Claims

1. A method for extracting a protein of interest from a precipitate, comprising:

    a. mixing the precipitate with a liquid in a first tank to form a suspension having a first dilution factor;

    b. feeding the suspension into a first filtration unit comprising a dynamic filter element adapted to produce a first retentate and a first permeate enriched with the protein of interest;

    c. diluting the suspension in the first tank by adding liquid to a second dilution factor, optionally by streaming the first retentate into the first tank; and

    d. recovering the first permeate enriched with the protein of interest in a second tank,

wherein steps b and c are repeated until one or both of (i) a final dilution factor has been achieved in the first tank and (ii) a protein concentration of the suspension in the first tank of 0.001 g/L to 0.1 g/L has been achieved.

2. The method according to claim 1, wherein the first dilution factor is from 1 to 10.

3. The method according to claim 1, wherein steps b and c are repeated until a final dilution factor of is from 6 to 70 has been achieved in the first tank.

4. The method according to claim 1, wherein steps b and c are repeated until a protein concentration of the suspension in the first tank of 0.001 g/L to 0.1 g/L has been achieved.

5. The method according claim 1, wherein the precipitate is an intermediate product of an alcohol fractionation process of blood plasma.

6. The method according to claim 5, wherein the intermediate product is selected from the group consisting of Cohn Fraction I (Fr I), Cohn Fraction II+III (Fr II+III), Cohn Fraction

I+II+III (Fr I+II+III), Kistler/Nitschmann Precipitate A (KN A), and combinations of KN A and one or more of Fr I, Fr II+III and Fr I+II+III.

7. The method according to claim 1, wherein the precipitate is a culture supernatant or a fermentation product.

8. The method according to claim 1, wherein the protein of interest is an immunoglobulin (Ig).

9. The method according to claim 1, wherein the first filtration unit comprises a pressure vessel.

10. The method according to claim 9, wherein the first filtration unit is equipped with rotating filter discs comprising ceramic membranes and optionally baffles for turbulence mixing of the content of the first filtration unit.

11. The method according to claim 10, wherein a transmembrane pressure across the ceramic membrane is from 0.1 bar to 2.5 bar.

12. The method according to claim 1, wherein the dynamic filter element is a dynamic cross flow filter element.

13. The method according to claim 12, wherein the dynamic cross flow filter element is a rotational cross-filter element having a rotating speed of is from about 600 rpm to about 1200 rpm.

14. The method according to claim 1, wherein the temperature in the first filtration unit is controlled at 2° C. to 25° C.

15. The method according to claim 1, wherein the precipitate comprises a filter aid.

16. The method according to claim 15, wherein the filter aid is removed prior to the first filtration.

17. The method according to claim 1, wherein the extraction process is further assisted by regulating one or more of a flow rate of the suspension in the first filtration unit, a residence

time of the suspension in the first filtration unit, a flow rate of the first retentate, and a flow rate of the first permeate.

18. The method according to claim 1, wherein the suspension has a pH of from about 3.0 to 9.0.

19. The method according to claim 1, wherein the precipitate has a total protein concentration of about 0.5 to 6.5% w/v.

20. The method according to claim 1, wherein the liquid comprises a buffer comprising one or more of sodium acetate, sodium phosphate, and citric acid.

21. The method according to claim 1, wherein the precipitate is added to the first tank in the form of a suspension, pellet or paste.

22. The method according to claim 1, wherein the product of the method is subjected to further processing including one or more of chromatography steps, virus inactivation steps, concentration and formulation such that the end product is suitable for administration to a subject.

23. A method for extracting a protein of interest from a precipitate, comprising:

a. mixing the precipitate with a liquid in a first tank to form a suspension having a first dilution factor;

b. feeding the suspension into a first filtration unit comprising a dynamic filter element adapted to produce a first retentate and a first permeate enriched with the protein of interest;

c. diluting the suspension in the first tank by adding liquid to a second dilution factor, optionally by streaming the first retentate into the first tank;

d. recovering the first permeate enriched with the protein of interest in a second tank;

e. subjecting the first permeate in the second tank to a continuous concentration

process in a second filtration unit comprising a cross flow filter element, thereby producing a second retentate enriched with the protein of interest and a second permeate depleted of the protein of interest;

f. optionally diluting the suspension in the first tank by streaming the second permeate to the first tank, thereby diluting the suspension to a further dilution factor; and

g. one or both of (i) returning second retentate enriched with the protein of interest to the second tank and (ii) collecting second retentate enriched with the protein of interest;

wherein either steps b and c or steps b-f are repeated until one or both of (i) a final dilution factor has been achieved in the first tank and (ii) a protein concentration of the suspension in the first tank of 0.001 g/L to 0.1 g/L has been achieved.

24. The method according to claim 23, wherein the first permeate is continuously fed into the concentration process of step e.

25. The method according to claim 23, wherein the concentration process of step e is an ultrafiltration performed in the second filtration unit.

26. The method according to claim 23, wherein the first permeate is collected in the second tank at step d, and once the suspension of the first tank is completely filtrated, the first permeate from the second tank is subjected to the continuous concentration process of step e.

27. The method according to claim 23, wherein the dynamic filter element or the cross-flow filter element comprises a filtration membrane having an average pore size of 5 nm to 5000 nm.

28. The method according to claim 23, wherein a flow velocity of the first permeate and the second permeate are controlled such that a constant product volume is maintained in the second tank.

29. An industrial scaled method for extracting a protein of interest in high yield from a

precipitate, comprising:

a. mixing the precipitate with a liquid in a first tank to form a suspension having a first dilution factor;

b. continuously feeding the suspension into a first filtration unit comprising a rotational cross flow filter element comprising a filter disc having a ceramic membrane with an average pore size between 5 nm and 5000 nm, the filter element adapted to produce a first retentate, and a first permeate enriched with the protein of interest;

c. diluting the suspension in the first tank by adding liquid to a second dilution factor in part by streaming the first retentate into the first tank;

d. recovering the first permeate enriched with the protein of interest in a second tank;

e. subjecting the first permeate in the second tank to a continuous concentration process in a second filtration unit comprising a cross flow filter element, thereby producing a second retentate enriched with the protein of interest and a second permeate depleted of the protein of interest;

f. optionally diluting the suspension in the first tank by continuously streaming the second permeate to the first tank, thereby diluting the suspension to a further dilution factor; and

g. one or both of (i) returning second retentate enriched with the protein of interest to the second tank and (ii) collecting second retentate enriched with the protein of interest,

wherein either steps b and c or steps b-f are repeated until one or both of (i) a final dilution factor has been achieved in the first tank and (ii) a protein concentration of the suspension in the first tank of 0.001 g/L to 0.1 g/L has been achieved.