

Biopharma Technology Limited - Poster presentation

Clare Ross, Tony Gaster and Kevin Ward

The importance of Critical Temperatures in the Freeze Drying of Pharmaceutical Products

Every formulation will have a critical temperature, below which it should be cooled for complete solidification and maintained during primary drying in order to minimise processing defects. Therefore, in order to design freeze drying cycles on a rational, product specific basis, such information should be identified (Pikal 1990, Frank 1990). The most commonly identified ones are, collapse temperature (Tc), eutectic temperature (Teu) and glass transition (Tg').

Freeze drying microscopy can be used to identify the temperatures at which visible changes occur, together with relative drying rates (Zhai et al 2003). Biopharma Technology Limited (BTL) has developed *Lyostat2* for this purpose.

Historically, it has often been assumed that Tg' and Tc occur at similar temperatures however, this is not always the case, especially for complex formulations. Furthermore, even with sensitive calorimetric methods, Tg' can often be elusive, and it is known that changes in mobility in the frozen structure can occur below Tg'. BTL has developed a further instrument - *Lyotherm2* to measure ZSin ϕ , a function of electrical impedance of a frozen formulation (Martin et al, 2007). This has enabled mobility increases to be identified below the "traditional" critical temperatures mentioned above.

Use of data from *Lyostat2* and *Lyotherm2* has enabled the development of safe yet efficient freeze drying cycles for a wide range of formulations. The benefits of using this approach are that once analysis has been carried out, a cycle can be developed that is energy efficient, economic, safe and robust for that formulation. The resulting product should then exhibit consistent quality in terms of being a cosmetically acceptable cake with good stability, long shelf life, high activity, low moisture and rapid rehydration. A case study is included to demonstrate the benefits of establishing critical temperatures in this way.

References

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