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Application of differential scanning calorimetry to the study of latex stability

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Abstract

Differential scanning calorimetry was used to study the effect of temperature, shaking, and pH on the stability of an aqueous dispersion of ethylcellulose latex particles (Aquacoat™, 0.3 μm in diameter) obtained by emulsion polymerization, and frequently used as an excipient in pharmaceutical formulations. Of the three factors studied, pH had the most marked effect on latex stability, followed by shaking and temperature. We conclude that differential scanning calorimetry is a reliable method for the study of factors that modify the stability of some components of pharmaceutical formulations.

Keywords: DSC; Latex; pH; Stability

1. Introduction

Calorimetric methods, because of their speed and reliability [1–3], are being used with increasing interest [4,5] to analyse stability and detect impurities in such fields as polymer formation and solid dispersion structures [6,7]. The aim of this study is to investigate the use of differential scanning calorimetry (DSC) to analyse the stability of pharmaceutical excipients.

The excipient chosen in this work is an ethylcellulose latex (Aquacoat™) which is widely used at present because of its potential pharmaceutical applications [8,9].

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The effect of pH, temperature, and ultrasonic shaking of the latex is analysed by the DSC technique.

2. Experimental

The polymer dispersion used, Aquacoat, is a registered trade mark of the FMC Corp., USA, and was kindly supplied by Foret, S.A., Spain. It is manufactured as a latex of ethylcellulose with high (approx. 30% v/v) particle concentration. In order to enhance stability, amounts of sodium dodecyl sulphate (SDS) and cetyl alcohol are also adsorbed on the polymer particles [8,9].

The DSC analysis of the samples was carried out with a Mettler FP80 differential scanning calorimeter, at a heating rate of 5°C min^{-1} over a temperature range of 30–400°C. The sample weight was between 5 and 6 mg.

DSC experiments were first carried out with Aquacoat latex alone. To check for the effect of temperature on the latex stability, samples were desiccated at 25, 40 and 80°C, respectively. When the pH was the variable under study, HCl or NaOH solutions were added to latex samples in order to adjust their pH to between 2 and 12. The samples were then desiccated at room temperature before running the DSC experiments. The effect of shaking on the latex excipient was tested by running samples for different periods in a Branson 5200E4 ultrasonic bath set at 450 W ultrasound power.

3. Results and discussion

Fig. 1, a thermogram of ethylcellulose latex, shows an endothermal peak at 55°C and an exothermal peak at 147°C. To find the possible origin of these thermal events, we analysed the behaviour of the three major components of Aquacoat, namely, ethylcellulose, cetyl alcohol and SDS, separately [10]. Fig. 2 illustrates the thermograms of each component. Ethylcellulose showed two peaks, an endothermal peak at 56°C and an exothermal peak at 184°C, while the melting temperature of cetyl alcohol appears to be 53°C. This explains the two peaks found in Fig. 1. However, the peaks characteristic of SDS (see Fig. 2, curve A) are not observed in the Aquacoat thermogram. Probably, the amount of sodium dodecyl sulphate in the latex preparation is too small in relation to the other two components to be detectable (the minimum detectable amount in our system is approximately 1 mg).

The effect of temperature on the stability of the latex is depicted in Fig. 3, which shows the thermograms obtained after desiccating Aquacoat samples at 25, 40 and 80°C. The characteristic endothermal and exothermal peaks are observed at the two lower temperatures, but at 80°C the differences are more pronounced (the destruction of latex at this temperature was more pronounced).

Ultrasonic shaking at 450 W for 4 h did modify the latex, see Fig. 4. Although the Aquacoat endothermal peak occurring at 55°C was preserved (slight shifts), the area under the curve was smaller in comparison with the results obtained with

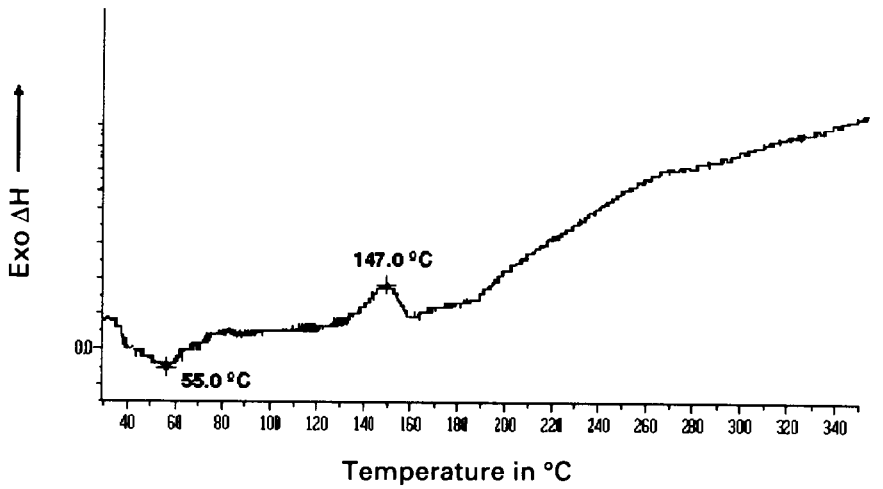

Fig. 1. Representative DSC thermogram of Aquacoat latex.

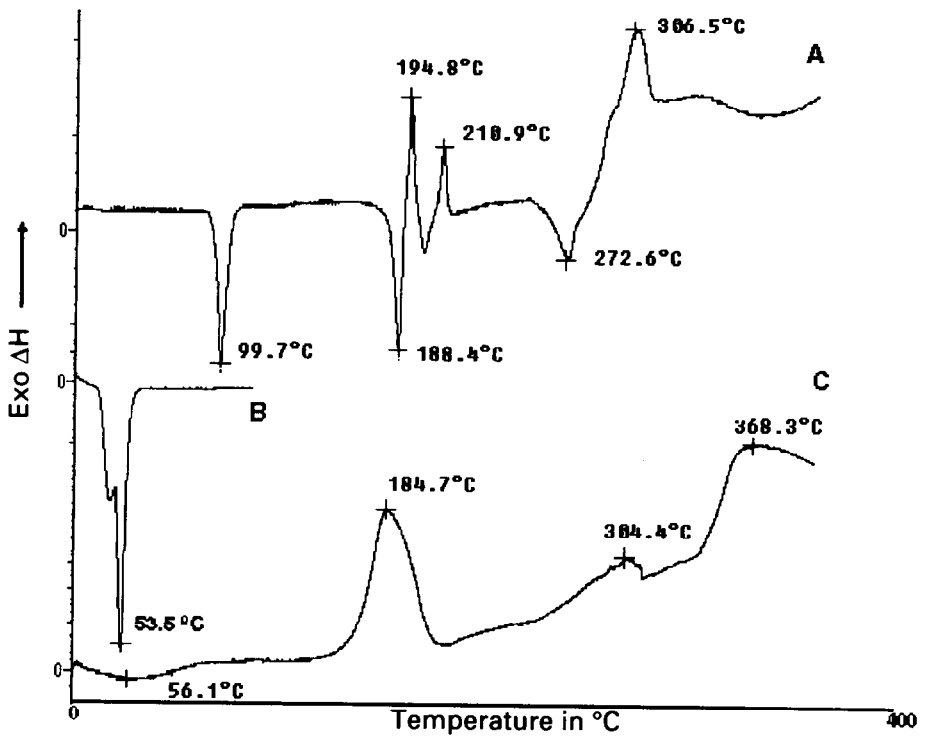

Fig. 2. DSC thermograms of pure components: curve A, lauryl sulphate sodium; curve B, cetyl alcohol; and curve C, ethylcellulose.

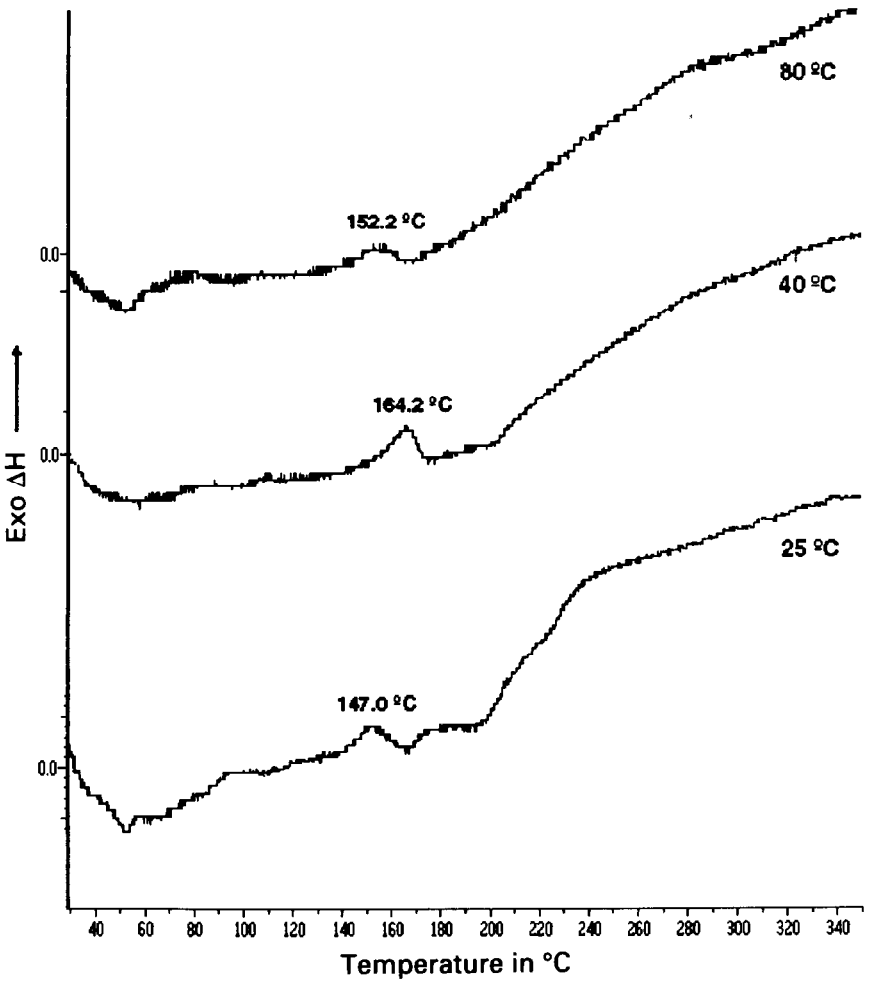

Fig. 3. DSC thermograms of Aquacoat latex at 25, 40 and 80°C.

untreated latex. Apparently, ultrasonic energy may destroy part of the Aquacoat particles (the same effect as obtained with desiccation at 40°C), thus reducing the area of the peaks corresponding to its two major components.

The effect of pH can be seen in Fig. 5, which shows representative Aquacoat thermograms obtained at pH 2, 5 and 12. Although a wider range of pH values was studied, the results over a large part of the range were similar. Therefore only the extreme values, together with the results at pH 5 (the normal pH value of the latex), are illustrated. No change in the endothermal peak (55°C) was seen when the pH was modified between 2 and 12. However, acid pH values shifted the exothermal peak (147°C at pH 5) to the right (149°C), whereas basic pH values changed the temperature of the exothermal event towards higher temperatures (199°C). These

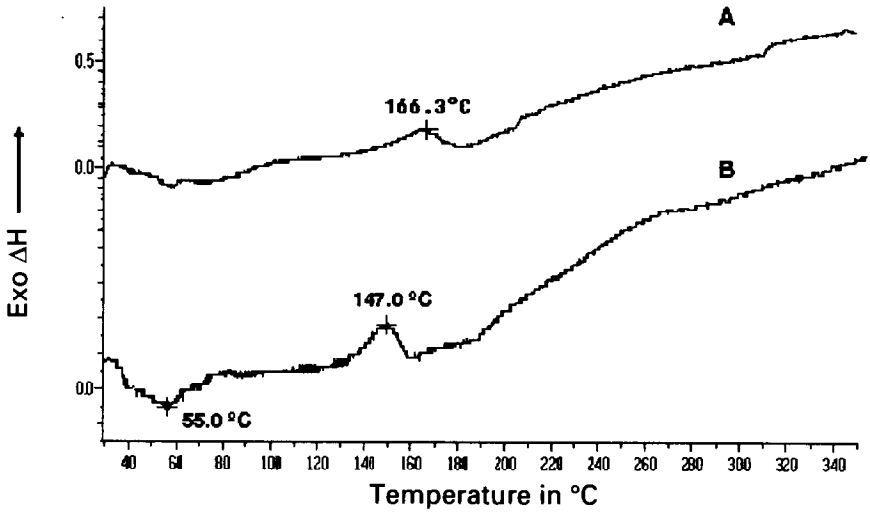

Fig. 4. DSC thermograms of Aquacoat latex with shaking (A) and without shaking (B).

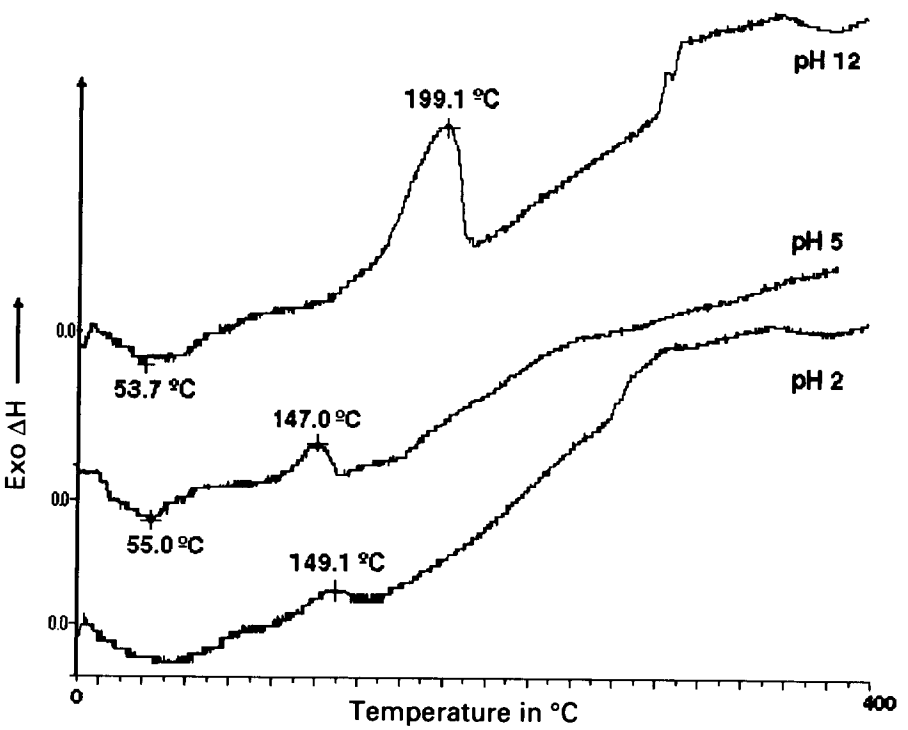

Fig. 5. DSC thermograms of Aquacoat latex at pH 2, 5 and 12.

findings suggest that pH affects the stability of latex. Jacobson and Gibbs [11] found a similar behaviour in entirely different systems, namely, injectable formulations of Cephradine. Note also that in Fig. 5 the thermogram corresponding to pH 12 differs more significantly than that obtained at pH 5. Ethylcellulose seems to be less stable when the dispersion medium is sufficiently acid. The differences observed could be due to the fact that at pH 12, the latex breaks and the principal component, ethylcellulose, a very stable component in an alkaline medium, can be obtained; this explains the extreme peak at 199°C in this medium. This does not occur at pH 2 in an acid medium where ethylcellulose is more sensitive.

All the changes observed in the samples under different conditions have been confirmed by means of an infrared study. The IR spectrum shows that the instability of the latex is physical and no chemical changes appear in its structure. Thus when using this polymer in pharmaceutical formulations, one must avoid extreme conditions of pH, temperature and shaking, as all of them can cause an irreversible coagulation of the latex, leading to its tearing with subsequent formation of its principal component, ethylcellulose, which is sensitive in an acid medium and which at high temperature undergoes a degradation process through oxidation.

4. Conclusions

Preliminary results shown in this work suggest that latex is more affected by the pH condition than by temperature fluctuations, and therefore extreme pH should be avoided even when it is necessary for the preparation of the pharmaceutical formulation. We can state that the advantage of using DSC for studying some components (excipients) in pharmaceutical formulations is not only that it gives a rapid estimation of the chemical stability, but also that it can possibly be used as a rapid method for estimating the effect of different factors that modify the stability of the formulation.

Acknowledgments

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