Claims:

1. A method for purifying recombinant a disintegrin-like and metallopeptidase with thrombospondin type 1 motif 13 (ADAMTS13) protein from a sample comprising ADAMTS13 protein and non-ADAMTS13 impurities, the method comprising chromatographically contacting the sample with hydroxyapatite under conditions that allow said ADAMTS13 protein to appear in an eluate or a supernatant from said hydroxyapatite.

2. The method according to claim 1, further comprising chromatographically contacting said eluate with a cation exchange/hydrophobic interaction resin that binds said ADAMTS13 protein.

3. The method according to claim 1 or 2, further comprising chromatographically contacting said sample with an anion exchange resin and eluting said ADAMTS13 protein from said anion exchange resin before chromatographic contact with said hydroxyapatite.

4. The method according to claim 1 or 2, further comprising concentrating said ADAMTS13 protein in said sample by ultrafiltration; and stabilizing said ADAMTS13 protein by diafiltration exchange into a buffer comprising calcium ions and zinc ions before chromatographic contact with said hydroxyapatite.

5. The method according to claim 2, further comprising, following contact with said hydroxyapatite or said cation exchange/hydrophobic interaction resin, the step of preparing said ADAMTS13 protein for cation exchange by reducing buffer conductivity.

6. The method according to claim 5, wherein said preparing step is performed by ultrafiltration/diafiltration.

7. The method according to claim 5, wherein said preparing step is performed by dialysis, said dialysis consisting of no more than 2 passes through a single dialysis module.

8. The method according to claim 5, wherein said preparing step is performed by gel filtration.

9. The method according to any one of claims 1, 2, or 5, further comprising subjecting said ADAMTS13 protein to at least one virus inactivation step.

10. The method according to 9, wherein said virus inactivation step comprises adding a solvent-detergent mixture comprising a non-ionic detergent and an organic solvent to said ADAMTS13 protein.

11. The method according to claim 10, wherein said ADAMTS13 protein is immobilized.

12. The method according to claim 11, wherein said ADAMTS13 protein is immobilized on a cation exchange resin.

13. The method according to claim 10, wherein said solvent-detergent mixture comprises 1% TRITONX-100, 0.3% Tri-N-butyl phosphate, and 0.3% TWEEN 80.

14. The method according to claim 9, wherein said virus inactivation step comprises filtering said ADAMTS13 protein with a nanofilter to remove viruses and/or viral particles.

15. The method according to claim 9, wherein said virus inactivation step is performed after said preparing step.

16. The method according to claim 12, further comprising eluting said ADAMTS13 protein from said resin using gradient elution, said gradient elution using a first buffer having low salt content and a second buffer having higher salt content.

17. The method according to claim 12, further comprising eluting said ADAMTS13 protein from said resin using step elution.

18. The method according to claim 17, wherein said step elution comprises eluting said ADAMTS13 protein from said resin with a storage buffer.

19. The method according to claim 18, wherein said storage buffer has a pH of greater than 7.0 and comprises less than 10 mM calcium ions, a buffering compound, 0.05% non-ionic detergent, and a salt.

20. The method according to claim 18, wherein there is no subsequent concentration or buffer exchange step.

21. A composition comprising a recombinant ADAMTS13 protein prepared according to the method of any one of claims 1, 2, or 5.

22. A composition comprising a recombinant ADAMTS13 protein prepared according to the method of claim 12.

23. A method for inactivating virus contaminants in a protein sample, said method comprising:

immobilizing said protein on a support; and

treating said immobilized protein with a solvent-detergent mixture comprising a non-ionic detergent and an organic solvent.

24. The method according to claim 23, wherein said protein is at least one selected from ADAMTS13, Advate, Factor VIIa, Factor IX, von Willebrand factor, and anti-MIF antibody.

25. The method according to claim 23, wherein said support is a chromatographic resin.

26. The method according to claim 23, wherein said solvent-detergent mixture comprises 1% Triton X-100, 0.3% Tri-N-butyl phosphate, and 0.3% Polysorbate 80.

27. The method according to claim 23, wherein said solvent-detergent mixture treatment continues for 30 minutes to 1 hour.

28. The method according to claim 23, further comprising eluting said protein from said support with a storage buffer.

29. The method according to claim 28, wherein said storage buffer has a pH of greater than 7.0 and comprises less than 10 mM calcium ions, a buffering compound, 0.05% non-ionic detergent, and a salt.

30. The method according to claim 28, wherein there is no subsequent concentration or buffer exchange step.

CLAIMS

1. An *in vitro* method for inactivating lipid-enveloped virus contaminants in a protein solution in the purification of a therapeutic protein composition, said method comprising:

providing a protein solution comprising a therapeutic protein and possibly comprising lipid-enveloped virus contaminants;

immobilizing said therapeutic protein on a support *in vitro*, wherein said immobilization occurs via bonds between a group on said support and a group on said immobilized protein;

wherein said immobilization is not in the presence of a solvent-detergent mixture, said mixture comprising a non-ionic detergent and an organic solvent; and

subsequently treating said therapeutic protein, while said therapeutic protein remains immobilized on said support, with a solvent-detergent mixture comprising a non-ionic detergent and an organic solvent at concentrations and for a time period suitable to effect inactivation of said lipid-enveloped virus contaminants;

wherein said solvent-detergent treatment results in reduced formation of aggregates of said therapeutic protein compared to solvent-detergent treatment while said therapeutic protein is in solution;

whereby said lipid-enveloped virus contaminants are inactivated.

2. The method according to claim 1, wherein said therapeutic protein is at least one selected from ADAMTS13, Factor VIII, Factor VIIa, Factor IX, von Willebrand factor, and anti-MIF antibody.

3. The method according to claim 1, wherein said support is a chromatographic resin.

4. The method according to claim 1, wherein said solvent-detergent mixture comprises 1% Triton X-100, 0.3% Tri-N-butyl phosphate, and 0.3% Polysorbate 80.

5. The method according to claim 1, wherein incubation in said solvent-detergent mixture continues for 30 minutes to 1 hour.

6. The method according to claim 1, further comprising eluting said therapeutic protein from said support with a storage buffer.

7. The method according to claim 6, wherein said storage buffer has a pH of greater than 7.0 and comprises less than 10 mM calcium ions, a buffering compound, 0.05% non-ionic detergent, and a salt.

8. The method according to claim 6, wherein said support is a cation exchange resin; and

wherein there is no ultrafiltration, diafiltration, or buffer exchange step subsequent to the eluting step from the cation exchange resin with the storage buffer.