

of a solute to function as a cryoprotectant or lyoprotectant, however, requires that the compound remain amorphous. The fact that glycine is a crystallizing agent disqualifies it as a protectant.

**[0015]** As crystallizing agents crystallize they separate from the protein phase thus leaving the protein without protection.

**[0016]** Amino acids are often included in protein formulations. L-arginine, L-isoleucine, and L-glutamic acid are used as a mixture to stabilize recombinant factor VIII in lyophilized form. Bush et al. (Seinin Hematol., 35 (2 Suppl 2): 18-21 (1998)) have developed a formulation for recombinant factor IX, which contains 10 mM histidine, 0.26 mM glycine, 1% sucrose, and 0.005% polysorbate-80. According to the authors, polysorbate 80 and sucrose protect the protein from freezing- and freeze-drying induced damage, respectively. Histidine provides buffering stability. Glycine serves as a bulking agent, providing high-quality cake morphology. A sucrose/glycine formulation is utilized for factor VIII lyophilization as well.

**[0017]** Glucose/dextrose also poses a challenge for lyophilized whole plasma preparations. Glucose is a reducing sugar that causes protein glycation and inactivation via the Mailard reaction. This reaction involves protein amino groups reacting with glucose to form a Schiff base and Amadori products. The Mailard reaction is considered extremely deleterious for lyophilized proteins. Therefore, glucose and other reducing sugars are generally avoided in lyophilized protein formulations. However, glucose is a natural plasma constituent, which is also included in all anticoagulants used for plasma collection. (Generally referred to as ACD and CPD- or acid citrate-dextrose or citrate-phosphate-dextrose). We measure reduced glucose levels in lyophilized whole plasmas subjected to accelerated aging. Pre-lyophilization glucose concentration in plasma is approx.  $334.4 \pm 10$  mg/dl. After lyophilization, and consequent storage of plasma at 40° C. for 6 days, the glucose concentration is significantly reduced (approx.  $290 \pm 7$  mg/dl). The reduced glucose levels in lyophilized and stored plasmas, we attribute to the fact that glucose, being a reducing sugar, binds to plasma proteins in lyophilized state, and the latter results in a reduced concentration of free glucose in plasma. Protein glycation by glucose in lyophilized plasma may be a main damaging factor to plasma proteins. Accordingly, there is a challenge to develop lyophilized plasma preparations with suitable anti-coagulant protection that is not dependent on glucose/dextrose based anticoagulants.

**[0018]** Numerous stabilization approaches, utilizing various lyoprotectants, have been undertaken to prepare lyophilized factors VIII, IX or fibrinogen. There are, however, no reported stabilization approaches for the preparation of lyophilized whole plasma. The challenge is to stabilize not an individual protein but a complex system consisting of coagulation factors and inhibitors thereby maintaining the balance in the system.

**[0019]** Accordingly, it is desired by those of skill in the art to have a lyophilized whole plasma preparation that can be reconstituted in a short time frame possibly with water, that exhibit properties the same or similar to that of frozen plasma.

#### SUMMARY OF THE INVENTION

**[0020]** The present invention addresses the problems and disadvantages associated with current strategies and designs and provides new tools and methods for preserving and storing plasma.

**[0021]** Accordingly, in an embodiment, a plasma preparation comprises lyophilized, glycine stabilized whole plasma configured for reconstitution with water.

**[0022]** In an embodiment, the preparation further comprises at least one protectant selected from the group consisting of calcium chloride, trisodium citrate, HES, ammonium sulfate and/or combinations thereof.

**[0023]** In an embodiment, the preparation further comprises calcium chloride, trisodium citrate, HES or ammonium sulfate.

**[0024]** In some embodiments, the HES is amylopectin-2-hydroxyethyl ether.

**[0025]** In some embodiments, the water is selected from the group consisting of distilled, deionized, distilled-deionized, autoclaved, sterile saline, and ultra pure pathogen free water and/or combinations thereof.

**[0026]** In an embodiment, the plasma is autologous.

**[0027]** In an embodiment, the plasma is allogenic.

**[0028]** In some embodiments, the preparation can be reconstituted with water to approximate the original volume of the pre-lyophilized plasma.

**[0029]** In some embodiments, the preparation can be reconstituted with water to approximate 50% of the original volume of the pre-lyophilized plasma.

**[0030]** A method for preparing freeze-dried plasma according to an embodiment comprises adding glycine to sterile, pathogen free plasma under sterile conditions, freeze drying said glycine comprising sterile pathogen free plasma under conditions that suppress recrystallization of glycine, and storing the lyophilized product.

**[0031]** In some embodiments, a method further comprises freezing the plasma by loading the plasma at room temperature into a freezable container, placing the freezable container into a lyophilizer, freezing the plasma to -4° C. at 2° C. per minute, holding the temperature for 10 minutes, freezing the plasma to -40° C. at 1° C. per minute, and holding the temperature for 120 minutes.

**[0032]** In some embodiments a method further comprises drying the plasma by setting the lyophilizer chamber pressure to 0.6 mbar, increasing the temperature to 20° C. at 0.2° C. per minute, holding for 10 hour, reducing the chamber pressure to 0.0 mbar, and holding the temperature at 20° C. for 7 hour.

**[0033]** A system for lyophilizing plasma according to an embodiment comprises a blood-collection bag, tubing, and a freeze-dry tray, wherein the tubing fluidly connects the blood collection bag and the freeze dry tray in a substantially sterile manner.

**[0034]** In some embodiments, the blood-collection bag comprises an amount of a blood component. In some embodiments, the blood component is transferred from the blood-collection bag to said freeze-dry tray. In some embodiments, the blood component in the freeze-dry tray is lyophilized. In some embodiments, up to one liter of plasma is lyophilized. In some embodiments, the blood component is transferred to a second blood-collection bag reversibly connected to the freeze-dry bag. In some embodiments, the second blood-collection bag is sealed.

**[0035]** Other embodiments and advantages in accordance with the invention are set forth in part in the description,