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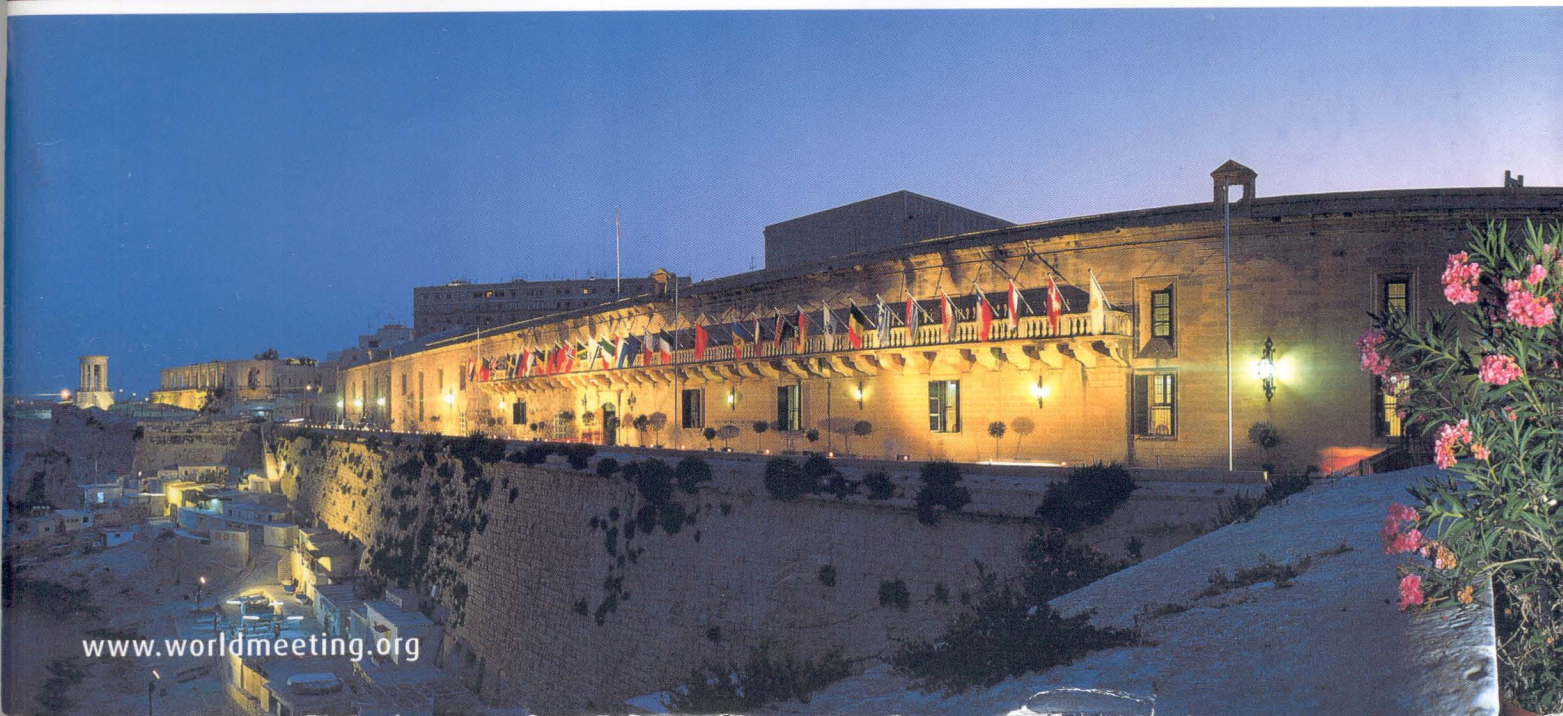and Pharmaceutical Technology

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Effect of Lactose on the thermogelation properties of Poloxamer 407

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INTRODUCTION

Poloxamers are block copolymers of ethylene oxide (EO) and propylene oxide (PO) used in different industrial areas such as detergents, foaming, lubrication, dispersion, stabilization, cosmetics, inks [1] and pharmaceutical field [2].

Their temperature-dependent self-assembling and thermogelling behaviour is well known. In fact, Poloxamers (above a certain concentration and at a specific temperature) possess in water the ability to change from individual block copolymer molecules (unimers) to self-assembling micelles. Moreover, some kind of Poloxamers are also characterized by a specific temperature at which micelles organized (cmT, critical micelle temperature or gel point) generating the transition from a viscous solution to a strong gel. Both micellization and gelation depend on different factors: temperature, polymer concentration, PEO block length [3] and presence of several additives.

In this paper the thermogelling properties of Poloxamer 407 have been analysed in order to determine modification in samples behaviour after the addition of lactose. The work is part of larger project focussing on the development of a thermogel system able to work as a crystallization medium, being gelled at ambient temperature and liquid at a lower temperature, so that the crystals can be easily harvested. The effect of solute and Poloxamer concentration have been very well characterized in order to generate a system with the right condition for crystallization and gelation.

EXPERIMENTAL METHODS

Materials

Poloxamer 407 (Lutrol F127, Acef, Italy; molecular weight 12600 and PEO/POP ratio 2:1) and ά-Lactose monohydrate (Pharmatose 150M, DMV International, The Netherlands) were used as received. Deionised water was produced with a laboratory deionizer (Osmo Lab UPW 2, Gamma 3, Italy).

Samples preparation

Concentrated solutions of Poloxamer 407 (Poloxamer stock solutions, PSS) were prepared by dispersing the polymer in the required amount of degassed and deionised water using the "cold" procedure . PSS were stored at 4-5 °C for at least 48 hours before the use. Concentrated solutions of lactose (Lactose stock solutions, LSS) were instead prepared by dissolving the disaccharide in the required amount of degassed and deionised water at 70°C. Suddenly after the preparation, the LSS were left at room temperature until they reach the temperature of 25°C, and then added to the PSS stored in an ice bath. The final solutions were mixed for 10 minutes while is still in ice bath.

Rheological characterization

Rheological analyses were performed using a stress control rheometer (Stress-Tech, Reologica) equipped with cone-plate geometry (4/40), automatic gap. All the systems were analysed suddenly after the preparation using a temperature sweep test (from 5 to 30 °C, 1°C/min, 1Hz, 1Pa)

RESULT AND DISCUSSION

The temperature sweep test allows the determination of the gelation temperature and the quantification of the variation in samples elasticity. The sol/gel transition temperature is the temperature characterised by a drastic increase in the elastic and viscous modulus and by a drastic decrease of the phase angle (Fig. 1A). The gel point is represented by the temperature where the phase angle drop to a value of 45° and the two moduli present similar values. Rheological tests showed that not all the composition analysed had the same behaviour in term of gelling performance and three different kind of systems have been observed: gelling, partially gelling and no gelling (Fig. 1A, 1B and 1C respectively). Similar results were evident also from a visual examination of the flow gel attitude.
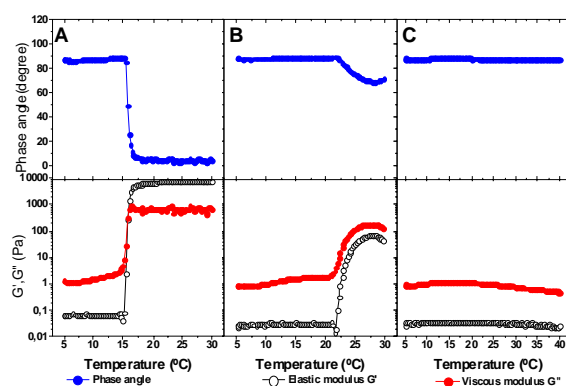

Figure 1. Effect of temperature on the rheological parameters G',G" and phase angle for the A) gelling, B) partially gelling and C) no gelling systems.

The component ratio of the different gelling systems and the influence of the system composition on the gel point (only for the gelling samples) are shown in fig. 2. The gel point is strongly dependent on the Poloxamer and lactose concentration, particularly it decreases as the concentration of the two components increases. The results clearly indicate that lactose interacts with the system Poloxamer/water altering its gelation properties, in term of gel point as well as rheological behaviour.
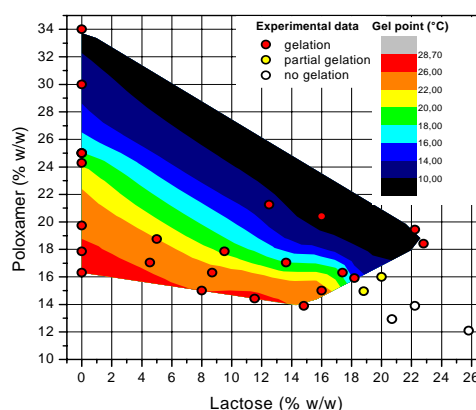

Figure 2. Effect of composition in rheological behaviour and gel point.

The same systems considered for gel point analysis were analysed also in term of complex viscosity in the temperature range below the gel point. As expected, results (not shown) showed an increase of the viscosity as the Poloxamer and lactose concentration increase, however the viscosity values were much less variable compared to gel point results.

CONCLUSIONS

Lactose interacts with poloxamer-water sysytems affecting the gelation temperature as well as their rheological behaviour. For a constant poloxamer concentration an increase of lactose amount decreases the gel point up to a threshold value over which it depress the gelling attitude until a complete inhibition of such process.

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