THE EFFECT OF ADDITIVES ON THE GELATION PROPERTIES OF PLURONIC F-127 SOLUTIONS

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Pluronic F-127 (PF-127), a block ABA copolymer of low toxicity and high solubilising capacity, has been considered as a possible depot drug delivery system (Howard, 1983). Aqueous solutions of the polymer in concentrations above 20% w/w exhibit reverse thermal gelation, remaining as solutions at refrigerated temperatures and gelling upon warming to ambient levels. The release of drug injected in a solution of PF-127 will thus be modified by the formation of a gel depot site within the body tissue. This study reports the effect of additives on the gelation properties of PF-127 solutions using benzoic acid (BZ) and water soluble polymers, the polyethylene glycols (PEG).

The effect of concentration of BZ, 0-2% w/v, and different molecular weight PEGs, 0-4% w/v, was considered. Gelation was assessed using a modification of the technique described by Vadnere et al, 1984. Solutions of PF-127 and additives were prepared using the "cold" method (Schmolka, 1972) and stored in a cold room. Aliquots (2ml) were transferred to test tubes in a water bath at 4°C, and sealed with Nescofilm. The temperature of the bath was increased in increments of 3°C and left to equilibrate for 15 minutes at each new setting. The samples were then examined for gelation which was said to have occurred when the meniscus would no longer move upon tilting through 90°.

Increasing BZ concentration decreased the gel-sol transition temperature over a range of PF-127 concentrations (Fig. 1). The opposite was observed when PEG was incorporated into the PF-127 solutions, the effect being dependent upon the chain length (Fig. 2) and concentration. Simultaneous inclusion of PEG with BZ allows the restoration of the optimum gelation temperature. Gelation is attributed to the dehydration of the polymer chains, promoting micellar association and subsequent entanglement, forming a three dimensional gel network (Rassing et al, 1984). Therefore these results may be interpreted in terms of the influence of the solute and polymer molecules on the micellar structure of the copolymer in aqueous solution. This study demonstrates that incorporation of both the BZ and PEG into PF-127 solutions permits the control of gelation temperature while increasing solute loading, a necessary requirement for successful formulation of a drug delivery system.

FIGURE 1.

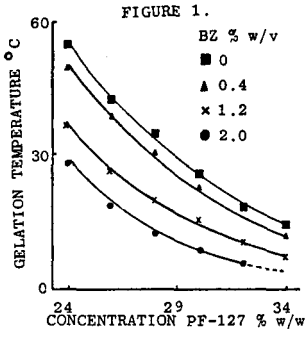
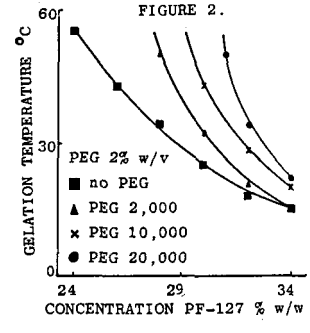


FIGURE 2.



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