

which follows, and in part, may be obvious from this description, or may be learned from the practice of the invention.

DESCRIPTION OF THE FIGURES

[0036] FIG. 1 is a graphic representation of the results of DSC Thermograms of glycine in a 0.5% solution in water, and in plasma.

[0037] FIG. 2 is a graphic representation of the effects of the addition of calcium chloride on the stability of lyophilized plasma.

[0038] FIG. 3 is a graphic representation of the effects of the addition of calcium chloride on the stability of Factors V and VII in lyophilized plasma.

[0039] FIG. 4 is a graphic representation of the effect of the addition of tri-sodium citrate and calcium chloride on the stability of lyophilized plasma.

[0040] FIG. 5 is a graphic representation of the effect of the addition of ammonium sulfate on the stability of lyophilized plasma.

[0041] FIG. 6 is a graphic representation of the effect of the addition of ammonium sulfate on the stability of Factors V and VIII lyophilized plasma.

[0042] FIG. 7 is a representation of the effect of the addition of glycine-based protectant cocktails on the stability of lyophilized plasma.

[0043] FIG. 8 is a representation of the effect of the addition of glycine-based protectant cocktails on the stability of Factors V, VII, VIII and IX in lyophilized plasma.

[0044] FIG. 9 is a representation of the effect of the addition of glycine-based protectant cocktails on the stability of coagulation inhibitors in lyophilized plasma.

[0045] FIG. 10 is a graphic representation on the effects of the concentration of reconstituted lyophilized plasma on plasma clotting factors.

[0046] FIG. 11 is a graphic representation on the effects of the concentration of reconstituted lyophilized plasma coagulation factors V, VII, VIII and X.

[0047] FIG. 12 is a graphic comparison of the effect of the concentration of reconstituted lyophilized plasma on coagulation inhibitors.

[0048] FIG. 13 compares the effect of glycine with other stabilizers on the stability of lyophilized plasma.

DESCRIPTION OF THE INVENTION

[0049] Preservation of blood plasma can be performed by many different conventional processes that maintain the basic components of the plasma, but do not preserve the integrity or functionality of proteins and other macromolecules themselves. It has been surprisingly discovered that plasma can be lyophilized and the overall integrity of the plasma and the components therein can be stabilized by lyophilizing in the presence of glycine. Plasma lyophilized according to the invention can also be reconstituted with water, a saline solution or another suitable buffer, and exhibit physiological characteristics comparable to control or untreated plasma.

[0050] According to the process of the invention, plasma to be stabilized can be autologous, allogenic or a combination thereof. In an embodiment of the invention, glycine can preserve the function of a plasma protein matrix. In a preferred embodiment, plasma protein matrix can comprise complex proteins. In another embodiment, glycine can prevent recrystallization. In this regard, glycine has been shown to be superior to other recognized "polyol" stabilizers for lyophilized

plasma. Mother embodiment further comprises the use of glycine as a stabilizing agent to facilitate the preparation of "protectant cocktails."

[0051] FIG. 1 shows the difference in behavior of glycine in plasma when compared to glycine in water. Using differential scanning calorimetry, it can be seen that whole human plasma inhibits glycine crystallization during freezing. Thus, in an embodiment according to the invention, glycine can act as a protein stabilizer, in the presence of plasma, during freeze drying by remaining amorphous. The freeze drying protocol according to the invention minimizes recrystallization events thus inhibits crystallization of glycine during. This assures that glycine remain amorphous. This is a surprising because glycine is a poor candidate for use as a stabilization agent because it is well characterized as a crystallizing agent. The surprising failure of glycine to crystallize is attributable to the relatively high NaCl concentration in plasma.

[0052] Another feature of the invention is reconstitution of lyophilized plasma. In another feature of the invention, lyophilized plasma is reconstituted with water. For purposes of the invention, "water" includes, but is not limited to distilled, deionized, distilled-deionized, autoclaved, sterile saline, ultra pure pathogen free water and/or combinations thereof. In a further embodiment, lyophilized plasma can be reconstituted to 50% of its original volume. In this illustrative form, increased functionality of the reconstituted plasma can be seen. In another embodiment, glycine stabilized lyophilized plasma can be combined with at least one of tri-sodium citrate, calcium chloride, hydroxyethyl starch (HES), ammonium sulfate and combinations thereof which can serve as cryoprotectants. In another embodiment, the HES can be amylopectin-2-hydroxyethylether. In a preferred construction, citric acid can be added to maintain physiological pH. Also surprisingly, the addition of citric acid does not adversely effect the stability of the of the plasma preparation.

[0053] Further still, in an embodiment according to the invention, a system for lyophilizing plasma 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. In another embodiment, the blood bag comprises a blood component. For purposes of the invention, blood component includes but is not limited to whole blood, plasma, red blood cells, white blood cells and platelets. In another embodiment, a blood component is transferred from the blood bag to the freeze dry tray. In still another embodiment, the blood component in the freeze dry tray is lyophilized. In yet another embodiment, up to 1 liter of plasma can be lyophilized. In yet still another embodiment, the freeze dried blood component can be transferred to a second blood bag that is reversibly connected to the freeze dry bag. Further still, the second bag may be sealed.

[0054] This invention may be further understood by reference to examples set forth below, which both describe preparation of the glycine-stabilized lyophilized plasma of the invention and its stability in terms of performance and protein activity. The following examples illustrate embodiments of the invention, but should not be viewed as limiting the scope of the invention.

EXAMPLES

Plasma Supply

[0055] Fresh donor plasma (FDP) units were obtained, frozen and stored at -80°C ., and used within three months of