody.

15. The method of claim 12 wherein the pH is about 1 to about 2 pH units above the pI of the antibody.

16. The method of claim 12 wherein the pH is about 1 pH unit above the pI of the antibody.

17. The method of claim 12 wherein the conductivity is < about 20 mS/cm.

18. The method of claim 12 wherein the conductivity is < about 10 mS/cm.

19. The method of claim 12 wherein the anion exchange membrane is replaced with an anion exchange monolith or depth filter.

20. The method of any of claims 1 to 19 wherein the membrane is a mixed mode adsorber.

21. The method of any of claims 1 to 20 wherein the contaminant is a host cell protein.

22. The method of claim 21 wherein the host cell protein is a Chinese Hamster Ovary Protein (CHOP).

23. The method of claim 21 wherein the host cell protein is an E.coli protein (ECP).

24. The method of any of claims 1 to 20 wherein the contaminant is an aminoglycoside antibiotic.

25. The method of claim 24 wherein the aminoglycoside antibiotic is gentamicin.

26. The method of any of claims 1 to 20 wherein the contaminant is an ionic polymer.

27. The method of claim 26 wherein the ionic polymer is polyethyleneimine (PEI).

28. The method of any of claims 1 to 27 wherein the antibody is a monoclonal antibody.

29. The method of any of claims 1 to 28 wherein the further purification step(s) comprises ion exchange chromatography.

30. The method of any of claims 1 to 28 wherein the further purification step(s) run continuously during steps a through e, said purification step being ion exchange chromatography.

31. The method of claim 29 or 30, wherein the ion exchange chromatography comprises a cation exchange column.

32. The method of claim 29 or 30, wherein the ion exchange chromatography comprises an anion exchange column.

33. The method of any of claims 1 to 32 further comprising preparing a pharmaceutical composition by combining the purified polypeptide with a pharmaceutically acceptable carrier.