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Effect of different salts on the ionotropic gelation of pectin and formulation of oral drug delivery systems based on pectinate gels

Farklı tuzların pektinin iyonotropik jelleşmesine etkileri ve pektinat jelleri ile hazırlanmış oral ilaç salım sistemlerinin formülasyonu

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Abstract

The aim of the study was to prepare formulations of oral drug delivery systems based on pectinate gels for controlled release and to find out the effect of the water solubility of the drug loaded. For this purpose pectin beads carrying water soluble drug propranolol hydrochloride and water insoluble drug ketoprofen were prepared by using ionotropic gelation method. The effects of different formulation parameters on the particle size, encapsulation efficiency and *in vitro* release profiles of the beads were investigated. Encapsulation efficiency of ketoprofen was higher (51-78 %) than that of propranolol HCl (12-29 %). Within 3 hours both drugs were totally released from the beads. Tablets were prepared by using pectin, pectin beads and zinc pectinate in order to achieve controlled release. By using zinc pectinate, the release of ketoprofen from the tablets could be controlled, about 60% of ketoprofen was released in 7 h.

Keywords: pectin, ionotropic gelation, bead, tablet, propranolol HCl, ketoprofen

Introduction

Hydrogels of natural polymers especially polysaccharides have been widely used because of their unique advantages such as being non-toxic, biocompatible, biodegradable and abundant. They can also be used to prepare particulate drug delivery systems, thus the use of organic solvents needed to solubilize water insoluble polymers can be avoided. A widely used natural polymer, pectin is a gelling and stabilizing agent in food, pharmaceutical and cosmetic industries (May 1990, Dimitriu 2001, Mohnen 2008, Vriesmanna et al. 2011). It is a polysaccharide present in cell walls of all plant tissues which function as an intercellular cementing material. One of the richest sources of pectin is lemon or orange rind which contains about 30% of this polysaccahride. Pectin occurs naturally as the partial methyl ester of α-(1→4) linked D-polygalacturonate sequences interrupted with (1→2) -L- rhamnose residues (Merck Index, 1996). The composition of pectin depends on the plant source and conditions employed during

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pectin isolation and purification. Extraction is an important step in the recovery of pectins. Extraction conditions depend upon the raw material and the desired product (Rolin 1993, Vriesmanna et al. 2011).

The ability of pectin to form rigid gels with divalent cations such as calcium (Aydın and Akbuğa 1996, Munjeri et al. 1997, Sriamornsak 1998, Sriamornsak et al. 2007 and 2008) and zinc (El-Gibaly 2002, Hagesaether et al. 2008, Khoder et al. 2010, Das et al. 2011, Assifaoui et al. 2011) has been used in the production of pectin microspheres or beads by some authors previously. Pectin also has a potential as tabletting excipient and drug carrier to the colon. This soluble polysaccharide passes through the stomach and small intestine with limited digestion, but is totally metabolized by the colonic microflora (Kim et al. 1998). Pectin-based matrix tablets (Ashford et al. 1994, Ahrabi et al. 2000, Sriamornsak et al. 2007), compression coated tablets of pectin (Wakerly et al. 1996), enteric coated calcium pectinate matrix tablet formulations (Adkin et al. 1997), pectin-hydroxypropylmethycellulose (HPMC) coated core tablets for colonic delivery (Turkoğlu and Uğurlu 2002), HPMC/pectin/calcium matrix tablets (Wu et al. 2007 and 2008) were prepared.

The aim of this work was to prepare formulations of oral drug delivery systems based on pectinate gels for controlled release and to find out the effect of the water solubility of the drug loaded. For this purpose the effect of different salts on the ionotropic gelation of pectin was investigated and pectin beads carrying water soluble drug propranolol hydrochloride and water insoluble drug ketoprofen were prepared by using ionotropic gelation method. Furthermore, tablets were prepared by using pectin, pectin beads and zinc pectinate in order to achieve controlled release of ketoprofen.

Materials and Methods

Materials

Propranolol HCl (Doğu İlaç, Turkey), ketoprofen (Nobel İlaç, Turkey) and pectin (Copenhagen Pectin, Denmark) were donations of the manufacturers. Other substances used were all of pharmaceutical grade.

Solubility measurement

Drug in an amount of excess of its solubility was placed in glass bottles containing 25 mL pH 7.4 phospate buffer solution and 0.1 N hydrochloric acid solution separately and shaken in a constant temperature water bath maintained at 37±0.5°C (Certamat WRB. Braun, Biotech International). At appropriate times aliquots were taken, filtered and assayed spectrophotometrically at 290 nm for propranolol HCl and at 260 nm for ketoprofen (Shimadzu UV 2100 S, Japan). Calibration curves were used for these assays.

Preparation of pectin beads

In order to obtain an optimum bead formulation, various salts at different concentrations were tested with different pectin concentrations as shown in Table 1. The formulations of the drug carrying beads are shown in Table 2. The beads were prepared by dropping the drug containing pectin solution into the salt solution while stirring with a magnetic stirrer (Ikamag RH, Germany). The beads formed were filtered under vacuum, washed with distilled water and dried in hot air oven at 50°C (Aydın and Akbuğa 1996).

Scanning electron microscope analysis of the beads

Shapes and surface characteristics of the beads were analyzed using Scanning Electron Microscope (SEM) (Joel JSM-5200, Japan).

Determination of particle size distribution and mean size of the beads

Particle size distribution of the beads was determined by a vibrational sieve analysis system (Retsch, Germany) with sieves having apertures of 0.71- 0.85- 1.18 and 2 mm, vibrating at a speed of 50 rpm for 10 min. Mean particle sizes of the formulations were calculated.

Table 1. Bead formulation studies with various salts and concentrations

Salt type	Salt %	Pectin %	Hardening	Result
Sodium chloride	2	6	-	-
Sodium chloride	10	6	-	-
Sodium acetate	2	5	-	-
Potassium chloride	1	6	-	-
Ammonium acetate	2	5	-	-
Calcium acetate	2	6	-	-
Magnesium chloride	2	5	-	-
Aluminium sulphate	2 or 3	6	-	-
Aluminium sulphate	2 or 3	5	-	-
Calcium chloride	2	6	in alcohol	+
Calcium chloride	10	6	in alcohol	+
Calcium chloride	2	5	in alcohol	+
Calcium chloride	10	5	in alcohol	+
Barium chloride	1	5	+	+
Barium chloride	2	1	+	+
Barium chloride	5	5	+	+
Barium chloride	10	5	+	+
Zinc acetate	0.25	5 or 6	+	+
Zinc acetate	0.50	5 or 6	+	+
Zinc acetate	1	5 or 6	+	+
Zinc acetate	2	5 or 6	+	+

Table 2. Mean particle sizes and encapsulation efficiencies of ketoprofen and propranolol HCl containing pectin beads

Code	Drug (%)	Zinc acetate (%)	Inner phase / outer phase ratio	Mean particle size (mm ± SD)	Encapsulation efficiency (%±SD)
K1	1	0.5	10:50	0.907 ± 0.008	51 ± 1.52
K2	2	0.5	10:50	0.928 ± 0.024	62 ± 5.00
K3	3	0.5	10:50	0.934 ± 0.001	68 ± 5.50
K4	3	0.25	10:50	1.034 ± 0.001	78 ± 1.00
K5	3	1.0	10:50	0.880 ± 0.010	68 ± 2.52
K6	2	0.5	5:100	0.869 ± 0.005	57 ± 1.50
P1	0.5	0.5	10:100	0.810 ± 0.003	28 ± 4.00
P2	1	0.5	10:100	0.820 ± 0.003	25 ± 3.00
P3	2	0.5	10:100	0.821 ± 0.032	29 ± 1.00
P4	2	0.25	10:100	0.835 ± 0.003	20 ± 0.58
P5	2	1.0	10:100	0.852 ± 0.004	12 ± 5.00
P6	1	0.5	10:50	0.830 ± 0.003	28 ± 0.70

Encapsulation efficiency of the beads

Beads were crushed and a sample of exactly 25 mg was extracted in pH 7.4 phosphate buffer solution. After filtration the sample was assayed spectrophotometrically. Pectin did not interfere with the drug absorbances.

In vitro release studies of the beads

The dissolution rates of the pure drugs and the drug release rates from the beads were measured according to the USP paddle method. Accurately weighed samples of 30 mg pure ketoprofen and 30 mg pure propranolol hydrochloride were tested in 500 mL pH 7.4 phosphate buffer solution and in 500 mL 0.1 N hydrochloric acid solution at 37±0.5°C. Accurately weighed samples of 100 mg beads were tested in 500 mL pH 7.4 phosphate buffer solution at 37±0.5°C. At preset time intervals aliquotes were withdrawn and replaced by the same volume of dissolution medium. The amount of drug dissolved / released was determined spectrophotometrically. The kinetics data obtained from release rates were evaluated.

Pectin- based matrix tablets

Preparation of zinc pectinate

Pectin solution (4 % w/v) was adjusted to pH 8.0 using 0.1 N NaOH and stirred at 4°C for 48 h. After acidification (pH 4.5) and dilution to final pectin concentration of 1.5 % (w/v), the solution was heated to 80°C. Aqueous solution of zinc acetate (1.32 % w/v) was added while mixing. The gel formed was cooled to room temperature, lyophilized (Leybold-Heraeus Lyovac GT2, Germany) and powdered (Rubinstein and Radai 1995).

Preparation of the tablets

Tablets were prepared by direct compression method using instrumental hydrolic press (Yeniyurt, Turkey). The compositions of the formulations prepared are shown in Table 3.

Table 3. Codes of tablet formulations prepared

Code	Ketoprofen (mg)	Drug containing pectin beads (mg)	Pectin (mg)	Zinc pectinate (mg)	Pectin beads (mg)	HPMC* granules (mg)	Compaction force (kg)
T1	50	-	450	-	-	-	1000
T2	-	200	300	-	-	-	1000
T3	-	200	-	300	-	-	1000
T4	25	-	-	225	-	-	2000
T5	25	-	-	225	-	-	1500
T6	25	-	-	225	-	-	1000
T7 **	-	100	-	-	100	-	1000
T8 **	-	100	-	-	100	100	1000

* Hydroxypropylmethylcellulose; ** Could not be compressed

Physical properties of the tablets

Diameter and height of 10 tablets was determined by using compass (LLG, Digital Caliper). Friability of 10 tablets was determined at 100 rpm for 4 min in a Roche type friabilitor (Aymes, Turkey). Hardness of 3 tablets was determined with hardness tester (Schleuniger, Switzerland).

Swelling behaviour of the tablets

Tablets were kept in pH 7.4 phosphate buffer for 2 h and the swelling values ρ and q were determined according to the formulas below :

$$\rho = \frac{\text{wet weight}}{\text{dry weight}} = g/g \qquad q = \frac{\text{wet volume}}{\text{dry volume}} = mm^3/mm^3$$

In vitro release studies of the tablets

Drug release profiles of the tablets were measured according to the USP basket method. The dissolution medium was pH 7.4 phosphate buffer solution at 37±0.5°C. At preset intervals aliquots were withdrawn, replaced by the same volume of the dissolution medium and the drug amount was determined spectrophotometrically. The kinetics data obtained from release rates were evaluated.

Statistical analysis

The data obtained from particle size, encapsulation efficiency and release rate determination studies were analysed statistically with ANOVA by using Sigma Stat. The results were expressed as means ± standard deviations. Unpaired, two-tailed t-tests were performed at each time point. The threshold for statistical significance was at $p < 0.05$.

Results And Discussion

Solubility measurement

The equilibrium solubilities of ketoprofen in pH 7.4 phosphate buffer solution and in 0.1 N hydrochloric acid solution were found to be 9.979 mg/mL and 0.085 mg/mL respectively. The equilibrium solubilities of propranolol hydrochloride in pH 7.4 phosphate buffer solution and in 0.1 N hydrochloric acid solution were 186.857 mg/mL and 66.463 mg/mL respectively. The results are indicating the sink condition limits for the dissolution and release rate studies.

Preparation of pectin beads

In order to obtain optimum bead formulation various salts at different concentrations were investigated with different pectin concentrations (Table 1). No gelation was formed by dropping the pectin solution into sodium chloride, sodium acetate, potasium chloride, amonium acetate, calcium acetate and magnesium chloride solutions of different concentrations. On the other hand the required gelation was obtained with calcium chloride, barium chloride, aluminium sulphate and zinc acetate solutions. When using calcium chloride, beads formed had to be kept in alcohol for hardening, therefore this salt was eliminated, as ketoprofen and propranolol hydrochloride are soluble in alcohol. With aluminium sulphate disks instead of beads were obtained after the drying process. When using zinc acetate and barium chloride, spherical beads were obtained. A very low concentration of zinc acetate solution (0.25 %) was enough to form spherical and rigid pectin beads, thus zinc acetate was chosen for further studies. Barium pectinate beads were not preferred because of its potential toxicity to cells (Wideroe and Danielsen 2001).

SEM analysis, particle size and encapsulation efficiency of the pectin beads

The beads containing the water soluble drug propranolol hydrochloride were spherical in shape and had a smooth surface (Fig. 1a and 1b). The beads containing the water insoluble drug

ketoprofen were also spherical in shape, but had a surface with salient parts when examined by SEM (Fig. 1c and 1d).

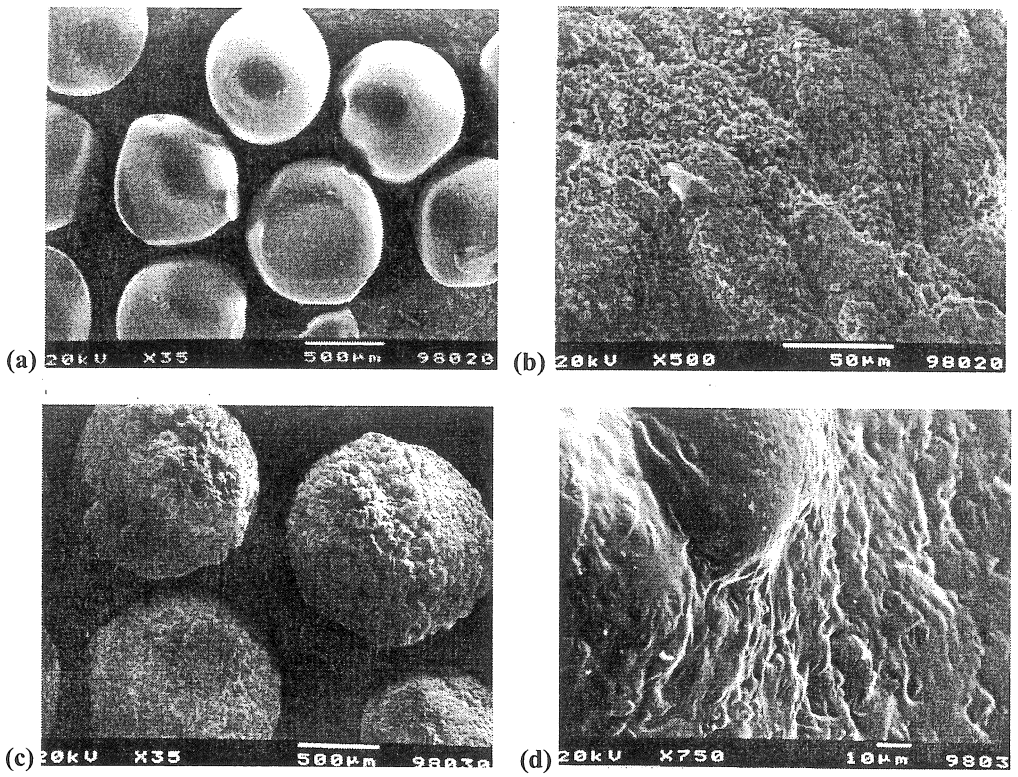

Figure 1: Scanning micrographs of *(a)* shape and *(b)* surface of formulation P3 and *(c)* shape and *(d)* surface of formulation K3

Ketoprofen containing beads were in the size range of 0.880-1.034 mm and propranolol hydrochloride containing beads were in the size range of 0.810- 0.852 mm (Table 2). The size of the ketoprofen beads was not affected by drug concentration and inner phase/ outer phase ratio ($p>0.05$) but was decreased as the concentration of zinc acetate increased ($p<0.05$). The size of the propranolol hydrochloride beads was not affected by drug and zinc acetate concentration ($p>0.05$).

The encapsulation efficiencies were found to be 51- 78 % for ketoprofen and was increased with increasing drug concentration ($p<0.05$). The same effect was reported by El-Gibaly et al. (1996) for the ketoprofen containing cellulose acetate butyrate-polystiren microcapsules prepared by w/o/w complex emulsion technique. In another work, the encapsulation efficiency of ketoprofen of the zinc pectinate microparticles were varied from 73.94 to 91.66%. This high encapsulation efficiency of ketoprofen might be due to the factor that zinc pectinate microparticles prepared were allowed to stand in the crosslinking solution to be cured for 24 h (El-Gibaly et al. 1996, El-Gibaly 2002). Zinc acetate concentration and inner phase/ outer phase ratio had no effect on the encapsulation efficiency of ketoprofen ($p>0.05$). The encapsulation efficiencies were found to be 12-29 % for propranolol hydrochloride. Zinc acetate concentration was effective ($p<0.05$),

whereas propranolol hydrochloride concentration and inner phase/outer phase ratio had no effect on the encapsulation efficiency of these beads ($p>0.05$).

In vitro release studies of the beads

The drug release profiles of water soluble model drug propranolol hydrochloride and water insoluble model drug ketoprofen are shown in Fig. 2.

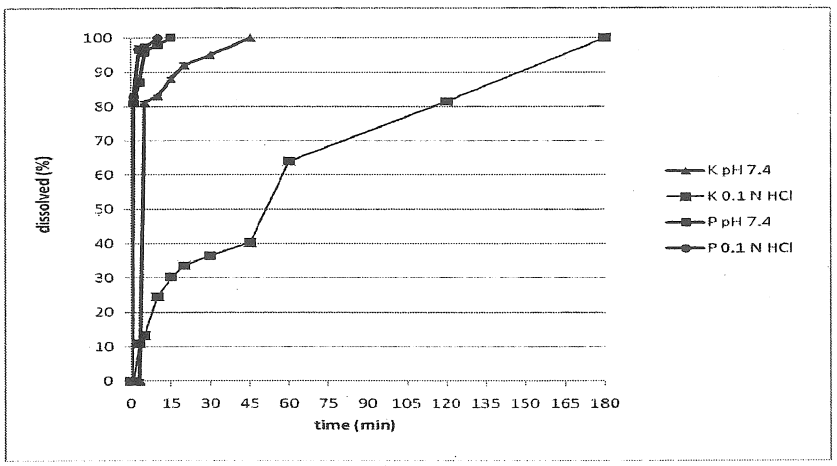

Figure 2. Dissolution rates of pure drugs at 37±0.5°C (n=3). 25 mg ketoprofen and 25 mg propranolol HCl in 500 mL pH 7.4 phosphate buffer solution, 30 mg ketoprofen in 900 mL and 30 mg propranolol HCl in 500 mL 0.1 N HCl solution

Ketoprofen concentration, zinc acetate concentration and inner phase/ outer phase ratio had no effect on the in vitro release rates of ketoprofen containing pectin beads ($p>0.05$) (Fig. 3)

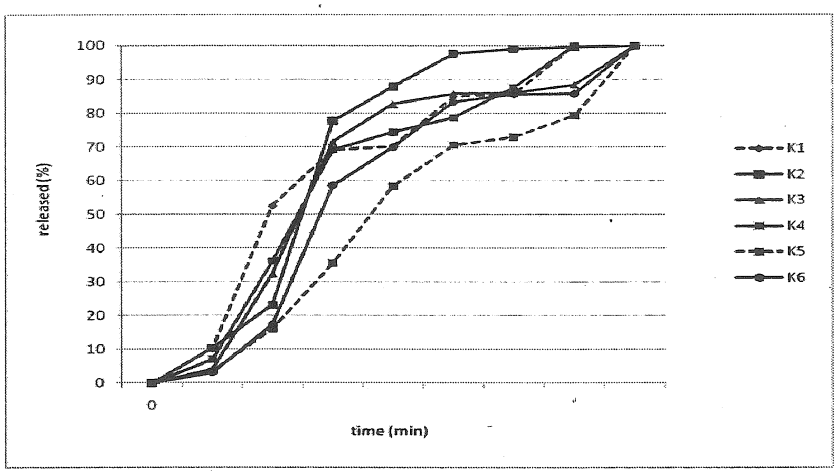

Figure 3. *In vitro* release rate of ketoprofen from pectin beads with 1 % (K1), 2 % (K2), 3 % (K3) drug content; from pectin beads with 0.25 % (K4), 1.0 % (K5) zinc acetate concentration and from pectin beads with an inner phase/ outer phase ratio of 5:100 (K6) (n=3).

The pH of the dissolution medium was found to be effective on the in vitro release of ketoprofen ($p<0.05$), but for propranolol hydrochloride it was not significant ($p>0.05$) This result is due to the ketoprofen solubility being more in pH 7.4 than in 0.1 N HCl. Similar results were reported

for the *in vitro* release of ketoprofen from ketoprofen microcapsules prepared by w/o/w complex emulsion technique (El-Gibaly et al. 1996), spray drying technique (Giunchedi et al. 2004) and ionotropic gelation method (Maestrelli et al. 2008).

Drug concentration, zinc acetate concentration and inner phase/ outer phase ratio had no effect on the *in vitro* release rate of propranolol hydrochloride from pectin beads ($p>0.05$) (Fig. 4).

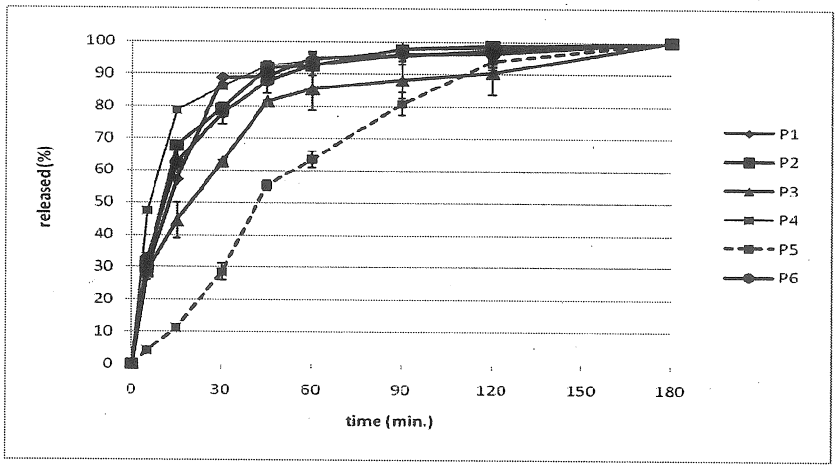

Figure 4: *In vitro* release rate of propranolol HCl from pectin beads with 1 % (P1), 2 % (P2), 3 % (P3) drug content; from pectin beads with 0.25 % (P4), 1.0 % (P5) zinc acetate concentration and from pectin beads with an inner phase/ outer phase ratio of 5:100 (P6) (n=3).

To sum up it was found out that the pH of the dissolution medium and the water solubility of the drug were the effective factors on the in vitro release rates of the drugs from pectin beads. Correlation coefficients of different mathematical models for ketoprofen and propranolol hydrochloride that are shown in Table 4 were obtained using the software (DISSOL) (Ağabeyoğlu 1991).

Table 4. Correlation coefficients of different mathematical models for ketoprofen and propranolol HCl release from pectin beads

Code	Hixson Crowell	Modified Hixson Crowell	Higuchi	Hopfenberg
K1	0.8891	0.9209	0.9027	0.8891
K2	0.8268	0.9235	0.7691	0.8268
K3	0.8726	0.8812	0.8983	0.8726
K4	0.9015	0.9448	0.9148	0.9015
K5	0.9187	0.9711	0.9089	0.9187
K6	0.9158	0.9315	0.9374	0.9158
P1	0.8550	0.9385	0.8038	0.8550
P2	0.9070	0.9629	0.8511	0.9070
P3	0.9274	0.9670	0.9440	0.9294
P4	0.9016	0.9646	0.8369	0.9016
P5	0.9937	0.9908	0.9815	0.9937
P6	0.9163	0.9759	0.8842	0.9163

Correlation coefficients of different mathematical models for ketoprofen and propranolol hydrochloride leads us to the conclusion that the Modified Hixson Crowell provides the best

correlation. Hixson and Crowell model initially proposed as a kinetic model for the dissolution of powders was modified and used for multiparticulate systems (Abdou 1989).

When the release rate data were evaluated according to the equation $Mt / M\infty = k. t^n$,

it was found out that "n" is greater than 1.0 in all cases except for one propranolol hydrochloride containing pectin bead formulation coded as P3. For P3 beads n = 0.436 and it is not fitting to Fick's diffusion law, the drug release occurs according to the diffusion and loosening of the polymer chains. All the other formulations where "n" is more than 1.0 show that the drugs were released with super case II mechanism (Peppas 1987). In this release mechanism diffusion coefficient is related to both concentration and time and drug release occurs according to the swelling of the polymer and the loosening of the polymer chains and surface erosion (Ritger and Peppas 1987).

Preparation, physical and swelling properties of pectin tablets

As ketoprofen containing pectin beads were not succesful in slowing down the release of ketoprofen, tablets were prepared with pectin, pectin beads and zinc pectinate in order to achieve controlled release. According to the physical characterization of tablets, it was found out that the friability % of T2 and T4 were lower than 1 and hardness of the tablets increased as the compaction force increased (Table 5).

Table 5. Physical characterization (weight, diameter, height, friability, hardness) and swelling properties (in phosphate buffer solution (pH 7.4) at the end of two h by weight (ρ) and by volume (q) of the tablets

Code	Weight (mg ±SD)	Diameter (mm)	Height (mm ±SD)	Friability (%)	Hardness (kp ±SD)	ρ ± SD	q ± SD
T1	505.6 ± 6.87	10.15	4.98 ± 0.26	1.34	5.77 ± 0.15	2.251 ± 0.13	2.559 ± 0.62
T2	505.8 ± 2.25	10.15	4.68 ± 0.12	0.92	9.63 ± 1.50	2.211 ± 0.11	2.332 ± 0.11
T3	470.5 ± 6.20	10.15	4.64 ± 0.10	1.62	11.50 ± 0.70	2.660 ± 1.08	6.053 ± 0.12
T4	234.6 ± 4.88	10.15	2.55 ± 0.25	0.72	15.33 ± 0.56	2.612 ± 0.48	2.985 ± 0.04
T5	241.3 ± 5.66	10.15	2.65 ± 0.09	1.59	10.40 ± 0.20	4.905 ± 0.37	5.345 ± 0.48
T6	243.8 ± 3.46	10.15	2.76 ± 0.11	1.89	5.20 ± 0.20	4.344 ± 0.70	5.034 ± 0.57

Tablets prepared with pectin beads and zinc pectinate (T3) swelled most by volume and the tablets prepared with ketoprofen and zinc pectinate (T5) swelled most by weight. Using zinc pectinate as a tablet excipient instead of pectin allows the tablets to swell more. One exception of these results is the T4 formulation prepared with ketoprofen and zinc pectinate using 2000 kg as a compaction force. Increased compaction force resulted a decrease in the swelling of tablets (Table 5).

In vitro release studies of pectin tablets

Tablet formulations prepared with zinc pectinate showed a slow release (Fig. 5). Using ketoprofen containing pectin beads (T2) instead of ketoprofen (T1) resulted in a slower release rate after 3h ($p<0.05$), although there was no difference in the first 3h ($p>0.05$) (Fig. 5). In order to slow down the release, zinc pectinate (T3) instead of pectin (T2) was added to ketoprofen containing pectin beads as an excipient. When compared with T2, no difference was observed during the first 5h ($p>0.05$), in the last 2h ketoprofen was released even more rapidly from T3 ($p<0.05$) (Fig. 5). In the study of Rubinstein A. and Radai R., 4.1 % cumulative release of the

low water soluble drug indomethacin was observed at 6 h from the plain matrix tablets prepared with calcium pectinate (Rubinstein and Radai 1995).

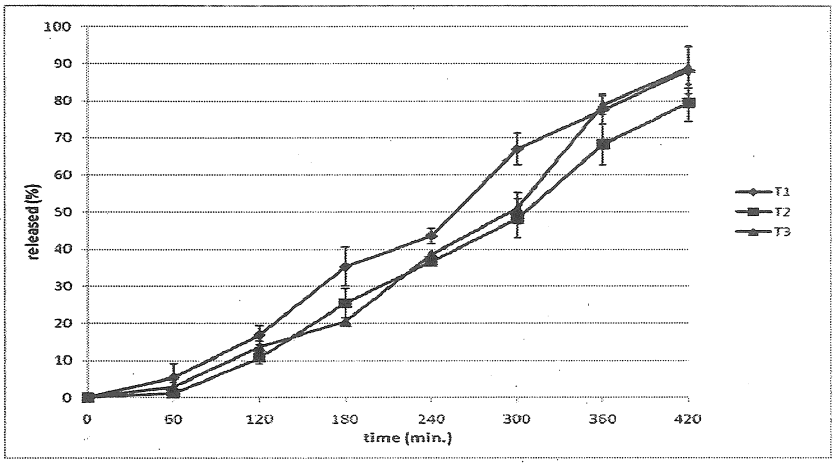

Figure 5. Ketoprofen release from tablets prepared with pectin, ketoprofen containing pectin beads and zinc pectinate (n=3)

Tablets prepared with ketoprofen and zinc pectinate using various compaction forces showed different release profiles of ketoprofen ($p<0.05$). After 7 h the total amount released from tablets compacted with 2000 kg (T4) was 48.27 ± 5.05 % , while it was 51.67 ± 0.87 % for the tablet compacted with 1500 kg (T5) and 59.07 ± 0.78 % for the tablet compacted with 1000 kg (T6) (Fig. 6).

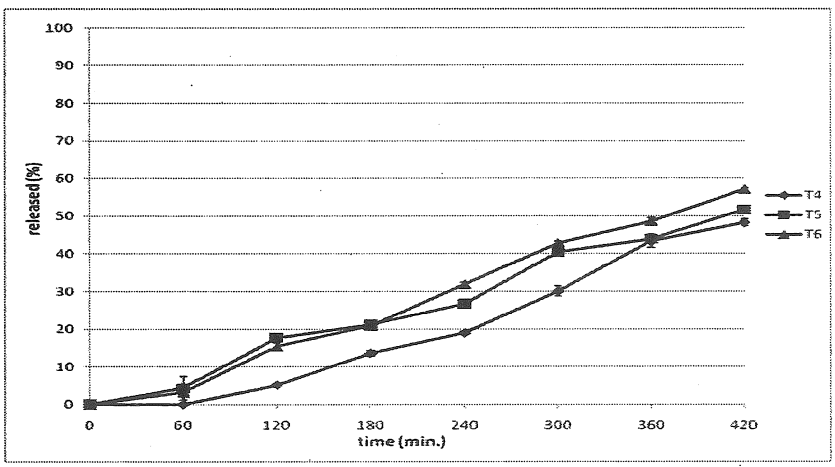

Figure 6. Ketoprofen release from tablets prepared with ketoprofen and zinc pectinate (n=3)

When ketoprofen release from the tablets prepared with pectin (T1) and with zinc pectinate (T6) as a tablet excipient were compared the first 3h there was no difference ($p>0.05$) but after 3h release from T6 was slower. At the end of the release study the total amount of ketoprofen released from T6 was 48.27±5.05 % as compared to 88.26±6.55 % from T1 ($p<0.05$) (Fig. 5,6). Using ketoprofen beads (T6) instead of pure drug (T3) in the tablets prepared with zinc pectinate, the release was better controlled after 3 h ($p<0.05$) (Fig. 5 and 6).

Correlation coefficients of different mathematical models for ketoprofen that are shown in Table 6 were obtained using the software (DISSOL) (Ağabeyoğlu, 1991). Correlation coefficients of different mathematical models for ketoprofen leads us to the conclusion that slab erosion equation provides the best correlation. When the release rate data were evaluated according to the $Mt / M\infty = k. t^n$ equation, it was found that "n" is higher than 1, indicating a "super case II" release mechanism (Table 7) (Peppas 1987).

Table 6. "r^2" values of the release kinetic equations

Code	Slab erosion (Hopfenberg)	Cylindirical erosion (Hopfenberg)
T1	0.9901	0.9815
T2	0.9919	0.9698
T3	0.9795	0.9432
T4	0.9836	0.9783
T5	0.9771	0.9788
T6	0.9904	0.9836

Table 7. Estimated values of "k" and "n" by regression of log (Mt/M∞) on log (t) of ketoprofen containing tablets

Code	r^2	n	k
T1	0.989	1.576	-2.065
T2	0.897	2.940	-5.471
T3	0.944	2.270	-3.800
T4	0.985	1.790	-2.960
T5	0.953	1.199	-1.396
T6	0.991	0.919	-0.657

Conclusion

Drug containing pectin beads were prepared by ionotropic gelation method. Propranolol hydrochloride and ketoprofen were both released totally in 3 h from the pectin beads prepared. These pectin beads can be used as a multiparticulate drug delivery system, but controlled release of the drugs could not be achieved. Ketoprofen containing tablets were prepared by using pectin, pectin beads and zinc pectinate. It was observed that zinc pectinate was successful in controlling the release of ketoprofen from tablets. About 60% of ketoprofen was released at 7 h from the tablets prepared with zinc pectinate. This study has proved the usefulness of zinc pectinate as an excipient for the controlled release tablets of ketoprofen.

Özet

Bu çalışmanın amacı kontrollü salım için pektinat jellerinden hazırlanmış oral ilaç salım sistemlerinin hazırlanması ve yüklü ilacın suda çözünürlüğünün etkisini belirlemektir. Bu amaçla suda çözünen bir ilaç olan propranolol hidroklorür ve suda çözünmeyen bir ilaç olan ketoprofen içeren pektin boncukları iyonotropik jelleşme yöntemi ile hazırlanmıştır. Farklı formülasyon parametrelerinin boncukların partikül boyutu, enkapsülasyon etkinliği ve in vitro salım profillerine olan etkileri belirlenmiştir. Ketoprofenin enkapsülasyon etkinliği (51-78 %), propranolol HCl'e (12-29 %) göre daha yüksektir. 3 saat içerisinde boncuklardan ilaçlar tamamen salınmıştır. Kontrollü salımı sağlamak amacıyla pektin, pektin boncukları ve çinko pektinat kullanılarak tabletler hazırlanmıştır. Çinko pektinat kullanılarak ketoprofenin tabletlerden salımı kontrol edilebilmiş, ketoprofenin yaklaşık % 60'ı 7 saat içerisinde salınmıştır.

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