CLAIMS

1. A method of purifying or enriching a biomolecule, the method comprising the steps:

(a) providing an aqueous solution containing the biomolecule;

(b) contacting the aqueous solution with a multimodal resin;

(c) optionally washing the multimodal resin with an aqueous washing buffer;

(d) eluting the biomolecule from the multimodal resin by an aqueous buffer solution, wherein the aqueous buffer solution comprises:

(i) at least 15 mM N-(2-acetoamido)iminodiacetic acid (ADA), N-(2-acetamido)-2-aminoethanesulfonic acid (ACES), N,N-bis(2-hydroxyethyl)-2-aminoethanesulfonic acid (BES), N,N-bis(2-hydroxyethyl)glycine (Bicine), 3-(cyclohexylamino)-1-propanesulfonic acid (CAPS), 3-(cyclohexylamino)-2-hydroxy-1-propanesulfonic acid (CAPSO), 2-(cyclohexylamino)ethanesulfonic acid (CHES), 4-(2-hydroxyethyl)piperazine-1-ethanesulfonic acid (HEPES), 3-(N-morpholino)propanesulfonic acid (MOPS), 1,4-piperazinediethanesulfonic acid (PIPES), N-[tris(hydroxymethyl)methyl]-3-aminopropanesulfonic acid (TAPS), or 2-[(2-hydroxy-1,1-bis(hydroxymethyl)ethyl)amino]ethanesulfonic acid (TES); and

(ii) one or both of:

between 10 and 400 mM alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; and

between 10 and 400 mM guanidium chloride, guanidium thiocyanate, ammonium chloride, ammonium sulfate, ammonium phosphate, ammonium acetate, sodium chloride, sodium citrate, sodium caprylate, sodium phosphate, sodium iodide, potassium chloride, potassium citrate, potassium sulfate, potassium phosphate, potassium iodide, magnesium chloride, magnesium sulfate, magnesium phosphate, calcium chloride, calcium sulfate, calcium phosphate, or taurine; and

optionally, further comprising (iii) between 1% and 60% (v/v) of ethylene glycol or propylene glycol or a mixture of ethylene glycol and propylene glycol; and

(e) collecting biomolecule containing fractions, thereby obtaining the biomolecule in purified or enriched form.

2. The method according to claim 1, wherein the aqueous buffer solution comprises 15 mM to 2.5 M of ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES.

3. The method according to claim 1 or claim 2, wherein the aqueous buffer solution comprises MES.

4. The method according to claim 1 or claim 2, wherein the aqueous buffer solution comprises MOPS.

5. The method according to any one of claims 1 to 4, wherein the biomolecule is a protein.

6. The method according to claim 5, wherein the protein is an enzyme.

7. The method according to claim 6, wherein the enzyme is glycosidase.

8. The method according to claim 7, wherein the glycosidase is an alpha-galactosidase.

9. The method according to claim 8, wherein the alpha-galactosidase is selected from the group consisting of agalsidase alfa and agalsidase beta.

10. The method according to any one of claims 1 to 9, wherein the multimodal resin is selected from the group consisting of Capto™ Adhere, Capto™ MMC, Pall PPA HyperCel™, Pall HEA HyperCel™, Pall MEP HyperCel™, and Eshmuno® HCX.

11. A purified biomolecule obtained by the method according to any one of claims 1 to 10.

12. A preparation comprising:

(a) a biomolecule; and

(b) an aqueous buffer solution comprising ~~one or more of~~:

(i) at least 15 mM ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES;

(ii) one or both of:

between 10 and 400 mM alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; and

between 10 and 400 mM guanidium chloride, guanidium thiocyanate, ammonium chloride, ammonium sulfate, ammonium phosphate, ammonium acetate, sodium chloride, sodium citrate, sodium caprylate, sodium phosphate, sodium iodide, potassium chloride, potassium citrate, potassium sulfate, potassium phosphate, potassium iodide, magnesium chloride, magnesium sulfate, magnesium phosphate, calcium chloride, calcium sulfate, calcium phosphate, or taurine; and

optionally, further comprising (iii) between 1% and 60% (v/v) of ethylene glycol or propylene glycol or a mixture of ethylene glycol and propylene glycol.

13. The preparation according to claim 12, wherein the aqueous buffer solution comprises 15 mM and 2.5 M ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES.

14. The preparation according to claim 12 or 13, wherein the aqueous buffer solution comprises MES.

15. The preparation according to claim 12 or 13, wherein the aqueous buffer solution comprises MOPS.

16. The preparation according to any one of claims 12 to 15, wherein the biomolecule is a protein.

17. The preparation according to claim 16, wherein the protein is an enzyme.

18. The preparation according to claim 17, wherein the enzyme is a glycosidase.

19. The preparation according to claim 18, wherein the glycosidase is an alpha-galactosidase.

20. The preparation according to claim 19, wherein the alpha-galactosidase is selected from the group of agalsidase alfa and agalsidase beta.

21. A method for desorbing a biomolecule from a multimodal resin, comprising contacting a biomolecule bound to a multimodal resin with an aqueous buffer, wherein the aqueous buffer solution comprises:

(i) at least 15 mM ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES; and

(ii) one or both of:

between 10 and 400 mM alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; and

between 10 and 400 mM guanidium chloride, guanidium thiocyanate, ammonium chloride, ammonium sulfate, ammonium phosphate, ammonium acetate, sodium chloride, sodium citrate, sodium caprylate, sodium phosphate, sodium iodide, potassium chloride, potassium citrate, potassium sulfate, potassium phosphate, potassium iodide, magnesium chloride, magnesium sulfate, magnesium phosphate, calcium chloride, calcium sulfate, calcium phosphate, or taurine; and

optionally, further comprising (iii) between 1% and 60% (v/v) of ethylene glycol or propylene glycol or a mixture of ethylene glycol and propylene glycol.

22. A method for increasing the recovery rate of a biomolecule absorbed on a multimodal resin by contacting the multimodal resin onto which the biomolecule has been absorbed with an aqueous buffer solution, wherein the ~~said~~ aqueous buffer solution comprises:

(i) at least 15 mM ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES; and

(ii) one or both of:

between 10 and 400 mM alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; and

between 10 and 400 mM guanidium chloride, guanidium thiocyanate, ammonium chloride, ammonium sulfate, ammonium phosphate, ammonium acetate, sodium chloride, sodium citrate, sodium caprylate, sodium phosphate, sodium iodide, potassium chloride, potassium citrate, potassium sulfate, potassium phosphate, potassium iodide, magnesium chloride, magnesium sulfate, magnesium phosphate, calcium chloride, calcium sulfate, calcium phosphate, or taurine; and

optionally, further comprising (iii) between 1% and 60% (v/v) of ethylene glycol or propylene glycol or a mixture of ethylene glycol and propylene glycol.

23. The method of claim 21 or claim 22, wherein the aqueous buffer solution comprises between 15 mM and 2.5 M ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES.

24. The method of any one of claims 21 to 23, wherein the aqueous buffer solution comprises MES.

25. The method of any one of claims 21 to 23, wherein the aqueous buffer solution comprises MOPS.

26. The method of any one of claims 21 to 25, wherein the biomolecule is a protein.

27. The method of claim 26, wherein the protein is an enzyme.

28. The method of claim 27, wherein the enzyme is a glycosidase.

29. The method of claim 28, wherein the glycosidase is an alpha-galactosidase.

30. The method of claim 29, wherein the alpha-galactosidase is selected from the group consisting of agalsidase alfa and agalsidase beta.

31. The method of any one of claims 21 to 30, wherein the multimodal resin is selected from the group consisting of Capto™ Adhere, Capto™ MMC, Pall PPA HyperCel™, Pall HEA HyperCel™, Pall MEP HyperCel™, and Eshmuno® HCX.

32. An article of manufacture comprising:

(a) a packaging material or container;

(b) an aqueous buffer solution comprising:

(i) at least 15 mM ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES; and

(ii) one or both of:

between 10 and 400 mM alanine, arginine, asparagine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, or valine; and

between 10 and 400 mM urea, guanidium chloride, guanidium thiocyanate, ammonium chloride, ammonium sulfate, ammonium phosphate, ammonium acetate, sodium chloride, potassium chloride, potassium citrate, potassium sulfate, potassium phosphate, potassium iodide, magnesium chloride, magnesium sulfate, magnesium phosphate, calcium chloride, calcium sulfate, calcium phosphate, or taurine; and

optionally, further comprising (iii) between 1% and 60% (v/v) of ethylene glycol or propylene glycol or a mixture of ethylene glycol and propylene glycol; and

(c) a data carrier containing instructions for carrying out a method according to any one of claims 1 to 10.

33. The article of manufacture according to claim 32, wherein the data carrier is a label present on the packaging material or container or a packaging insert.

34. The article of manufacture according to claim 32 or claim 33, wherein the data carrier comprises written information, visual information, or computer-readable information.

35. The article of manufacture according to any one of claims 32 to 34, wherein the data carrier further comprises one or more of the following information:

(i) instructions for use of aqueous buffer solution;

(ii) quality information such as information about the lot/batch number, the manufacturing or assembly site or the expiry or sell-by date of the aqueous buffer solution; or information concerning the correct storage or handling of the article;

(iii) information concerning the composition of the aqueous buffer solution;

(iv) information concerning the interpretation of information obtained when performing methods according to any one of claims 1 to 10;

(v) a warning concerning possible misinterpretations or wrong results when applying unsuitable methods; and

(vi) a warning concerning possible misinterpretations or wrong results when using unsuitable reagent(s) and/or buffer(s).

36. The article of manufacture according to any one of claims 32 to 35, further comprising one or more of the following components:

(d) a chromatography medium;

(e) a chromatography column; and

(f) a reference biomolecule usable for calibrating a method for purifying or enriching a biomolecule.

37. The article of manufacture according to claim 36, wherein the chromatography column is prepacked with the chromatography medium.

38. The article of manufacture according to claim 36 or claim 37, wherein the chromatography medium is a multimodal chromatography resin.

39. The article of manufacture according to claim 38, wherein the multimodal chromatography resin is selected from the group consisting of Capto™ Adhere, Capto™ MMC, Pall PPA HyperCel™, Pall HEA HyperCel™, Pall MEP HyperCel™, and Eshmuno® HCX.

40. The article of manufacture according to any one of claims 36 to 39, wherein the reference biomolecule is a protein or a nucleic acid.

41. The article of manufacture according to any one of claims 32 to 40, wherein the aqueous buffer solution comprises between 15 mM and 2.5 M ADA, ACES, BES, Bicine, CAPS, CAPSO, CHES, HEPES, MOPS, PIPES, TAPS, or TES.

42. The article of manufacture according to any one of claims 32 to 41, wherein the aqueous buffer solution comprises MES.

43. The article of manufacture according to any one of claims 32 to 42, wherein the aqueous buffer solution comprises MOPS.

44. The method according to claim 3 or claim 4, wherein the aqueous buffer solution comprises 10 mM to 400 mM arginine.

45. The method according to claim 44, wherein the aqueous buffer solution comprises 150 mM to 400 mM arginine.

46. The preparation according to claim 14 or claim 15, wherein the aqueous buffer solution comprises 10 mM to 400 mM arginine.

47. The preparation according to claim 46, wherein the aqueous buffer solution comprises 150 mM to 400 mM arginine.

48. The method according to claim 24 or claim 25, wherein the aqueous buffer solution comprises 10 mM to 400 mM arginine.

49. The method according to claim 48, wherein the aqueous buffer solution comprises 150 mM to 400 mM arginine.

50. The article of manufacture according to claim 42 or claim 43, wherein the aqueous buffer solution comprises 10 mM to 400 mM arginine.

51. The article of manufacture according to claim 50, wherein the aqueous buffer solution comprises 150 mM to 400 mM arginine.

52. The method according to claim 9, wherein the agalsidase beta is Fabrazyme®.

53. The method according to claim 9, wherein the agalsidase alfa is Replagal™.

54. The preparation according to claim 20, wherein the agalsidase beta is Fabrazyme®.

55. The preparation according to claim 20, wherein the agalsidase alfa is Replagal™.

56. The method according to claim 30, wherein the agalsidase beta is Fabrazyme®.

57. The method according to claim 30, wherein the agalsidase alfa is Replagal™.