CLAIMS

1. A composition for reducing adsorption of a therapeutic protein to one or more components of an intravenous drug delivery system, the composition comprising succinate and polysorbate 80.

2. The composition of claim 1, wherein the composition comprises:
about 1 to about 10 mM succinate, and
about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80.

3. The composition of claim 2, wherein the composition comprises about 4 mM to about 6 mM succinate; and optionally wherein the composition comprises about 5 mM succinate.

4. The composition of any one of claims 2-3, wherein the composition comprises about 0.002% (w/v) to about 0.008% (w/v) polysorbate 80; and optionally wherein the composition comprises about 0.004% (w/v) polysorbate 80.

5. The composition of any one of claims 2-4, wherein the pH of the composition is about 5.0 to about 7.0; and optionally wherein the pH of the composition is about 6.0.

6. The composition of any one of claims 1-5, wherein the composition comprises the therapeutic protein.

7. The composition of claim any one of claims 1-6, wherein the therapeutic protein comprises at least a first binding domain; and optionally wherein the first binding domain is a single chain variable fragment (scFv).

8. The composition of any one of claims 1-7, wherein the therapeutic protein comprises at least a first binding domain and a second binding domain; and optionally wherein the first binding domain is a single chain variable fragment (scFv) and the second binding domain is a scFv.

9. The composition of claim 8, wherein the first binding domain specifically binds to CD123; and optionally wherein the second binding domain specifically binds CD3ε.

10. The composition of claim 8 or 9, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:

(a) the first binding domain

(b) a hinge region;

(c) an immunoglobulin constant region; and

(d) the second binding domain; and optionally wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.

11. The composition of any one of claims 8-10, wherein the first binding domain comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

12. The composition of claim 11,

(i) wherein the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HDCR3 comprises SEQ ID NO: 12;

(ii) wherein the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15; or

(iii) wherein:

the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HDCR3 comprises SEQ ID NO: 12; and

the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15.

13. The composition of any one of claims 8-12, wherein the first binding domain comprises a sequence at least 95% identical to SEQ ID NO: 18.

14. The composition of any one of claims 8-13, wherein the second binding domain comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

15. The composition of claim 14,

(i) wherein the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HDCR3 comprises SEQ ID NO: 21;

(ii) wherein the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24; or

(iii) wherein:

the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HDCR3 comprises SEQ ID NO: 21; and

the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.

16. The composition of any one of claims 8-15, wherein the second binding domain comprises a sequence at least 95% or 100% identical to SEQ ID NO: 27.

17. The composition of any one of claims 8-16, wherein the therapeutic protein comprises the sequence of SEQ ID NO: 31.

18. The composition of claim 8, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain,

wherein the CD86 binding domain comprises a variable heavy chain and a variable light chain that specifically bind CD86,

wherein the immunoglobulin Fc domain is an IgG1 Fc domain that comprises two or more mutations that prevent or significantly reduce binding to Fc receptors FcγR, FcγRIIa, FcγRIIb, and FcγRIIIb,

wherein the monomeric IL-10 domain comprises two subunits of human IL-10 separated by a short linker, and

wherein the therapeutic protein is a homodimer.

19. The composition of clam 18, wherein the CD86 binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (2) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3; and optionally wherein the amino acid sequence of HCDR1 is SEQ ID NO: 1, the amino acid sequence of HCDR2 is SEQ ID NO: 2, the amino acid sequence of HCDR3 is SEQ ID NO: 3, the amino acid sequence of LCDR1 is SEQ ID NO: 4, the amino acid sequence of LCDR2 is SEQ ID NO: 5, and the amino acid sequence of LCDR3 is SEQ ID NO: 6.

20. The composition of any one of claims 18-19,

wherein the CD86 binding domain comprises a variable heavy chain with an amino acid sequence at least 95% identical to SEQ ID NO: 7 and a variable light chain with an amino acid sequence at least 95% identical to SEQ ID NO: 8;

optionally wherein the CD86 binding domain comprises an amino acid sequence that is at least about 95% or 100% identical to SEQ ID NO: 9;

optionally wherein the monomeric IL-10 domain comprises an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 28; and

optionally wherein the therapeutic protein comprises SEQ ID NO: 30 or an amino acid sequence at least about 90%, at least about 95%, at least about 98%, or at least about 99% identical to SEQ ID NO: 30.

21. The composition of any one of claims 6-20, wherein the concentration of the therapeutic protein is about 0.01 μg/mL to about 2.0 μg/mL; and optionally

(i) wherein the concentration of the therapeutic protein is about 0.01, about 0.02, about 0.03, about 0.04, about 0.05, about 0.06, about 0.07, about 0.08, or about 0.09 µg/mL;

(ii) wherein the concentration of the therapeutic protein is about 0.1, about 0.2, about 0.3, about 0.4, about 0.5, about 0.6, about 0.7, about 0.8, or about 0.9 µg/mL; or

(iii) wherein the concentration of the therapeutic protein is about 1.0, about 1.1, about 1.2, about 1.3, about 1.4, about 1.5, about 1.6, about 1.7, about 1.8, about 1.9, or about 2.0 µg/mL.

22. The composition of any one of claim 1-21, wherein the composition comprises about 5 mM succinate and about 0.0004% (w/v) polysorbate 80 in water, wherein the pH of the composition is about 6.0, and wherein the composition is formulated for injection.

23. The composition of claim 1, wherein the composition comprises about 25 to about 150 mM succinate, and about 0.01% to about 0.1% (w/v) polysorbate 80.

24. The composition of claim 23, wherein the composition is at a 10X-50X concentration; and optionally wherein the composition is at a 20X concentration.

25. The composition of any one of claims 23-24, wherein the composition comprises about 75 mM to about 125 mM succinate; and optionally wherein the composition comprises about 100 mM succinate.

26. The composition of any one of claims 23-25, wherein the composition comprises about 0.05% (w/v) to about 0.1% (w/v) polysorbate 80; and optionally wherein the composition comprises about 0.08% (w/v) polysorbate 80.

27. The composition of any one of claims 23-26, wherein the pH of the composition is about 5.0 to about 7.0; and optionally wherein the pH of the composition is about 6.0.

28. The composition of any one of claims 23-27, wherein the composition comprises about 100 mM succinate and about 0.08% (w/v) polysorbate 80 in water, wherein the pH of the composition is about 6.0, and wherein the composition is formulated for injection.

29. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 100 mM succinate;

about 0.08% (w/v) polysorbate 80; and

about therapeutically effective amount of a therapeutic protein.

30. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 μg/mL to about 2.0 μg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:

(a) a first binding domain that specifically binds to a first target;

(b) a hinge region;

(c) an immunoglobulin constant region; and

(d) a second binding domain that specifically binds to a second target.

31. The composition of claim 30,

(i) wherein the first target is CD86;

(ii) wherein the first target is CD123;

(iii) wherein the second target is a receptor of IL-10;

(iv) wherein the second target is CD3ε;

(v) wherein the first target is CD86 and the second target is a receptor of IL-10; or

(vi) wherein the first target is CD123 and the second target is CD3ε.

32. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate,

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:

(a) a first binding domain;

(b) a hinge region;

(c) an immunoglobulin constant region; and

(d) a second binding domain;

wherein the first binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3; wherein the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HDCR3 comprises SEQ ID NO: 12; and wherein the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15;

wherein the second binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3; wherein the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HDCR3 comprises SEQ ID NO: 21; and wherein the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.

33. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;

wherein the therapeutic protein comprises the sequence of SEQ ID NO: 31.

34. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 μg/mL to about 2.0 μg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus: a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain,

wherein the CD86 binding domain comprises a variable heavy chain and a variable light chain that specifically bind CD86,

wherein the immunoglobulin Fc domain is an IgG1 Fc domain that comprises two or more mutations that prevent or significantly reduce binding to Fc receptors FcγR, FcγRIIa, FcγRIIb, and FcγRIIIb,

wherein the monomeric IL-10 domain comprises two subunits of human IL-10 separated by a short linker, and

wherein the therapeutic protein is a homodimer.

35. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 μg/mL to about 2.0 μg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus: a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain;

wherein the CD86 binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (2) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3, wherein the amino acid sequence of HCDR1 is SEQ ID NO: 1, the amino acid sequence of HCDR2 is SEQ ID NO: 2, the amino acid sequence of HCDR3 is SEQ ID NO: 3, the amino acid sequence of LCDR1 is SEQ ID NO: 4, the amino acid sequence of LCDR2 is SEQ ID NO: 5, and the amino acid sequence of LCDR3 is SEQ ID NO: 6;

wherein the monomeric IL-10 domain has an amino acid sequence of SEQ ID NO:28.

36. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;

wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus: a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain;

wherein the CD86 binding domain comprises the amino acid sequence of SEQ ID NO: 9; and

wherein the monomeric IL-10 domain comprises the amino acid sequence of SEQ ID NO: 28.

37. A composition for reducing protein adsorption to one or more components of an intravenous drug delivery system, the composition comprising:

about 1 to about 10 mM succinate;

about 0.001% (w/v) to about 0.01% (w/v) polysorbate 80; and

about 0.01 µg/mL to about 2.0 µg/mL of a therapeutic protein;

wherein the therapeutic protein comprises the amino acid sequence of SEQ ID NO: 30.

38. A container adapted for holding a therapeutic protein, wherein an interior surface of the container is first contacted with the composition of any one of claims 1-37 before it is contacted with a composition comprising the therapeutic protein.

39. The container of claim 38, wherein the container is substantially free of latex; optionally wherein the container is substantially free of bis(2-ethylhexyl) phthalate (DEHP); and optionally wherein the container is selected from the group consisting of an IV bag, a syringe, and a tube.

40. A method of preparing an intravenous drug delivery system for delivery of a therapeutic protein, the method comprising:

providing at least one container adapted to hold the therapeutic protein; and

before the therapeutic protein is added to the at least one container, contacting an interior surface of the at least one container with a composition comprising about 1 to about 10 mM succinate, and about 0.001% to 0.01% (w/v) polysorbate 80.

41. The method of claim 40, wherein the composition coats the interior surface of the at least one container and prevents the therapeutic protein from binding to the interior surface of the container.

42. The method of any one of claims 40-41, wherein the at least one container is substantially free of latex; optionally wherein the at least one container is substantially free of bis(2-ethylhexyl) phthalate (DEHP); and optionally wherein the at least one container is selected from the group consisting of an IV bag, a syringe, and a tube.

43. A method of reducing adsorption of a therapeutic protein to one or more components of an intravenous drug delivery system, the method comprising:

providing at least one container adapted to hold the therapeutic protein;

contacting an interior surface of the container with a composition comprising about 1 to about 10 mM succinate and about 0.001% to about 0.01% (w/v) polysorbate 80; and

contacting the interior surface of the container with a composition comprising the therapeutic protein.

44. The method of claim 43, wherein the therapeutic protein comprises at least a first binding domain; and optionally wherein the first binding domain is a single chain variable fragment (scFv).

45. The method of claim 43, wherein the therapeutic protein comprises at least a first binding domain and a second binding domain; optionally wherein the first binding domain is a single chain variable fragment (scFv) and the second binding domain is an scFv; optionally wherein the first binding domain specifically binds to CD123; and optionally wherein the second binding domain specifically binds CD3ε.

46. The method of claim 45, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus:

(a) the first binding domain;

(b) a hinge region;

(c) an immunoglobulin constant region; and

(d) the second binding domain; and optionally wherein the immunoglobulin constant region comprises immunoglobulin CH2 and CH3 domains of IgG1, IgG2, IgG3, IgG4, IgA1, IgA2 or IgD.

47. The method of any one of claims 45 to 46, wherein the first binding domain comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

48. The method of claim 47,

(i) wherein the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HDCR3 comprises SEQ ID NO: 12;

(ii) wherein the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15; or

(iii) wherein:

the HCDR1 comprises SEQ ID NO: 10, the HCDR2 comprises SEQ ID NO: 11, and the HDCR3 comprises SEQ ID NO: 12; and

the LCDR1 comprises SEQ ID NO: 13, the LCDR2 comprises SEQ ID NO: 14, and the LCDR3 comprises SEQ ID NO: 15.

49. The method of claim any one of claims 45 to 48, wherein the first binding domain comprises a sequence at least 95% or 100% identical to SEQ ID NO: 18.

50. The method of claim 45, wherein the second binding domain comprises:

(i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and

(ii) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3.

51. The method of claim 50,

(i) wherein the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HDCR3 comprises SEQ ID NO: 21;

(ii) wherein the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24; or

(iii) wherein:

the HCDR1 comprises SEQ ID NO: 19, the HCDR2 comprises SEQ ID NO: 20, and the HDCR3 comprises SEQ ID NO: 21; and

the LCDR1 comprises SEQ ID NO: 22, the LCDR2 comprises SEQ ID NO: 23, and the LCDR3 comprises SEQ ID NO: 24.

52. The method of any one of claims 45-51, wherein the second binding domain comprises a sequence at least 95% identical to SEQ ID NO: 27.

53. The method of any one of claims 45-51, wherein the therapeutic protein comprises the sequence of SEQ ID NO: 31.

54. The method of claim 45, wherein the therapeutic protein comprises, in order from amino terminus to carboxyl terminus a CD86 binding domain, an immunoglobulin hinge domain, an immunoglobulin Fc domain, and a monomeric IL-10 domain;

wherein the CD86 binding domain comprises a variable heavy chain and a variable light chain that specifically bind CD86;

wherein the immunoglobulin Fc domain is an IgG1 Fc domain that comprises two or more mutations that prevent or significantly reduce binding to Fc receptors FcγR, FcγRIIa, FcγRIIb, and FcγRIIIb;

wherein the monomeric IL-10 domain comprises two subunits of human IL-10 separated by a short linker; and

wherein the therapeutic protein is a homodimer.

55. The method of clam 54, wherein the CD86 binding domain comprises (i) an immunoglobulin heavy chain variable region (VH) comprising HCDR1, HCDR2, and HCDR3; and (2) an immunoglobulin light chain variable region (VL) comprising LCDR1, LCDR2, and LCDR3; and optionally wherein the amino acid sequence of HCDR1 is SEQ ID NO 1, the amino acid sequence of HCDR2 is SEQ ID NO: 2, the amino acid sequence of HCDR3 is SEQ ID NO: 3, the amino acid sequence of LCDR1 is SEQ ID NO: 4, the amino acid sequence of LCDR2 is SEQ ID NO: 5, and the amino acid sequence of LCDR3 is SEQ ID NO: 6.

56. The method of any one of claims 54-55, wherein the CD86 binding domain comprises a variable heavy chain with an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 7 and a variable light chain with an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 8; and optionally wherein the CD86 binding domain comprises an amino acid sequence with at least about 95% or 100% identical to SEQ ID NO: 9.

57. The method of any one of claims 54-56, wherein the monomeric IL-10 domain comprises an amino acid sequence at least 95% or 100% identical to SEQ ID NO: 28.

58. The method of any one of claims 54-57, wherein the therapeutic protein comprises SEQ ID NO: 30 or an amino acid sequence at least about 90%, at least about 95%, at least about 98%, or at least about 99% identical to SEQ ID NO: 30.

59. The method of any one of claims 43-58, wherein the composition coats an interior surface of the at least one container and prevents the therapeutic protein from binding to the interior surface of the container.

60. A drug delivery system for delivering a therapeutic protein to a patient, the system comprising:

at least one container adapted to hold the therapeutic protein;

wherein an interior surface of the at least one container is contacted with a composition comprising about 1 to about 10 mM succinate, and about 0.001% to 0.01% (w/v) polysorbate 80 before it is contacted with a composition comprising the therapeutic protein.