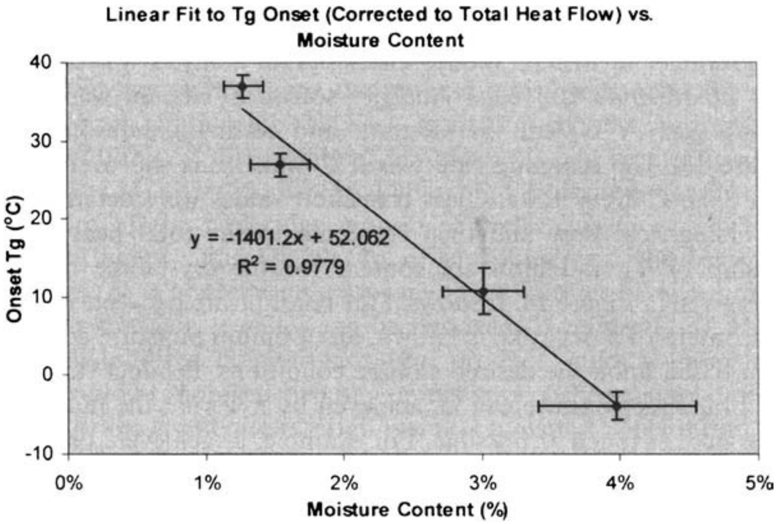

FIGURE 14 T_g of dry cakes as a function of moisture content. *Abbreviation*: T_g, glass temperature.

INTERPRET DATA FOR CYCLE DEVELOPMENT

With a thorough understanding of the formulation, we can reduce the amount of trial and error in cycle development. Results from DSC and the freeze-drying microscope, as we described in previous sections, indicate an annealing step is necessary to crystallize glycine in the formulation. Consequently, this allows us not only to conduct the primary drying aggressively at a relatively high product temperature but also to obtain a good cake appearance. In addition, it also provides a scientific rationale to determine freezing temperature, annealing temperature, primary drying shelf temperature, and primary drying pressure. Data from the adsorption study and moisture optimization studies, on the other hand, demonstrate a characteristic of the drier, the better for this formulation. As a result, it guides us to confidently design secondary drying processes such as determining optimal drying temperature, pressure, and time to provide uniform moisture content in the final containers. The information from the formulation characterization studies also assists in the validation of the cycle, particularly in bracketing the process parameters.

A typical lyophilization cycle for a crystalline matrix-type formulation, such as the one discussed here, is illustrated in Figure 15. The cycle includes the following:

1. An annealing step in freezing to slowly warm the product to −20°C and then hold for one hour.
2. An aggressive primary drying with a shelf temperature of 5°C and a chamber pressure of 300 mTorr.
3. An overdrying secondary drying with a ramped shelf temperature of 25°C and a chamber pressure of 100 mTorr for a total of 24 hours.