THE INVENTION CLAIMED IS:

1. A mammalian cell culture medium formulation comprising at least one of mannose at about 3.5 g/L or more and calcium in a range from about 1.5 mM to about 9.5 mM.

2. The formulation of claim 1, wherein the medium comprises mannose at about 3.5 g/L or more and calcium at less than about 1.5 mM or more than about 9.5 mM.

3. The formulation of claim 1, wherein the medium comprises mannose at less than about 3.5 g/L and calcium in a range from about 1.5 mM to about 9.5 mM.

4. The formulation of claim 1, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

5. The formulation of claim 2, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

6. The formulation of claim 1, wherein the medium comprises calcium in a range from about 2 mM to about 5 mM.

7. The formulation of claim 3, wherein the medium comprises calcium in a range from about 2 mM to about 5 mM.

8. The formulation of claim 1, wherein the formulation comprises DMEM/F12 in 1:1 ratio, and includes at least one of mannose in a range from about 4 g/L to about 5 g/L and calcium in a range from about 2 mM to about 5 mM.

9. A method of producing a recombinant protein in cell culture, comprising:

providing recombinant protein expressing cells; and

culturing the cells in a cell culture medium including at least one of mannose at about 3.5 g/L or more and calcium in a range from about 1.5 mM to about 9.5 mM.

10. The method of claim 9, wherein the medium comprises mannose at about 3.5 g/L or more and calcium at less than about 1.5 mM or more than about 9.5 mM.

11. The method of claim 9, wherein the medium comprises mannose at less than about 3.5 g/L and calcium in a range from about 1.5 mM to about 9.5 mM.

12. The method of claim 9, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

13. The method of claim 10, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

14. The method of claim 9, wherein the medium comprises calcium in a range from about 2 mM to about 5 mM.

15. The method of claim 11, wherein the medium comprises calcium in a range from about 2 mM to about 5 mM.

16. The method of claim 9, wherein the cells are mammalian cells.

17. The method of claim 16, wherein the mammalian cells are selected from BHK cells, CHO cells, HKB cells, HEK cells, and NS0 cells.

18. The method of claim 17, wherein the mammalian cells are BHK cells.

19. The method of claim 9, wherein the cells express a blood-coagulation pathway recombinant protein.

20. The method of claim 19, wherein the cells express recombinant human factor VIII (rhFVIII), or a variant thereof.

21. The method of claim 20, wherein the variant factor VIII is a genetic variant.

22. The method of claim 21, wherein the genetic variant is a B-domain deleted FVIII.

23. The method of claim 20, wherein the variant factor VIII is a pegylated FVIII.

24. The method of claim 9, wherein the cells are BHK cells expressing recombinant factor VIII, and wherein the medium comprises DMEM/F12 in 1:1 ratio, and includes at least one of mannose in a range from about 4 g/L to about 5 g/L and calcium in a range from about 2 mM to about 5 mM.

Claims

1. A mammalian cell culture medium formulation comprising mannose at about 3.5 g/L or more and calcium at more than about 9.5 mM.

2. The formulation of claim 1, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

3. The formulation of claim 1 or claim 2, wherein the formulation comprises DMEM/F12 in 1:1 ratio.

4. A method of producing a recombinant protein in cell culture, comprising:
providing recombinant protein expressing mammalian cells; and
culturing the mammalian cells in a cell culture medium including mannose at about 3.5 g/L or more and calcium in a range from about 1.5 mM to about 9.5 mM, wherein the mammalian cells are selected from BHK cells, CHO cells, HKB cells, and NS0 cells.

5. The method of claim 4, wherein the medium comprises mannose at about 3.5 g/L or more and calcium at less than about 1.5 mM or more than about 9.5 mM.

6. The method of claim 4, wherein the medium comprises mannose at less than about 3.5 g/L and calcium in a range from about 1.5 mM to about 9.5 mM.

7. The method of claim 4, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

8. The method of claim 5, wherein the medium comprises mannose in a range from about 4 g/L to about 5 g/L.

9. The method of claim 4, wherein the medium comprises calcium in a range from about 2 mM to about 5 mM.

10. The method of claim 6, wherein the medium comprises calcium in a range from about 2 mM to about 5 mM.

11. The method of claim 4, wherein the cells express a blood-coagulation pathway recombinant protein.

12. The method of claim 11, wherein the cells express recombinant human factor VIII (rhFVIII), or a variant thereof.

13. The method of claim 12, wherein the variant factor VIII is a genetic variant.

14. The method of claim 13, wherein the genetic variant is a B-domain deleted FVIII or a pegylated FVIII.

15. The method of claim 4, wherein the cells are BHK cells expressing recombinant factor VIII, and wherein the medium comprises DMEM/F12 in 1:1 ratio, and includes at least one of mannose in a range from about 4 g/L to about 5 g/L and calcium in a range from about 2 mM to about 5 mM.