

chloride) can inhibit or reduce the crystallization of either excipient thereby also limiting the extent of crystallization.

While several attempts have been made to lyophilize aqueous pharmaceutical formulations, there remains a need for effective lyophilization methods and compositions prepared therefrom.

SUMMARY OF THE INVENTION

In one aspect, the present invention provides a method of lyophilizing a composition comprising at least one active ingredient and at least one crystallizing excipient. The method comprises: exposing the composition to a first temperature for a first period of time sufficient to obtain a first composition having the at least one crystallizing excipient partially or completely crystallized.

In one aspect, there is provided a method of lyophilizing a composition comprising AT-III and at least one crystallizing excipient, the method comprising exposing the composition to a first temperature for a first period of time sufficient to obtain a first composition having the at least one crystallizing excipient partially or completely crystallized, wherein the first temperature is -48 °C or below and wherein the first period of time is 4 to 10 hours.

In another aspect, there is provided a method of lyophilizing a liquid composition comprising plasma-derived AT III, NaCl, and alanine, the method comprising:

(a) exposing the composition to -54 °C or below for 4 to 10 hours such that the temperature of the composition is -48 °C or below in order to provide a first composition having one or more components therein completely or near completely crystallized; and

(b) drying the first composition to obtain a lyophilized cake.

In another aspect, the present invention provides a method of lyophilizing a liquid composition comprising plasma-derived AT III, NaCl, and alanine. The method comprises:

(a) exposing the composition to about 54 °C or below such that the temperature of the composition is about 48 °C or below for about 5 hours or more in order to provide a first composition having one or more components therein completely or near completely crystallized; and

(b) drying the first composition to obtain a lyophilized cake.

In some aspects, the present invention provides compositions including lyophilized cakes prepared in accordance with the methods disclosed herein.

In other aspects, the present invention provides a kit comprising one or more of the compositions and/or the lyophilized cakes prepared in accordance with the methods disclosed herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1. DSC thermogram during freezing and warming of NaCl solution (0.15M).

Figure 2. DSC thermograms during freezing (A) and warming (B) of alanine solution (0.1M).