Molecular and Structural Stability of Infliximab: Spray-Dried Powder versus Freeze-Dried Cake.

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Abstract

The current study compared the stability of Infliximab powder following 2 drying procedures namely spray drying and freeze drying.

Introduction: Infliximab as a chimeric anti-TNFα monoclonal antibody was approved for the treatment of inflammatory diseases namely Crohn's disease and rheumatoid arthritis. In prospect of preparing stable formulation of Infliximab, freeze drying and spray drying were compared as processing method.

Methods and Results: Spray-dried formulation was prepared in the presence of Trehalose and Sucrose besides Cysteine. Powders were characterized via SEC-HPLC to quantify the level of induced aggregates/fragments after process along with upon 1 and 3 months of storage at 45℃. Kinetic of aggregation and fragmentation was calculated for each sample. FTIR-spectroscopic assessments were employed to determine the secondary structure of antibody. Trehalose generated more stable particle within spray drying, with least aggregation and fragmentation rate constants of 0.22 and 0.27 (1/month). Combination of Cysteine and Trehalose significantly reduced aggregation upto 0.87, 1.07 and 2.26 % after process, up on 1 and 3 months of storage (rate constant of aggregation of 0.14,(1/month)). Fragmentation was 0.31, 0.38 and 0.98 % respectively with 0.17 (1/month) rate constant of fragmentation. The induced aggregates in Remicade were 0.11, 0.18 and 0.32% (aggregation rate constant:0.15 (1/month)) and fragments were 0.1, 0.14 and 0.29% after process, 1 month and 3 months at 45℃ (fragmentation rate constant of 0.15 (1/month)). The conformation of antibody was shown to be composed of 66.68% and 69.43% beta-sheet in spray-dried powder and freeze-dried cake (Remicade®) respectively.

Conclusions: This study demonstrated that, both spray drying and freeze drying may be efficient for powder production of Infliximab with regards to molecular and structural stability after storage at high temperatures.

Key words: Infliximab, Spray drying, Freeze drying, Molecular Stability, Structure

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