International Journal of Pharmaceutics, 98 (1993) 235–238

IJP 03107

Polycarbophil as a controlled release matrix

Ehab A. Hosny

Department of Pharmaceutics, College of Pharmacy, King Saud University, P.O. Box: 2457, Riyadh 11451 (Saudi Arabia)

(Received 6 July 1992)
(Modified version received 27 October 1992)
(Accepted 9 November 1992)

Key words: Polycarbophil; Controlled release; Propranolol hydrochloride; Indomethacin; Release mechanism

Summary

The hydrophilic polymer, polycarbophil, was used as a sustained release delivery system for propranolol hydrochloride and indomethacin as water soluble and water insoluble drugs, respectively. The rate of release of either drug was found to be dependent on the polymer content of the tablet formulations. As the polycarbophil content increased, the amount released of either drug decreased. The mechanism of release of either drug was found to be dependent on the drug as well as on the polycarbophil content in the tablets.

Polycarbophil (Markus, 1965), a synthetic hydrophilic resin of the polyacrylic acid type, a copolymer of acrylic acid loosely cross-linked with divinyl glycol able to contain a considerable amount of water without dissolving, is a polymeric material which could be used as a drug delivery system.

Polycarbophil, as a bioadhesive material has been used to increase the bioavailability of chlorothiazide in rat stomach (Longer et al., 1985). Also, polycarbophil has been used to improve the rectal bioavailability of ketoprofen from sustained release suppositories in both dogs (Hosny and Robinson, 1991) and humans (Hosny, 1988). Polycarbophil has not previously been used as a drug delivery system.

The purpose of the present work was to investigate the usefulness of polycarbophil as a sustained release matrix. The effect of polycarbophil content on the release rate and mechanism of release of both a water soluble drug (propranolol hydrochloride) and a water insoluble drug (indomethacin) from sustained-release tablets prepared using polycarbophil was also studied.

Six different tablet formulations of each of indomethacin and propranolol hydrochloride were prepared by direct compression using a single punch tabletting machine (Korsch, Type EKO) fitted with a 6 mm flat faced punch. All propranolol HCl tablets formulations contain 20% drug (w/w) 5, 20, 40, 60, 70 and 77% (w/w) polycarbophil in formulations I, II, III, IV, V and VI, respectively. Indomethacin tablets contain 25%

Correspondence to: E.A. Hosny, Department of Pharmaceutics, College of Pharmacy, King Saud University, P.O. Box: 2457, Riyadh 11451, Saudi Arabia.

drug (w/w), 5, 10, 20, 40, 60 and 72% polycarbophil in formulations I–IV, respectively. All formulations for both tablets contained 1% magnesium stearate and 2% talc. The final weights were completed to 100 mg using spray dried lactose.

The dissolution of each of the tested formulation tablets was carried out using the USP dissolution apparatus I (USP, 1980) at 50 rpm based rotational speed. The dissolution media were 900 ml of phosphate buffer pH 6.5 and distilled water for indomethacin and propranolol HCl tablets, respectively. The absorbance and % drug dissolved were recorded continuously at 265 and 288 nm for indomethacin and propranolol HCl, respectively, using a Philips PU 8620 spectrophotometer (U.K.) connected to an IBM computer Model PS 30 using TDS software from Philips. The release data were evaluated using different release models. The correlation coefficients of each formulation were calculated for each of the release models chosen.

Figs 1 and 2 show the percent of propranolol hydrochloride and indomethacin released vs time from different tablet formulations, respectively.

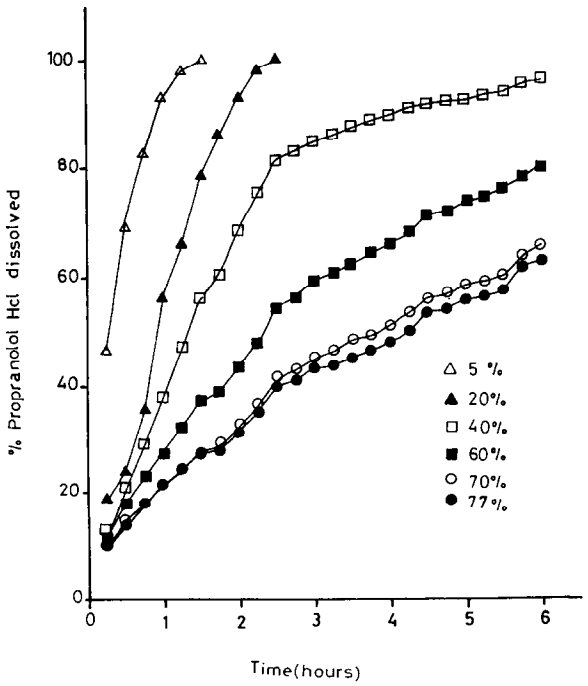

Fig. 1. Effect of polycarbophil content on release of propranolol hydrochloride from tablet matrix.

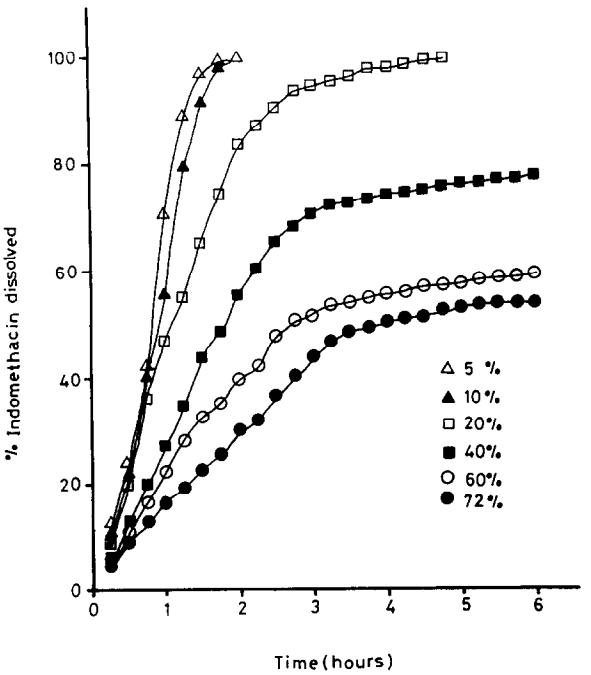

Fig. 2. Effect of polycarbophil content on release of indomethacin from tablet matrix.

The release rate of either drug from these formulations appears to decrease and is inversely proportional to the polycarbophil content. From Figs 1 and 2, it can also be seen that formulations that contained propranolol hydrochloride showed faster release than that containing indomethacin at the same level of polycarbophil. Of course, this can be attributed to the different water solubility of these drugs and to the difference in operative principle controlling their release from matrix tablets. For propranolol HCl, a water soluble drug, when the tablet surface is exposed to aqueous fluids it becomes wet and the polycarbophil begins to partially hydrate to form a gel layer, and an initial burst of propranolol hydrochloride from the external layer is released. On further expansion of the gel layer, more soluble drug diffuses through the gel barrier. Water continues to penetrate towards the tablet core until all drug is dissolved. Concomitantly, the outer layers of polycarbophil become fully hydrated and erode. For indomethacin, a drug of limited water solubility, it will not be completely dissolved when poly-

carbophil is hydrated, so diffusion will commence from a saturated solution (Ford et al., 1985). Therefore, propranolol hydrochloride is released by diffusion from the swollen polycarbophil and by tablet erosion, while indomethacin is released by exposure through tablet erosion.

The effect of polycarbophil content on the mechanism of release of propranolol hydrochloride and indomethacin from their tablet matrices was determined by fitting the release profiles to various models, viz., zero-order, first-order and Higuchi square root models. The correlation coefficients were determined to select the model which yielded the best fit. Models with higher correlation coefficients were judged to be more appropriate for the dissolution data, showing release of $\leq 60\%$. To further examine the kinetic behavior, the data were analyzed according to the equation of Peppas (1985):

$$M_t/M_\infty = Kt^n$$

where M_t/M_∞ is the fraction of drug released, t denotes the time for release, K is a constant incorporating structural and geometric characteristics of the controlled release system and n represents the diffusional release exponent indicative of the release mechanism.

From Table 1, the release mechanism of propranolol hydrochloride from the tablet matrix containing 5% polycarbophil appears to follow first-order kinetics. For higher polycarbophil concentrations, zero-order kinetics appear to be followed. This is according to the correlation coefficient values and also to the exponent n, where n values > 0.5 and < 1 indicate non-Fickian diffusion controlled by a combination of diffusion and chain relaxation mechanisms due to the slow swelling of tablets which leads to a transition of the overall system for the glassy to rubbery state (Ponchel et al., 1987).

Table 1 also shows that the release mechanism of indomethacin from tablet matrices containing 5 and 10% polycarbophil was according to a zero-order mechanism as judged by the higher correlation coefficients and also by values of n that were close to unity. The slightly higher values of n may be explained on the basis that this equation was derived for release from a planar surface and not from an erodible matrix (Ford et al., 1987). For higher concentrations of polycarbophil of 20–75%, the release mechanism followed first-order kinetics as judged by correlation coefficient values and larger deviations of n values from unity.

The data presented in this work clearly demonstrate that polycarbophil can be a useful controlled and sustained release matrix for formulating both water soluble and water insoluble drugs. Also, the data show that the polycarbophil

TABLE 1

Comparison of correlation coefficients from dissolution data of propranolol hydrochloride and indomethacin fit to various models

Model	Correlation coefficient					
	I	II	III	IV	V	VI
Propranolol HCl						
Zero-order	−0.9902	−0.9636	−0.9974	−0.9960	−0.9942	−0.9934
First-order	−0.9998	−0.9418	−0.9959	−0.9948	−0.9917	−0.9928
Higuchi	0.9980	0.9328	0.9932	0.9939	0.9883	0.9909
n	0.5295	0.8162	0.8287	0.6603	0.6126	0.5999
Indomethacin						
Zero-order	−0.9827	−0.9955	−0.9934	−0.9979	−0.9922	−0.9983
First-order	−0.9471	−0.9863	−0.9970	−0.9967	−0.9974	−0.9980
Higuchi	0.9600	0.9830	0.9943	0.9931	0.9978	0.9928
n	1.1850	1.1965	0.7929	0.7824	0.7471	0.8045

content is an important factor that can affect both the rate and mechanism of release of drugs from tablet matrices.

References

Ford, J.L., Rubinstein, M.H. and Hogan, J.E., Formulation of sustained release promethazine hydrochloride tablets using hydroxypropylmethyl- cellulose matrices. *Int. J. Pharm.*, 24 (1985) 327–338.

Ford, J.L., Rubinstein, M.H., McCaul, F., Hogan, J.E. and Edgar, P.J., Importance of drug type, tablet shape and added diluents on drug release kinetics from hydroxypropylmethylcellulose matrix tablets. *Int. J. Pharm.*, 40 (1987) 223–234.

Hosny, E.A. and Robinson, J.R., Rectal drug delivery of ketoprofen using a bioadhesive containing suppository, *2nd Anglo-Egyptian Conference of Pharmaceutical Scientists*, Abstract Book, 18, Alexandria, Nov. 9-12, 1991.

Hosny, E.A., Rectal drug delivery using a bioadhesive containing dosage form. Ph.D. Thesis, School of Pharmacy, University of Wisconsin, Madison, 1988.

Longer, M.A., Ch'Ng, H.S. and Robinson, J.R., Bioadhesive polymers as platforms for oral controlled drug delivery: III. Oral delivery of chlorothiazide using a bioadhesive polymer. *J. Pharm. Sci.*, 74 (1985) 406–411.

Markus, R.L., *US Patent, 3, 202, 577*, 1965.

Peppas, N., Analysis of Fickian and non-Fickian drug release from polymers. *Pharm. Acta Helv.*, 60 (1985) 110–111.

Ponchel, G., Touchard, F., Wouessidjewe, D., Duchene, D. and Peppas, N., Bioadhesive analysis of controlled-release systems: I. Bioadhesive and release behavior of metronidazole-containing poly (acrylic acid) hydroxypropylmethylcellulose systems. *Int. J. Pharm.*, 38 (1987) 65–70.

US Pharmacopoeia, XX Rev., US Pharmacopoeial Convention, Rockville, MD, 1980, p. 959.