Targeting Non-Steroidal Drug Using Polymer Encapsulation

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Flurbiprofen is an effective anti-inflammatory and analgesic agent of the phenylalkanoic acid series (ibuprofen, naproxen and ketoprofen) which is used to treat pain, tenderness, swelling, and stiffness caused by osteoarthritis and rheumatoid arthritis. Studies have shown that Flurbiprofen is a valuable alternative to other non-steroidal anti-inflammatory drugs in the management of rheumatoid arthritis. It is superior to others in terms of formal symptomatic measures (pain, stiffness and swelling), as well as having a high efficacy/tolerance ratio [1].

Polyethylene-polypropylene-polyethylene tri-block copolymers have shown significant potential as drug carriers, in particular for encapsulation of hydrophobic drugs. Because of the hydrophobic character of PPO blocks, multi-molecular micelles form [2] above the critical micellisation concentration (CMC) and critical micellisation temperature (CMT). However, the sensitivity of micellisation highlights difficulties in predicting aggregation characteristics. A critical issue in drug delivery using Pluronic polymers is the control of the Critical Micelle Concentration.

In this paper we discuss the use of surface tension measurements, a dye solubilisation method and PFGSE NMR spectroscopy in order to determine the CMC of Pluronics P103, P123 and L43. The effect of the addition of Flurbiprofen to the three Pluronic solutions was examined by surface tension measurements and the results showed a remarkable reduction in CMC values and decrease in surface area occupied by each molecule. The aggregation behaviour of the Pluronic P103, in the presence of Flurbiprofen, was also studied by pulsed field gradient stimulated-echo NMR. A substantial increase in the hydrodynamic radius of Pluronic P103 from 5nm to 10nm was observed, along with an increase in the fraction of polymer micellised (Figure 1). This clearly shows that nearly all of the Flurbiprofen interacted with the polymer micelles with possible application to drug deliveries [3].

Figure 1: Attenuation plots for 5%w/w P103, 0.5% w/w Flurbiprofen in D₂O/d₆-ethanol (90:10). The data was taken from the CH₃ resonance at δ ~ 3.6ppm for P103 and the attenuation of the Flurbiprofen aromatic group at δ ~ 7.5ppm.