

Application of Vial Impedance Spectroscopy for Lyophilization

Bhaskar Pandya¹, Geoff Smith¹, Eugene Polyglov, Irina Ermolina¹

¹Leicester School of Pharmacy, De Montfort University, The Gateway, Leicester LE1 9BH, United Kingdom

Corresponding author: gsmith02@dmu.ac.uk, +44 (0)116 250 6298

PURPOSE

To demonstrate the impact of vial location on the drying rate using two parameters of non-product invasive through vial impedance spectroscopy (TVIS). These include: (i) the peak imaginary amplitude, C''_{PEAK} , which is a direct measure of ice mass in the vial, and (ii) the peak frequency, F_{PEAK} , which is sensitive to a change in the shape of the ice interface.

METHODS

160 standard 10 mL vials (manufactured by Schott) were used in this work, out of which 5 were modified TVIS measurement vials, with copper electrodes (19 by 10 mm) attached on the outside of the glass wall. One TVIS vial was placed at the halfway point of each of the 4 edges of the shelf and one was placed in the core. After pre-weighing these vials, freeze drying was carried out in a Virtis Advantage Plus laboratory freeze dryer, by freezing at a shelf temperature of $-40\text{ }^{\circ}\text{C}$ at $30\text{ }^{\circ}\text{C h}^{-1}$, and then primary drying for 30 min at a shelf temperature of $-15\text{ }^{\circ}\text{C}$ and a chamber pressure of $30\text{ }\mu\text{bar}$. The loss of ice mass over the first 30 min was also recorded by the gravimetric method.

RESULTS

A brief period (5 min) of steady state conditions were observed after the first 20 min of primary drying as indicated by a constant chamber pressure and a constant F_{PEAK} profile. During this period, the surrogate drying rate, $d(C''_{PEAK})/dt$, of the ice cylinder in the front edge vial was found to be 50 % higher than the core vial owing to the additional heat contribution via radiation from the Plexiglass door. This agrees well with one experimental study based on mathematical modelling, where the difference in the heat flow to the product in the edge v/s the core vial was found to be 50%. However, an 8 % discrepancy between the average gravimetric drying rate and the surrogate drying rate suggests the shape of the ice interface had changed over the 30 min period.

CONCLUSION

TVIS serves as a valuable non product invasive development tool for demonstrating the heterogeneity in the freeze drying process due to the location of the vial on the shelf.

REFERENCES

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