Research Article Arch Pharm Sci & Res Vol 1 No 1 40-42 July 2009

Formulation and Evaluation of Biodegradable Poly (ϵ-caprolactone) Microspheres of Cefuroxime Axetil

S.Tamizharasi, Jagdish Chandra Rathi[1*], Vaishali Rathi[1]

Nandha College of Pharmacy, Perundurai Main Road, Erode-638 052, Tamil Nadu, India

[1]NRI institute of pharmaceutical sciences, 3, sajjan singh nagar, opp. patel nagar, Bhopal-462 026, Madhya Pradesh, India

Cefuroxime axetil loaded Poly(ϵ-caprolactone) microspheres were prepared by solvent evaporation technique with different drug to carrier ratio F_1 (1:3), F_2 (1:4), F_3 (1:5) and F_4 (1:6). The microspheres were characterized for particle size, scanning electron microscopy, FT-IR study, percentage yield, drug entrapment, stability studies and for *in-vitro* release kinetics. The shape of microspheres was found to be spherical by SEM. The size of microspheres was found to be ranging 47.31 ± 5.67 µm to 88.34 ± 6.89 µm. Among the four drug to carrier ratio, F_3 (1:5) showed maximum percentage yield of 75.89 ± 4.35% and F_2 (1:4) showed highest drug entrapment of 71.28 ± 1.87 % w/w. It was found that there was no interaction between drug and polymer by FT-IR study. No appreciable difference was observed in the extent of degradation of product during 60 days in the microspheres which were stored at various temperatures. In the *in-vitro* release study formulation F_2 (1:4) showed 76.36% drug release at 12 hours and found to be sustained.

Keywords : Cefuroxime axetil, Microspheres, Poly (ϵ-caprolactone), Biodegradable.

INTRODUCTION

The main objective of any drug therapy is to achieve a desire concentration of the drug in blood or tissue which is therapeutically effective and nontoxic for extended period of time, this goal can be achieved by proper design of sustain release dosage regimen[1-2]. Microspheres have been widely accepted as a mean to achieve oral and parenteral controlled release[3]. The microspheres require a polymeric substance as a coating material or carrier. A number of different substances biodegradable as well as non – biodegradable have been investigated[4] for the preparation of microspheres. Of the various biodegradable polymers used for the development of sustained release formulations, Poly(ϵ-caprolactone) has been reported to be advantageous since they are biocompatible[5-6]. Poly(ϵ-caprolactone) is aliphatic polyester polymer, suitable for controlled drug delivery due to a high permeability to many drugs and at the same time being free from toxicity[7].

Cefuroxime axetil is a broad spectrum, β-lactamase stable cephalosporin. Cefuroxime axetil has saturation kinetics that could be overcome by slow release of drug from the formulation, by incorporating Cefuroxime axetil in sustained drug delivery system[8]. The aim of this study was to prepare poly(ϵ-caprolactone) microspheres containing cefuroxime axetil to achieve a controlled drug release profile suitable for peroral administration.

* For correspondence
S.Tamizharasi
E-Mail: roshan_rathi2005@yahoo.co.in

MATERIAL AND METHOD

Cefuroxime axetil was obtained as a gift sample from Zorex Pharmaceutical Ltd, Ahmedabad, India. Poly(ϵ-caprolactone) was obtained from Fulka chemika, Sigma-Aldrich chemie, Switzerland. Dichloromethane was procured from loba Chem. Pvt. Ltd.,Mumbai. All other reagents used were of analytical grade.

Preparation of microspheres

Poly(ϵ-caprolactone) microspheres were prepared by solvent evaporation technique[9]. Drug to carrier ratio for different formulation was 1:3 (F_1), 1:4 (F_2), 1:5 (F_3) and 1:6 (F_4). Accurately weighed quantity of the poly (ϵ-caprolactone) was dissolved in 10 ml of dichloromethane than 200mg of cefuroxime axetil was dissolved in this polymer phase. This solution was poured in 100ml of liquid paraffin containing 1.3% Tween 80 and continuous stirred for 5 hours at 1100 rpm. The

TABLE 1: YIELD, DRUG ENTRAMENT AND AVERAGE PARTICLE SIZE OF CEFUROXIME AXETIL LOADED POLY(Ε-CAPROLACTONE) MICROSPHERES

Formulation Code	Drug: polymer	Percent * yield	Drug * Entrapment (% w/w)	Average * Particle Size (µm)
F1	1 : 3	66.48 ±1.56	69.67 ± 3.42	47.31 ± 5.67
F2	1 : 4	72.95 ± 2.87	71.28 ± 1.87	60.62 ± 4.78
F3	1 : 5	75.89 ± 4.35	68.98 ± 2.44	76.89 ± 5.67
F4	1 : 6	68.56 ± 2.89	67.52 ± 3.86	88.34 ± 6.89

* Average of three preparation ± S.D.

microspheres were filtered and washed three times with 50ml of n-hexane and dried at room temperature for 12 hours. Microspheres dried at room temperature were then weighed and the yield of microspheres preparation was calculated using the formula[10].

$$\text{The Amount of Microspheres Obtained (g)} = \frac{\text{Percent Yield}}{\text{The Theoretical Amount (g)}} \times 100$$

Encapsulation efficiency of the microspheres

Cefuroxime axetil was extracted from the microspheres after crushing with phosphate buffer pH 7.4 and absorbance was measured using UV/Vis spectrophotometer at 274nm. Amount of cefuroxime axetil in the microspheres was estimated with the help of a standard graph.

Particle size analysis and scanning electron microscopy (SEM)

Particle size analysis was carried out by using optical microscopy[11]. About 200 microspheres were selected randomly and their size was determined using optical microscope fitted with a standard micrometer scale. The surface morphology and the internal textures of microsphers were observed under a scanning electron microscope.

FT-IR study

FT-IR spectra of cefuroxime axetil, and Poly(ϵ-caprolactone) microsphere loaded with cefuroxime axetil were taken to check drug polymer interaction and degradation of drug during microencapsulation

Stability studies

The microspheres were placed in screw capped glass container and stored at ambient humidity conditions, at room temperatures (27±2°), oven temperature (40 ±2°) and in refrigerator (5 -8°) for a period of 60 d, the microspheres were analyzed for drug content[12].

***In Vitro* release studies**

The *in vitro* release profile of cefuroxime axetil from microspheres was examined in phosphate buffer pH 7.4 using the rotating paddle method under sink conditions. Accurately weighed samples of microspheres were added to dissolution medium kept at 37 ±0.5°C. At preset time intervals aliquots were withdrawn and replaced by an equal volume of dissolution medium to maintain constant volume. After suitable dilution the samples were analyzed spectrophotometrically at 274ηm[13].

Fig.1: Scanning electron microphotograph of cefuroxime axetil loaded Poly(ϵ-caprolactone) microspheres

RESULT AND DISCUSSION

Poly(ϵ-caprolactone) microspheres of cefuroxime axetil were prepared by solvent evaporation technique. Poly(ϵ-caprolactone) was selected as a polymer for the preparation of microspheres due to its biodegradable and biocompatible properties. The scanning electron microphotograph of microspheres is shown in fig.1, it indicated that microspheres were spherical and discrete. The particle size was analyzed by optical microcopy. The particle size differed due to variation in the composition of the formulation. The particle size gradually increased with increasing in the proportion of poly (ϵ-caprolactone). The mean particle size of the microspheres is shown in

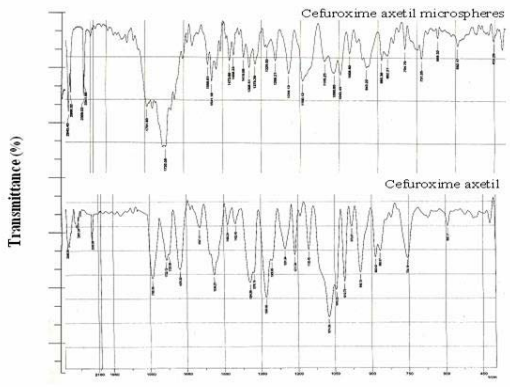

Fig.2: FT-IR spectra obtained for pure cefuroxime axetil and cefuroxime axetil loaded poly (ϵ-caprolactone) microspheres

ta ble 1. T he pe rcentage yi eld a nd e ntrapment efficiency were high for all the formulations and were in the range of 66.48 ±1.56 – 75.89 ± 4.35% and 67.52 ± 3.86 – 71.28 ± 1.87 % w/ w respectively a s shown i n t able 1. Among t he 4 drugs to carrier ra tio F_3 showed m aximum percentage yield of 75.89 ± 4.35% and F_2 showed highest drug entrapment of 71.28 ± 1.87 % w/w.

The FT-IR spectra obtained for cefuroxime axetil and cefuroxime ax etil loaded Poly(ϵ-caprolactone) microspheres (fig.2). T he r esult indicated that the characteristic peaks due to pure cefuroxime axetil have appeared in microspheres, without a ny c hange i n t heir pos ition a fter successful e ncapsulation, indicating no chemical interaction between cefuroxime axetil and Poly(ϵ-caprolactone) and the stability of dr ug dur ing microencapsulation process.

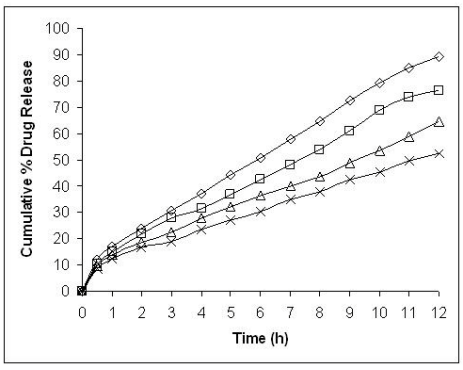

Fig.3: In vitro drug release of cefuroxime axetil from poly(ϵ-caprolactone) microspheres
In vitro dissolution profiles of cefuroxime axetil from poly(ϵ-caprolactone) microspheres formulation F1 (-♦-), F2 (-■-), F3 (-△-) and F4 (-×-)

In the stability studies, no appreciable difference was obs erved i n t he e xtent of de gradation of products du ring 60 d in the m icrospheres w hich were stored at various temperatures.

The cum ulative pe rcent r elease of cefuroxime axetil from different f ormulations is s hown i n fig 3. C efuroxime a xetil release f rom al l t he formulations was slow and sustained over 12 h. The drug release r ate w as de creasing on increasing the polymer ratio. By the end of 12 h formulation F_1, F_2, F_3 and F_4 released 89.45, 76.36, 64.74 a nd 52.34 % of l oaded dr ug respectively. T he pol ymer dr ug ratio 1: 4 (F_2) showed be tter d rug e ntrapment a nd r elease pattern. It controlled the drug release over 12h and w as f ound t o be t he m ost s uitable a mong other formulations.

ACKNOWLEDGEMENTS

The a uthor w ould l ike t o t hank Zorex Pharmaceutical L td, Ahmedabad for pr oviding gift sample of cefuroxime axetil

REFERENCES

1. Singh D., S araf S., D ixit V.K., S araf. S; Biol. Pharm. Bull. 2008; 31, 662-667.
2. Torrado J.J., Illum L., Devis S.S; Int. J. Pharm.1989; 51, 85-93.
3. Das M.K., Senapati P.C; Indian J. Pharm. Sci. 2008; 70, 77-84.
4. Vyas S.P., Khar R.K; Targeted and Controlled Drug Delivery Novel Carrier Systems, 1st ed; CBS Publishers, New Delhi, 2002, 418.
5. Sinha V.R., B ansal K., K aushik R., k umriq R., Trehan A; Int J Pharm. 2004; 278, 1-23.
6. Tamizharasi S., Rathi J.C., Rathi V; Indian J. Pharm. Sci. 2008; 70, 332-336.
7. Wang S., Guo S., Cheng L; Int. J. Pharm. 2008; 350, 130-137.
8. Patel V.F., Patel N.M; AAPSPharmSciTech. 2007; 7, E1-E7.
9. Anperiqdou A ., Geogarakis M ; Int. J. Pharm. 1995; 115, 1-8.
10. Haznedar S., Dortunc B; Int. J. Pharm. 2004; 269, 131-140.
11. Martin A., Bu stamante P., Chun A .H.C; Physical p harmacy.; 4th ed; B.I.Waverty P vt. Ltd, New Delhi, 1991, 431.
12. Shabaraya A.R., Narayanacharyulia R; Indian J. Pharm. Sci. 2003; 65, 250-252.
13. Sant V .P., P aradkar A .R., N agarsenker M .S; Indian J. Pharm. Sci. 2002; 64, 459-464.
14. Rajesh K .S., B howmik B .B., Sa B; Indian J . Pharm. Sci. 2003; 65, 526-529.
15. Higuchi T ; J. Pharm. Sci. 1963; 52, 1145–1149.