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Preparation and *in vitro* Evaluation of Eudragit Microspheres Containing Cephalexin

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The aim of this study was to prepare and evaluate Eudragit microspheres containing cephalexin. Microspheres were prepared by emulsion solvent diffusion method. The prepared microspheres were analyzed for particle shape, particle size, percentage field, entrapment efficiency, stability studies and for *in vitro* release study. The size range of microspheres varies from 260.5-292.8 µm. Percentage yield and entrapment efficiency were found in the range of 72.8-79.6 % and 56.4-66.8 % w/w, respectively. The *in vitro* release studies indicated that cephalexin loaded Eudragit microspheres provide sustained release over a period of 12 h.

Key Words: Microspheres, Cephalexin, Eudragit, Emulsion solvent diffusion.

INTRODUCTION

Cephalexin is the first generation antibiotic and active against many gram-positive organisms including pencellinase reducing *S. aureus* and *S. epidermis*, *S. pneumoniae*. Susceptible gram-negative organisms include *Klebsiella pneumoniae*, *Escheria coli, Proteus mirabilis* and *Shigella*. It is commonly used antibiotic but has short biological half-life[1,2].

Microspheres are one of the multiparticulate delivery system and are prepared to obtain prolonged or controlled drug delivery, to improve bioavailability or stability and to target drug to specific sites. Microspheres can also offer advantages like limiting fluctuation within therapeutic range, reducing side effects, decreasing dosing frequency and improving patient compliance[3,4]. Methacrylate copolymers (Eudragit) have received increased attention for preparing sustained dosage forms because of their inertness, solubility in relatively non-toxic solvents and availability of resins with different properties[5,6].

The aim of this study was to prepare Eudragit microspheres containing cephalexin to achieve a controlled drug release profile suitable for peroral administration.

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EXPERIMENTAL

Cephalexin was a gift sample from Apex laboratories, Chennai. Eudragit RS 100 was obtained from Rohm pharma, Germany. Dichloromethane was obtained from Merck Ltd., Mumbai. Other substances used were all of pharmaceutical grade.

Preparation of microspheres: Microspheres containing cephalexin were prepared using the emulsion solvent diffusion technique[7,8]. Different amount of Eudragit RS 100 and cephalexin (1 g) were dissolved in a mixture of ethanol (8 mL) and dichloromethane (8 mL). This solution was dropped in to 0.2 sodium lauryl sulphate solution. The solution was stirred with a propeller type agitator at room temperature for 1 h at 500 rpm. The formed microspheres were filtered, washed with water and dried at room temperature in a desiccator.

Microspheres dried at room temperature were then weighed and yield of microspheres preparation was calculated using the formula

$$\text{Yield (\%)} = \frac{\text{Amount of microspheres obtained (g)}}{\text{Theoretical amount (g)}} \times 100$$

Encapsulation efficiency of the microspheres: Cephalexin was extracted from the microspheres after crushing with phosphate buffer pH 7.4 and absorbance was measured using UV/Vis spectrophotometer at 254 nm. Amount of cephalexin in the microspheres was estimated with the help of a standard graph.

Determination of the shape and mean particle size of microspheres: To study the shape of microspheres, the microspheres were dispersed in liquid paraffin and observed under optical microscope. The mean particle size was determined by optical microscopy. An average of about 300 particles was counted and determined[9].

Stability studies: The microspheres were placed in screw capped glass containers and stored at ambient humidity conditions, at room temperature (27 ± 2 ºC), oven temperature (40 ± 2 ºC) and in refrigerator (5-8 ºC) for a period of 60 d. The microspheres were analyzed for drug content.

***in vitro* release study:** The *in vitro* release profile of cephalexin was examined in phosphate buffer pH 7.4 using rotating paddle method at 100 rpm and 37 ± 0.5 ºC. Accurately weighed samples of microsphers equivalent to 100 mg of drug were added to dissolution medium. At preset time intervals aliquots were withdrawn and replaced by an equal volume of dissolution medium to maintain sink conditions. After suitable dilution the samples were analyzed spectrophotometrically at 254 nm.

RESULTS AND DISCUSSION

The shape of microspheres was found to be spherical by microscopic studies. The mean particle size was in the range of 260.5-292.8 μm and was not affected by the ratio of polymers for all formulation. The percentage yield and entrapment efficiency were in the range of 72.8-79.6 and 56.4-66.8 % w/w, respectively as shown in Table-1. Formulation F_2 showed highest entrapment of 66.8 % w/w and F_3 showed highest yield of 79.6 %. No appreciable difference was observed in the extent of degradation of products during 60 d in the microspheres which were stored at various temperatures. In the *in vitro* release study drug release was retarded on increasing the ratio of Eudragit RS 100 cephalexin release rate from formulation F_3 and F_4 was very slow and incomplete while from formulation F_1 it was fast as shown in the Fig. 1. Formulation F_2 drug to polymer ratio (1:2) showed 86.26 % drug release at 12 h and found the best for sustained release of cephalexin.

TABLE-1
MEAN PARTICLE SIZE, YIELD AND ENTRAPMENT EFFICIENTLY OF EUDRAGIT MICROSPHERES OF CEPHALEXIN

Formulation	Drug: polymer ratio	Mean particle* size (μm)	Percentage* yield (%)	Entrapment* efficient (w/w)
F_1	1:1	260.5	72.8	56.4
F_2	1:2	273.6	76.5	66.8
F_3	1:3	281.8	79.6	65.7
F_4	1:4	292.8	75.4	64.3

*Average of three preparation.

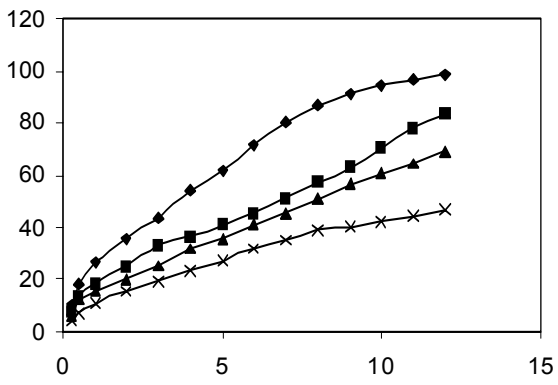

Fig. 1. *in vitro* release study of formulation of cephalexin from Eudragit microspheres in pH 7.4 buffer solution; Formulation F_1 (◆), F_2 (■), F_3 (▲) and F_4 (×)

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