Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 5538 - 5544
Received 05 March 2021; Accepted 01 April 2021.

Microspheres Preparation of Cefaclor (Solvent Evaporation) and Evaluation

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Abstract

The aim of the present study was to develop and characterize Cefaclor microspheres containing ethyl cellulose as sustained release delivery system. Cefaclor microspheres are prepared by solvent evaporation technique and were found to be intact and spherical shape. Their particle size range was found to be 178.0 to 245.3 µm. Scanning electron microscopy showed spherical shape of microspheres. The loading efficiency showed maximum value when the concentration of Cefaclor and ethyl cellulose was 1:4. Best retardation of Cefaclor release from ethyl cellulose in all formulations were showed, but formulation CF1 is the optimized formulation and the drug release showed 94.71% up to 12 hrs and order of release was zero order, it was best fitted in Korsmeyer Peppas model.

Key words: Microspheres, ethyl cellulose, Cefaclor and solvent evaporation

1. INTRODUCTION

Microcapsule system made up of polymers have been paid considerable attention for several years in controlling and sustaining of release rate of drugs .Recently dosage forms that can precisely control the release rate and targets drugs to a specific body site have made enormous impact in the formulation and development of novel drug delivery systems. Microspheres are

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small, solid and free flowing particulate carriers containing dispersed drug particles either in solution or crystalline form that allow a sustained release[1].

The microspheres maintain functionality under physiological conditions, can incorporate drug to deliver locally at high concentration ensuring that therapeutic levels are reached at the target site while reducing the side effects by keeping systemic concentration low. It will therefore be advantageous to have means for providing an intimate contact of the drug delivery system with the absorbing membranes.

Cefaclor is a broad spectrum antibiotic belonging to the family of second generation cephalosporin. Cefaclor is well absorbed in the body, with a peak serum concentration occurring within 30-60 min, which is significantly reduced in the presence of food, with no change in the total amount of drug absorbed. Cefaclor is rapidly excreted in urine, with an approximate half – life of two hours. Because of its short half – life and large dose, Cefaclor is considered a good candidate for sustained release dosage forms.[2]

2. MATERIALS AND METHODS:

Materials

Cefaclor monohydrate was obtained as a gift sample from Sance laboratories, palai, Cochin. Ethyl cellulose was purchased from Natco laboratories.

Method

Microspheres were prepared by Solvent evaporation method[3]. Required amount of ethyl cellulose (EC) was dissolved into a 12 ml mixture of dichloromethane: ethanol in a ratio of 1:1. Then, required amount of drug was added to EC solution by stirring with a magnetic stirrer. The resultant solution was poured into 100 ml 2% polyvinyl alcohol solution, in a 250ml beaker. The resulting microspheres were filtered through Whatman's filter paper. The residue was washed 4-5 times in distilled water each. Microspheres were dried at room temperature for 24 hrs. Drug and polymer are taken in 1:1, 1:2, 1:3, 1:4 ratio and coded as CF1, CF2, CF3 and Cf4 respectively. Different formulation composition of Cefaclor microspheres will be given in **Table 1.**

3. EVALUATION OF MICROSPHERES:

Micrometric properties [4]

Carr's index: A 50 ml glass cylinder was weighed and filled with 30 ml of sample and reweighed. The opening was secured with Para-film. The cylinder was gently reversed once and the powder was carefully leveled without compacting. Bulk volume was determined after one mechanical tap on a tap density tester (Dolphin^{TM}). Tap volume was measured after 2000 taps. Each analysis was repeated twice. Values of bulk density and tap density used to Calculate Carr's index.

Particle size analysis: Particle size of different batches of microspheres was determined by optical microscopy. The projected diameter of microspheres from each batch was determined using ocular micrometer and stage micrometer equipped with optical microscope. Analysis was carried out by observing the slide containing microspheres under the microscope. Mean particle size of all formulations were determined.

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Angle of repose: The flow properties of prepared microspheres were investigated by measuring the Angle of repose by using fixed funnel method. The value of Angle of repose was calculated by using the formula. The above results were given in the Table 2.

Angle of repose (θ) = $\tan^{-1}(h/r)$

h = cone height, r = radius of circular base formed by the microspheres on the ground.

Drug Entrapment efficiency [5]

Microspheres containing of drug (100mg) were crushed and then dissolved in 100ml of phosphate buffer (pH 6.5) solution and kept for 24hrs.It is stirred for 5min and was filtered then assayed by UV-Vis spectroscopy. Entrapment efficiency is equal to ratio of actual drug content to theoretical drug content.

$$DEE = (Pc / Tc) X 100$$

Where –Pc is practical content, Tc is the theoretical content.

Percentage yield [6]

The percentage yield of microcapsules of various batches are calculated using the weight of final product after drying with respect to the initial total weight of the drug and polymer used for preparation of microcapsules and percent yields is calculated as per the formula mentioned below.

Percentage yield =Weight of microsphere recovered / Weight (drug + polymer) X 100

Scanning electron microscopy (SEM)

For morphology and surface characteristics, prepared microspheres were coated with gold in an argon atmosphere. The surface morphology of the microspheres was then studied by scanning electron microscope.

Fourier Transform Infra Red spectroscopy (FT-IR)

Drug-polymer interactions were studied by FT/IR spectroscopy .The spectra were recorded for pure drug and drug-loaded microspheres using FT-IR (Perkin Elmer, Model No.883). Samples were prepared in KBr disks (2 mg sample in 200 mg KBr). The scanning range was 400-4000 cm^{-1} and the resolution was 2 cm^{-1}.

In-vitro drug release study [7]

The In-vitro release study of the microsphere was carried out using USP basket-type dissolution test apparatus. A weighed quantity of the microspheres was introduced into the basket, the dissolution chamber was filled with 900 mL of phosphate buffer of pH 6.5 and the whole system was stirred at 100 rpm and maintained at constant temperature (37 ± 1°C). At specific time intervals, 10 mL of the sample were withdrawn and replaced by an equal volume of fresh pre-warmed dissolution medium. After suitable dilution, the samples were analyzed at 265 nm using Hitachi U-2001 UV-Visible spectrophotometer.

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Release kinetics [8]

Data obtained from in-vitro release studies were fitted to various kinetic equations to find out the mechanism of drug release from the ethyl cellulose microsphere. The kinetic models used were:

$Q_t = K_0 . t$ (zero-order equation)

$\ln Q_t = \ln Q_0 - k_1 . t$ (first-order equation)

$Q_t = K . S. t^{1/2} = k_H . t^{1/2}$ (Higuchi equation based on fickian diffusion)

Where Q_t is the amount of drug release in time t, Q_0 is the initial amount of drug in the microsphere, S is the surface area of the microcapsule and k_0 , k_1 , and k_H are rate constants of zero order, first order and Higuchi equations, respectively. In addition to these basic release models, there are several other models as well. One of them is Korsenmeyer-Peppas equation (power law)

$M_t / M_\infty = k . t^n$

where M_t is the amount of drug release at time t and M_∞ is the amount release at time $t = \infty$, thus M_t / M_∞ is the fraction of drug released at time t, k is the kinetic constant, and n is the diffusion exponent which can be used to characterize both mechanism for both solvent penetration and drug release. Determining the correlation coefficient assessed fitness of the data into various kinetic models. The rate constants for respective models were also calculated from slope.

3. RESULTS AND DISCUSSION

3.1. Micrometric properties

Micromeritic properties of all formulations were given in table no. 2. Particle diameter was in the range of 178 to 245 µm. Values of Carr's index represents its good flow ability.

3.2. Scanning Electron Microscopy (SEM): SEM of microspheres was given in **Fig.1**. It showed that the microspheres were spherical in shape.

3.3. %Yield:

As shown in the table 2 sustained release Cefaclor microspheres by solvent evaporation method were found to be in the range of 85.62% to 94.66%.

3.4. Drug entrapment efficiency:

The drug entrapment efficiency of ethyl cellulose encapsulated Cefaclor microspheres were in the range 85.20+0.86 to 92.0+31.Drug entrapment showed more with increase in concentration of the polymer. The high viscosity of the polymer solution at highest polymer proportion would be expected decrease the diffusion of the drug into the external phase which would results higher entrapment efficiency. The results were shown in T**able 2**.

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3.5. In-vitro drug release studies:

The In-vitro release of the Cefaclor microspheres was enlisted in table 4. All the batches of Cefaclor exhibited sustained release for about period of 12 hrs. The drug release for all formulations was as given in Fig. 3. As concentration of ethyl cellulose increases drug release was decreased. For formulations with drug: ethyl cellulose ratio 1:4 drug release was sustained. No significant difference was observed in the percentage drug release for same concentration of ethyl cellulose with different rpm. Model fitting data for dissolution profile was as given in table no. 3. It showed that all the formulations follows zero order. It has indicated that drug release form homogenous matrix was through diffusion. It revealed that increase in concentration of ethyl cellulose decreases the drug diffusion from microsphere. The percentage release of was found 0.980 to 0.993%.

3.6. Release kinetics:

Further the drug release was subjected for mathematical treatment to check whether the release study is following first order kinetics or zero order kinetics. The r^2 values of zero order were between 0.980 to 0.993 and first order plot between 0.742-0.881.The r^2 values indicates all these preparations followed zero order kinetics. The values of co efficient correlation were best fitted to Korsemeyer peppas and Higuchi model. The r^2 values are closer to zero order kinetics, so it follows zero order kinetics. The results of In-vitro drug release studies of Cefaclor Microspheres were shown in **Table 3.**

CONCLUSION

Microspheres were prepared by solvent evaporation method successfully. The microspheres obtained were spherical; optimization of all the parameters was required to obtain better formulation with good encapsulation efficiency. Drug release rate from microspheres were depend on the concentration of polymer used. The optimized formulation was selected depending on the percentage of drug release, order of release and mechanism of drug from microspheres. All these parameters were found in CF1 and it was selected as optimized formulation.

Table 1. Different formulation composition of Cefaclor microspheres

Batch code	Drug(mg)	EC(mg)	Ethanol(ml)	DCM(ml)	PVA(ml)
CF1	250	250	6	6	100
CF2	250	500	6	6	100
CF3	250	750	6	6	100
CF4	250	1000	6	6	100

* EC= ethyl cellulose, DCM=dichloro methane & PVA=poly vinyl alcohol

Table 2: Percentage yield, Particle size, entrapment efficiency, Angle of repose & Carrs index of Cefaclor microspheres

Batch Code	% Yield	Drug entrapment	Particle size	Angle of repose	Carrs index

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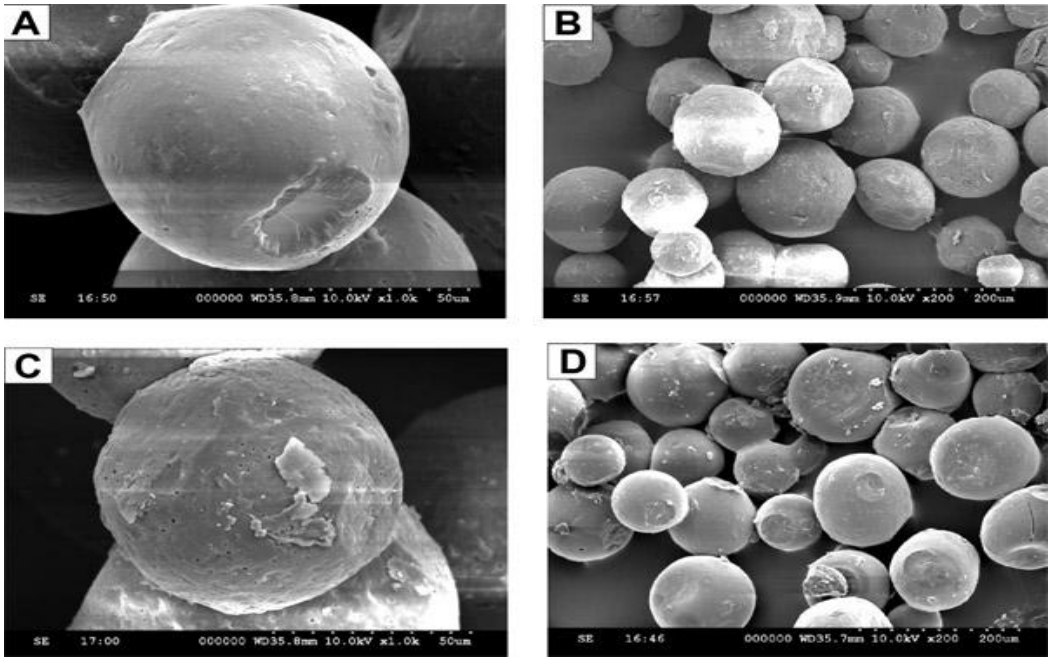
CF1	89.66	85.20±0.86	178.0±13.7	20±1	12±1
CF2	85.25	89.0±0.43	236.8±19.7	22±2	11±1
CF3	92.66	92.0±0.31	245.3±20.3	18±1	13±1
CF4	94.56	90.56±0.22	240.4±18.5	22±2	14±2

Table 3: In-vitro drug release studies of Cefaclor Microspheres

Time(hrs)	CF1	CF2	CF3	CF3
0	0	0	0	0
1	11.21	10.42	9.80	7.52
2	15.64	16.42	12.84	12.24
3	22.76	26.43	20.63	22.46
4	26.24	32.31	28.24	30.50
5	36.62	40.42	34.66	38.47
6	42.61	59.60	49.22	42.62
7	52.20	68.67	56.24	60.21
8	58.62	72.73	69.21	69.64
9	65.34	79.82	78.30	74.62
10	72.84	82.66	85.44	79.63
11	80.61	89.61	89.23	82.76
12	94.71	96.60	91.62	90.15



A = 1:1 ratio EC, B = 1:2 ratio EC. C=1:3 ratio EC, D=1:4 ratio EC.

Fig 1: SEM Photographs of Cefaclor microspheres

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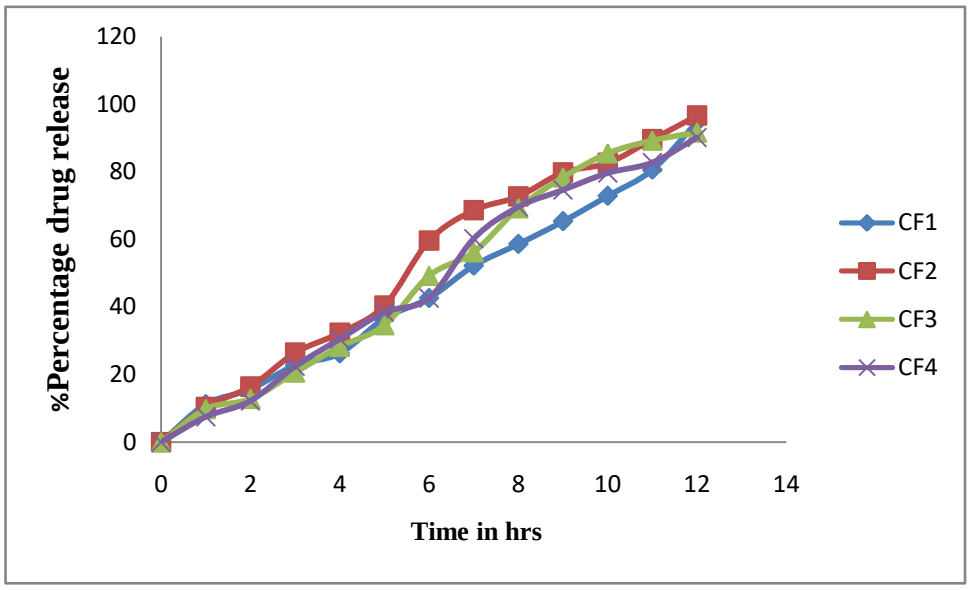

Fig 2: In-vitro drug percentage release studies of Cefaclor Microspheres

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