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Influence of selected variables on heat of fusion determinations by oscillating DSC

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Abstract

The influence of variables on the determination of the heat of fusion for phases with different crystallinity was investigated using oscillating differential scanning calorimetry (ODSC). The hydrophobic drug griseofulvin (GRIS) represented a crystalline substance and the polymer polyethylene glycol (PEG) 6000, a substance of semi-crystallinity. The influence of forty combinations of frequency, amplitude and underlying heating rate was analysed.

The parameters determined were melting interval, melting point and the three heat of fusion values, the conventional component ΔH, the reversible c_p-component ΔH_c, and the irreversible kinetic component ΔH_k. The selection of amplitude, frequency and heating rate did not significantly influence the conventional heat of fusion values but had a great impact on the values of the c_p and the kinetic components. To be able to predict the reproducibility of the heat of fusion determinations, a combined value of selected variables is introduced, denoted the *degree of oscillation*.

A tentative evaluation of the heat of fusion values showed that the ratio $\Delta H_c/\Delta H$ at an appropriate degree of oscillation might be an expression of the degree of crystallinity of the phases investigated.

Keywords: Crystallinity; Degree of oscillation; Griseofulvin; Heat of fusion; Oscillating DSC; PEG

1. Introduction

In recent years, oscillating or modulated DSC (ODSC, MDSC) has been developed in which an oscillating time–temperature wave is applied while simultaneously heating

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at a constant underlying rate. The technique allows a Fourier transform separation of the parent DSC signal into two distinct components, the c_p (reversible) component and the kinetic (irreversible) component [1,2].

The new capabilities of the ODSC method in comparison with conventional DSC include separation of reversible and irreversible thermal events, improved resolution of closely occurring and overlapping transitions, and increased sensitivity of heat capacity measurements [1,3,4]. In conventional DSC, the impact of heating rate on DSC peak shape is evaluated. As heating rate increases, there is an increase in the peak height on melting and the melting occurs in a broader temperature interval. Significant variations in the slope of the peak are obtained for samples containing a polymer [5].

With the ODSC equipment, three variables can be changed: the frequency of the oscillation, the amplitude and the underlying heating rate. No systematic investigation has so far been performed concerning the influence of the variables on the heat of fusion determinations by ODSC measurements. The importance of the investigations has, however, been stressed [1,6]. In an earlier study on a pharmaceutical model system containing griseofulvin and polyethylene glycol, problems concerning the reproducibility of the heat of fusion measurements were discussed [7].

The aim of this study has been to investigate the influence of the variables for the reversible and irreversible components, respectively, on the melting process for a highly crystalline material, griseofulvin [8], and for a semi-crystalline polymer, PEG 6000 [9], and to examine the possibility of predicting the reproducibility of the determination of the enthalpy components. The possibility of using the information on the enthalpy changes of the reversible component as an indication of the degree of crystallinity for the material was also investigated.

1.1. Theory

The response of an ideal DSC, where no temperature gradients exist, can be expressed [1,10]

$$\frac{\mathrm{d}Q}{\mathrm{d}t} = c_{p,t}\frac{\mathrm{d}T}{\mathrm{d}t} + f(t, T) \tag{1}$$

where Q is the amount of heat absorbed by the sample, $c_{p,t}$ is the thermodynamic heat capacity, T is the absolute temperature and t is the time; $f(t, T)$ is a function of time and temperature that governs the kinetic (irreversible) response of a process.The temperature program can be expressed as

$$T = T_0 + At + B\sin(\omega t) \tag{2}$$

where T_0 is the starting temperature, A is the underlying heating rate, B is the amplitude of the temperature modulation, and ω is the frequency in radians, or $\omega = 2\pi f$ where f is the frequency in Hz. The equation gives temperature curves like those in Fig. 1.

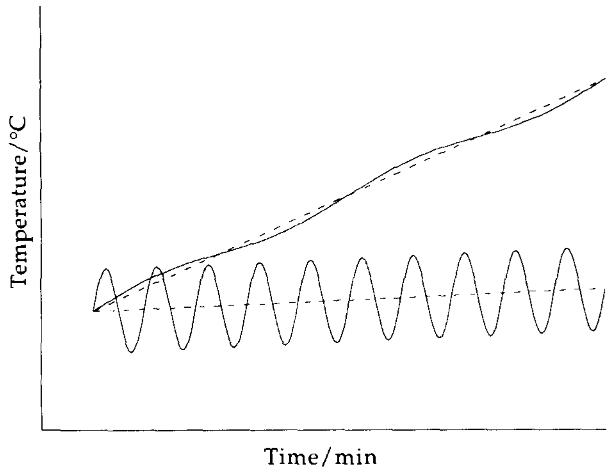

Fig. 1. Temperature curves for two different selections of amplitude, frequency and heating rate. Degree of oscillation is 0.06 for the upper curve, and 18 for the lower curve.

Over a small temperature interval, the kinetic process can be approximated as linear. Eq. (1) can be rewritten as

$$\frac{\mathrm{d}Q}{\mathrm{d}t} = c_{p,t}[A + B\omega\cos(\omega t)] + f'(t, T) + C\sin(\omega t) \tag{3}$$

where $f'(t, T)$ is the average underlying kinetic function once the effect of the sine wave oscillation has been subtracted, and C is the amplitude of the kinetic response to the sine wave oscillation. $A + B\omega\cos(\omega t)$ is the measured quantity $\mathrm{d}T/\mathrm{d}t$.

2. Experimental

2.1. Materials

Griseofulvin (GRIS), formula $C_{17}H_{17}ClO_6$ (Sigma, USA), a hydrophobic, crystalline drug, was used as supplied. Polyethylene glycol (PEG) 6000 (Janssen Chimica, Belgium) with the formula $OH\text{-}(C_2H_4\text{-}O)_nH$, where $n = 140$, average M_w 5600-7000, was pulverized and sieved to obtain the fraction 300-500 μm. Griseofulvin and PEG 6000 were characterised by X-ray diffraction and found to be high crystalline and semicrystalline, respectively.

2.2. Method

2.2.1. Oscillating differential scanning calorimetry

All samples were analysed using an oscillating Seiko DSC 220 differential scanning calorimeter SSC/5200H (Japan). The calorimeter was temperature- and heat-calibrated with indium, tin and gallium as standards. Samples of griseofulvin (2.5–3.5 mg) and PEG 6000 (4.0–5.0 mg) were analysed in an atmosphere of nitrogen with the samples kept in aluminium pans using, respectively, 40 and 24 different combinations of variables. All the combinations give both heating and cooling in the temperature cycle. The maximum of one period thus exceeds the minimum of the next period. The frequency interval was 0.01–0.05 Hz, the heating rate interval 1–10 K min^{-1} and the amplitude interval 1–6 K. The presented results are mean values of three determinations. The temperature program was performed in the range 170–270°C for griseofulvin, with melting point at 219°C, and in the range 20–140°C for PEG 6000, with melting point at 60°C.

3. Results and discussion

3.1. Influence of selected variables on heat of fusion values

Raw data from the ODSC measurements on the griseofulvin and PEG 6000 samples respectively, were separated into the three components, the conventional component (almost identical with the traditional DSC component), the reversible c_p-component and the irreversible kinetic component. For each combination of variables the energy associated with the melting was determined: ΔH (conventional), ΔH_c (reversible or c_p) and ΔH_k (irreversible or kinetic). For each combination, the peak temperature, T_m, was determined from the conventional curve together with the melting interval. The integration was performed over this melting interval.

In Table 1, a comparison of the results for 0.01 and 0.02 Hz is presented for crystalline griseofulvin and semi-crystalline PEG 6000. In Tables 2 and 3, detailed data of the heat of fusion measurements with standard deviations are presented for both compounds.

The reproducibility for the conventional component, ΔH, was very good for both griseofulvin and PEG 6000, with relative standard deviations less than 3%. The variation of the ΔH_c and ΔH_k values was, however, very large. Moreover, negative values were obtained, indicating exothermic components of the melting process. In particular, with the frequency 0.05 Hz (Table 2), the ΔH_c and ΔH_k values appeared in a very broad interval, very often leading to negative values of ΔH_k. The selected

Table 1
Average values and variations of heat of fusion components for 24 samples of griseofulvin and PEG 6000 (frequency 0.01 and 0.02 Hz)

	Griseofulvin		PEG 6000	
	Average value	Variation	Average value	Variation
$\Delta H_c/\mathrm{J\,g^{-1}}$	78.1	26.5–153	93.0	25.3–186
$\Delta H_k/\mathrm{J\,g^{-1}}$	51.8	−57.5–99.3	93.9	5.1–157
$\Delta H/\mathrm{J\,g^{-1}}$	130	123–135	187	183–191
T_m, peak/°C	219	216–225	60.1	58.1–63.9

Table 2

Heat of fusion values ΔH_c, ΔH_k and ΔH with standard deviations, melting interval and melting point with standard deviation for griseofulvin obtained by 40 different combinations of variables

Sample number	Frequency /Hz	Heating rate/K min^{-1}	Amplitude /K	ΔH_c/ J g^{-1}	SD of ΔH_c	ΔH_k/ J g^{-1}	SD of ΔH_k	ΔH/ J g^{-1}	SD of ΔH	$T_{m,peak}$/ °C	SD of $T_{m,peak}$	ΔT_m/°C
1	0.01	1.0	1	97.3	3.0	30.3	3.0	127	1.9	219	0	10
2	0.01	1.0	2	54.8	0.80	75.1	0.25	128	0.90	219	1	13
3	0.01	1.0	4	31.9	1.9	96.4	1.3	128	0.70	217	1	9.0
4	0.01	1.0	6	28.6	3.2	99.3	3.6	127	1.2	216	0	8.5
5	0.01	2.5	1	190	7.3	−57.5	9.1	132	2.5	220	0	17
6	0.01	2.5	2	113	4.5	19.0	4.2	131	0.70	220	0	15
7	0.01	2.5	4	65.9	4.7	63.9	6.5	129	2.1	217	1	13
8	0.01	2.5	6	36.1	1.3	88.8	0.90	123	0.20	216	1	10
9	0.01	5.0	4	101	6.2	29.8	5.4	130	1.1	221	1	26
10	0.01	5.0	6	76.4	11	58.4	10	134	1.5	220	0	25
11	0.01	10	6	97.4	15	34.8	13	134	2.7	225	0	47
12	0.02	1.0	1	63.8	2.0	63.2	2.6	127	1.2	219	0	9.0
13	0.02	1.0	2	49.4	1.8	79.9	2.0	129	0.90	219	0	9.0
14	0.02	1.0	4	30.9	0.70	96.6	1.9	127	2.5	218	0	10
15	0.02	1.0	6	26.5	1.0	98.0	0.50	124	1.0	218	0	8.0
16	0.02	2.5	1	124	26	7.40	24	131	2.8	219	0	11
17	0.02	2.5	2	82.1	12	46.1	10	128	1.6	219	0	12
18	0.02	2.5	4	63.3	2.2	65.2	1.1	129	1.5	219	0	10
19	0.02	2.5	6	43.3	2.4	83.4	3.1	126	0.90	218	1	9.0
20	0.02	5.0	2	89.2	4.5	39.0	3.7	131	1.0	220	0	18

Table 2 (*continued*)

Sample number	Frequency /Hz	Heating rate/K min^{-1}	Amplitude /K	ΔH_c/ J g^{-1}	SD of ΔH_c	ΔH_k/ J g^{-1}	SD of ΔH_k	ΔH/ J g^{-1}	SD of ΔH	$T_{m,peak}$/ °C	SD of $T_{m,peak}$	ΔT_m/°C
21	0.02	5.0	4	63.3	2.0	68.0	2.8	131	1.1	219	0	17
22	0.02	5.0	6	69.0	16	63.0	15	132	3.5	219	1	20
23	0.02	10	4	153	15	−18.0	17	135	1.4	222	0	32
24	0.02	10	6	123	10	12.3	13	135	2.7	222	0	33
25	0.05	1.0	1	46.4	5.90	78.7	5.90	128	0.90	219	0	10
26	0.05	1.0	2	37.3	2.50	87.9	1.80	125	0.90	219	0	10
27	0.05	1.0	4	31.6	0.600	93.8	1.00	124	0.30	219	0	7.0
28	0.05	1.0	6	27.1	1.40	100	1.70	127	1.8	219	0	8.0
29	0.05	2.5	1	131	16.1	−6.60	16.6	129	0.50	219	0	11
30	0.05	2.5	2	64.9	1.00	63.6	0.400	130	1.0	219	0	10
31	0.05	2.5	4	44.5	2.50	82.6	3.30	128	1.3	219	0	10
32	0.05	2.5	6	39.3	3.30	90.1	4.10	130	1.1	219	0	10
33	0.05	5.0	1	315	20.4	−185	21.2	129	0.80	219	0	12
34	0.05	5.0	2	158	19.0	−29.9	18.3	131	1.4	220	0	15
35	0.05	5.0	4	130	37.7	1.30	39.7	131	2.7	220	0	13
36	0.05	5.0	6	90.3	10.0	38.8	10.1	131	0.40	220	0	14
37	0.05	10	1	581	39.6	−448	40.7	133	1.6	220	0	21
38	0.05	10	2	623	222	−489	223	133	1.5	220	1	21
39	0.05	10	4	246	27.1	−112	28.3	134	1.2	220	0	17
40	0.05	10	6	168	24.9	−34.1	22.9	134	2.3	220	0	21

Table 3
Heat of fusion values ΔH_c, ΔH_k and ΔH with standard deviations, melting interval and melting point with standard deviation for PEG 6000 obtained by 24 different combinations of variables

Sample number	Frequency /Hz	Heating rare/K min^{-1}	Amplitude /K	ΔH_c/ J g^{-1}	SD of ΔH_c	ΔH_k/ J g^{-1}	SD of ΔH_k	ΔH/ J g^{-1}	SD of ΔH	$T_{m,peak}$/ °C	SD of $T_{m,peak}$	ΔT_m/°C
1	0.01	1.0	1	88.9	4.0	99.9	3.7	189	0.80	60.2	0.1	17
2	0.01	1.0	2	74.6	4.7	113	4.2	188	0.60	60.0	0.1	17
3	0.01	1.0	4	55.8	1.8	130	1.3	186	2.1	59.7	0	14
4	0.01	1.0	6	44.3	0.90	139	0.90	183	1.7	58.2	0	13
5	0.01	2.5	1	184	41	5.60	41	190	2.0	59.9	0.1	22
6	0.01	2.5	2	147	16	40.0	16	188	0.90	59.8	0.7	24
7	0.01	2.5	4	102	2.6	85.6	2.9	188	0.40	59.5	0.2	21
8	0.01	2.5	6	81.5	1.3	104	0.90	186	0.70	59.6	0	21
9	0.01	5.0	4	104	1.5	83.4	2.1	188	0.60	58.7	0.1	37
10	0.01	5.0	6	83.9	3.3	105	2.3	189	1.5	58.1	0	37
11	0.01	10	6	186	9.0	5.10	7.7	191	1.7	63.9	0.1	55
12	0.02	1.0	1	56.8	4.2	129	0.70	186	3.9	60.3	0	13
13	0.02	1.0	2	44.0	0.40	142	1.2	185	0.80	60.3	0	13
14	0.02	1.0	4	29.6	0.80	153	0.70	183	1.5	60.1	0	14
15	0.02	1.0	6	25.3	0.20	157	0.50	183	0.50	59.8	0	13
16	0.02	2.5	1	90.6	4.5	95.1	5.2	186	1.3	60.4	0.1	21
17	0.02	2.5	2	70.6	1.0	114	0.70	185	0.80	60.2	0	20
18	0.02	2.5	4	57.0	1.9	129	2.4	186	0.70	60.2	0	22
19	0.02	2.5	6	56.8	0.60	130	0.10	187	0.70	60.2	0.1	18
20	0.02	5.0	2	168	3.8	18.0	4.2	186	1.4	60.3	0.2	26
21	0.02	5.0	4	103	14	83.4	13	187	0.50	60.3	0.2	26
22	0.02	5.0	6	82.8	2.4	104	1.8	187	0.70	60.3	0.1	26
23	0.02	10	4	163	13	28.2	13	191	1.5	60.9	0.1	45
24	0.02	10	6	133	11	58.0	12	191	1.4	60.8	0.1	39

variables thus have a tremendous impact on the size and the sign of the enthalpy that is measured.

3.1.1. Degree of oscillation

The reproducibility of certain variable combinations is also low. This is especially in the case when the ratio amplitude (K)/heating rate (K min^{-1}) is less than 1. In these cases, griseofulvin has very low ΔH_k values, that are sometimes also negative. This means that ΔH_c is larger than ΔH. By also including the variable frequency, a dimensionless quantity of the combination of variables can be obtained, denoted the *degree of oscillation*. It is calculated using the expression

$$\text{Degree of oscillation} = \frac{Amplitude(K) \times Frequency(s^{-1})}{Heating\ \ rate(K\ \ s^{-1})}$$

Using the symbols from Eq. (3) we arrive at

$$\text{Degree of oscillation} = \frac{Bf}{A} \quad or \quad \frac{B\omega}{2\pi A}$$

If we use this expression for the variable combinations illustrated in Fig. 1, we arrive at 0.06 for the upper curve and 18 for the lower curve. If a low degree of oscillation is used, the temperature resembles a linear heating with only a small cyclic heating, while for higher values of the degree of oscillation there is greater deviation from the underlying heating rate.

In Figs. 2 and 3, the $\Delta H_c/\Delta H$ values and the standard deviations of ΔH_c relative to the conventional component ΔH, respectively, are plotted as a function of the degree of oscillation. This way of representing a certain reproducibility was chosen instead of the ordinary way to express relative standard deviation because of the great variation in the values of ΔH_c. It was observed that a high degree of oscillation gives a low value of $\Delta H_c/\Delta H$, whereas low degrees of oscillation give ratios in a wide range. For PEG 6000, all values are less than 1, whereas for griseofulvin, values higher than 1 are also obtained. The latter values result in a negative ΔH_k. Using 0.05 Hz, ratios are obtained that are much higher than 1 if the degree of oscillation is lower than 2–3. The corresponding relative standard deviations are also very high.

If Eq. (3) is evaluated for the cyclic reversible component, $c_p\,\mathrm{d}T/\mathrm{d}f$, and c_p is assumed to be constant for a certain material, then

$$\frac{\mathrm{d}T}{\mathrm{d}t} = A + B\omega\cos(\omega t) \tag{4}$$

or

$$\frac{\mathrm{d}T}{\mathrm{d}t} = A\left[1 + \frac{B\omega}{A}\cos(\omega t)\right] \tag{5}$$

$(B\omega)/(2\pi A) = (Bf)/A$ is the degree of oscillation mentioned above.

At high heating rate (A), low amplitude (B) and frequency (f) respectively, i.e. a low degree of oscillation, the second term in Eq. (5) is small. The cyclic part is thus small and

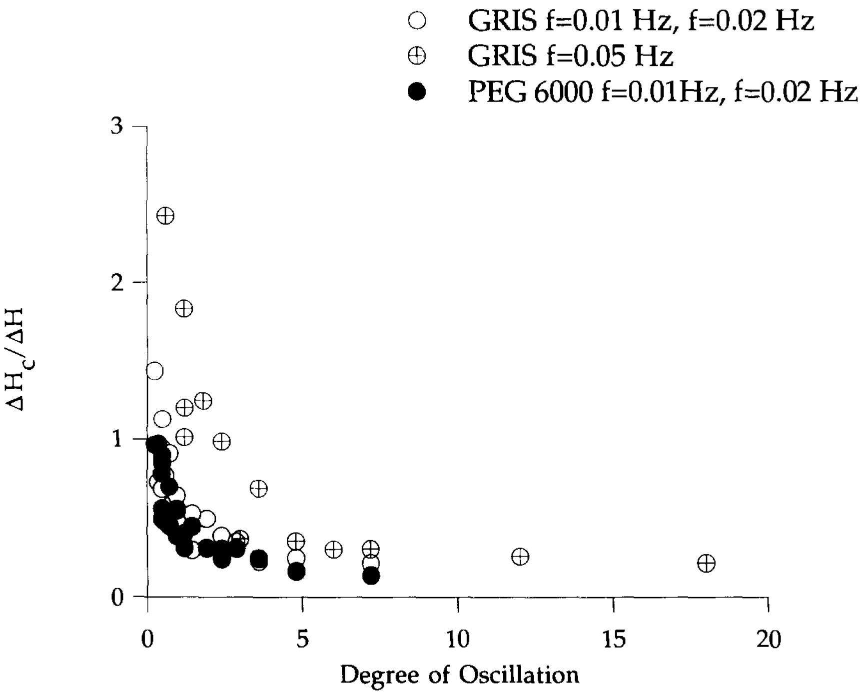

Fig. 2. Ratio of the reversible and conventional component of the heat of fusion, $\Delta H_c/\Delta H$, versus the degree of oscillation for griseofulvin and PEG 6000.

the real heating temperature is close to the underlying heating rate. When the degree of oscillation is higher, the impact of the cyclic part increases. The real heating rate then becomes more dependent upon amplitude and frequency. If the degree of oscillation, for example, is 0.5, the second term in the parenthesis of Eq. (5) has a maximum value of 3.1, while for a degree of oscillation of 2, the same value is 12.6.

The experiment shows that an increasing degree of oscillation gives a lower and constant value of ΔH_c. There might be a critical value of the degree of oscillation to reach that ΔH_c. Different materials give different responses to the cyclic temperature. A perfect crystalline material should give a distinct melting process, with an almost 100% response to the temperature cycling and thus a large reversible component, whereas a low crystalline material might have a more complex melting process in which the enthalpy changes also involve a large kinetic component. Our results show that the relation between the type of solid phase and the reversible or irreversible responses is very complex.

The best reproducibility of the three components ΔH, ΔH_c and ΔH_k is obtained when the degree of oscillation is higher than 1, but some combinations with lower degrees of oscillation also show good reproducibility. Since a high degree of oscillation means a low underlying heating rate or high frequencies or amplitudes with poor reproducibility, practical reasons indicate that a degree of oscillation that is as low as possible

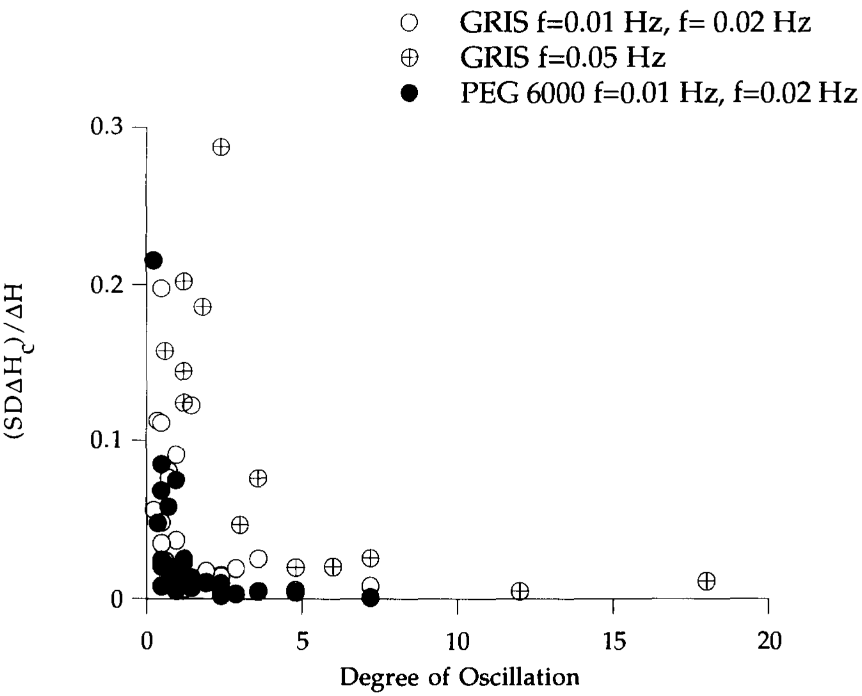

Fig. 3. Ratio of the standard deviation for the reversible component and the conventional component of the heat of fusion, $(SD\Delta H_c)/\Delta H$, versus the degree of oscillation for griseofulvin and PEG 6000.

ought to be selected. A minimum of 1.4 is quite sufficient for the polymer phase investigated here.

In Table 4, varying combinations of variables, degrees of oscillation and number of periods that the samples griseofulvin or PEG 6000 are modulated in the melting interval are presented. All represent combinations where $\Delta H_c/\Delta H$ is less than 1 and relative standard deviations are less than 2%. According to Ref. [1], the number of modulations should be at least six over the course of a thermal event for good reproducibility. For griseofulvin, as low as 2.4 modulations per melting interval give a reproducible result if the degree of oscillation is appropriate. However, a certain high degree of oscillation does not always give a reproducible result, even though the number of modulations is high. For PEG 6000, however, the results show a strong correlation between the degree of oscillation, the number of modulations in the melting interval and the reproducibility. The degree of oscillation is obviously not the ideal quantity, but it can better predict suitable variables for determination of the heat of fusion than the number of modulations over the course of a single thermal event.

3.2. *Influence of selected variables on melting interval and melting point*

In Tables 2 and 3, the melting interval ΔT_m and the peak temperatures T_m of the melting endotherm are presented together with standard deviations. As reported

Table 4
Comparison between degree of oscillation and number of modulations in the melting interval for samples of griseofulvin and PEG 6000. All combinations have relative standard deviations $\leq 2\%$ and $\Delta H_c/\Delta H < 1$.

Sample number	Frequency/ Hz	Heating rate K min^{-1}	Amplitude/ K	Degree of oscillation	Modulations/ ΔT_m GRIS	Modulations/ ΔT_m PEG 6000
2	0.01	1.0	2	1.2	7.8	10
3	0.01	1.0	4	2.4	5.4	8.3
7	0.01	2.5	4	0.96	3.1	5.0
8	0.01	2.5	6	1.4	2.4	5.0
9	0.01	5.0	4	0.48	3.1	4.4
10	0.01	5.0	6	0.72	3.0	4.4
13	0.02	1.0	2	2.4	11	15
14	0.02	1.0	4	4.8	12	16
15	0.02	1.0	6	7.2	9.6	15
17	0.02	2.5	2	0.96	5.8	9.7
18	0.02	2.5	4	1.9	4.8	11
19	0.02	2.5	6	2.9	4.3	8.8
22	0.02	5.0	6	1.4	4.8	6.3

earlier, an increased heating rate induces a broader melting interval for a sample [3]. The variations can be explained by the fact that the temperature of the whole sample cannot follow the changes in the temperature program if the heating rate is too high. Several regions are formed within the sample, each of them at different stages of the melting process. At a low heating rate, there is enough time for the temperature of the sample to adapt to the programmed temperature homogeneously and the melting interval becomes narrower.

In this study, a similar influence was observed for an increasing amplitude. An oscillating temperature means that the absolute value of the derivative of the temperature–time function is much higher than the derivative of the underlying temperature during a certain time. This fact might then have the same impact on the sample as an increasing heating rate and thereby induce a broader melting interval when the amplitude is increased.

An increased frequency decreases the melting interval. This effect on the melting interval can be a function of the thermal resistance and the nucleus rate of the sample concerned. At higher frequencies the sample might not form nuclei large enough for crystallisation to start before the temperature program raises the temperature above the melting temperature. This means that the melting seems to occur over a relatively narrow temperature interval. At lower frequencies the sample has time enough to melt and crystallise several times and therefore a broader melting interval is observed.

The peak temperatures are moved to higher temperature with increased heating rate since the peak temperature corresponds to the point where the inner core of the sample is melting. Variation of the amplitude and frequency seemed, however, to have no influence on the peak temperature.

For certain degrees of oscillation, especially with a low heating rate, the shape of the peaks for PEG 6000 showed two endothermic overlapping peaks. At crystallisation, a PEG structure with folded polymer chains can be formed [11]. At the melting, the first endotherm represents unfolding of the chains, and the second endotherm represents melting of extended chains. The peak temperature measured here corresponds to the second melting endotherm.

3.3. Crystallinity

A tentative evaluation of the ODSC measurements as a means to determine the crystallinity of the compounds was performed. The melting is an endothermic process which involves both reversible and irreversible events. In the ODSC measurements, the variables can be selected in such a way that they involve both cooling and heating in the melting interval, so that the temperature program passes the melting temperature more than once. Theoretically, both melting and crystallisation can occur in each of the modulations. A material with a high degree of crystallinity should melt and recrystallise in a smaller temperature interval than a semi-crystalline one. The material should, in a thermodynamic sense, undergo a reversible process during several modulations. This would be observed by a greater reversible component in the ODSC signals.

The ratio $\Delta H_c/\Delta H$ could thus be a measure of the crystallinity in a system. In Fig. 4(a) and (b), this ratio is presented for griseofulvin and PEG 6000 as a function of the degree

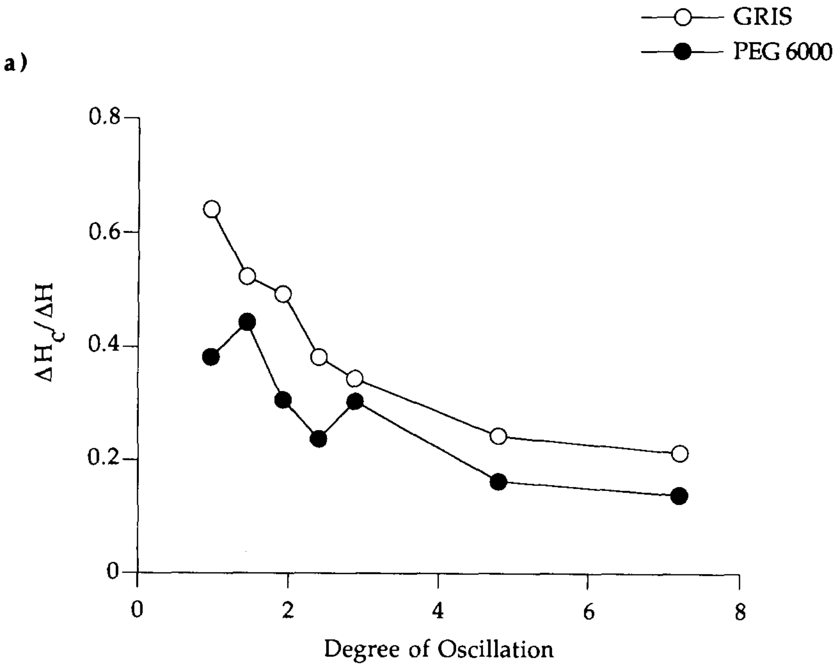

Fig. 4. Ratio of the reversible and the conventional component of the heat of fusion versus the degree of oscillation for some samples of griseofulvin and PEG 6000. The samples represent combinations of variables where the relative standard deviations are <2% and $\Delta H_c/\Delta H < 1$. (a) Frequency 0.02 Hz and (b) frequency 0.01 Hz.

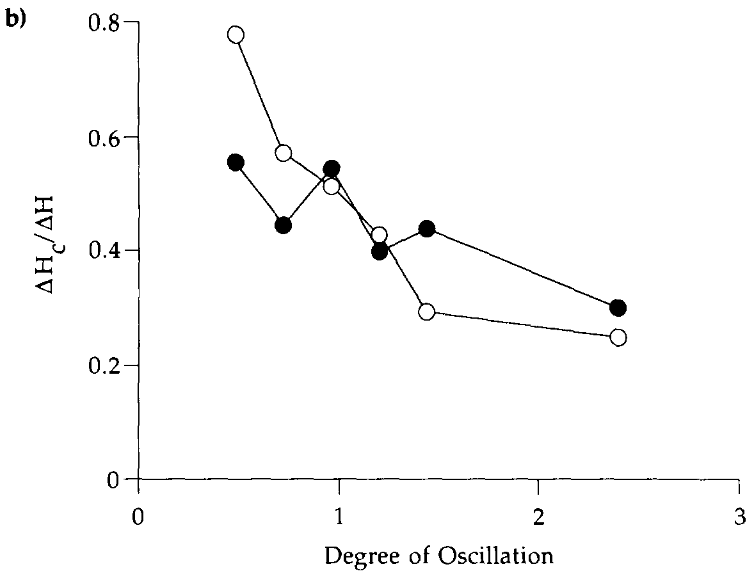

Fig. 4 (*Continued*)

of oscillation for the frequencies 0.02 and 0.01 Hz, respectively. The relative standard deviation is less than 2% and the ratio $\Delta H_c/\Delta H$ is less than 1 for all samples. The relation between crystallinity and the ratio is, however, not unambiguous. For 0.02 Hz, the expected relation is obtained, i.e. a higher ratio for the more crystalline griseofulvin, whereas for the lower frequency there is no simple relation. For 0.01 Hz, combinations with a high degree of oscillation also give results that are confusing. Work is underway to evaluate further the correlation between crystallinity and the reversible component in this and other systems.

4. Conclusions

For the materials investigated here, crystalline griseofulvin and semi-crystalline PEG 6000, the selection of variables (amplitude, frequency and heating rate) did not significantly influence the conventional heat of fusion values, ΔH, but had a great impact on the values of the reversible c_p-component, ΔH_c, and the irreversible kinetic component, ΔH_k. The latter values appeared in a very broad interval, including negative components. Especially when the highest frequency was used, low reproducibility of the results of the separate components was obtained.

To improve the reproducibility of the measurements of all components of the heat of fusion, a combined value of the variables is suggested, denoted the degree of oscillation, expressed by

$$\frac{Amplitude(K) \times Frequency(s^{-1})}{Heating\ rate(K\ s^{-1})}$$

or

$$\frac{B\omega}{2\pi A}$$

This expression can be associated with the weight the cyclic component is given in the heat flow equation (Eqs.(1) and (5)).

The reproducibility as expressed by the standard deviation of the ΔH_c or ΔH_k component relative to ΔH was essentially increased when a certain degree of oscillation was used. A degree of oscillation >1–2 for frequencies of 0.01 Hz and 0.02 Hz gave reliable results for a variety of combinations. The degree of oscillation seemed to predict better suitable variables for determination of the heat of fusion than the number of modulations over a course of a single thermal event.

Both the melting interval and the melting point of griseofulvin and PEG 6000 were affected by the selection of variables. An increased heating rate or amplitude broadened the melting interval whereas an increased frequency narrowed it. The melting point was influenced only by changes in heating rate and moved to higher temperature with an increasing heating rate. The changes can be related to the real heating rate accomplished by the oscillation and to the effect of the oscillation temperature history on the crystallisation process.

The reversible component of the heat of fusion, ΔH_c, might express the character of a system as the amount of material that is crystalline enough to respond reversibly to the temperature modulation. If an appropriate degree of oscillation is used, the ratio $\Delta H_c/\Delta H$ can be a measure of the degree of crystallinity in the system. However, the choice of frequency seems to be crucial.

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