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Optimization of Freeze Drying Process Using Isomalt as Bulking Agent

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Freeze dried products form a special group of sterile medications because of the unique manufacturing process. Their importance is ever growing due to the appearance of a number of unstable active pharmaceutical ingredients and nanosystems. This instability can be overcome with the formulation of a freeze dried product in most cases, thus ensuring a pharmaceutically acceptable shelf-life. On the other hand, in a number of compositions which comprise low concentrations of active ingredients the addition of a bulking agent is necessary to produce an optimal product [1].

Isomalt is a disaccharide sugar alcohol, which offers several important health benefits. The most important is its suitability for diabetics as it does not raise blood glucose or insulin levels. Its glycaemic index is very low [2].

The aim of our work was to assess isomalt as a new bulking agent. Furthermore, our purpose was to determine and optimize the parameters for freeze drying and to compare important properties (e. g. water content, water uptake) of freeze dried isomalt to conventionally used excipients (lactose).

Our experiment led us to the elaboration of the optimal parameters for freeze drying. We determined the acceptable rate of freezing and the time of primary sublimation during lyophilisation using statistical analysis of data. Latter was performed using the TableCurve[®]3D v4.0 (Systat Software Inc., London, UK). The effect of the independent variables on response y was modelled by the following polynomial equation:

$$y = b_0x_0 + b_1x_1 + b_2x_2 + b_{11}x_1^2 + b_{22}x_2^2 + b_{12}x_1x_2$$

where x_1 and x_2 are the factors (x_1 : time, x_2 : temperature) and b parameters mark the coefficients characterizing the main (b_1 , b_2), the quadratic (b_{11} , b_{22}), and the interaction effects (b_{12}). These equations were used in a two factorial, three level study to determine the water content of the product.

Furthermore we determined the water uptake of freeze dried isomalt over time and compared it to lactose lyophilised under the same process parameters.

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