CONTROLLED DRUG RELEASE FROM PLURONIC MATRICES

J C Gilbert and M Whiteman - SmithKline Beecham Pharmaceuticals, Mundells, Welwyn Garden City, Herts. AL7 1EY

Matrix systems for controlled release are easy to formulate, and relatively cheap to produce. Developments in capsule filling technology have enabled a wide range of polymers to be used as controlled release matrices (Cole, 1989).

The Pluronics are a group of structurally related block ABA copolymers (known generically as poloxamers), offering a wide range of physicochemical properties. They are relatively non-toxic, highly efficient solubilizing agents and certain members of the group have the ability to form gels in aqueous solution. The purpose of this study was to determine whether the gelling potential of Pluronics offered the opportunity to develop novel controlled release systems.

Four Pluronics were used, exhibiting a range of properties as shown in Table 1; the model drug chosen for the studies was methylparahydroxybenzoate (MEPB). 400 mg of MEPB was added to 4 g of molten Pluronic at 60°C and the mixture was stirred until a clear solution formed. Capsules were prepared by filling 440 mg ($\pm$ 10 mg) of the solution into size 0 hard gelatin shells. These were allowed to solidify under ambient conditions.

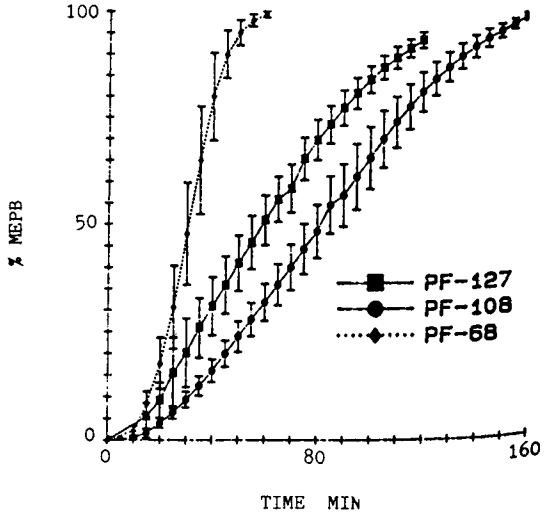
Dissolution testing was performed within 24 hours of capsule preparation using a Beckman DU70 multi-sample spectrophotometer attached to a BP/USP basket apparatus, rotating at 50 rpm; the dissolution medium was 900 mL of 0.1M HCl at 37°C. Release of MEPB was monitored over a 3 hour period.

Dissolution profiles for three of the four polymers are shown in Figure 1. The results obtained for F98 lie between the lines for F127 and F108 but have been omitted for the sake of clarity. It was found that F127, supposedly the surfactant producing the strongest gels (Schmolka, 1972), was not as efficient at retarding MEPB release as F108. These data clearly confirm that poloxamers can be used as controlled release capsule matrices and that drug release can be modulated by selecting the block copolymer. What is less clear is whether differences in drug release profiles can be attributed to the relative abilities of the copolymers to form gels or correlates more closely with other properties such as molecular weight and HLB. In an effort to clarify this point, the next phase of this work will consider the effect of varying the hydrophilic content of the block copolymers.

TABLE 1: Physicochemical Properties of Pluronics

Pluronic Grade	Molecular Weight	Melting Point °C	Viscosity (77°C) cps	HLB	Hydrophilic Content %	Min. Gelling Conc. % w/w
F 68	8400	52	1000	29	80	60
F 98	13000	58	2700	27.5	80	40
F 108	14600	57	2800	27	80	30
F 127	12600	56	3100	22	70	20

Figure 1: MEPB RELEASE FROM PLURONIC MATRICES



Cole, E., (1989) Pharm. Tech. 9: 124-138
Schmolka, I.R., (1972) J. Bio. Mat. Res. 6: 571-582