UV Imaging Studies on Pluronic F127-based Hydrogel Formulations of Ibuprofen

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ABSTRACT SUMMARY
UV imaging studies have been carried out on hydrogel formulations of ibuprofen, and complemented by rheology studies. Gels where ibuprofen was present below its solubility limit demonstrated a correlation between gel viscosity and drug release. An increase in gel viscosity retarded ibuprofen release from the gels. The saturated (5% w/w ibuprofen) gel demonstrated a statistically significant increase in the rate of drug release compared to the unsaturated (1% w/w ibuprofen) gel, despite the greater viscosity of the latter. This is consistent with supersaturation increasing the thermodynamic activity of the formulation, thus drug release.

INTRODUCTION
Ibuprofen is a potent, non-steroidal anti-inflammatory drug (NSAID). This class of drugs encompasses a wide spectrum of indications from the reduction of pain, inflammation and fever to the long and short-term management of various conditions, including intra-articular disorders (osteoarthritis and rheumatoid arthritis) and musculoskeletal pain. The associated risk of gastrointestinal bleeding¹ and cardiovascular disease²,³ has brought increased attention to non-systemic administration of ibuprofen. The aim of the project was to prepare Pluronic F127 gel formulations containing ibuprofen and correlate their rheological and drug release properties. The effects of variation of Pluronic F127 concentration (15%, 20% and 25%) and ibuprofen (1% and 5%) concentration were investigated.

EXPERIMENTAL METHODS

Pluronic F127 gels containing 1% or 5% w/w ibuprofen were prepared on a weight basis using the cold method at 15%, 20% and 25% w/w Pluronic concentrations. Propylene glycol was used as a co-solvent. Saturation concentration of ibuprofen in each gel was determined using an Olympus BH2 microscope fitted with a camera (AxioCamMRc-Zeiss, UK) and AxioVision vs4.4 software. Viscometry was performed at 32°C to characterise the flow behaviour of the gels, using a sandblasted stainless steel cone-plate (4°/40 mm) with 150 µm gap size. UV imaging of ibuprofen diffusion from the gels in PBS buffer was carried out using an Actipix SD1300 surface dissolution imaging system at 214 nm (Paraytec, UK).

RESULTS AND DISCUSSION
Polarised microscopy confirmed that gels (15%, 20% and 25%) containing 1% ibuprofen were unsaturated. The viscosity of the gels was found to increase with the increase of the F127 concentration from 15% to 25%. The rate of ibuprofen release from the gels was found to decrease in response to increasing gel viscosity as the polymer content increased from 15 to 25% w/w. The reduction in the number and dimension of aqueous channels within the gel matrix, increase in intermicellar cross-linking and thereby gel viscosity⁴ in response to the increase in F127 content from 15-25% are believed to be the key factors accounting for the retardation of drug release.

The presence of crystals in the 15% w/w gel containing 5% w/w ibuprofen indicated that ibuprofen was present above its solubility limit within the gel matrix (Fig. 1).
The 15% w/w gel with 5% w/w ibuprofen had higher viscosity compared to the corresponding gel with 1% w/w ibuprofen (Fig. 2). The average increase over the shear rate range was 0%.

Figure 3 shows the time dependence of drug concentration released from two formulations. In the first 30 minutes, a phosphate buffer solution pH 7.4 was flowed over the gel surface at a rate of 0.2 mL/min. In the second phase (30 – 60 min), the flow was stopped. Depletion is seen to occur at the end of the first phase. In the second phase, concentration in the dissolution medium builds back up again. The rate of drug release from the gel with 5% ibuprofen was higher when compared to the gel with 1% ibuprofen. The effect of increased drug loading and supersaturation seems to outweigh the effect of gel viscosity in terms of drug release. Supersaturation has previously been found to be a means of enhancing flux from formulations by increasing the thermodynamic activity beyond the saturation level as illustrated in the Higuchi equation.

Experiments are being extended to lower concentrations of the API, and to provide a more detailed study of depletion in the surface layer of the gel.

Figure 3. Concentration of drug released from two gel formulations as a function of time. Flow rate from 0-30 minutes = 0.2 mL/min; 30-60 minutes = 0.0 mL/min.

CONCLUSION

Gels where ibuprofen was present below its solubility limit demonstrated a correlation between gel viscosity and drug release. An increase in gel viscosity retarded ibuprofen release from the gels. The saturated (5% w/w ibuprofen) gel demonstrated a statistically significant increase in the rate of drug release compared to the unsaturated (1% w/w ibuprofen) gel, despite the greater viscosity of the latter. This is consistent with supersaturation increasing the thermodynamic activity of the formulation, thus drug release.

REFERENCES