CLAIMS

1. A method for the purification of immunoglobulins, the method comprising:

- contacting a sample of blood-derived plasma with a medium chain fatty acid, in conditions comprising a pH range of between about 4.6 to about 5.0, for enabling the selective precipitation of albumin from the sample,
- thereby forming a suspension comprising a soluble protein-containing component comprising immunoglobulins and an insoluble protein-containing component comprising albumin;
- separating the soluble protein-containing component from the insoluble protein-containing component to obtain a solution of purified immunoglobulins.

2. A method for the purification of immunoglobulins from plasma, the method comprising:

a) in a first tank: mixing a sample of blood-derived plasma with a medium chain fatty acid, in conditions comprising a pH range of between about 4.6 to about 5.0, for enabling the selective precipitation of albumin from the sample, thereby forming a suspension comprising soluble immunoglobulins and insoluble albumin;

b) feeding the suspension into a first filtration unit comprising a dynamic filter element adapted to produce a first retentate, comprising the insoluble albumin and a first filtrate comprising the soluble immunoglobulins; and

c) recovering the first filtrate in a second tank.

3. A method for the purification of immunoglobulins and albumin, the method comprising:

- contacting a sample of blood-derived plasma with a medium chain fatty acid, in conditions comprising a pH range of between about 4.2 to about 5.0, for enabling the selective precipitation of albumin from the sample,

- thereby forming a suspension comprising a soluble protein-containing component comprising immunoglobulins and an insoluble protein-containing component comprising albumin;

- separating the soluble protein-containing component from the insoluble protein-containing component to obtain a solution of purified immunoglobulins and a suspension comprising albumin;

4. A method for the purification of immunoglobulins and albumin from plasma, the method comprising:

a) in a first tank: mixing a sample of blood-derived plasma with a medium chain fatty acid, in conditions comprising a pH range of between about 4.2 to about 5.0, and optionally, a conductivity of between about 8 mS/cm to about 12 mS/cm, for enabling the selective precipitation of albumin from the sample, thereby forming a suspension comprising soluble immunoglobulins and insoluble albumin;

b) feeding the suspension into a first filtration unit comprising a dynamic filter element adapted to produce a first retentate comprising the insoluble albumin and a first filtrate comprising the soluble immunoglobulin;

c) recovering the first filtrate in a second tank.

5. The method of claim 2 or claim 4, wherein the method further includes step bii) diluting the suspension in the first tank by streaming the retentate into the first tank.

6. A method for the purification of albumin, the method comprising:

- contacting a sample of blood-derived plasma with a medium chain fatty acid, in conditions comprising a pH range of between about 4.15 to about 4.25, for enabling the selective precipitation of albumin from the sample,

- thereby forming a suspension comprising a soluble protein-containing component comprising immunoglobulins and an insoluble protein-containing component comprising albumin;

- separating the soluble protein-containing component from the insoluble protein-containing component to obtain a precipitate or suspension comprising albumin;

7. The method of any one of claims 1, 3 and 6, wherein the step of separating the soluble protein-containing component from the insoluble protein-containing component comprises feeding the suspension into a filtration unit comprising a dynamic filter element adapted to produce a first retentate and a first filtrate.

8. The method of any one of claims 1, 3 and 6-7, wherein the method further comprises recovering the first filtrate.

9. The method of any one of claims 1-8, wherein the method further comprises concentrating the first filtrate.

10. The method of claim 9, wherein the filtrate is concentrated using a filtration unit comprising a dynamic filter element or Tangential Flow Filtration (TFF).

11. The method of any one of claims 1 to 10, wherein the immunoglobulins purified comprise immunoglobulin G (IgG) preferably human immunoglobulin G (IgG).

12. A method for the purification of albumin from plasma, the method comprising:

a) in a first tank: mixing a sample of blood-derived plasma with a medium chain fatty acid, in conditions comprising a pH range of between about 4.15 to about 4.25, and optionally, a conductivity of between about 8 mS/cm to about 12 mS/cm, for enabling the selective precipitation of albumin from the sample, thereby forming a suspension comprising soluble immunoglobulins and insoluble albumin;

b) feeding the suspension into a first filtration unit comprising a dynamic filter element adapted to produce a first retentate comprising the insoluble albumin and a first filtrate comprising the soluble immunoglobulin;

c) recovering the first retentate.

13. The method of claim 12, wherein the method further includes step bii) diluting the suspension in the first tank by streaming the retentate into the first tank.

14. The method of claim 12 or 13, wherein the pH of the first retentate is adjusted to 6.4 – 7.2 to solubilize the albumin.

15. The method of claim 14, wherein the pH of the first retentate is adjusted to 6.8 – 7.2.

16. The method of any one of claims 12 to 15, wherein the solubilized albumin is fed into a further filtration unit comprising a dynamic filter element to produce a retentate depleted of albumin and a filtrate enriched in albumin.

17. The method of any one of claims 12 to 16, wherein the enriched albumin solution is heated in the range of 60 to 65°C.

18. The method of claim 17, wherein the heating occurs for a time period of over 90 min.

19. The method of anyone of claims 12 to 18, wherein after the heating step, the pH of the solution is adjusted to, or about, 4.20 to precipitate proteins denatured during the above-mentioned heating step.

20. The method of claim 19, wherein when the pH is adjusted the solution is at the same time cooled to 4°C.

21. The method of any one of claims 12 to 20, wherein the precipitate is removed by filtration whereby the filtrate comprises purified albumin.

22. The method of claim 21, wherein the albumin purity is equal to or greater than 95%, 96%, 97%, or 98% total protein and albumin yield of equal to or greater than 85%, 86%, 87%, 88%, 89% or 90%.

23. The method of claim 2 or 4, wherein the step of concentrating the first filtrate, comprises subjecting the filtrate to a continuous concentration process in a second filtration unit comprising a dynamic filter element or static Tangential Flow Filtration

(TFF), adapted to produce a second retentate enriched for immunoglobulins and a second filtrate, depleted of immunoglobulins.

24. The method of claim 23, wherein the second filtrate, depleted for immunoglobulins is streamed back into the first tank; and/or the second retentate, enriched for the immunoglobulins, is streamed back into the second tank.

25. The method of claim 23 or 24, wherein the dynamic filter element in the first filtration unit adapted to produce a filtrate (permeate) enriched with soluble protein (immunoglobulins), is a dynamic cross flow filter element and/or wherein the dynamic filter element in the second filtration unit adapted to produce a retentate enriched with immunoglobulins, is a dynamic cross flow filter element or Tangential Flow Filtration (TFF).

26. The method of claim 25, wherein the dynamic cross flow filter element is a rotational cross flow filter element.

27. The method of claim 26, wherein the rotational cross flow filter element comprises a filter disc.

28. The method of claim 27, wherein the filter disc is a ceramic membrane.

29. The method of claim 28,wherein the filter disc is mounted on a shaft member.

30. The method of claim 29, wherein the rotational cross flow filter element comprises more than one filter disc and more than one shaft member.

31. The method of any one of claims 1 to 30, wherein:

(i) the sample of plasma is derived from human blood;

(ii) the sample of blood-derived plasma comprises fresh plasma, cryo-poor plasma or cryo-rich plasma;

(iii) the sample of plasma does not comprise filter aid and/or has not been subjected to an alcohol or other fractionation processes;

(iv) the conductivity of the plasma sample is about 5 mS/cm to about 12 mS/cm;

(v) the pH of the plasma sample is adjusted without substantial dilution of the plasma prior to contact with the medium chain fatty acid; or

the plasma sample is diluted in a buffer prior to the step of being mixed with the medium chain fatty acid; and/or

(vi) the medium chain fatty acid is selected from a fatty acid that comprises a general structural formula of $CH_3(CH_2)_nCOOH$, wherein the fatty acid is a C 6 to C 12 carboxylic acid.

32. The method of claim 31, wherein for (v) the dilution of the plasma sample is of about 1 : 0.5, about 1 : 0.75, about 1 : 1, about 1 : 1.25, about 1 : 1.5, about 1 : 1.75, about 1 : 2, about 1 : 3, or about 1 : 4.

33. The method of claim 32, wherein the fatty acid is selected from: enanthic (heptanoic) acid, caprylic (octanoic) acid, pelargonic (nonanoic) acid, or capric (decanoic) acid, or a salt or ester thereof.

34. The method of claim 1 or 2, wherein the amount of fatty acid, mixed with the plasma sample, is about 0.30 g/g total protein (in the plasma sample), about 0.35 g/g total protein, about 0.40 g/g total protein, about 0.45 g/g total protein or about 0.50 g/g total protein.

35. The method of claim 34, wherein the amount of fatty acid is about 0.300 g/g total protein, or about 0.325 g/g total protein, or about 0.350 g/g total protein, or about 0.375 g/g total protein, or about 0.400 g/g total protein, or about 0.425 g/g total protein, or about 0.450 g/g total protein.

36. The method of claim 35, wherein the amount of fatty acid is at least about 0.350 g/g total protein.

37. The method of claim 3 or 4, wherein the amount of fatty acid mixed with the plasma sample, is about 0.35 g/g total protein (in the plasma sample), about 0.40 g/g total protein, about 0.45 g/g total protein, about 0.50 g/g total protein or about 0.55 g/g total protein.

38. The method of any one of claims 12 to 22, wherein the amount of fatty acid mixed with the plasma sample, is equal to or greater than about 0.35 g/g total protein.

39. The method of claim 38, wherein the amount of fatty acid mixed with the plasma sample, is equal to or greater than about 0.35 g/g total protein but less than, or less than about, 1.1 g/g total protein.

40. The method of any one of claims 1 to 39, wherein

(i) the step of contacting the plasma sample with the medium chain fatty acid comprises mixing of the plasma sample and fatty acid to obtain a homogeneous emulsion of the medium chain fatty acid and plasma sample, preferably wherein the mixing is vigorous mixing, so as to enable formation of the homogeneous emulsion;

(ii) the plasma sample and the medium chain fatty acid, preferably caprylic (octanoic) acid, are mixed for a period of at least about 10 minutes, at least about 15 minutes, at least about 20 minutes, at least about 25 minutes, at least about 30 minutes, at least about 35 minutes, at least about 40 minutes, at least about 45 minutes, at least about 50 minutes or at least 60 minutes;(iii) the mixing step is followed by a period of incubation, prior to separating the soluble protein-containing component (soluble immunoglobulins) from the insoluble protein-containing component (insoluble albumin);

(iv) the steps of the method are performed at a temperature of between about 18 °C to about 37 °C ;

(v) the immunoglobulin solution, or concentrated immunoglobulin is subjected to further processing in order to further purify the immunoglobulins; ;

(vi) the purified immunoglobulin solution contains one or more of the following impurities: IgA, IgM, albumin, α (alpha)-2 macroglobulin, α (alpha)-1 anti-trypsin, a lipid, and a lipoprotein; and/or

(vii) the insoluble protein-containing component of the suspension (i.e., obtained from contacting the plasma sample with the medium chain fatty acid), is retained following a step of separating the soluble protein-containing component from the insoluble protein-containing component.

41. The method of claim 40, wherein the period of incubation at step (iii) is at least about 20 minutes, at least about 30 minutes, at least about 40 minutes, at least about 50 minutes, at least about 60 minutes, at least about 70 minutes, at least about 80 minutes, at least about 90 minutes, at least about 100 minutes, at least about 110 minutes, at least about 120 minutes, at least about 130 minutes, at least about 140 minutes, at least about 150 minutes or more.

42. The method of claim 40 or 41, wherein the steps of the method are performed at a temperature of between about 18 °C to about 24 °C.

43. The method of any one of claims 40 to 42, wherein the further processing at step (v) does not comprise a further step of continuous filter extraction.

44. The method of claim 43, wherein the immunoglobulins are subjected to further processing such as low pH treatment, chromatography steps (including anion exchange chromatography and/or immunoaffinity chromatography), virus filtration and inactivation steps, concentration and formulation so that the end product can be administered for example to the human body.

45. The method of any one of claims 31 to 44, wherein the fatty acid is caprylic (octanoic) acid, or a salt or ester of thereof.

46. The method of claim or 4, wherein the method further comprises:

d) adjusting the pH of the insoluble protein-containing component comprising albumin to a pH of between about 6.4 to 7.2, to obtain solubilised albumin;

e) recovering purified albumin from the solubilised albumin;

47. The method of claim 46, wherein the solubilised albumin is subjected to further processing steps to remove impurities therefrom.

48. The method of claim 46 or 47, wherein:

(i) the insoluble albumin is residual insoluble protein remaining in the first tank and/or may further comprise the first retentate, and/or

the pH of the insoluble protein-containing component is adjusted without substantial dilution of the insoluble protein-containing component, and/or

the conductivity of the insoluble protein-containing component is adjusted to between about 8 to about 15 mS/cm; or

(ii) step d) comprises first contacting the insoluble protein-containing component (insoluble albumin) with a buffer, having a pH of between 7.1 to 7.4, to form a further suspension, and adjusting the pH of this further suspension to a pH of at least about 6.4.

49. The method of any one of claims 46 to 48, wherein the buffer at step d) has a conductivity of between about 8 to about 15 mS/cm.

50. The method of any one of claims 46 to 49, wherein at step d) the pH is adjusted to a neutral pH, thereby obtaining solubilised albumin.

51. The method of any one of claims 46 to 49, wherein at step d) the pH is adjusted to between about 6.4 to about 7.2.

52. The method of claim 47, comprising further processing steps to remove impurities(i) comprising:

- feeding the solubilised albumin into a filtration unit comprising a dynamic filter element adapted to produce a retentate depleted of albumin and a filtrate enriched in soluble albumin;
- recovering the filtrate enriched with albumin; or

(ii) comprising:

- providing the solubilised albumin in a first tank:
- feeding the solution of solubilised albumin into a first filtration unit comprising a dynamic filter element adapted to produce a retentate depleted of albumin and a filtrate enriched in albumin;
- recovering the filtrate, enriched in albumin, in a second tank.

53. The method of claim 52, wherein (ii) further comprises a step of diluting the solution in the first tank by streaming the retentate into the first tank.

54. The method of claim 52 or 53, where the method further comprises concentrating the filtrate.

55. The method of claim 54, wherein:

(i) concentrating the filtrate comprises subjecting the filtrate to a continuous concentration process in a second filtration unit comprising a dynamic filter element, adapted to produce a retentate enriched for albumin and a filtrate, depleted of albumin;

(ii) the filtrate, depleted of albumin is streamed back into the first tank;

(iii) the retentate, enriched for the albumin, is streamed back into the second tank;

(iv) the dynamic filter element in the first filtration unit adapted to produce a filtrate (permeate) enriched with albumin is a dynamic cross flow filter element; and/or

(v) the dynamic filter element in the second filtration unit adapted to concentrate the albumin solution, and produce a retentate enriched with albumin, is a dynamic cross flow filter element or a TFF.