apheresis platelets. The platelets or platelet derivatives can retain at least about 15% of the lactate dehydrogenase activity of donor apheresis platelets. The platelets or platelet derivatives can retain at least about 20% of the lactate dehydrogenase activity of donor apheresis platelets. The platelets or platelet derivatives can have an annexin V percent positivity of at least 70%. The platelets or platelet derivatives can have an annexin V percent positivity of at least 75%. The platelets or platelet derivatives can have an annexin V percent positivity of at least 80%. The platelets or platelet derivatives can have CD47 percent positivity of at least 8%. The the platelets or platelet derivatives can have CD47 percent positivity of at least 10%. The platelets or platelet derivatives can have CD47 percent positivity of at least 15%. The platelets or platelet derivatives can have CD47 percent positivity of at least 20%. The platelets or platelet derivatives can have CD62 percent positivity of at least 80%. The platelets or platelet derivatives can have CD62 percent positivity of at least 82%. The platelets or platelet derivatives can have CD62 percent positivity of at least 85%. The platelets or platelet derivatives can have CD62 percent positivity of at least 90%. The platelets or platelet derivatives can have fibrinogen associated with the cell membrane. The aqueous medium can have a lactate concentration of less than 2.0 mmol/L. The aqueous medium can have a lactate concentration of less than 1.5 mmol/L. The aqueous medium can have a lactate concentration of about 0.4 to about 1.3 mmol/L. The aqueous medium can have a lactate concentration of about 0.5 to about 1.0 mmol/L. The platelet derivatives can include thrombosomes.

[0009] Also provided herein is a process for preparing a composition comprising platelets and an aqueous medium, the process including tangential flow filtration (TFF) of a starting material comprising platelets, centrifugation of a starting material comprising platelets, or a combination thereof, wherein the aqueous medium has a protein concentration less than 50% of the protein concentration of donor apheresis plasma.

[0009a] In one aspect, the present disclosure refers to a process for preparing a thermally-treated platelet derivative composition, the process comprising:

performing tangential flow filtration (TFF) of a platelet composition comprising whole platelets in a preparation agent comprising a biologically compatible buffer having a concentration in the range of 5 mM to 100 mM, one or more saccharides comprising trehalose having a concentration in the range of 10 mM to 1,000 mM, and polysucrose having a concentration in the range of 3% to 10% w/v, wherein the preparation agent has a pH in the range of 6.0 to 7.4, thereby preparing a TFF-treated composition in an aqueous medium having less than 5.0% microparticles by scattering intensity,

freeze drying the TFF-treated composition comprising platelets in the aqueous medium to form a freeze-dried platelet derivative composition comprising freeze-dried platelet derivatives; and

heating the freeze-dried platelet derivative composition at a temperature in the range of 60°C to 85°C for at least 1 hour to not more than 36 hours to thermally treat the freeze-dried platelet derivatives in the freeze-dried platelet derivative composition to form the thermally-treated platelet derivative composition comprising thermally-treated platelet derivatives, wherein the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition, have an *in vitro* occlusion activity, such that when forced through a collagen-coated microchannel at a concentration of at least 255 x 10^3 particles/μL they are capable of attaining a pressure of 80 kPa in less than 14 minutes in platelet-reduced citrated whole blood in an in vitro total thrombus-formation analysis system (T-TAS) assay, and wherein at least 70% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD62 positive when measured using flow cytometry.

[00010] Implementations can include one or more of the following features. The starting material can be (a) positive for HLA Class I antibodies based on a regulatory agency approved test, (b) positive for HLA Class II antibodies based on a regulatory agency approved test, (c) positive for HNA antibodies based on a regulatory agency approved test, or (d) one or more of of a), b), and c). The starting material can have a protein concentration of about 60 to about 80

to form a lyophilized composition. The method can further include treating the lyophilized composition at about 80 °C for about 24 hours.

[00016] Also provided herein is a composition comprising platelets or platelet derivatives prepared by any of the methods described herein.

[00017] The materials and methods described herein can provide several advantages. First, they can allow for the collection of otherwise deferred donors and reduce the competition for apheresis materials.

[00017a] In one aspect, the present disclosure refers to the use of a dried, thermally-treated platelet derivative composition comprising thermally-treated platelet derivatives in the manufacture of a medicament for the treatment of a clotting-related disease or condition in a subject in need thereof, wherein the composition has less than 5.0% microparticles by scattering intensity, wherein at least 65% of the dried, thermally-treated platelet derivatives are positive for CD 42 when measured using flow cytometry, wherein at least 55% of the dried, thermally-treated platelet derivatives are positive for CD 41 when measured using flow cytometry, wherein at least 70% of the dried, thermally-treated platelet derivatives are positive for CD 62 when measured using flow cytometry, wherein at least 70% of the dried, thermally-treated platelet derivatives are positive for Annexin V binding when measured using flow cytometry, wherein the thermally-treated platelet derivatives have less than 10% crosslinking of platelet membranes via proteins and/or lipids present on the membranes, wherein the dried, thermally-treated platelet derivatives in the thermally-treated platelet derivative composition, have an *in vitro* occlusion activity, such that when forced through a collagen-coated microchannel at a concentration of at least 255 x 10^3 particles/µL they are capable of attaining a pressure of 80 kPa in less than 14 minutes in platelet-reduced citrated whole blood in an *in vitro* total thrombus-formation analysis system (T-TAS) assay, and wherein the clotting-related disease or the condition is selected from the group consisting of von Willebrand Disease, hemophilia, thrombasthenia, and thrombocytopenia.

DESCRIPTION OF THE DRAWINGS

[00018] Figure 1A shows initial gate placement for identification of Class I and Class II HLA FLOWPRA™ beads in PBS using side scattering vs. forward scattering.

[00019] Figure 1B shows initial gate placement for identification of Class I and Class II HLA FLOWPRA™ beads in PBS using phycoerythrin fluorescence vs. forward scattering.

[00020] Figure 2A shows an exemplary FITC-H histogram of FLOWPRA™ beads in PBS, supplier platelet-poor plasma (PPP) (in triplicate), and donor platelet-poor plasma gated on Class I HLA (in triplicate).

[00021] Figure 2B shows an exemplary FITC-H histogram of FLOWPRA™ beads in PBS, supplier platelet-poor plasma (PPP) (in triplicate), and donor platelet-poor plasma gated on Class II HLA (in triplicate).

[00022] Figure 2C shows an exemplary FITC-H histogram of FLOWPRA™ beads in PBS, supplier platelet-poor plasma (PPP) (single data set), and donor platelet-poor plasma gated on Class I HLA (single data set).

[00023] Figure 2D shows an exemplary FITC-H histogram of FLOWPRA™ beads in PBS, supplier platelet-poor plasma (PPP) (single data set), and donor platelet-poor plasma gated on Class II HLA (single data set).

CLAIMS

What is claimed is:

1. A process for preparing a thermally-treated platelet derivative composition, the process comprising:

performing tangential flow filtration (TFF) of a platelet composition comprising whole platelets in a preparation agent comprising a biologically compatible buffer having a concentration in the range of 5 mM to 100 mM, one or more saccharides comprising trehalose having a concentration in the range of 10 mM to 1,000 mM, and polysucrose having a concentration in the range of 3% to 10% w/v, wherein the preparation agent has a pH in the range of 6.0 to 7.4, thereby preparing a TFF-treated composition in an aqueous medium having less than 5.0% microparticles by scattering intensity,

freeze drying the TFF-treated composition comprising platelets in the aqueous medium to form a freeze-dried platelet derivative composition comprising freeze-dried platelet derivatives; and

heating the freeze-dried platelet derivative composition at a temperature in the range of 60℃ to 85℃ for at least 1 hour to not more than 36 hours to thermally treat the freeze-dried platelet derivatives in the freeze-dried platelet derivative composition to form the thermally-treated platelet derivative composition comprising thermally-treated platelet derivatives,

wherein the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition, have an *in vitro* occlusion activity, such that when forced through a collagen-coated microchannel at a concentration of at least 255 x 10^3 particles/µL they are capable of attaining a pressure of 80 kPa in less than 14 minutes in platelet-reduced citrated whole blood in an in vitro total thrombus-formation analysis system (T-TAS) assay, and wherein at least 70% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD62 positive when measured using flow cytometry.

2. The process of claim 1, wherein the trehalose has a concentration in the range of 50 mM to 500 mM, and the polysucrose has a concentration in the range of 3% to 7% w/v, and wherein the TFF-treated composition in an aqueous medium has less than 3.0% microparticles by scattering intensity.

3. The process of any one of claims 1 or 2, wherein the biologically compatible buffer is one or more selected from the group consisting of phosphate buffered saline (PBS), sodium-bicarbonate ($NaHCO_3$), N-2-hydroxyethylpiperazine-N'-2- ethanesulfonic acid (HEPES), tris-buffered saline (TBS), propane-1,2, 3-tricarboxylic acid (tricarballylic), benzenepentacarboxylic acid, maleic acid, 2, 2-dimethylsuccinic acid, 3,3-dimethylglutaric acid, bis(2- hydroxyethyl)imino- tris(hydroxymethyl)-methane (BIS-TRIS), benzenehexacarboxylic (mellitic), N-(2- acetamido)imino-diacetic acid (ADA), butane-1, 2, 3, 4-tetracarboxylic acid, 1,1-cyclopentanediacetic (3,3 tetramethylene-glutaric acid), piperazine-1,4- bis-(2-ethanesulfonic acid) (PIPES), N-(2-acetamido)-2- aminoethane sulfonic acid (ACES), 1,1-cyclohexanediacetic acid, 3, 6-endom ethylene-1,2,3,6-tetrahydrophthalic acid (EMTA), 2- (aminoethyl)trimethylammonium chloride (CHOLAMINE), N,N- bis(2- hydroxy ethyl)-2-aminoethanesulfonic acid (BES), 2-methylpropane- 1,2,3 - triscarboxylic (beta-methyltricarballylic), 2-(N-morpholino)propane-sulfonic acid (MOPS), and N-tris(hydroxymethyl)methyl-2-amminoethane sulfonic acid (TES).

4. The process of any one of claims 1 to 3, wherein the preparation agent further comprises one or more salts selected from the group consisting of phosphate salts, sodium salts, potassium salts, calcium salts, and magnesium salts, and having a concentration in the range of 0.5 mM to 100 mM.

5. The process of any one of claims 1 to 4, wherein the biologically compatible buffer comprises N-2-hydroxyethylpiperazine-N'-2- ethanesulfonic acid (HEPES), and sodium-bicarbonate ($NaHCO_3$), and has a concentration in the range of 5 mM to 50 mM.

6. The process of claim 5, wherein the trehalose has a concentration in the range of 50 mM to 500 mM, the polysucrose has a concentration in the range of 3% to 7% w/v, the preparation agent further comprises a salt having a concentration in the range of 2 mM to 90 mM, and the salt is a sodium salt and a potassium salt, and an organic solvent comprising ethanol in a concentration range of 0.1% to 5%.

7. The process of claim 1, wherein prior to performing TFF, the process comprises diluting the platelet composition with a mass of preparation agent equal to at least 25% of the mass of the platelet composition.

8. The process of any one of claims 1 to 7, wherein at least 75% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD62 positive when measured using flow cytometry, at least 55% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD41 positive when measured using flow cytometry, and at least 65% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD42 positive when measured using flow cytometry.

9. The process of any one of claims 1 to 8, wherein the step of performing TFF comprises diluting the platelet composition with a mass of the preparation agent equal to at least 25% of the mass of the platelet composition to form a diluted platelet composition;

concentrating the diluted platelet composition to form a concentrated platelet composition such that the platelets in the concentrated platelet composition have a concentration in the range of 2000×10^3 cells/µl to 2500×10^3 cells/µl; and

performing TFF of the concentrated platelet composition with at least 2 dia-volumes (DV) of the preparation agent, thereby preparing the TFF-treated composition.

10. The process of any one of claims 1 to 8, wherein the TFF is carried out until a particular residual plasma protein endpoint is reached, wherein the particular residual plasma protein endpoint is set at less than or equal to 10% residual plasma protein, and wherein an absorbance at 280 nm of the aqueous medium is measured to determine the particular residual plasma protein endpoint is reached.

11. The process of any one of claims 1 to 8, wherein at least 65% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD41 positive when measured using flow cytometry, at least 70% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are positive for annexin V binding when measured using flow cytometry, and at least 80% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are CD62 positive when measured using flow cytometry.

12. The process of any one of claims 1 to 8, wherein the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition have fibrinogen associated with their cell membrane.

13. The process of any one of claims 1 to 8, wherein the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition, when at a concentration of $4.8x10^3$ particles/µL generate a thrombin peak height (TPH) of at least 25 nM when in the presence of a reagent containing tissue factor and phospholipids.

14. The process of any one of claims 1 to 8, wherein the microparticles are less than 0.5 µm in diameter, and at least 70% of the thermally-treated platelet derivatives in the thermally-treated platelet derivative composition are in between the diameter of 0.5 µm to 5.0 µm.

15. The process of any one of claims 1 to 8, wherein the TFF-treated composition comprises platelets in the range of 1000×10^3 to 4000×10^3 platelets/µl in the aqueous medium.

16. The process of any one of claims 1 to 8, wherein the thermally-treated platelet derivative composition is:

a) negative for HLA Class I antibodies based on a regulatory agency approved test for HLA Class I antibodies;

b) negative for HLA Class II antibodies based on a regulatory agency approved test for HLA Class II antibodies; and

c) negative for HNA antibodies based on a regulatory agency approved test for HNA antibodies.

17. The process of any one of claims 1 to 8, wherein the TFF is performed using a membrane with a pore size in the range of 0.45 to 0.65 µm, wherein the TFF-treated composition has less than 3.0% microparticles by scattering intensity, and wherein the heating the freeze-dried platelet derivative composition is performed at a temperature in the

range of 70℃ to 85℃ for between 6 hours and 36 hours to thermally treat the freeze-dried platelet derivatives to form the thermally-treated platelet derivative composition.

18. Use of a dried, thermally-treated platelet derivative composition comprising thermally-treated platelet derivatives in the manufacture of a medicament for the treatment of a clotting-related disease or condition in a subject in need thereof, wherein the composition has less than 5.0% microparticles by scattering intensity, wherein at least 65% of the dried, thermally-treated platelet derivatives are positive for CD 42 when measured using flow cytometry, wherein at least 55% of the dried, thermally-treated platelet derivatives are positive for CD 41 when measured using flow cytometry, wherein at least 70% of the dried, thermally-treated platelet derivatives are positive for CD 62 when measured using flow cytometry, wherein at least 70% of the dried, thermally-treated platelet derivatives are positive for Annexin V binding when measured using flow cytometry, wherein the thermally-treated platelet derivatives have less than 10% crosslinking of platelet membranes via proteins and/or lipids present on the membranes, wherein the dried, thermally-treated platelet derivatives in the thermally-treated platelet derivative composition, have an *in vitro* occlusion activity, such that when forced through a collagen-coated microchannel at a concentration of at least 255 x 10^3 particles/μL they are capable of attaining a pressure of 80 kPa in less than 14 minutes in platelet-reduced citrated whole blood in an *in vitro* total thrombus-formation analysis system (T-TAS) assay, and wherein the clotting-related disease or the condition is selected from the group consisting of von Willebrand Disease, hemophilia, thrombasthenia, and thrombocytopenia.

19. The use of claim 18, wherein at least 75% of the dried, thermally-treated platelet derivatives are positive for CD 42 when measured using flow cytometry, and wherein at least 75% of the dried, thermally-treated platelet derivatives are positive for CD 41 when measured using flow cytometry.

20. The use of claim 18, wherein at least 80% of the dried, thermally-treated platelet derivatives are positive for CD 62 when measured using flow cytometry, and wherein a therapeutically effective amount of the composition is to be administered to the subject.