International Journal of Pharmaceutics, 58 (1990) 89–91
Elsevier

IJP 01979

Short Communication

Drug release through aqueous-based film coatings of acrylate-methacrylate, a water-insoluble copolymer

R.S. Okor and C.E. Obi

Department of Pharmaceutics, School of Pharmacy, University of Benin, Benin City (Nigeria)

(Received 8 August 1989)
(Accepted 24 August 1989)

Key words: Tablet film coating; Acrylate-methacrylate copolymer coating; Drug release; Ephedrine hydrochloride

Summary

An aqueous-based system of a water-insoluble acrylate-methacrylate copolymer was prepared by a coarcevation technique. The composition of the fluid included ethanol (10 ml), polymer (5 g) and a non-solvent, water (90 ml). Polymer film coatings were applied on a porous substrate (Whatman No. 1 filter paper) by immersion of the substrate (10 s) in the fluid. After drying, the performance of the film coatings as barriers in drug release studies compared favourably with that of film coatings cast from ethanol and were considerably more permeable than those cast from acetone. This difference relates to the higher polarity of water or ethanol compared with acetone. The indication is that the aqueous-based system could be substituted for the more expensive ethanol in the polymeric coating of drug particles.

Polymer films find use as controlled release barriers in drug delivery systems. Previous studies (Okor, 1982a,b) have demonstrated the potential of films derived from acrylate-methacrylate copolymers in this area of use. These polymers are, however, not soluble in water, therefore their coatings can only be deposited from organic solvents which are expensive. In this study, an aqueous-based system of the water-insoluble polymer was developed using a coarcevation technique. The procedure involved addition of excess water (non-solvent) to an ethanolic solution of the polymer.

An acrylate-methacrylate copolymer (trade name, Eudragit RL100) was obtained from Rhom Pharma (Darmstadt, F.R.G.). It contains a small proportion of quaternary ammonium (cation) groups (66 mol per mol polymer chain) which imparts some hydrophilic swelling character. Ethanol (i.e. absolute alcohol BP) and acetone (analar grade BDH) were used as solvents in film coating. Ephedrine-HCl (analar grade, BDH) was the test drug.

The polymer (5 g) was dissolved in ethanol (10 ml) using overnight stirring, water (90 ml) being added with continuous shaking. 5% w/v solutions of the polymer in ethanol or acetone were also made.

A porous substrate (Whatman No. 1 filter paper) was impregnated and coated with the polymer by dipping it for 10 s into the polymer fluid followed by drying at 70°C for 20 min. The procedure was repeated but with a drying time of

Correspondence: R.S. Okor, Department of Pharmaceutics, School of Pharmacy, University of Benin, Benin City, Nigeria.

40 min. The first dipping would impregnate (i.e. plug) surface pores of the substrate while the second forms a film coating on it. Microscopic examination of a section of the coated substrate therefore revealed an asymmetric structure characterized by a loose porous core (representing the substrate) bounded by compact skins (i.e. the film coats). The substrate conferred mechanical rigidity to the barrier thus obviating the need for an additional mechanical support for the film in the design of the dialysis cell. The thickness of the substrate was determined at 10 random points before and after coating and from the difference the thickness of the film coat was calculated. This simple technique of applying a film coat on a porous substrate has been frequently used in the formation of dialysis membranes (Richards, 1972).

The coated substrate formed the barrier in drug release experiments which were carried out by dialysis methods. Barriers of mean thickness 166 $\pm$ 3.1 μm and film coat thickness 10 $\pm$ 1.2 μm were used: the area exposed to drug source (donor fluid) was 5 cm^2. The apparatus consisted of a dialysis cell similar in design to that described by Luttinger and Cooper (1967), but without a mechanical support for the membrane; also, the donor fluid was not stirred to simulate practical situations of drug release from coated pellets (Friedman et al., 1979). The donor fluid in the dialysis cell was the drug solution (10 ml) and the receptor fluid, 800 ml water in a 1 l glass beaker. The considerably larger volume of the receptor fluid was intended to create near-sink conditions. With stirring of the receptor fluid at 100 rpm, the experiment was conducted at 30 $\pm$ 0.5 °C. Samples (5 ml) were taken at 30-min intervals for 3 h and analysed spectrophotometrically (Unicam, SP500) for content of ephedrine-HCl at λ_{max} 253 nm. Methylene blue (1 ml, 1% aq.) was added to the donor fluid at the end of each experiment to test for leakage. The experiment was carried out in triplicate and mean results calculated; individual results were reproducible to $\pm$ 12.5% of the mean.

Drug release through this type of barrier is expected to be controlled by the rate of permeation through the film coats, these being the high-resistance layers in the asymmetric structure. The amounts of drug released through the aqueous and ethanol cast film coats were virtually equal but considerably higher as compared to those for acetone (Fig. 1). The mutual repulsion between cationic groups in the polymer structure results in the formation of a more porous film structure (Okor and Anderson, 1987); the extent of this repulsion in turn depends on the degree of dissociation of the cationic groups. Dissociation is favoured in the polar solvents (water and ethanol) as compared with the non-polar solvent (acetone). It was expected that the larger (colloidal) particle size in the aqueous coarcevated system (compared with the molecular sizes in ethanol solution of the polymer) would lead to the formation of a more heterogeneous structure with greater permeability. The results (Fig. 1) suggest that any such differences were slight.

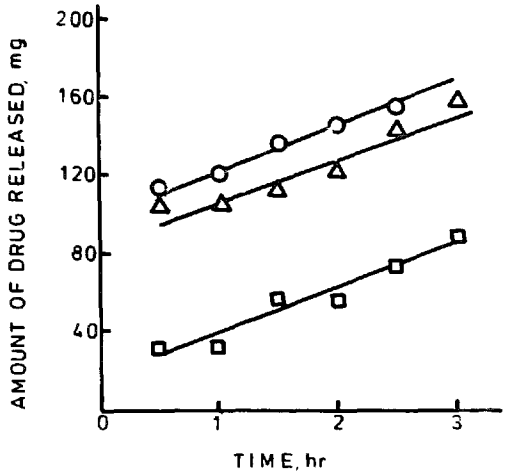

Fig. 1. Effect of type of casting fluid on drug release through the film coatings. (△) Ethanol, (○) aqueous, (□) acetone. Permeant: ephedrine-HCl (10 ml, 5% w/v aq.).

Results (Fig. 1) were obtained using a 5% w/v drug solution. During the course of an increase in permeant concentration of 1 to 5%, a marked rise in drug release was observed up to 25% permeant concentration, while beyond this point the increase was slight (Table 1). This finding suggests that at this critical drug concentration (2.5% w/v), film permeability was determined by the availability of surface pores of suitable size for permeant penetration rather than the number of permeant molecules at the film upstream surface. The retard-release property of the barriers was therefore

TABLE 1

Effect of permeant concentration on drug release through the film coatings

(a) Aqueous cast and (b) ethanol cast films.

Permeant concentration (% w/v)	Amount released (mg) in time (h)					
	0.5	1	1.5	2	2.5	3
(a) 1	48	56	70	88	88	90
2.5	104	112	112	120	136	136
5	112	120	136	144	152	160
(b) 1	48	56	56	80	80	88
2.5	104	104	112	120	144	155
5	112	125	140	150	152	160

more pronounced at higher drug concentration because of the greater residual content after 3 h.

The results of this preliminary study indicate that the aqueous coarcevated system of the polymer has a potential in the polymeric coating of drug particles for controlled release applications, and could be substituted for the more expensive ethanol as casting fluid.

References

Friedman, M., Donbrow, M. and Samuelor, Y., Placebo granules as cores for timed release drug delivery systems. *J. Pharm. Pharmacol.*, 31 (1979) 396–399.

Luttinger, M. and Cooper, C.W., Improved hemodialysis membranes for the artificial kidney. *J. Biomed. Mater. Res.*, 1 (1967) 67–81.

Okor, R.S., Effect of polymer cation content on certain film properties *J. Pharm. Pharmacol.*, 34 (1982a) 83–86.

Okor, R.S., Influence of hydrophilic character of plasticizer and polymer on certain film properties. *Int. J. Pharm.*, 11 (1982b) 1–9.

Okor, R.S. and Anderson, W., Casting solvent effects on the permeability of polymer films of differing cation content. *J. Pharm. Pharmacol.*, 39 (1987) 547–548.

Richards, J.H., Disperse systems. In S.J. Carter (Ed.), *Cooper & Gunn's Tutorial Pharmacy*, 6th edn., Pitman, London 1972, pp. 72–73.