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PREPARATION AND EVALUATION OF CONTROLLED RELEASE PROPRANOLOL HYDROCHLORIDE BEADS

E.A. Hosny, G.M. El-Mahrouk and A Al-Angary,
Department of Pharmaceutics, College of Pharmacy,
King Saud University, P.O. Box: 2457,
Riyadh 11451, Saudi Arabia.

ABSTRACT

Conventional pan coating method was utilized to prepare propranolol-HCl sustained release coated beads. Eudragit RS100 was used as release controlling materials. Overcoating of the beads with beeswax was also investigated. The beads were characterized for their particle size distribution, drug loading efficiency and their dissolution behaviour in 0.1N HCl. Most of the finished beads (72.4%) fall in the particle size range 800-1700 um. The actual drug content, calculated as opposed to the theoretical drug content were 77.6% and 74.2% of the drug for the beads having particle size range 1700-1250 um and 1250-800 um respectively. The coating level of the polymer, the particle size of the beads and overcoating with beeswax play a major role in determining the release rate of the drug from the coated beads.

INTRODUCTION

Coated beads are generally better suited than ordinary coated tablets as retarded release dosage forms

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since slight damage to the coating will not lead to immediate release of high doses intended for sustained release. The use of spherical particles as a drug vehicle for pharmaceutical delivery system in controlled release dosage forms has received significant attention(1-3).

Eudragit RS100 was used in preparation of sustained release beads using different techniques(4-6).

The objective of this study was to prepare sustained release propranolol hydrochloride beads using Eudragit RS100 in different concentrations. The effect of overcoating of the polymer coated beads with beeswax, particle size of the beads and concentration of the polymer on the dissolution profile of the beads were also investigated.

MATERIALS & METHODS

Materials

Eudragit RS100 was obtained from Rhom Pharma (GmbH, Germany), Carboxymethylcellulose sodium from BDH Chemicals Ltd. (Poole, England), Beeswax from E. Merk (Darmstadt, Germany), Propranolol hydrochloride from Kahira Pharm. & Chem Ind. Co. (Cairo, Egypt). All other ingredients and chemicals were of analytical grade while sucrose was of food grade.

Methods

1 Preparation of Propranolol Hydrochloride Beads:

Beads were prepared from a powdered mixture of 200 g sucrose, 8 g corn starch, 8 g carboxymethyl cellulose sodium and 10 g propranolol hydrochloride. This mixture was dry blended and placed in 8-inch conventional coating pan rotated at 30 rpm. The processes of wetting with water,

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dusting with 8 g talc and drying the seeds were repeated until the seeds were built to the desired size. The seeds were then screened for particle size distribution using sieve analysis (14).

2. Coating of Propranolol Hydrochloride Beads:

The drug loaded beads were coated by spraying Eudragit RS100 solution in acetone-isopropranolol mixture(1:1) in a coating pan and drying it using a stream of hot air. Different batches were prepared using different concentrations of Eudragit RS100. Half of the amount of each batch of the polymer coated beads were further treated with 5% beeswax solution in chloroform.

3. Determination of Drug Content:

One hundred mg of each of the prepared batches was grinded carefully and dissolved in 100 ml distilled water. The solutions were then filtered and their propranolol hydrochloride content was determined spectrophotometrically at 288 nm.

4. In-Vitro Dissolution Studies:

Dissolution studies were carried out on coated beads using the USP dissolution apparatus II (Paddle) at 37°C with a 50 rpm rotational speed. The dissolution medium was 500 ml of 0.1N HCl. Samples were withdrawn at 15 minute intervals using automated PU 8605/60 tablet dissolution monitoring system (Philips PU 8620, England).

RESULTS AND DISCUSSION

Table 1 shows that most of the seeds (72.4%) fall in the diameter range 800-1700 um with mean drug content 75.3±3.2%. The two particle size ranges chosen for

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TABLE 1

Physical Testing of Propranolol Hydrochloride Beads

Particle diameter range (um)	Yield of the process (%)	Drug Content (%)
>2000	0.9	87.8
2000 - 1700	4.9	85.0
1700 - 1250	25.3	77.6
1250 - 1000	26.6	76.6
1000 - 800	20.4	71.7
800 - 500	17.7	64.9
500 - 315	2.9	56.5
<315	1.4	50.2

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coating were 1700-1250 and 1250-800 um with yield value of 25.3 and 23.5%, with efficiency of loading 77.6 and 74.2%, respectively.

The results of the dissolution studies for propranolol hydrochloride beads particle size range 1.25-0.80 mm coated with 5, 10 and 15% Eudragit RS100 solution with and without beeswax overcoat are shown in Fig. 1. That of particle size range 1.70-1.25 are shown in Fig. 2. From Fig. 1 & 2, it is clear that as the concentration of Eudragit RS100 coating solution increases from 5 to 15%, the release rates decreased. These results also indicate that the drug release from beads of larger particle size is non-significantly ($P>0.5$) faster than from smaller ones. These release data indicate that Eudragit RS100 coating will not produce satisfactory delayed release beads since all of

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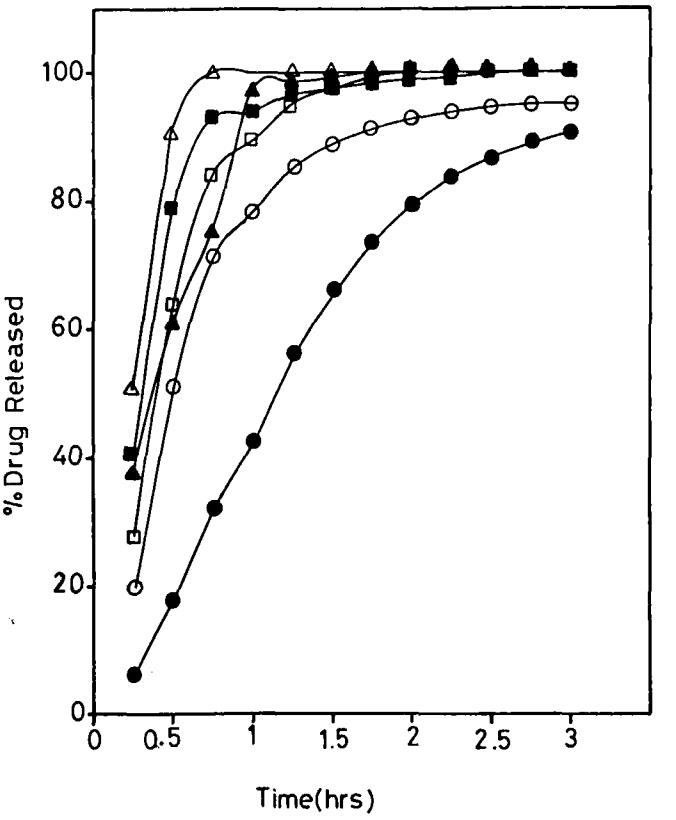

FIGURE 1

Release of propranolol hydrochloride from 1.25-0.80 mm beads coated with Eudragit RS100(W/V): 5%(△),10% (▲), 15%(□) or Eudragit RS100 with beeswax overcoat:5%(■), 10%(○), 15%(●).

the drug is released within the first 1-2 hours. Therefore, additional coating of the beads with another hydrophobic material such as beeswax was added. On addition of beeswax overcoat, the amount of drug release decreased significantly ($P<0.01$) for both particle size beads. These results are in agreement with that of previous workers (15).

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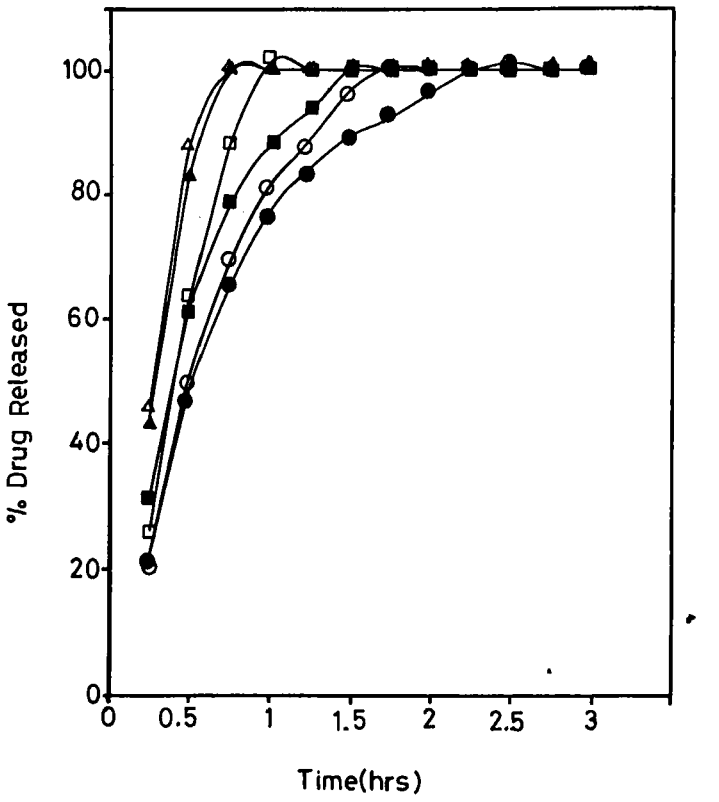

FIGURE 2

Release of propranolol hydrochloride from 1.75-1.25 mm beads coated with Eudragit RS100(W/V): 5%(△),10% (▲), 15%(□) or Eudragit RS100 with beeswax overcoat:5%(■), 10%(○), 15%(●).

The release of propranolol hydrochloride from the waxed coated beads is significantly ($P<0.05$) lower from smaller size beads (1.25-0.80) than from larger size beads (1.75-1.25). This may be due to the higher drug loading capacity of the larger particles which consequently shift the ratio between drug and polymer in favor of the drug.

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In conclusion, Eudragit RS100 with beeswax overcoat is suitable for preparation of sustained release beads of water soluble drugs.

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