CROSSLINKED POLOXAMER HYDROGELS AS CONTROLLED RELEASE SYSTEMS

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Crosslinked, swelling hydrogels derived from the acryloyl derivatives of poloxamer co-polymeric, surfactants have been prepared and their morphology and swelling properties described (Law et al., 1984). Varying proportions of the modified poloxamer 188 (Pluronic F68, $(PEO)_{75}$-$(PPO)_{30}$-$(PEO)_{75}$) and poloxamer 181 (Pluronic L61, $(PEO)_3$-$(PPO)_{30}$-$(PEO)_3$) have been polymerised to give swelling hydrogels in which benzoic and p-hydroxybenzoic acids and prostaglandin E_2 have been incorporated. Such systems provide an approach to zero-order drug release rates.

Release rate data for swelling hydrogels are best described by the equation $Mt/M = kt^n$ where Mt/M is the fraction released at time t and k and n are constants. When n=1, zero order release rate kinetics are indicated and n=0.5 corresponds to diffusion controlled or Higuchi type release rate kinetics (Korsmeyer et al., 1983).

Release rates were determined by stirring (125rpm) the gel slabs in 500ml phosphate buffer, pH7.4 at 37°C in round bottomed flasks. Solute concentrations were determined by absorbance measurements at 264nm.

Table 1 shows the values of n and the time for 60% release (t_{60}) for the release of benzoic acid and p-hydroxybenzoic acids from hydrogels with varying proportions of modified poloxamers 188 and 181.

TABLE 1

Ratio of poloxamer 188:181	n	t_{60} (p-hydroxy benzoic acid) mins.	t_{60}(benzoic acid) mins.
pure 188	0.73	400	-
4.1	0.69	480	230
3.2	0.57	510	280
2.3	0.51	720	400
1.4	0.50	810	520
pure 181	0.49	910	560

The pure 181 hydrogel shows a value of n=0.49, indicating diffusion controlled release as expected for a non-swelling gel. The value of n increases to a maximum value of 0.73 with increasing content of the more hydrophilic poloxamer 188. Extent of swelling also increases in this manner.The rate of release of the p-hydroxybenzoic acid was in all cases slower than that of benzoic acid, probably due to hydrogen bonding to the oxyethylene ether oxygens in the gel network.

The hydrogel system with the value of n closest to 1 (0.73 for pure poloxamer 188) was chosen for studies with prostaglandin E2: a similar value of n was obtained (0.71) with a time for 60% of 670 min. These swellable poloxamer hydrogels provide drug release systems with controllable release rates approaching zero-order.

Law et al (1984) Int.J.Pharm., 21, 277
Korsmeyer et al (1983) Int.J.Pharm., 15, 25