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Crystallization and Relaxation Dynamics of Amorphous Loratadine under Different Quench-cooling Temperatures

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Theoretical Background

Non-isothermal cold crystallization kinetics

Avrami equation is used to describe the non-isothermal crystallization kinetics:

\[ X_t = 1 - \exp\left(-K(t - t_0)^n\right) \]  

(S1)

where \( X_t \) is the degree of crystallization, \( K \) is the crystallization rate constant depending on the nucleation and growth rate, \( t_0 \) is the induction time of crystallization and \( n \) is the Avrami exponent depending on the nucleation rate and the dimensionality of the crystallization.\(^{1-4}\)

Given the non-isothermal character of the investigated process, Jeziorny\(^4\) suggested that the rate parameter should be corrected and given by \( \log Z_t = \log K / \Phi \) where \( Z_t \) is same as \( K \) as mentioned above, meaning the crystallization rate constant.

In the DSC measurements, \( X_t \) is defined by the follow equation:

\[
X_t = \frac{\int_{t_0}^{t} \frac{dH}{dt} \, dt}{\int_{t_0}^{\infty} \frac{dH}{dt} \, dt} = \frac{A_t}{A_\infty}
\]

(S2)

where \( \frac{dH}{dt} \) is the rate of heat evolution, \( t_0 \) and \( t_\infty \) are respectively the time when crystallization starts and ends and \( A_t \) and \( A_\infty \) are the areas of partially and fully crystallized materials under normalized DSC curve, respectively.

Moreover, the non-isothermal crystallization kinetics of amorphous drugs could be analyzed through the logarithmic form of primary crystallization based on eq S2:

\[
lg[-\ln(1 - X(t))] = \log Z_t + n \log(t - t_0)\]

(S3)

Molecular dynamics

Imaginary complex permittivity could be described by Havriliak–Negami (HN)\(^5,6\), which is employed as:
\[ \varepsilon^*(\omega) = \varepsilon_\infty + \sum_k \left( \frac{\Delta \varepsilon}{1 + \left(i \omega \tau_{HN_k}\right)^{a_{HN_k}} \beta_{HN_k}} \right) \]

where \( \varepsilon_\infty \) is the high frequency limit of the real part \( \varepsilon'(\omega) \), \( k \) sums over different relaxation processes (primary or secondary processes), \( \omega = 2\pi f \) is the angular frequency, \( \tau_{HN} \) is the characteristic relaxation time that is related to the frequency of maximal loss \( f_{\text{max}} \), \( \Delta \varepsilon \) is the dielectric relaxation strength of the process under investigation; \( a_{HN} \) and \( \beta_{HN} \) are fractional shape parameters (\( 0 < a_{HN} \leq 1 \) and \( 0 < a_{HN} \beta_{HN} \leq 1 \)) describing the symmetric and asymmetric broadening of the dielectric spectrum. And for secondary relaxation process (\( \beta \)-relaxation), when \( \beta_{HN} = 1 \) the HN function reduces to Cole–Cole distribution function.\(^7\)

**Fragility parameter**

Fragility parameter \((m_p)\) is calculated as:\(^8\)

\[ m_p \equiv \frac{d \log \tau_\alpha}{d (T_g/T)} \bigg|_{T=T_g} \]

(S5)

This parameter is often used to predict the tendency of glass-forming liquids toward crystallization. The values of \( m_p \) for different materials typically range between \( m_p = 16 \) and about 200.\(^9\) The liquids characterized by small values of \( m_p \) are classified as strong systems \((m < 30)\), whereas large values of \( m_p \) are a feature of fragile materials \((m > 100)\).\(^{10}\) When \( m_p \) falls within the 30 < \( m_p \) < 100 range, the super-cooled liquid is classified as intermediate glass-former.\(^{11}\) The strong liquids usually have a strong thermodynamic stability and a small tendency toward crystallization near \( T_g \). In contrast with the low values found for the strong liquids, it varies rapidly at the temperature near \( T_g \) for fragile glass-formers.

In DSC test, the thermodynamic fragility could be calculated by the following equation:

\[ m_p = 56 \frac{T_g \Delta C_p(T_g)}{\Delta H_m} \]

(S6)

where \( \Delta C_p(T_g) \) is the heat capacity at \( T_g \) and \( \Delta H_m \) is the enthalpy of fusion.\(^{12,13}\)
References