CLAIMS

What is claimed is:

1. A composition, ~~method for increasing the safety and efficacy of blood transfusions comprising administering to a patient a pharmaceutical composition~~ comprising:~~an effective amount of~~ a polyoxyethylene/polyoxypropylene copolymer having the ~~following~~ chemical formula:

$HO(C_2H_4O)_a - (C_3H_6O)_b - (C_2H_4O)_aH$; and

a blood or packed red blood cells that was compromised by storage lesion,

wherein:

the amount of copolymer is effective to increase the safety and efficacy of the storage lesion-compromised blood or packed red blood cells for transfusion;

b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of ~~approximately~~ 950 to 4000; ~~, preferably approximately 1200 to 3500,~~ and

each a is an integer that can be the same or different such that the hydrophile portion represented by (C_2H_4O) constitutes ~~approximately~~ 50% to 90% by weight of the copolymer ~~compound, and a pharmaceutically acceptable carrier, and wherein the pharmaceutical composition is admixed with blood to be transfused prior to transfusion in the patient or the pharmaceutical composition is administered to the patient prior to, concomitant with or immediately after transfusion with blood~~.

2. The composition of claim 1,~~A method for reducing the adverse effects of transfusing a patient with blood compromised by storage lesion comprising administering to a patient a pharmaceutical composition comprising an effective amount of a polyoxyethylene/polyoxypropylene copolymer having the following chemical formula:~~

~~$HO(C_2H_4O)_a-(C_3H_6O)_b-(C_2H_4O)_aH$~~

wherein b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of ~~approximately 950 to 4000, preferably approximately~~ 1200 to 3500~~, and a is an integer such that the hydrophile portion represented by (C_2H_4O) constitutes approximately 50% to 90% by weight of the compound, and a pharmaceutically acceptable carrier, and wherein the pharmaceutical composition is admixed with blood to be transfused prior to transfusion in the patient or the pharmaceutical composition is administered to the patient prior to, concomitant with or immediately after transfusion with blood~~.

3. The composition ~~method~~ of claim 1 or 2, wherein:

the polyoxyethylene/polyoxypropylene copolymer is a poloxamer 188, which has the ~~following~~ chemical formula:

$$HO(CH_2CH_2)_a(CHCH_2O)_b(CH_2CH_2O)_aH \quad (CH_3)$$

$$HO(CH_2CH_2O)_a(CHCH_2O)_b(CH_2CH_2O)_aH \quad (CH_3)$$

;

~~wherein~~ the molecular weight of the hydrophobe (C_3H_6O) is ~~approximately~~ 1750 daltons; and the total molecular weight of the ~~compound~~ copolymer is ~~approximately~~ 8400 daltons.

4. The ~~method~~ composition of any of claims 1-3~~ of claim 1 or 2~~, wherein the polyoxyethylene/polyoxypropylene copolymer is purified to reduce low and high molecular weight contaminants so that the polydispersity value is less than or equal to ~~approximately~~ 1.07.

5. The ~~method~~ composition of any of claims 1-3 ~~of claim 1 or 2~~, wherein the polyoxyethylene/polyoxypropylene copolymer is purified to reduce low molecular weight substances.

~~6. The method of claim 1 or 2, wherein the pharmaceutical composition is admixed with the blood to be transfused to form a blood admixture prior to transfusion.~~

~~7. The method of claim 1 or 2, wherein the pharmaceutical composition is administered to the patient after transfusion with the blood.~~

~~8. The method of claim 1 or 2, wherein the method increases the ability of the blood having red blood cells to deliver oxygen to a tissue in the patient.~~

~~9. The method of claim 8, wherein the tissue is jeopardized by anemia, trauma, hypovolemia, inflammation, sepsis, or microvascular compromise.~~

~~10. The method of claim 8, wherein compromised deformability of the red blood cells is reversed or improved.~~

~~11. The method of claim 8, wherein red blood cell adhesiveness is reduced or prevented.~~

~~12. The method of claim 8, wherein the red blood cell aggregation is reduced or prevented.~~

6. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or a packed red blood cells that had been stored for at least 1 week.

7. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or a packed red blood cells had been stored for 2 weeks or longer.

8. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or a packed red blood cells that had been stored for 3 weeks or longer.

9. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or packed red blood cells that had been stored for 4 weeks or longer.

~~13~~10. The ~~method~~ composition of ~~claim 1 or 2~~any of claims 1-9, wherein the composition comprises the copolymer in an amount of from ~~about~~ 0.5% to ~~about~~ 15% by weight of the composition.

~~14. The method of claim 1 or 2, wherein administering the pharmaceutical composition results in a concentration of the copolymer in the circulation of the patient of about 0.5 mg/mL.~~

~~15. The method of claim 1 or 2, wherein the concentration in the circulation is targeted for up to 72 hours following transfusion.~~

~~16~~11. The ~~method~~ composition of ~~claim 1 or 2~~any of claims 1-10, wherein the composition is formulated for ~~administered via~~ intravenous infusion.

~~17~~12. The ~~method~~ composition of claim ~~16~~11, wherein the composition is formulated for administration ~~formulation is administered~~ as a single continuous infusion, multiple continuous infusions, a single bolus administration, or multiple bolus administrations.

13. The composition of any of claims 1-12 for use for treating a disease or condition in which treatment includes transfusion of blood or a packed red blood cells.

14. The composition of claim 13, wherein the disease or condition in which treatment includes transfusion of blood or packed red blood cells is selected from among sickle cell disease, acute chest syndrome, peripheral artery disease, myocardial infarction, stroke, peripheral vascular disease, macular degeneration, acute respiratory distress syndrome (ARDS), multiple organ failure, ischemia, hemorrhagic shock, septic shock, acidosis, hypothermia, anemic decomposition, surgery, trauma, acute blood loss and blood disorders.

15. A polyoxyethylene/polyoxypropylene copolymer for use for increasing the safety and efficacy of a blood or packed red blood cells, which has been stored for at least 1 week, for transfusion, wherein:

the blood or packed red blood cells is compromised by storage lesion;

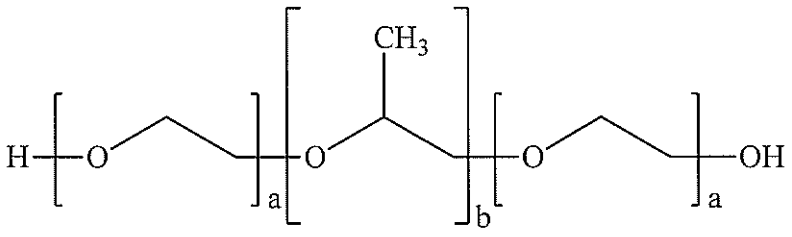
the copolymer has the chemical formula:

$HO(C_2H_4O)_a-(C_3H_6O)_b-(C_2H_4O)_aH$;

b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 950 to 4000; and

a is an integer such that the hydrophile portion represented by (C_2H_4O) constitutes 50% to 90% by weight of the copolymer.

16. The use of claim 15, wherein the copolymer is a poloxamer 188 that has the formula:



, wherein the molecular weight of the hydrophobe (C_3H_6O) is 1750 daltons and the total molecular weight of the copolymer is 8400 daltons.

17. The use of claim 15 or claim 16, wherein the blood or packed red blood cells is compromised by storage for two weeks or longer.

18. The use of claim 15 or claim 16, wherein the blood or packed red blood cells is compromised by storage for three weeks or longer.

19. The use of any of claims 15-18, wherein the blood or packed red blood cells is compromised by storage for four weeks or longer.

20. A method of improving the safety and efficacy of blood or packed red blood cells for transfusion, comprising mixing the blood or packed red blood cells with a polyoxyethylene/polyoxypropylene copolymer to produce a composition for transfusion, wherein:

the blood or packed red blood cells is compromised by storage lesion; and

the copolymer has the chemical formula:

$HO(C_2H_4O)_a-(C_3H_6O)_b-(C_2H_4O)_aH$, wherein:

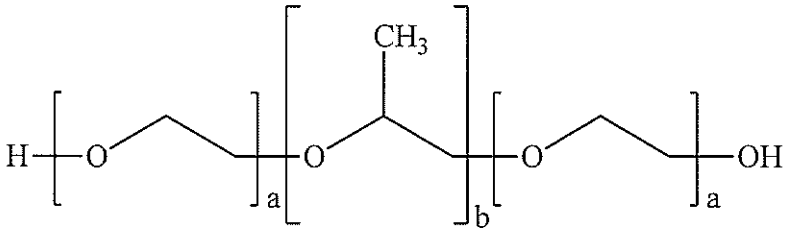
b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 950 to 4000; and

a is an integer such that the hydrophile portion represented by (C_2H_4O) constitutes 50% to 90% by weight of the copolymer.

21. The method of claim 20, wherein b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 1200 to 3500.

22. The method of claim 20 or claim 21, wherein:

the copolymer is poloxamer 188 that has the formula:



;

the molecular weight of the hydrophobe (C_3H_6O) is 1750 daltons; and

the total molecular weight of the copolymer is 8400 daltons.

23. The method of any of claims 20-22, wherein the polyoxyethylene/polyoxypropylene copolymer is purified to reduce low and high molecular weight contaminants so that the polydispersity value is less than or equal to 1.07.

24. The method of any of claims 20-23, wherein the composition comprises the copolymer in an amount of from 0.5% to 15% of the composition.

25. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for at least 1 week before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

26. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for 2 weeks or longer before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

27. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for 3 weeks or longer before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

28. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for 4 weeks or longer before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

29. The method of any of claims 20-28, further comprising storing the composition.

30. A method of improving the safety and efficacy of blood or packed red blood cells for transfusion, comprising mixing the blood or packed red blood cells with a polyoxyethylene/polyoxypropylene copolymer to produce a composition of any of claims 1-14.

CLAIMS

What is claimed is:

1. A composition, comprising:
a polyoxyethylene/polyoxypropylene copolymer having the chemical formula:
$HO(C_2H_4O)_a - (C_3H_6O)_b - (C_2H_4O)_aH$; and
a blood or packed red blood cells that was compromised by storage lesion,
wherein:
the amount of copolymer is effective to increase the safety and efficacy of the storage lesion-compromised blood or packed red blood cells for transfusion;
b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 950 to 4000; and
each a is an integer that can be the same or different such that the hydrophile portion represented by (C_2H_4O) constitutes 50% to 90% by weight of the copolymer.

2. The composition of claim 1, wherein b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 1200 to 3500.

3. The composition of claim 1 or 2, wherein:
the polyoxyethylene/polyoxypropylene copolymer is a poloxamer 188, which has the chemical formula:

$$HO(CH_2CH_2O)_a(\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2O)_b(CH_2CH_2O)_aH$$
;

the molecular weight of the hydrophobe (C_3H_6O) is 1750 daltons; and
the total molecular weight of the copolymer is 8400 daltons.

4. The composition of any of claims 1-3, wherein the polyoxyethylene/polyoxypropylene copolymer is purified to reduce low and high molecular weight contaminants so that the polydispersity value is less than or equal to 1.07.

5. The composition of any of claims 1-3, wherein the polyoxyethylene/polyoxypropylene copolymer is purified to reduce low molecular weight substances.

6. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or a packed red blood cells that had been stored for at least 1 week.

7. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or a packed red blood cells had been stored for 2 weeks or longer.

8. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or a packed red blood cells that had been stored for 3 weeks or longer.

9. The composition of any of claims 1-5, wherein the blood or packed red blood cells that was compromised by storage lesion is blood or packed red blood cells that had been stored for 4 weeks or longer.

10. The composition of any of claims 1-9, wherein the composition comprises the copolymer in an amount of from 0.5% to 15% by weight of the composition.

11. The composition of any of claims 1-10, wherein the composition is formulated for intravenous infusion.

12. The composition of claim 11, wherein the composition is formulated for administration as a single continuous infusion, multiple continuous infusions, a single bolus administration, or multiple bolus administrations.

13. The composition of any of claims 1-12 for use for treating a disease or condition in which treatment includes transfusion of blood or a packed red blood cells.

14. The composition of claim 13, wherein the disease or condition in which treatment includes transfusion of blood or packed red blood cells is selected from among sickle cell disease, acute chest syndrome, peripheral artery disease, myocardial infarction, stroke, peripheral vascular disease, macular degeneration, acute respiratory distress syndrome (ARDS), multiple organ failure, ischemia, hemorrhagic shock, septic shock, acidosis, hypothermia, anemic decomposition, surgery, trauma, acute blood loss and blood disorders.

15. A polyoxyethylene/polyoxypropylene copolymer for use for increasing the safety and efficacy of a blood or packed red blood cells, which has been stored for at least 1 week, for transfusion, wherein:

the blood or packed red blood cells is compromised by storage lesion;

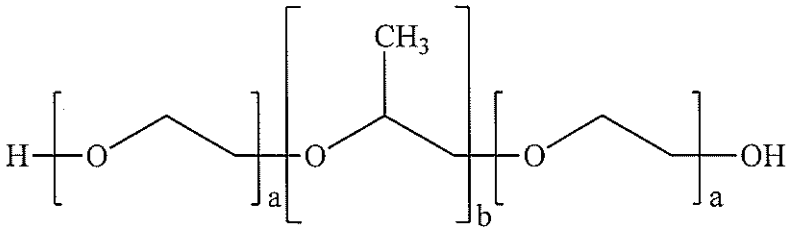
the copolymer has the chemical formula:

$HO(C_2H_4O)_a - (C_3H_6O)_b - (C_2H_4O)_aH$;

b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 950 to 4000; and

a is an integer such that the hydrophile portion represented by (C_2H_4O) constitutes 50% to 90% by weight of the copolymer.

16. The use of claim 15, wherein the copolymer is a poloxamer 188 that has the formula:



, wherein the molecular weight of the hydrophobe (C_3H_6O) is 1750 daltons and the total molecular weight of the copolymer is 8400 daltons.

17. The use of claim 15 or claim 16, wherein the blood or packed red blood cells is compromised by storage for two weeks or longer.

18. The use of claim 15 or claim 16, wherein the blood or packed red blood cells is compromised by storage for three weeks or longer.

19. The use of any of claims 15-18, wherein the blood or packed red blood cells is compromised by storage for four weeks or longer.

20. A method of improving the safety and efficacy of blood or packed red blood cells for transfusion, comprising mixing the blood or packed red blood cells with a

polyoxyethylene/polyoxypropylene copolymer to produce a composition for transfusion, wherein:

the blood or packed red blood cells is compromised by storage lesion; and

the copolymer has the chemical formula:

$HO(C_2H_4O)_a - (C_3H_6O)_b - (C_2H_4O)_aH$, wherein:

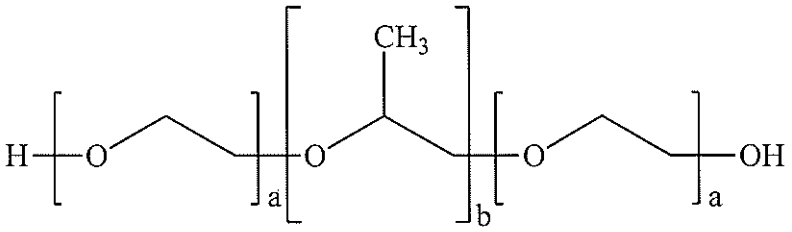
b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 950 to 4000; and

a is an integer such that the hydrophile portion represented by (C_2H_4O) constitutes 50% to 90% by weight of the copolymer.

21. The method of claim 20, wherein b is an integer such that the hydrophobe represented by (C_3H_6O) has a molecular weight of 1200 to 3500.

22. The method of claim 20 or claim 21, wherein:

the copolymer is poloxamer 188 that has the formula:



;

the molecular weight of the hydrophobe (C_3H_6O) is 1750 daltons; and

the total molecular weight of the copolymer is 8400 daltons.

23. The method of any of claims 20-22, wherein the polyoxyethylene/polyoxypropylene copolymer is purified to reduce low and high molecular weight contaminants so that the polydispersity value is less than or equal to 1.07.

24. The method of any of claims 20-23, wherein the composition comprises the copolymer in an amount of from 0.5% to 15% of the composition.

25. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for at least 1 week before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

26. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for 2 weeks or longer before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

27. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for 3 weeks or longer before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

28. The method of any of claims 20-24, wherein the blood or packed red blood cells that is compromised by storage lesion was stored for 4 weeks or longer before it is mixed with the polyoxyethylene/polyoxypropylene copolymer.

29. The method of any of claims 20-28, further comprising storing the composition.

30. A method of improving the safety and efficacy of blood or packed red blood cells for transfusion, comprising mixing the blood or packed red blood cells with a

polyoxyethylene/polyoxypropylene copolymer to produce a composition of any of claims 1-14.