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Application of a novel impedance-based freeze-drying microscope for product formulation development

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Abstract

This work demonstrates the application in freeze-drying of a single analytical instrument (Z-FDM) combining impedance (Z) spectroscopy with freeze-drying microscopy (FDM). The electrical impedance spectrum and visual appearance of a 5% sucrose solution was analysed with an interdigitated micro-electrode array placed on a freeze-drying microscope stage. The critical process parameters of ice growth, sublimation drying rate and end-point were studied using Z-FDM technique in addition to observing the collapse temperature. This early study indicates that by using this combined approach it is possible to obtain further information that can be obtained currently by two separate instruments.

Introduction

Over the past few decades, a number of analytical instruments have been developed for the characterization of product formulations intended for Lyophilization. Freeze-drying microscopy (FDM) is now used routinely to determine the critical temperature at which the product may collapse during primary drying (Tc) whereas a combination of differential thermal analysis (DTA) with electrical impedance analysis has been used to study the critical temperatures of a sample in a frozen state (i.e. the glass transition, ice crystallisation and eutectic melting temperatures)[1]. In this study, a combination of impedance spectroscopy with freeze-drying microscopy has been reported for the first time.

Materials and Methods

A gold interdigitated electrode IDE (Micrux) was integrated into the stage of Lyostat 5 freeze dying microscope using fine copper cable on the inside and a RG316 coaxial cabel on the outside which connects the electrode array to an ISX3-mini impedance analyser (Sciospec). A 5% w/v solution of sucrose (Sigma-Aldrich) was prepared using ultrapure water and a sample of 0.5 µL was placed on the IDE. A glass cover slip was placed on the top of the liquid and then spectra were recorded during freeze-drying.

Results & Conclusions

Fig.1 shows how critical parameters can be recorded by the monitoring the real and imaginary capacitance of the IDE at 1.6 kHz: (A) nucleation onset; (B) solidification endpoint, (B-C) loss of excess heat; (C-D) thermal equilibrium, and the position of the drying front (e.g. E & F) from which the drying rate was determined.

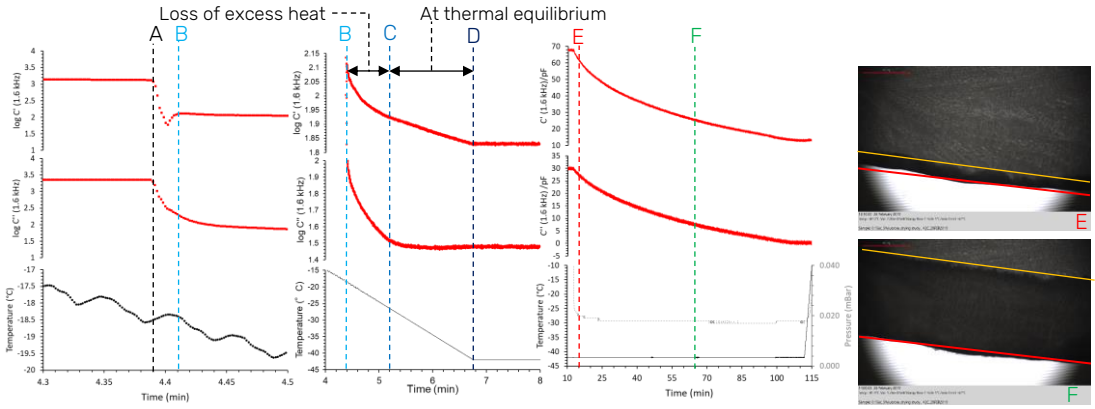

Fig. 1 *Real (C') and imaginary (C") capacitance (at 1.6 kHz) of an IDE on a freeze-drying microscope stage, with a solution of 5% sucrose during freezing and drying*

In a separate experiment, the onset of collapse for the 5% sucrose solution was recorded at -34.5°C by a change in the gradient of the real part capacitance at 1 kHz (Fig.2, see point B).

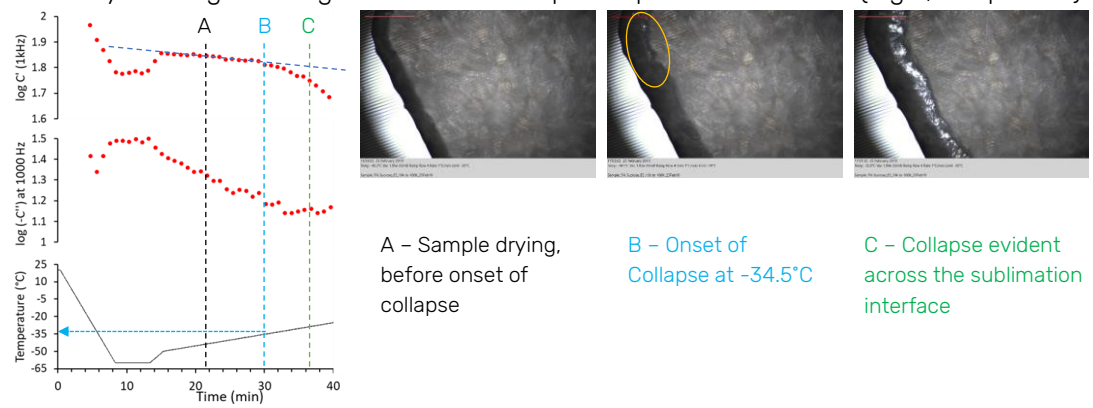

Fig. 2 *The real part capacitance profile shows a discontuinuity with time at the onset of collapse*

References

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