Study on the impact of annealing on the primary drying times using impedance spectroscopy

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Abstract - This study was performed to evaluate the application of impedance spectroscopy in the characterization of a frozen matrix during annealing and in the recording of the impact of annealing on the duration of primary drying. The results shows increments in the product capacitance during annealing that can be applied to explain the decrease in primary drying of the matrix.

INTRODUCTION

The annealing step is commonly included in the freeze drying cycle as it is believed to facilitate the sublimation of ice by optimizing the ice structure in such a way as to reduce the resistance to vapour flow. Traditionally the impact of annealing is monitored either by off-line retrospective characterization of the product or by process analytical technologies which measure the average response of the entire batch in terms of a mean sublimation rate. Single vial measurement technologies often poorly characterize the annealing stage as they perturb ice structure and/or introduce thermal inputs. The impedance measurement technique, being non-invasive with an ability to record glass transition and primary drying times (Smith et al., 2011) may be applied to provide a rationale for setting up annealing cycle which results in optimum drying time. The current works presents the application of impedance measurement technology to optimize the annealing step of freeze drying cycle.

MATERIALS AND METHODS

The impedance spectra (10^1-10^6Hz) were recorded from aliquots (3.0 ml) of surrogate formulation containing maltodextrin DE 16.5-19.5 (10% w/v). Impedance spectra were recorded throughout the freeze drying cycles (Pre-freezing at -35C 5hr Annealing at -10 °C for 1-5 hrs. primary drying at -25 °C for 20 h and secondary drying at 20 °C 4hr) with scan intervals 3 min^{-1}.

RESULTS AND DISCUSSION

Features of the pseudo-relaxation process (i.e. peak position, f_{peak} and peak amplitude C''_{peak}) arising from the interfacial polarization between the product and the glass wall were sensitive to the temperature and phase behaviour of the product and the sublimation of ice from the product. The impedance response during freezing and annealing was also characterized by modelling the spectrum with an equivalent circuit comprising a combination of CPE; R and C. The circuit element CPE denotes a constant phase element, R is resistor and C is capacitor; the former assimilate the glass–formulation interface while the latter two describe the formulation response.

The primary drying time was calculated from the time slice of capacitance at frequencies corresponding to the position of peak during primary drying (Smith et al., 2013).

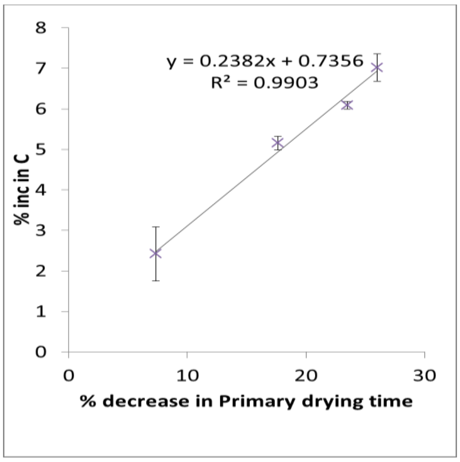

Fig. 1. Predictive control plot for the annealing of maltodextrin 10% w/v.

Increasing the annealing hold time from 1 to 5 h resulted in an increase in the product capacitance by 10%, and a 25% decrease in the drying time. Increments in the product capacitance may be explained in terms of the increase in the ice phase which decreases the resistance to vapour flow and hence reduces the drying time. The results showed a good correlation (R^2=0.99) between the product capacitance and the primary drying time as the annealing hold time was increased from 1-5 h. This linear correlation suggests the potential application of impedance measurement to predict the formulation performance during primary drying.

CONCLUSIONS

Impedance measurement provides a criterion to ascertain an optimal conditioning of the frozen formulations before advancing to the irreversible primary drying stage.

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