# Probing Amorphous Relaxation and Crystallization using Master Curves and X-Ray Diffraction

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Variability in the time to crystallization is a major technical and economic hurdle in using amorphous solids in dosage forms. It is known that amorphous solids "age", and that the older they are the more relaxed and the higher the probability of crystallization. At present, there is no method that allows the "effective age" of an amorphous raw material to be assessed relative to its unrelaxed initial condition. A method has been developed that may satisfy this unmet need and provide a first step in subsequent investigation of the crystallization "event". This method consists of using master curves to enable the determination of the effective age ('aging') of an amorphous compound given normal excursions in storage conditions. The present study shows that master curves can be prepared for different storage conditions and subsequently be used to predict the relaxation or aging behavior of amorphous compounds with expected variations in storage conditions.

Given the constraint that the system remain within the area enclosed by the equilibrium supercooled liquid line and the glass on the enthalpy-temperature diagram, experimental results using indomethacin and salicin as model compounds show that master curves can be used to predict aging behavior under non-isothermal conditions, with temperature excursions as large as 10°C. The non-isothermal relaxation behavior can be modeled by combining the Kohlrausch-Williams-Watts (KWW) stretched exponential function, the relaxation function and a shift factor. In addition, a model was developed that extends the range of applicability to time/temperature regions in which partial crystallization occurs.

The continuation of our studies is focused on estimating the time to crystallization onset with temperature and elucidating the underlying mechanism. It is hypothesized that the molecular events that result in the generation of heterogeneity within the amorphous state result from the most relaxed segments of the population. Preliminary X-ray diffraction experiments using both Cu-Kα and synchrotron radiation have been performed on aged amorphous compacts of indomethacin and seem to support the feasibility of using these techniques to provide a detailed map of crystallization from the amorphous phase and serve to compliment the master curves based on thermal analysis.

**References**

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