Application of impedance based technology to investigate the collapse of freeze-dried sugar-salt solutions.

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PURPOSE

During primary drying, an increase in product temperature above the glass transition temperature of a freeze-concentrated solution (T'_g) may cause dramatic changes in the microstructure of a freeze-dried cake with the potential for batch failure. In this study, through vial impedance spectroscopy (TVIS) is used for evaluating the impact of collapse on the sublimation rate during a freeze-drying cycle.

METHODS

The electrical capacitance spectra of three solutions (containing 5% sucrose and either 0%, 0.26% or 0.55% sodium chloride (NaCl)) were measured within a TVIS vial over the frequency range of 10 Hz to 1 MHz during the entire freeze-drying cycle in a VirTis Advantage Plus Freeze-dryer. The peak frequency (F_{PEAK}) and peak amplitude (C''_{PEAK}) of the imaginary capacitance spectrum were then determined. One of the plain vials close to the TVIS vials had a thermocouple placed therein to provide a representative temperature for the temperature in the TVIS vial and an annealing cycle used to calibrate F_{PEAK} for temperature. The product was forced through the collapse temperatures by ramping shelf temperature during primary drying. Any evidence of visual collapse was taken by using images taken by a digital camera. Differential scanning calorimetry (DSC) was used for analyzing T'_g of formulations.

RESULTS

The in-vial temperatures ($T_{F(PEAK)}$) as predicted from the TVIS measurement system and before the temperature was ramped, were -36, -37 and -38 °C respectively for the solutions of 5% sucrose with 0%, 0.26% and 0.55% NaCl. Only pure sucrose had a product temperature lower than its respective T'_g (-33.7 °C from DSC). Higher surrogate drying rates (i.e. the rate of change of the C''_{PEAK} value which is proportional to the amount of ice) of 0.06 and 0.09 pF/h were found in sample with 0.26 and 0.55% NaCl as compared with the formulation without NaCl (0.04 pF/h). This finding suggests an alteration in microstructure that was not seen in the photographic evidence, which could promote mass flux due to an increase in pore size (microcollapse) (Milton, et al. 1997). Later in the cycle on a significant change in a capacitance spectrum, as the temperature was ramped, appeared to relate to the loss in macroscopic structure or macro-collapse (as confirmed by the photographic images).

CONCLUSION

TVIS is a promising tool that would allow to the design the efficient process whilst avoiding collapse.

REFERENCES

1. Milton, N., Pikal, M.J., Roy, M.L., Nail, S.L., 1997. Evaluation of manometric temperature measurement as a method of monitoring product temperature during lyophilization. PDA J Pharm Sci Technol, 51, 7-16.