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Note

Preparation and evaluation of pectin beads

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Abstract

Pectin beads were prepared by dropping drug-containing solutions of pectin into calcium chloride solutions. The droplets instantaneously formed gelled spheres by ionotropic gelation. Atenolol (cationic) and piroxicam (anionic) were used as model drugs. By using this method, beads with high drug contents were obtained. The effect of formulation and processing factors was also studied.

Keywords: Beads; Pectin; Ionotropic gelation; Atenolol; Piroxicam; Sustained-release

Pectin is a heterogeneous anionic polysaccharide present in the cell wall of most plants. It is non-toxic, almost totally degraded by colonic bacteria and is not digested by gastric or intestinal enzymes (Cummings et al., 1979). Pectin forms water-insoluble complexes with several drugs and may be useful additive for sustained-release preparations (Takahashi et al., 1978; McMullen et al., 1984; Bechard and McMullen, 1986; Naggar et al., 1992). Recently pectin has attracted attention as a carrier for colon targeting since it is easily degraded by colonic bacteria (Ashford et al., 1993; Radai and Rubinstein, 1993). However there is no information about the preparation of pectin gel beads. The aim of the present study is to prepare the pectin beads by ionotropic gelation method and to characterize the possible interactions between cationic (atenolol) and anionic (piroxicam) drugs, and pectin. The effect of formulation and processing variables on bead properties are examined.

Pectin beads were prepared using the method of Bodmeier et al. (1989) as follows. The drug atenolol (Doğu Pharm. Co.) or piroxicam (Deva Pharm Co., Turkey) was added to the 6% (w/v) solution of pectin (Apple 250, BDH, England). This phase was dropped into gently agitated calcium chloride solution (2% w/v). The beads formed were separated and washed with distilled water and dried at 50°C. All batches were prepared at least three times. Two different drugs, atenolol and piroxicam, were incorporated into pectin beads preparation. A number of variables such as drug and calcium chloride concentrations and drying conditions were investigated for optimization of bead properties (Table 1).

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For dissolution studies, pectin beads were suspended in dissolution medium (distilled water for atenolol; pH 7.4 phosphate buffer for piroxicam beads) at 25 ± 0.5°C. The medium was stirred at 100 rev./min in a shaker bath. Samples withdrawn at various time intervals were analyzed spectrophotometrically (Shimadzu UV 2100 S, Japan) at 274 and 253 nm, respectively, for atenolol and piroxicam. All tests were performed in triplicate. No interferance from pectin took place.

Particle size of beads was determined by sieve analysis. Drug content of beads was spectrophotometrically assayed after extraction.

By using ionotropic gelation method, pectin beads were obtained. Preliminary experiments showed that the necessary condition for the preparation of pectin beads were a low internal to external phases ratio, slow stirring rate, and low calcium chloride concentration (Aydin, 1995). In contrast to our expectations pectin formed beads with both anionic and cationic drugs. To confirm the occurence of a binding between the drug (atenolol and piroxicam) and pectin, IR studies were performed. The results indicated that drugs (atenolol and piroxicam) bind to pectin with hydrogen bonds. This was consistent with earlier report (Naggar et al., 1992). Drug-loading capacity and size of pectin beads were given in Table 2. Bead size was dependent on drug concentration and drying methods in atenolol beads ($P < 0.05$). In piroxicam beads, the size changed with the drying conditions ($P < 0.05$). Moreover, the concentration of calcium chloride has no importance in the size of beads containing atenolol or piroxicam ($P > 0.05$). On the other hand, as seen in Table 2, atenolol or piroxicam contents of beads were mainly dependent on the calcium chloride concentration and drug amount used for bead production ($P < 0.05$), but the method of drying has no effect on the encapsulation efficiency of the beads ($P > 0.05$). It can be said that high drug loadings (50–97%) were almost achieved for the two drugs.

When compared atenolol dissolution from beads and from powder form, a marked increase in drug dissolution was observed. Previously, Meshali et al. (1991) reported the increased dissolution rate of pectin-coated glafenine at pH 1.2 as compared to the drug alone. Our findings indicated similarity with the data as Meshali et al. (1991). On the other hand, a retardation was observed in the release profiles of piroxicam from pectin beads (Fig. 1). However, the effect of drug and calcium chloride concentrations on the dissolution of the drug from beads was not found in piroxicam- or atenolol-loaded beads ($P > 0.05$);

Table 1
Codes of pectin beads

Variables	Values	Designation	
		Atenolol	Piroxicam
Drug conc. (%)	2.0	A_1	P_1
	6.0	A_2	P_2
	12.0	A_3	P_3
	18.0	–	P_4
	333*	–	–
	999*	–	–
Drying methods	Oven 50°C/5h	C_1A	C_1P
	Freeze-drying	C_2A	C_2P
$CaCl_2$ conc.(%)	2	E_1A	E_1P
	10	E_2A	E_2P

A, atenolol (powder form).
P, piroxicam (powder form).

Table 2
Size and drug loading capacity of pectin beads containing atenolol or piroxicam

	Mean particle size (mm ± S.D.)	Incorporation efficiency (% ± S.D.)
A_1	0.882 ± 0.04	26.5 ± 2.2
A_2	0.939 ± 0.04	44.6 ± 4.4
A_3	1.158 ± 0.04	58.7 ± 1.0
C_1A	0.882 ± 0.04	26.5 ± 2.2
C_2A	1.566 ± 0.04	35.3 ± 2.6
E_1A	0.882 ± 0.04	26.5 ± 2.2
E_2A	0.988 ± 0.00	27.5 ± 2.4
P_1	0.844 ± 0.01	77.3 ± 5.2
P_2	1.180 ± 0.00	94.7 ± 4.7
P_3	1.180 ± 0.00	97.2 ± 1.4
P_4	1.180 ± 0.00	93.7 ± 1.6
C_1P	0.844 ± 0.01	77.3 ± 5.2
C_2P	1.853 ± 0.13	91.4 ± 2.8
E_1P	0.844 ± 0.01	77.3 ± 5.2
E_2P	1.180 ± 0.00	64.3 ± 1.2

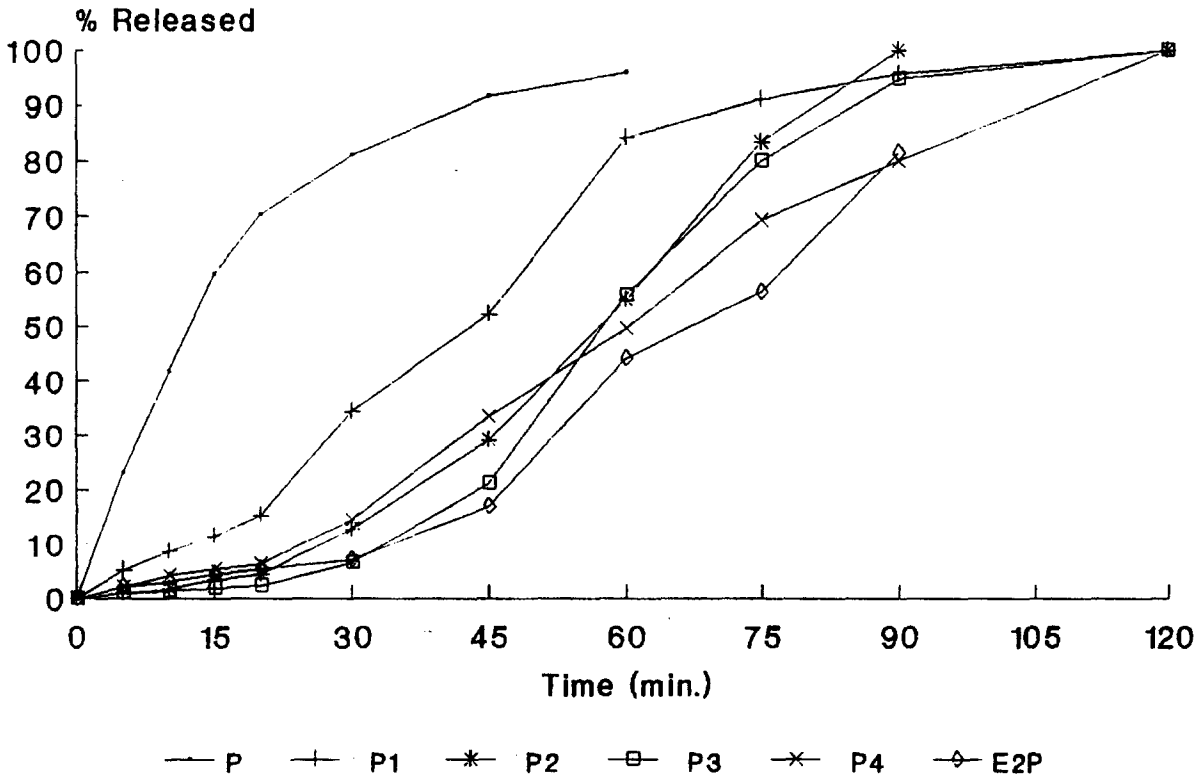

Fig. 1. Piroxicam release from pectin beads.

however, the method of drying affected the drug release from beads. Drug dissolution increased in piroxicam beads, whereas it was not changed in atenolol beads after the freeze-drying process ($P > 0.05$).

Table 3
Coefficients and exponents of drug release functions according to $M_t/M_\infty = Kt^n$ for pectin beads

	r^2	n	K
P_1	0.964	1.166	0.58
P_2	0.993	1.952	0.02
P_3	0.974	2.044	0.01
P_4	0.983	1.420	0.13
C_1P	0.993	1.166	0.58
C_2P	0.979	0.420	15.05
E_1P	0.993	1.166	0.58
E_2P	0.978	1.581	0.06

r^2, coefficient of determination; n release exponent in above equation; K coefficient in above equation.

In order to understand the mode of release of drug from swellable beads, except atenolol-loaded beads, the data ($\leq 60\%$) were fitted to the following power law equation (Ritger and Peppas, 1987): $M_t/M_\infty = Kt^n$. As seen in Table 3, the values of n fell within the range of 1.0–2.0 (except C_2P beads) indicating that piroxicam release from pectin beads are the case II type. This data is in accordance with the results of Naggar et al. (1992).

In summary, drug-containing pectin beads were successfully prepared by the ionotropic gelation method. This study has proved the usefulness of pectin as a matrix for encapsulation of both cationic and anionic drugs. The bead properties were regulated by the appropriate choice of experimental conditions for the preparation of beads.

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