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Measurement of enthalpic relaxation by differential scanning calorimetry—effect of experimental conditions

Rahul Surana[1], Abira Pyne[2], Meena Rani, Raj Suryanarayanan*

Department of Pharmaceutics, College of Pharmacy, 308 Harvard St. S.E., University of Minnesota, Minneapolis, MN 55455, USA

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Abstract

Differential scanning calorimetry (DSC) is the most commonly used technique for studying enthalpic relaxation in amorphous systems. Our objective was to study the effect of experimental conditions, specifically heating and cooling rates, on the enthalpic relaxation measurement by differential scanning calorimetry. Amorphous trehalose was prepared by freeze-drying an aqueous solution of trehalose dihydrate. It was subjected to differential scanning calorimetry. The enthalpic recovery (ER) at the glass transition temperature (T_g), for identically aged samples, depended on the heating rate (HR). The T_g onset increased as a function of the heating rate and so did the completion of enthalpic recovery, i.e., the temperature at which the enthalpy curve meets the super-cooled liquid line after the glass transition. Therefore, the enthalpic recovery, and by extension the observed extent of relaxation, was influenced by the heating rate. As the aging time increased, there was an increase in the T_g onset as well as the completion of enthalpic recovery. Since the calculated enthalpic recovery value is strongly dependent on this endpoint, there is a potential for overestimation of the relaxation below T_g. This is particularly important for longer aging times and higher heating rates. It is generally believed that the enthalpic recovery can be minimized by keeping the cooling and heating rates identical. This observation can also be explained by the effect of heating rate on T_g onset and the endpoint of enthalpic recovery. The enthalpic recovery at T_g may not reflect the state of the sample, and may be strongly influenced by the experimental conditions. Thus, the effects of experimental conditions need to be carefully evaluated in order to obtain meaningful results.

Keywords: Differential scanning calorimetry; Glass transition temperature; Enthalpic relaxation

1. Introduction

Glasses are thermodynamically non-equilibrium systems but can approach equilibrium over extended periods of time when stored in a limited temperature region close to glass transition temperature (T_g). This progressive change in the thermodynamic properties of the glass towards equilibrium is also called the physical aging or relaxation process. The relaxation results in a decrease in the mobility and loss of enthalpy and specific volume [1–3].

Since the physical properties of the freshly prepared glass change continuously with the extent of relaxation, the process has considerable commercial importance and has been studied widely. It has been shown that aging may lead to an increase in the yield stress and tensile modulus and a decrease in fracture toughness [4]. Moreover, aging may also have implications on the vapor sorption behavior of glasses [5,6].

The increased interest in characterization of the time scales of molecular motions in amorphous food and pharmaceutical systems arises from the fact that molecular motions, which are responsible for relaxation, may also be responsible for physical and chemical processes causing unwanted changes. These changes include loss of potency due to chemical reactivity, crystallization and collapse [7]. Several carbohydrates and polymers, used as bulking agents, stabilizers or coatings,

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* Corresponding author. Tel.: +1 612 624 9626; fax: +1 612 626 2125.
E-mail address: surya001@umn.edu (R. Suryanarayanan).

[1] Present address: Forest Laboratories Inc., 49 Mall Drive, Commack, NY 11725, USA.

[2] Present address: Millennium Pharmaceuticals, 35 Lansdowne Street, Cambridge, MA 02139, USA.

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exist in the glassy state at typical storage conditions. Changes in their properties over time may have a catastrophic impact on product performance. Thus, it becomes particularly important to study these relaxation processes and determine the storage conditions where significant changes in properties will not occur in the time scales of interest [8].

The primary effect of aging is the increase in relaxation times. Thus, it is possible to study the relaxation process by following the time evolution or frequency dependence of material properties such as enthalpy, volume, viscosity, and dipole relaxation [9]. So far, differential scanning calorimetry (DSC) has been one of the most popular tools to study the relaxation process where enthalpic relaxation is measured as a function of time. This relaxation is usually measured as the recovery of the lost enthalpy associated with the glass transition event during the heating cycle of an aged glass.

To understand the enthalpic relaxation and recovery processes, let us consider the example of a liquid being cooled rapidly from a temperature above the melting point. The sequence of events is schematically shown in Fig. 1. When a liquid fails to crystallize during cooling, it enters the rubbery state and then undergoes glass transition when the molecular motions are not able to keep up with the cooling rate. At T_g the excess enthalpy and entropy are ‘frozen in’, the amounts of which depend upon the conditions (e.g., cooling rate, sample geometry, etc.) of glass formation [10,11]. When this glass with excess enthalpy ‘frozen in’, is stored at a temperature T_1 close to T_g (aging time, t_1), it tends to lose its excess enthalpy and moves towards the super-cooled liquid (represented by the extrapolated liquid line). There is an increase in the density and decrease in entropy and free volume as a function of aging of a glass. As discussed above, when this aged glass is heated through T_g to the rubbery state, the lost enthalpy is regained and this event can be observed as an endotherm associated with the glass transition in the DSC profile. It is usually assumed that the enthalpy regained at T_g (ΔH) is equal to that lost during aging below the T_g.

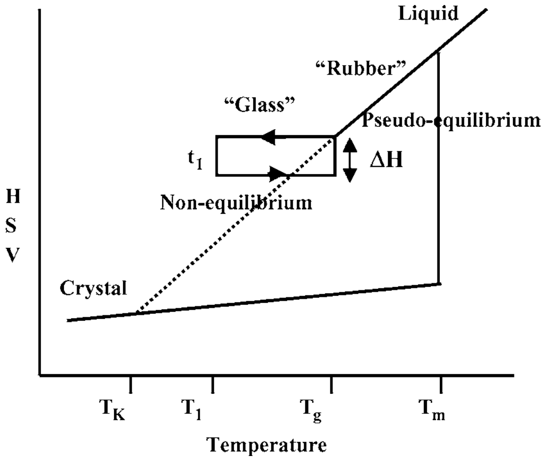

Fig. 1. Schematic representation of changes in enthalpy (or volume or entropy) as a function of temperature for a liquid undergoing crystallization or glass transition during cooling. Enthalpic relaxation on storage below the T_g and its recovery at T_g during heating are also depicted. T_K, T_1 and T_m are Kauzmann, aging and melting temperatures, respectively; t_1 is the aging time at T_1. Adapted from [10,11].

The relaxation rate in the glassy state depends upon the aging temperature relative to the T_g, and decreases with increase in the difference between the two temperatures. The temperature range for physical aging generally extends from T_g down to the first secondary relaxation temperature [4]. The relaxation rate below T_g is an indication of the molecular mobility of an amorphous material, a property influencing both physical (e.g., crystallization) and chemical (e.g., decomposition) instability of amorphous substances. Assuming relaxation processes to be directly related to the shelf-life of amorphous pharmaceuticals, some recent studies have utilized the enthalpic recovery (ER) at T_g (as a function of the aging time) as a predictor of shelf-life [7,8].

Relaxation in glasses has been studied by several techniques, including microcalorimetry and dielectric analysis, which monitor the relaxation process under isothermal conditions in real time [12,13]. DSC, however, is different from other techniques wherein the isothermal relaxation is measured non-isothermally during the heating profile. Though study of real time relaxation under isothermal conditions would be ideal, the instrumental sensitivity is a major limiting factor. The ease of both sample preparation and experimentation and the almost universal applicability of DSC make it a very attractive tool for the study of relaxation processes.

It is well accepted that the T_g of a material is dependent upon the experimental conditions [14–16]. Both the extent of relaxation of the glass and the DSC heating rate (HR) are known to increase the observed T_g value. It can be expected that enthalpic recovery, so closely associated with glass transition, will also be affected by the method of its determination. However, there are no detailed studies showing the effect of experimental conditions on the enthalpic relaxation determined by DSC.

The aim of this project was a phenomenological study of the effects of experimental conditions on the enthalpic recovery determined by DSC. The aging time and temperature, and the DSC heating and cooling rates were the variables. The isothermal and non-isothermal relaxation behavior through the cooling and heating cycle were also compared. The model compound was amorphous trehalose, a relatively fragile glass.

The working hypotheses of this project were based on the kinetic behavior of the glass transition event. It can be expected that, since the onset of T_g increases with an increase in the heating rate, the temperatures of the endpoint (also represented as the endpoint of enthalpic recovery) will also increase with an increase in the HR. It is hypothesized that relaxation not only increases the onset of T_g, but also raises the endpoint temperature of enthalpic recovery. The other hypothesis to be tested was that the rise in endpoint temperature of ER is responsible for the higher value of ER observed with an increase in the HR.

2. Materials and methods

2.1. Preparation of amorphous trehalose

α,α-Trehalose (α-D-glucopyranosyl α-D-glucopyranoside) dihydrate ($C_{12}H_{22}O_{11}\cdot 2H_2O$, Sigma, St. Louis, MO) was used as obtained. Aqueous trehalose solution (10%, w/v) was cooled to −45 °C in a tray freeze-drier (Model UNITOP 400L,Virtis) and subjected to primary drying for 48 h. Over the next 24 h, the temperature was gradually increased to 50 °C. The secondary drying was carried out at 50 °C for 24 h, after which the temperature was raised to 60 °C and the drying continued for 24 more hours. The samples were removed from the freeze-drier and stored in a desiccator at room temperature over anhydrous calcium sulfate (RH ∼0%) until used. The freeze-dried materials were X-ray amorphous. While preparing the samples for experiments, they were handled in a controlled humidity environment (<5% RH, in a glove box) under ambient temperature conditions.

2.2. Thermal analysis

A differential scanning calorimeter (MDSC, Model 2920, TA Instruments, New Castle, DE) with a refrigerated cooling accessory was used. The DSC was calibrated with pure samples of tin and indium at all the heating rates used. Samples (4–8 mg) were analyzed in crimped aluminum pans under a dry nitrogen purge. The lids of the sample pans had several holes, which facilitated the removal of residual moisture during the drying cycle. The samples were dried in the DSC pans for 2 h at 100 °C to remove any moisture present in the system. Unless otherwise stated, the sample history was erased by heating the sample to a temperature $>T_g$ (usually to ∼140 °C; $T_g \sim$ 114–120 °C depending upon the heating rate) and cooling it rapidly (20 °C/min) to the temperature of interest. The other experimental details are provided separately in each section.

3. Results and discussion

3.1. Dependence of enthalpic recovery on the heating rate

It is well documented that the T_g depends on the heating rate and also on a combination of the heating and cooling rates [14–16]. It was also observed that for a similarly relaxed material, the enthalpic recovery at T_g was dependent on the heating rate [17]. Our first objectives were to study the effect of heating rate (i) on the enthalpic recovery of samples that were aged isothermally in the same manner, and (ii) on the extent of relaxation of a material aged isothermally for different time periods.

A schematic outline of sample treatment is shown in Fig. 2a. The samples were heated to at least 15 °C above T_g to remove the thermal history and cooled back at 20 °C/min to 25 °C. It was then heated to 98 °C at 20 °C/min, aged for a preset time (t_a) and cooled back to 25 °C at 20 °C/min. After this aging process, the sample was heated past its T_g and from this final heating scan the T_g and enthalpic relaxation were measured. The aging times ranged from 0 to 480 min and the heating rates were 2, 5, 10, 20 and 40 °C/min. In order to ensure that complete enthalpic recovery occurred during the final heating scan, the samples heated at different rates, were cooled back at 20 °C/min to room temperature and reheated at 20 °C/min. The enthalpic recovery in this heating scan for all the samples was identical.

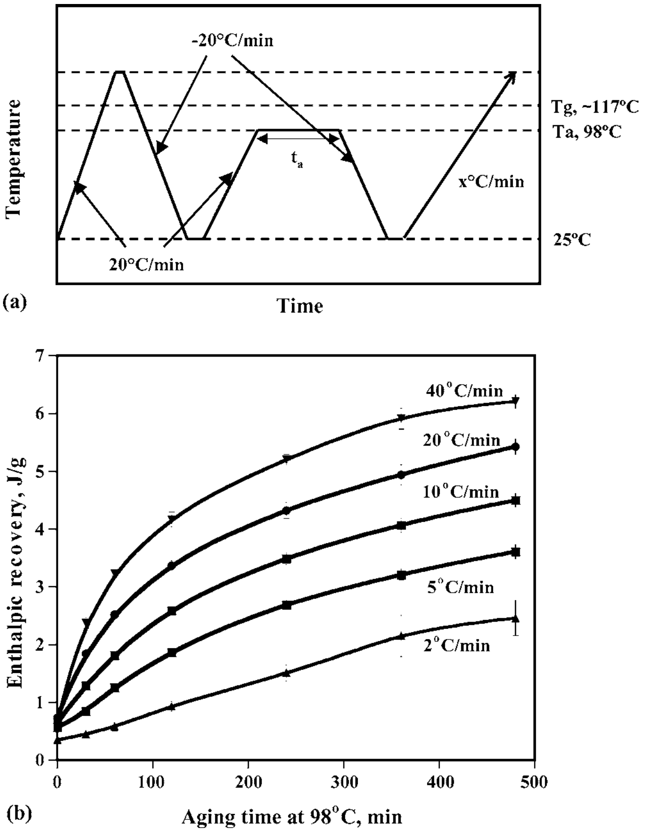

Fig. 2. (a) Schematic representation of the experimental conditions during the measurement of enthalpic recovery at T_g after isothermal aging at 98 °C (T_a) for different time periods. All the heating and cooling rates were 20 °C/min, except for the heating rate in the final scan; t_a = aging time. (b) Enthalpic recovery as a function of aging time at different heating rates. The aging temperature was 98 °C ($n \geq 3$).

The enthalpic recovery at T_g was plotted as a function of the aging time for various heating rates (Fig. 2b). For the unaged sample ($t_a = 0$), the enthalpic recovery was nearly identical at the different heating rates. Aging led to an increase in the ER at all heating rates. This effect was very pronounced at short aging times and reached a limiting value for longer aging times. For the same aging time, the ER determined from DSC differed with heating rate (Fig. 2b). Moreover, this difference varied with aging time. The longer the aging time, more was this difference. Thus, the heating rate had an effect on the ER determined by DSC.

When two samples with identical thermal history are heated at different rates, it is expected that the slowly heated sample would relax more during heating as the time spent below the T_g will be longer in that case. On the contrary, in case of amorphous trehalose, the sample that was heated at 2 °C/min showed less relaxation compared to the one heated at 40 °C/min (Fig. 2b). The increase in heating rate leads to an increase in the temperature of the onset of glass transition as well as the endpoint of ER. As discussed later on, this difference may be responsible for the observed differences in the enthalpic recovery at different heating rates.

As discussed earlier, the glass transition is a kinetic phenomenon and is dependent on the heating and cooling rate of the amorphous substance [14–16]. The increase in the heating rate increases the observed glass transition temperature. This may also change the temperature where the enthalpy curve meets the super-cooled liquid line following this transition (Fig. 1). The "enthalpy jump" at T_g from the glassy curve to the super-cooled liquid line is responsible for the endotherm associated with the T_g. Any change in the onset or end point of this enthalpy curve will change the calculated enthalpy value. Fig. 3a exemplifies the effect of heating rate on both the T_g onset and the temperature at which the enthalpic recovery is complete.

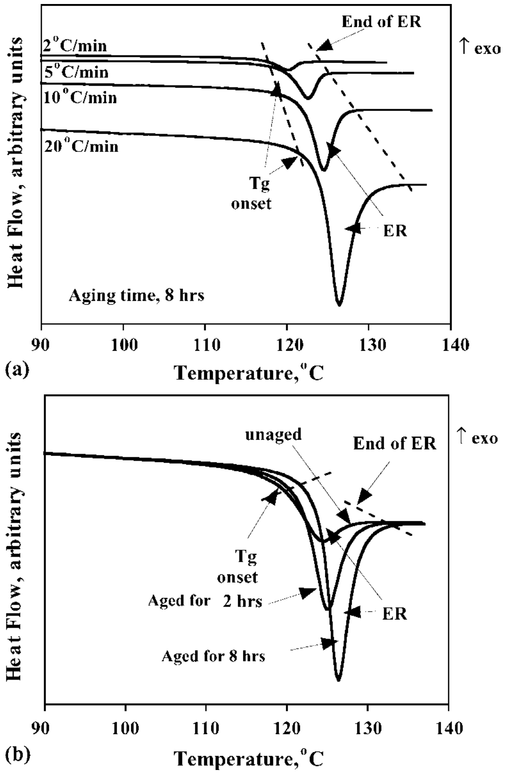

Fig. 3. (a) Effect of heating rate on T_g onset and the end-point of enthalpic recovery. Samples were aged at 98 °C for 8 h, cooled to room temperature at 20 °C/min and heated at different rates. (b) Effect of aging time on T_g onset and the end-point of enthalpic recovery in samples aged for 0 (unaged), 2 and 8 h at 98 °C. The heating rate was 20 °C/min.

Enthalpic relaxation leads to an increase in the structural relaxation time of a glassy material. This increases the observed T_g and the ER associated with it (Fig. 3b). If the T_g increases, it is possible that the end of enthalpic recovery, observed in the DSC, will also be at a higher temperature. The heat capacity of amorphous materials in the glassy and the rubbery state are different, with the latter having a higher value. This is evident from the slope values of the enthalpy curves (Fig. 1), with the rubbery state characterized by a steeper slope. The rubbery state is considered to be in pseudo-equilibrium and after glass transition, the thermodynamic properties of a material are no longer dictated by the thermal history. At constant pressure, the properties will depend only on the temperature of the system. Thus, if the "enthalpy jump" (Fig. 1) is occurring at a higher temperature, the aged sample will need to recover more enthalpy to reach the equilibrium rubbery state.

Fig. 4 summarizes the influence of aging time on both the onset temperature of the glass transition event and the endpoint of ER. These experiments were carried out at different heating rates. The T_g onset (Fig. 4a) and extrapolated endpoint of ER (Fig. 4c) were determined by drawing the tangents and extrapolating the onset and the end. The endpoint of ER (Fig. 4b) was determined to be the temperature at which the heat flow returns to the baseline after the ER endotherm. Several conclusions may be drawn from Fig. 4. The T_g onset (Fig. 4a) and endpoint (Fig. 4b and c) increased with an increase in the heating rate. Aging led to an increase in the T_g and this increase was more pronounced at higher heating rates (Fig. 4a). Similarly, the endpoint of ER, in general, occurred at a higher temperature at longer aging times (Fig. 4b and c). Moreover, this increase was more pronounced at higher heating rates.

Fig. 5a and b is schematic representation of the combined effect of heating rate and aging on the thermodynamic properties of a relaxed material. While our discussion will be restricted to enthalpy, the same arguments will also hold for the entropy and volume. Since the heat capacity of amorphous materials changes with temperature, the enthalpy increase with temperature is not expected to be linear. The profiles in the figures are linear only for the sake of simplicity.

For Fig. 5a, lets us consider a simple case where an amorphous substance is cooled from above the T_g at a predetermined rate and relaxed at a temperature, T_a, below the T_g for a specific time. Thus, the same thermal history was imparted to the sample in all cases. This sample is then heated at different rates across the T_g. To keep it simple, let us consider that the relaxation during this heating cycle is not significant and the sample traverses the same path up to the T_g at all heating rates. This will probably be true for a sample relaxed for a very long time, where not enough relaxation is expected during heating, or the heating rates are not very different from each other. At a slower HR, the glass transition occurs at a lower temperature. The width of the transition region is also shown to be low thus the event is complete at a lower temperature. As the HR is increased, the T_g onset and width of the

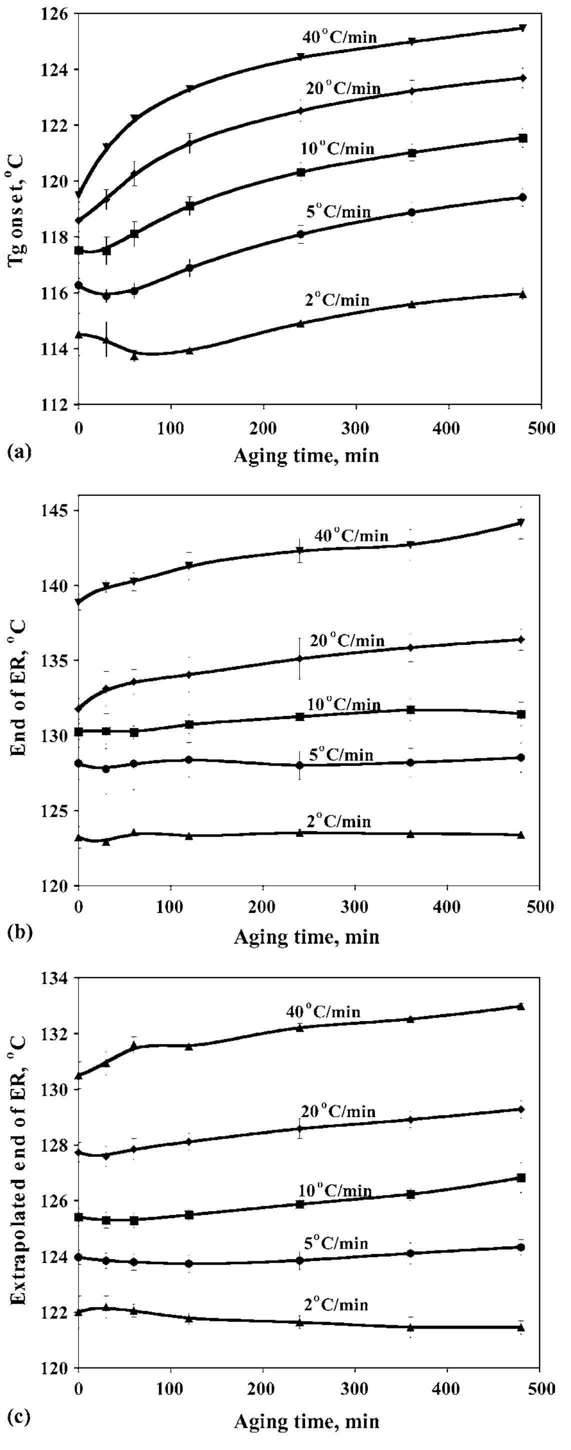

Fig. 4. Effect of heating rate and aging on (a) T_g onset, (b) endpoint of ER, and (c) extrapolated end of enthalpic recovery in amorphous trehalose. The experimental details are shown in Fig. 2(a). The heating rates were 2, 5, 10, 20 and 40 °C/min ($n \geq 3$).

transition region increases. There is also an increase in the endpoint of ER, which makes the total enthalpy jump more in this case. At a still higher heating rate, the effect becomes more pronounced and the observed ER is much higher.

To understand the effect of aging time on enthalpic recovery (Fig. 5b), let us consider a similar system with all the sample treatment being the same until the aging process. In this case, the aging is performed for different time periods and following aging, the sample is heated at a constant HR across T_g. As shown in Fig. 5b, an increase in the aging time increases the T_g. The ER endpoint also increases as shown earlier (Fig. 4b and c). It can be clearly seen from Fig. 5b that the increase in aging time disproportionately increases the observed ER. Thus, with an increase in the aging time, there is an overestimation of ER in the DSC. This effect is more pronounced at higher HR.

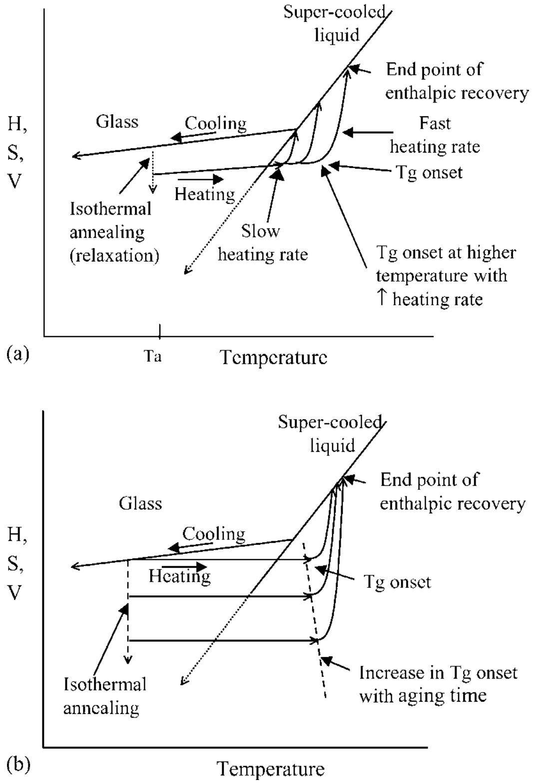

Fig. 5. Schematic representation of the predicted thermodynamic behavior of an aged amorphous substance. (a) A constant aging time followed by heating at different rates and (b) changing the aging time while keeping the heating rate constant.

Figs. 4 and 5 can be used to understand the effects of heating rate and aging time on the observed ER in amorphous trehalose (Fig. 2b). For the samples with the same thermal history, increase in HR increases the endpoint of ER and results in higher observed ER. The increase in the aging time causes a disproportionate increase in the endpoint of ER for different HR. Thus, the magnitude of increase in ER with aging time differs with the HR. The two observations listed above can explain the profiles in Fig. 2b.

In order to understand the real impact of heating rate and the aging time, the enthalpy curves for several samples were plotted together. While the effect of heating rate on T_g for a sample aged for 8 h is shown in Fig. 6a, the aging time effects on the enthalpy values are elucidated in Fig. 6b. The enthalpy curves were obtaind by assuming a fixed enthalpy value for all the samples at 140 °C (a temperature substantially above

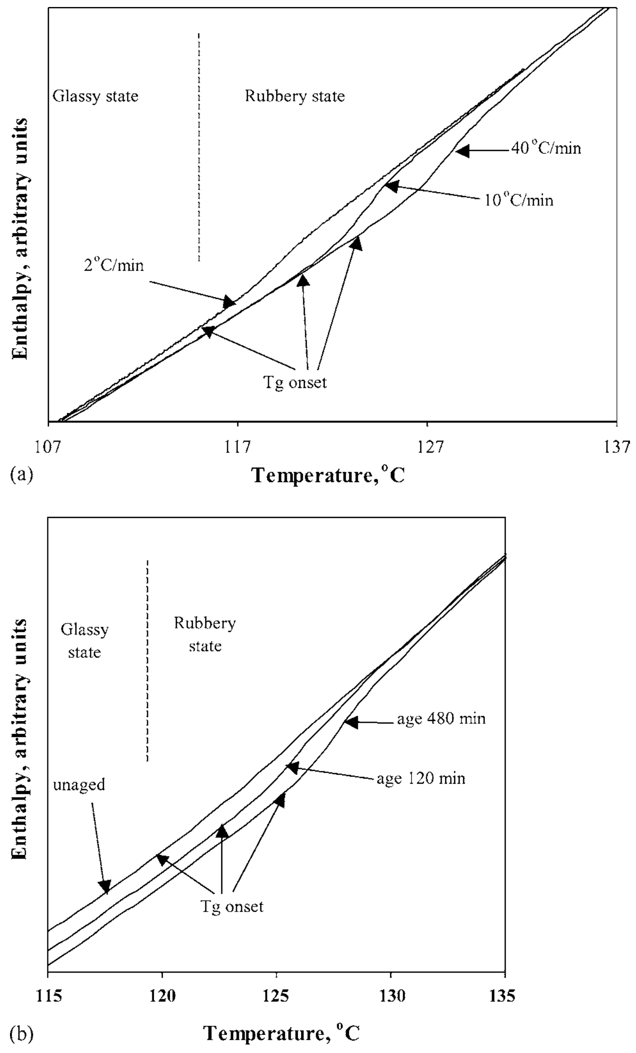

Fig. 6. Enthalpy curves of aged (98 °C) amorphous trehalose during heating. (a) A constant aging time of 8 h followed by heating at different rates and (b) changing the aging time while keeping the heating rate constant at 40 °C/min. The lowest observed glass transition temperature [∼116 °C in panel (a); ∼119 °C in panel (b)] formed the basis for the demarcation of the glassy and rubbery regions.

T_g) and calculating the enthalpy curves using the heat flow signal. While this method does not give an accurate measure of the enthalpy of the system, it was found to be acceptable for this comparison. While Fig. 5 is a schematic representation, Fig. 6 contains the experimental results.

Thus, the heating rate has a strong influence on the enthalpic recovery values obtained by DSC. The questions that arise are: (i) If the observed enthalpic recovery is a function of the heating rate, then how important is the choice of the heating and cooling rates during these studies? (ii) Will the calculated physicochemical parameters (such as fragility) be influenced by the choice of heating rate?

If there is a constant difference in the recovery values at different heating rates, a correction factor may be used to account for the effect of heating rate. However, as seen above (Fig. 2b), the difference in the recovery increases with an increase in the heating rate. If all the comparisons are made at the same heating rate, acceptable results may be obtained. The other option is to calculate the relaxation by real time loss of enthalpy at the temperature of interest rather than relying on the indirect DSC method.

3.2. *Effect of heating and cooling rate on the T_g and enthalpic relaxation of an amorphous system*

The ratio of cooling to heating rates is known to have an impact on the T_g and enthalpic relaxation of amorphous systems. Moynihan et al. showed that enthalpic relaxation could be minimized if the same cooling and heating rates are employed [14,15]. Seemingly, at the same cooling and heating rates, the material retraces its path from the glassy state to the rubbery state and the T_g value during cooling and heating are very close. Moreover, it has been seen that the enthalpic recovery at T_g is minimized when the same cooling and heating rates are employed for T_g determination [14,17]. However, as shown earlier, the ER at T_g is a function of the heating rate and thus it may not be feasible to compare the ER values obtained at different heating rates. A glassy amorphous material always relaxes below T_g, both during cooling and during heating. If the material always relaxes it would be difficult to retrace its path, more so at a slower heating and cooling rate.

As far as the effects of DSC experimental conditions are concerned, existing literature reports show that enthalpic recovery observed at T_g arises due to the differences in the heating and cooling rates [14]. Slow cooling followed by fast heating led to enthalpic relaxation. On the other hand, identical cooling and heating rates minimized enthalpic relaxation. Using amorphous trehalose as the model system, we studied the effect of the ratio of cooling rate to HR on the enthalpic recovery at T_g. Enthalpic recovery as a function of the cooling rate is plotted in Fig. 7. The samples were cooled at rates varying from 0.5 to 25 °C/min. These samples were then heated either at the same rate as was the cooling rate or at 5, 10 or 20 °C/min. It can be observed that with a decrease in the cooling rate, the enthalpic recovery at the three heating rates increased. This effect is more pronounced at 20 °C/min than at 5 °C/min. In other words with increase in the ratio of HR to cooling rate, there was an increase in the ER. The recovery associated with identical heating and cooling rates is shown in curve (d), where, irrespective of the heating and cooling rates, the enthalpic recovery values were not markedly different from each other.

The above observations are thus consistent with literature reports that minimum relaxation occurs if the heating and cooling rates are identical. According to another theory regarding relaxation in amorphous substances, the amorphous material always relaxes below the T_g, both during cooling and during heating [18]. Relaxation below T_g is a function of (i) ($T_g - T$), where T is the temperature of storage, and (ii) the time of aging. Increase in ($T_g - T$) decreases the relaxation rate. At a constant temperature, increase in aging time

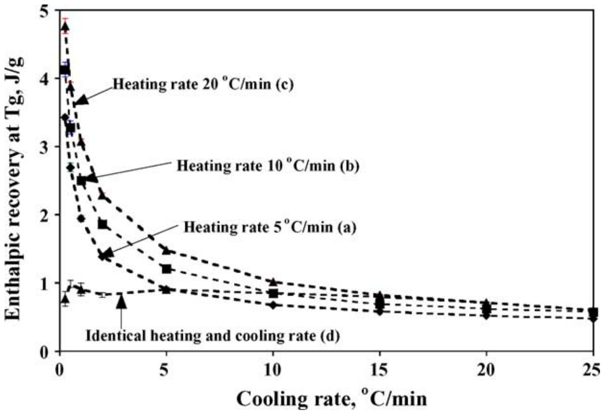

Fig. 7. Enthalpic recovery at T_g as a function of the heating and cooling rates ($n \geq 3$). The sample thermal history was removed by heating it to 140 °C. It was then cooled, at rates ranging from 0.5 to 25 °C/min (*x*-axis) to 25 °C and finally heated at the desired rate. The enthalpic recovery was calculated from the final heating scan. Curves (a–c) are enthalpic recoveries obtained on heating the samples at 5, 10 and 20 °C/min, respectively, following cooling at different rates. Curve (d) shows enthalpic recovery determined by using the same heating rate as was used during cooling.

increases the relaxation. Thus, it is apparent that relaxation should be more when slower cooling and heating rates are employed because of longer time periods allowed to the system below the T_g. If that is the case, why do we not "observe" more relaxation in a sample that has been cooled and heated at very slow rates (for example, 0.25 °C/min)? If a higher ER is not observed, is it really true that the slowly cooled material has not relaxed more than the fast cooled material?

Owing to their frequent use in calculation of the fragility parameters and mobility in glasses, it is important to ensure that the relaxation and recovery values that are obtained by DSC are not "apparent" values. From the earlier results, we observed that the recovery in similarly relaxed material varied on changing the heating rate.

We have tried to understand the effects of heating and cooling rates, on the thermodynamic properties of amorphous trehalose. Fig. 8 is a schematic representation of the changes in thermodynamic properties of amorphous materials cooled and heated through the T_g. Let us consider a system at point C in the plot which is the super-cooled liquid region existing under pseudo-equilibrium conditions. Let us take the first scenario when the material is cooled and heated very rapidly through T_g. This case is shown as the top profile in the schematic. At a fast cooling rate, the glass transition occurs at a higher temperature. Since the system does not get enough time, minimal relaxation occurs during the cooling cycle. During heating, the profile matches that obtained during cooling till the zero mobility temperature (shown by the vertical line AB in Fig. 8; zero mobility in the experimental time scales) and then deviates from that line. There could be two possible reasons for this deviation: (i) during heating there is some relaxation; (ii) because of the fast heating rate, the enthalpy of the material is not able to keep up with the rapidly increasing temperature. At a faster heating rate, the structural relaxation time becomes equal to the experimental time scales only at a high temperature. Thus, the material follows the heating curve across the super-cooled liquid line and takes up some enthalpy to reach the super-cooled liquid state. The enthalpy required to reach the super-cooled liquid line is important because this is revealed in the DSC experiment. This enthalpy recovery may not be equal to what is lost during the cooling cycle. The faster the heating rate, the higher will be the temperature where the enthalpy curve meets the liquid line (because of kinetic factors). As mentioned earlier, the higher is the endpoint of enthalpic recovery, the larger is the enthalpy required by the system.

The second profile is for a slowly cooled and heated sample. As expected, the T_g (during cooling) of a slowly cooled system is lower than that of the rapidly cooled system. The slope value of the cooling curve is higher than that of the sample cooled at a faster cooling rate, indicating more relaxation during cooling. In this case, the material is at a much lower enthalpy after cooling to the zero mobility temperature, compared to the fast cooled sample. Below the zero mobility temperature, negligible relaxation is expected, thus the slope of the enthalpy curve will be similar to that in the first profile. It is assumed that below this temperature, the decrease in enthalpy is because of the change in temperature and not due to relaxation. During heating, similar to the observation in the fast cooled and heated sample, the material first retraces the enthalpy curve to the zero mobility temperature. In the region where there is significant molecular mobility (that is, above the critical mobility temperature), the material relaxes even during heating. For the sake of simplicity, the enthalpy profile is linear with the understanding that it is not strictly true. The extent of deviation from linearity will be a function of the dependence of molecular mobility on temperature. Moreover, the relaxation during heating will also depend on the relaxation that has already occurred during cooling. On heating the material through T_g, the material undergoes transition at a lower temperature when compared with the faster heating rate and the width of the transition region is also decreased.

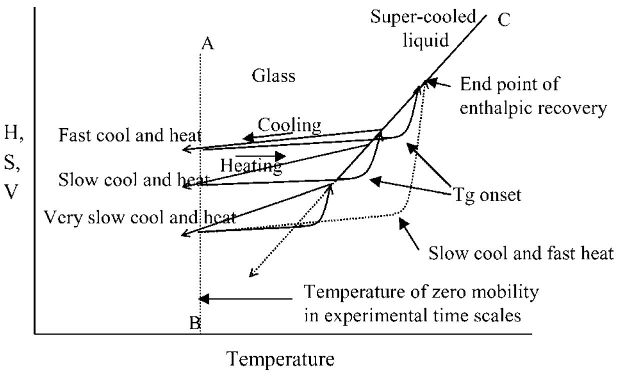

Fig. 8. Schematic representation of the change in thermodynamic properties in an amorphous system across the T_g as a function of heating and cooling rates. Line AB signifies the zero mobility temperature below which no mobility is expected in the experimental time scale.

Thus, the temperature where the enthalpy curve of the system meets the super-cooled liquid line is lower for a system heated at a slower rate. This translates to a lower enthalpy jump at T_g and so a smaller observed enthalpic recovery in this system.

The third profile shows the enthalpy as a function of temperature for a sample that was very slowly cooled and heated. The slower the cooling, the lower is the observed T_g and higher the relaxation. During heating, as in the other cases, the material retraces the cooling curve up to the zero mobility temperature. In the region of substantial mobility, the material relaxes during heating. The glass transition and enthalpic recovery occurs over a small temperature range translating to a smaller enthalpy jump at T_g and low observed enthalpic recovery.

So far, the discussion was limited to situations where the cooling and heating rates were identical. In these cases, it is expected that the system might retrace the cooling enthalpy curve during the heating cycle. Our next objective was to understand why a difference between the heating and cooling rates results in a higher enthalpic recovery in the DSC, especially at high HR to cooling rate ratios. The dashed heating curve in Fig. 8 is that of a very slowly cooled sample heated at a fast rate. In this case, there is considerable relaxation during the cooling cycle. When this low enthalpy system is heated at a fast rate, the T_g is higher than that of the fast cooled and heated system. This is because of the relaxation during the slow cooling. Consequently, the observed enthalpic recovery is very high. The end point of the recovery in this case is close to the end point of the first case (i.e., fast cooling and heating).

Fig. 8 explains very well, the trends seen in Fig. 7. A slower cooling rate gives rise to more enthalpic recovery during heating because there is more relaxation during cooling. This recovery is higher at faster heating rates because heating rate determines the end point of the enthalpic recovery on the enthalpy curve. This also explains the low enthalpic recovery observed when the heating and cooling rates are identical (Fig. 7, curve (d)). As mentioned above, the observed recovery at T_g is a function of two parameters, the extent of relaxation and the heating rate. Fig. 7 shows that when the heating and cooling rates are identical, recovery at T_g is similar in all cases. Though the relaxation during slower cooling and heating is more, the "observed" recovery at T_g is not significantly different because of the "smaller jump" to the super-cooled liquid line.

As can be observed from the above results, the loss in enthalpy is more in the case of slowly cooled samples than in the samples subjected to rapid cooling. As a result, the molecular mobility will be low and the relaxation time constant (τ) will be high for slowly cooled sample. Therefore, one needs to question whether the observed recovery it a true measure of relaxation. Moreover, low recovery observed at identical cooling and heating rates does not necessarily mean less relaxation during the cycle, but could be because of the limitations of the DSC technique.

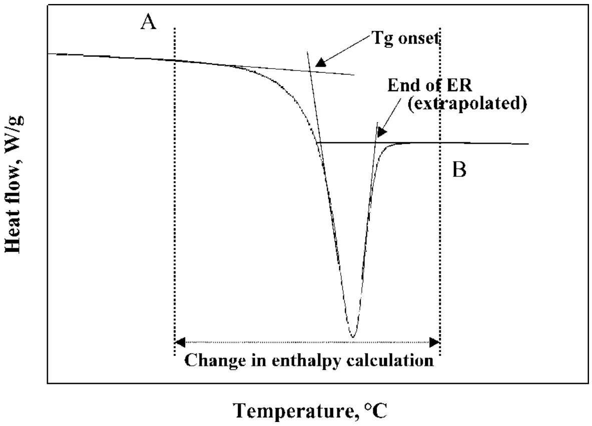

Fig. 9. Calculation of the change in enthalpy across T_g. The total enthalpy change was the sum of the area under the enthalpic recovery endotherm, enthalpy change between points A and T_g onset and between extrapolated end of enthalpic recovery and B.

In order to eliminate the heating rate artifact, we calculated the change in enthalpy in a constant temperature range encompassing the T_g. Using the heat capacity data for amorphous trehalose (obtained using MDSC), an enthalpy curve for amorphous trehalose was generated over the temperature range of 30–150 °C. The change in enthalpy from 110 to 140 °C was calculated for all the heating rates. The procedure for the calculation of enthalpy change across the temperature range is shown in Fig. 9. Extrapolated onset of T_g and the end point of ER were used. The total change in enthalpy was obtained as a sum of (i) the change in enthalpy of the system from 110 °C to T_g onset, (ii) area under the recovery endotherm associated with T_g, and (iii) the change in enthalpy from the endpoint of ER to 140 °C. The enthalpic recovery, T_g onset and ER values were obtained from the individual experiments. Enthalpy values for calculations (i) and (ii) were obtained from the generated enthalpy curve. It is recognized that some of these regions might be overlapping because of the extrapolated onset and endpoints and the calculations are at best semi-quantitative. Moreover, the heat capacities of the aged and unaged glass are slightly different and assuming them to be same will also add to the errors in the determination. However, due to practical limitations, this was considered to be an acceptable method for calculation.

The change in enthalpy across T_g was calculated for samples subjected to identical heating and cooling rates. In Fig. 10 the observed enthalpic recovery at T_g (curve (a); same as curve (d) in Fig. 7) and calculated change in enthalpy (curve (b)) in the desired temperature range (110–140 °C) are compared. As is evident from the plot, though the observed recovery at T_g is similar in all cases, the change in enthalpy in the temperature range increases with a decrease in the heating (and cooling) rate. This makes it clear that the loss in enthalpy at slower cooling rate is high even though it cannot be seen from the recovery in the DSC. Looking again at Fig. 5, it can

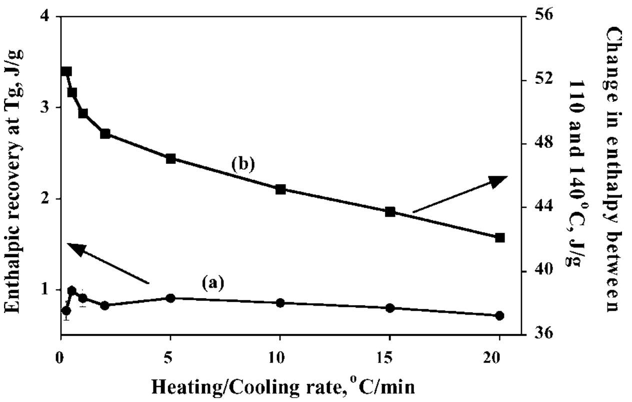

Fig. 10. Comparison of the enthalpic recovery at T_g obtained by DSC (curve (a)), and change in enthalpy across the T_g calculated by the method described in Fig. 9 (curve (b)) for samples cooled and heated at same rates. The sample thermal history was removed by heating it to 140 °C. It was then cooled at rates ranging from 0.5 to 20 °C/min (x-axis) to 25 °C and finally heated again at the same rate (used during cooling). The enthalpic recovery and change in enthalpy were calculated from the final heating scan ($n \geq 3$).

be seen that the enthalpy required to reach the super-cooled equilibrium liquid line (which is manifested as enthalpic recovery in DSC) is small at slow heating rates. Fig. 4a and b also reveals that the end point of recovery does not coincide with the onset of T_g during cooling. When the heating and cooling rates are identical, these numbers may be close but because of relaxation they also do not match. It is hypothesized that the end point of the recovery during heating will be higher, equal or lower than the T_g onset (during cooling) for very fast, moderate and very slow cooling (and heating) rates, respectively.

3.3. Practical implications

The enthalpic relaxation behavior as a function of aging time is often used to determine the fragility and relaxation time constants (τ) of amorphous materials [18]. These time constants can be defined as the average time taken for molecular motion of a particular type to occur. They are very useful in comparing the molecular mobility in different types of amorphous phases. Our results show that the DSC experimental conditions may have a strong impact on the enthalpic relaxation measurements (measure as enthalpic recovery), which may eventually lead to errors in the measurements of relaxation time constants.

The strong dependence of enthalpic relaxation measurement on the experimental conditions warrants comparison with other techniques. Isothermal relaxation studies in the DSC or isothermal microcalorimetry [13,19,20] may be better alternatives to the indirect measurement of enthalpic relaxation, as recovery, during the DSC heating scan. It will also be interesting to compare the isothermal relaxation data to that obtained at different heating rates in the DSC. Using that comparison, it may be possible to determine a heating rate where the non-isothermally obtained relaxation values will closely match those obtained from isothermal determinations. However, the added complication in this approach is that even if an appropriate heating rate is determined using a model system, it may not work for all amorphous substances, as the heating rate dependence will also be a function of the material properties including the T_g, fragility and heterogeneity of the material.

4. Conclusions

DSC is the most commonly used technique for studying the enthalpic relaxation in amorphous systems. Our results show that the heating rate used in DSC has a significant impact on the calculation of enthalpic relaxation. Our results also show that employing the same cooling and heating rate across the T_g may not ensure minimum relaxation during the cycle. The effect is possibly due to the dependence of T_g on the heating rate. Thus, the effects of DSC experimental conditions need to be carefully evaluated in order to obtain meaningful results.

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