Diode-array UV Spectrometric Evidence for a Concentration Dependent Phase Transition in Dilute Aqueous Solutions of Pluronic F87 (Poloxamer 237)

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Incubation of dilute polymer solutions with a KI–I_2 standard shows the presence of a concentration dependent phase transition for the poly(oxyethylene) + poly(oxypropylene) + poly(oxyethylene) block copolymer F87 (P237) using diode-array UV spectrometry; the transition is shown to be reversible and reproducible and is in agreement with previous data obtained *via* high-sensitivity differential scanning microcalorimetry (HSDSC).

In previous publications[1–7] we have reported the observation of phase transitions for a series of synthetic non-ionic block copolymers of general formula poly(oxyethylene)$_A$–poly(oxypropylene)$_B$–poly(oxyethylene)$_A$ (PEO_A–PPO_B–PEO_A) as determined *via* high-sensitivity differential scanning calorimetry (HSDSC). These polymers, termed poloxamers, Pluronics (BASF, Germany) or Synperonic PE non-ionic surfactants (ICI, UK), have found numerous industrial applications because of the varying hydrophobic/hydrophilic balance, and range of molecular masses, obtainable by alteration of their PEO : PPO ratio. Here, we report the phase transitions observed for a series of dilute solutions of the poloxamer F87 (M_w 7700, PEO content 5450, PPO content 2250 g mol^{-1}) as determined *via* diode-array UV spectrometry.

We have noted previously a temperature induced phase transition in 5 mg cm^{-3} F87 as studied *via* UV–VIS spectrometry.[4] Since F87 has no UV chromophores, the trace obtained was ascribed to scattering as the average particle size in solution increased. In this study, we enhanced the sensitivity of the technique by utilizing an indicator. We chose to use I_2, a comparatively small indicator molecule, in order to minimise possible disruption to the poloxamer system. This method was first described by Baleux.[8] The use of larger indicator molecules may lead to mixed aggregated. Alexandridis *et al.*[9] recently reported phase transitions for a series of poloxamers, determined using a comparatively large indicator molecule (1,6-diphenyl-1,3,5-hexatriene, DPH). Their published transition temperatures differed from those we determined *via* HSDSC. F87 was not included in their study and a direct comparison of our method with their technique is not possible. That the phase transitions determined in this study, compared directly with those we published previously using HSDSC, indicates that I_2 incorporation does not give rise to any observable effects on the aggregation process.

The sample of F87 was a gift from ICI (UK), purity being established by the presence of a single elution peak by GPC. Solutions were prepared by dissolution of the poloxamer in doubly distilled water at mass concentrations between 5–30 mg cm^{-3}, maintained at a constant temperature of 293 K before use, and used within 24 hours of preparation. The KI–I_2 standard was prepared by dissolution of iodine (1 g) and potassium iodide (2 g) in doubly distilled water (100 ml).

Dependent on the poloxamer concentration, between 30–50 μl of the solution of KI–I_2 standard was added to 10 ml of poloxamer solution. The absorbance of the resulting solution was recorded in the range 190–820 nm, from 293–343 K at a scan rate of 0.33 K min^{-1}, on a Hewlett–Packard 8452A diode–array UV spectrometer. A sealed cuvette was employed to prevent solvent and iodine loss. Data analysis was performed using the software package ORIGIN™ (Microcal Software Inc., MA, USA).

Fig. 1 shows the UV–VIS spectra for 5 mg cm^{-3} F87 at varying temperatures. The absorbance maximum at 366 nm corresponds to molecular iodine, and this was chosen as the analysis wavelength. Fig. 2 shows the variation in absorbance at 366 nm with temperature for the same sample. Previously, we reported a phase transition temperature for 5 mg cm^{-3} F87 determined *via* HSDSC. The value obtained (314.65 K) was derived from the peak calorimetric output of the sample, and did not reflect the onset of aggregation. A comparable result may be obtained from the data reported here, by taking the first differential of the curve presented in Fig. 2. The resulting plot is shown in Fig. 3. From this data set, a T_m value may be determined, which compares directly with the HSDSC value.

Previously, we have shown a time dependent relaxation process following dissolution of the poloxamer at 298 K.[5] This corresponds to the slow hydration of the hydrophobic PPO region as the molecule unfolds. At 293 K, the amount of solubilised I_2 in the experimental solutions is therefore low. As the temperature is increased, dehydration of the PPO moiety induces the formation of small aggregates. These aggregates consist of a hydrophobic PPO core, surrounded by a hydrophilic PEO layer, and are well documented.[10] Solubilised I_2 will preferentially partition into this hydrophobic core. The saturated

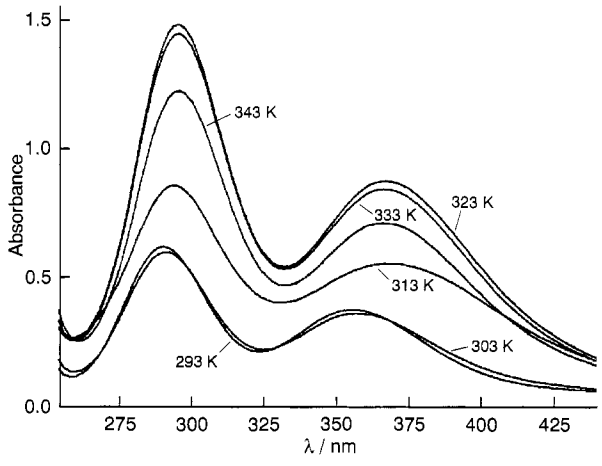

Fig. 1 Absorbance spectrum for F87 (5 mg cm^{-3})

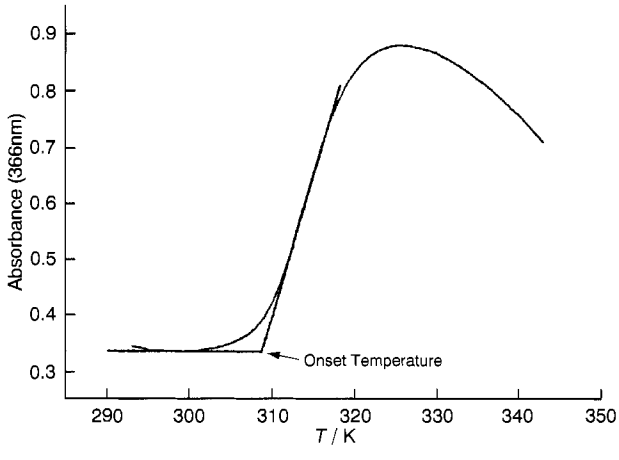

Fig. 2 Absorbance *vs.* temperature for F87 (5 mg cm^{-3}) at 366 nm

aqueous concentration of I_2 is maintained *via* the conversion of I_3^- to I_2, from the excess KI present in solution. The intensity of the I_2 maximum therefore increases with increasing temperature. At high temperatures, the poloxamer aggregates become large enough to induce scatter, and the observed absorption intensity decreases.

From the data shown in Fig. 2, the onset temperature (T_0) of aggregation, defined as the temperature at which aggregation is first observed by increased I_2 uptake, may be determined. As molecular I_2 is small, compared to the PPO moiety of the poloxamer, I_2 uptake can occur immediately that small hydrophobic regions form, and the resolution of the technique is high. The T_0 values obtained therefore correspond to the formation of small aggregates. As the temperature is increased further, the average number of poloxamer molecules in each aggregate increases. The increased scatter observed at higher solution temperatures in this study supports this increasing mass hypothesis.

Table 1 lists the T_0 values determined for F87 over the study concentration range. When plotted, these values give a good linear correlation, (A = 311.10 K, B = −0.510 K cm^3 mg^{-1}, r = 0.9957). That the gradient of the line obtained from this plot is not zero, indicates that the initial conformation of the poloxamer in solution is dependent on the mass concentration of F87. Since a van't Hoff analysis requires that the initial and final states of the system under study remain constant, and that the process involves only two states, it follows that this type of analysis is not applicable to our data.

Alexandridis *et al.*[9] recently published phase transitions for a series of poloxamers determined *via* dye solubilisation UV–VIS spectrometry. The range of poloxamers in their study was extensive, and they reported onset temperatures derived for mass concentrations between 0.01–200 mg cm^{-3}. The dye employed, DPH, is larger than I_2 and the possibility exists that mixed aggregates may form in their system. Their technique adds a standard quantity of DPH to varying mass concentrations of poloxamer solutions; the resultant change in molar ratio of DPH to poloxamer across the study concentration range would appear to affect the continuity of their results. Additionally, they state that DPH is too large to be solubilised by the PPO core of a single coiled poloxamer molecule. This implies an inherent lack of sensitivity in their technique, *i.e.* that the minimum aggregate size visualised by DPH is unknown.

In the comparable cases, their derived onset temperatures differed considerably from the values we obtained *via* HSDSC.[4] They did not study F87 and so a direct comparison with the data presented here is not possible. We have since studied some poloxamers included in their study, and our results differ from theirs and are in accord with the HSDSC data. From the data presented, it was impossible to ascertain if they observed the scattering at high solution temperatures that we observed in our study. Included in their data were ΔH values for the aggregation process derived *via* a van't Hoff analysis, *i.e.* from a plot of $1/T_0$ *vs.* ln[poloxamer].

As noted above, a prerequisite of a van't Hoff analysis is the existence of a simple two-state process. The organisational state of solutions of poloxamers which range in concentration from 0.01 to 200 mg cm^{-3} are known to differ significantly. Moreover, it is probable, as noted earlier, that (i) the presence of DPH at different concentrations at each poloxamer concentration and (ii) the effect of DPH on aggregation, contribute to this apparent correspondence with the van't Hoff isochore. Consideration of our data, over a narrower concentration range, shown in Table 1, and the linearity demonstrated there between T_0 and [poloxamer] implies that a van't Hoff analysis of such data is inappropriate.

In summary, I_2 incorporation UV spectrometry offers an affordable, reliable, simple and reproducible technique for studying poloxamer aggregation. Comparison of the data obtained in this study with previous HSDSC data reveals a good correlation and indicates that the incorporation of I_2 does not appear to significantly affect the aggregation process.

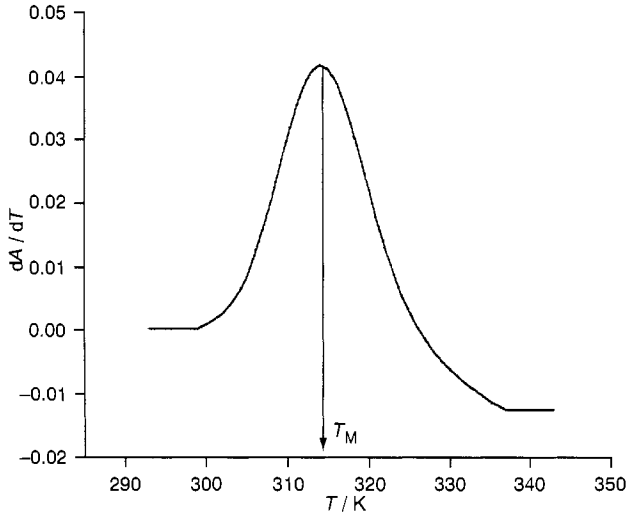

Fig. 3 First differential of absorbance *vs.* temperature for F87 (5 mg cm^{-3}) at 366 nm

Table 1 T_0 values for F87

Concentration F87/mg cm^{-3}	T_0/K
5	308.54
10	305.57
15	303.92
20	301.33
25	297.73
30	295.90

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