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Research Article

Formulation and Evaluation of Floating Drug Delivery System for Cefuroxime Axetil

ASHISH KUMAR VARMA* AND SWATANTRA KUSHWAHA

Pranvir Singh Institute of Technology, Kanpur, U.P, India. PIN-209305

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ABSTRACT

The main aim of present study was to build up multiparticulate gastro retentive drug delivery system of Cefuroxime which is used to treat a wide variety of bacterial infections. This medication is known as a cephalosporin antibiotic. It works by stopping the growth of bacteria. The gastro retentive drug delivery system can be formulated to enhance the bio-availability of Cefuroxime Axetil by retaining the system into the stomach for extended period of time. Cefuroxime Axetil is a poorly water-soluble drug (BCS Class-II drug) and its bioavailability is exceedingly low. The rate of absorption and the extent of bioavailability for such insoluble drug are restricted by the rate of dissolution in the gastrointestinal fluids. The gastroretentive drug delivery system of Cefuroxime Axetil was primed by emulsion solvent diffusion method by using ethyl cellulose, Eudragit L100, HPMC, Chitosan polymers in changeable concentration. All formulations were evaluated for percent yield, particle size, entrapment efficiency, *in vitro* buoyancy as well as *in vitro* release studies. The resultant formulations showed superior buoyancy and *in vitro* controlled release of Cefuroxime Axetil.

INTRODUCTION

Gastroretentive drug delivery system is novel drug delivery systems which has an upper hand owing to its ability of prolonged retaining ability in the stomach and thereby increase gastric residence time of drugs and also improves bioavailability of drugs. The gastroretentive microspheres alter the absorption of a drug, thus enhancing its bioavailability. They broaden dosing intervals which would permit improvement of once a day formulations and thereby boost better patient compliance outside the level of existing dosage forms by controlling over gastric residence time. When gastroretentive microspheres floats over gastric contents, the drug is released through diffusion at the preferred rate, resulting in better gastric retention with less fluctuations in plasma drug concentration [1 – 3].

Cefuroxime Axetil is a second-generation cephalosporin, proven to be relatively safe. It can be given orally as well as by parenteral administration.

Author for Correspondence:
Email: ashishfnd@gmail.com

Cefuroxime axetil is a prodrug of cefuroxime, which upon absorption undergoes immediate de-esterification to free cefuroxime. Cefuroxime axetil drug has an *in vitro* antibacterial spectrum against many Gram- positive and Gram-negative microorganisms [4, 5].

Cephalosporin antibiotic (b-lactam) stability makes it useful in treating a variety of infections caused by β-lactam-producing species of *Haemophilusinfluenzae*, *Moraxella catarrhalis* and *Staphylococcus aureus*. Chemically it is 5-Thia-1-azabicyclo [4.2.0] ct-2-ene-2-carboxylicacid, 3 [[(aminocarbonyl) oxy] methyl]-7-[[2- furanyl(methoxyimino)acetyl] amino]-8- oxo-, 1-(acetyloxy) ethylester, [6*R*-[6a7b (Z)]]. Mechanism of action of Cefuroxime is like the penicillin. It is a beta-lactam antibiotic. Through binding to specific penicillin-binding proteins situated within the bacterial cell wall, it retards the third and last stage of bacterial cell wall production. Cell lysis is then initiated by bacterial cell wall autolytic enzymes such as autolysins It is a possibility that Cefuroxime may interferes with an autolysin inhibitor [6, 7].

To prepare a drug delivery system for oral administration, the ideal route of administration,

it is necessary to optimize not only the release rate from the system but also the residence time of the system in gastrointestinal tract organ. Range of oral delivery systems has been developed including polymeric matrices, osmotic tablets, and microcapsules. Yet, very few numbers of techniques has been followed to increase the residence time of the delivery system within the GIT [8, 9].

Gastroretentive drug delivery system (GRDDS) is amongst the several approaches that have been developed in order to enhance the gastric residence time (GRT) of dosage forms. Development of floating delivery system utilizes use of many low density polymers. EC, HPMC, and Eudragit L and Chitosan are such low density polymers [10, 11].

A lot of controlled release dosage forms utilize hydrophilic polymers for slowing drug release. The mechanism of drug release is dependent on the swelling as well as dissolution practice. During early part of the discharge progression is marked by the swelling due to the conversion of the polymer from a glassy to a rubbery state due to water penetration [12, 13].

The floating microspheres constructively modify the absorption of a drug, thus enhancing its bioavailability. Cephalosporin antibiotic extend dosing intervals which allow expansion of once a day formulations and thereby increase in better patient compliance beyond the level of existing dosage forms by achieving control over gastric residence time. Cephalosporin gastroretentive microspheres or gastro-retentive drug delivery systems based on a non-effervescent approach. Since the system floats over gastric contents, the drug is released slowly at desired and predetermined rate, resulting in increased gastric retention with less fluctuation in plasma drug concentration [14 – 16].

MATERIALS AND METHODS

The drug Cefuroxime Axetil (CA) was received as a gift sample from Alkem Laboratories (Baddi, Himachal Pradesh, India). Ethyl Cellulose, Eudragit L100 and HPMC was purchased from Central drug house, New Delhi, whereas, Chitosan was received as a gift sample from Meron, Cochin, India.

Preparation of Floating Microspheres

Gastro retentive microspheres were prepared by emulsion solvent diffusion method. The drug and polymer were mixed in the solvent (ethanol/dichloride-methane, 1:1) as per the composition in Table 1. The resultant slurry was added into a 250 ml beaker containing 200 ml 0.2 % sodium lauryl sulfate (SLS)& stirred at 750 rpm with a mechanical stirrer for 1 hour at room temperature. The Gastro retentive micro-spheres were collected by decantation, washed with n-hexane and dried overnight in an oven at 40 ± 2°C, and reserved in a desiccators containing calcium chloride as desiccant.

Table 1: Composition of batches of floating micro spheres of Cefuroxime Axetil

Batch	Cefuroxime Axetil (mg)	Ethyl Cellulose (mg)	HPMC	Eudragit L100	Chitosan
F-1	100	200	-	-	-
F-2	100	400	-	-	-
F-3	100	800	-	-	-
F-4	100	100	100	-	-
F-5	100	200	200	-	-
F-6	100	100	400	-	200
F-7	100	-	-	100	100
F-8	100	-	-	200	200
F-9	100	-	-	400	200

In-Vitro Evaluation of Floating Microspheres of Cefuroxime Axetil Determination of Percent Yield

All dried microspheres were collected as well as weighed accurately. Then the percentage yield was calculated.

Determination of Entrapment Efficiency

The drug content of Cefuroxime Axetil loaded microspheres was calculated by dispersing 100 mg microspheres in 10 ml of methanol, which was stirred with a magnetic bead for 8 hours to extract the drug. The samples were diluted and analyzed by UV photometer at 281 nm and the percentage drug entrapment was determined.

Particle Size Analysis

Particle size of prepared microspheres was determined by using an optical microscope, and the mean particle size was calculated by measuring 100 particles with the help of a calibrated ocular micrometer.

Floating Behaviour (Buoyancy)

50 mg of the microspheres were kept in 100 ml of simulated gastric fluid (pH 1.2) containing 0.02% w/v tween 20. The resultant mixture was stirred at 100 rpm on a magnetic stirrer. Following 4 h, the layer of buoyant microspheres

was pipette and separated by filtration. Particles in the submerged particulate layer were also isolate by filtration. Particles of both types were dried in desiccators. Both the parts of cephalosporin microspheres were weighed and buoyancy was calculated by the weight ratio of floating particles to the sum of floating and sinking particles.

Characterization of Microspheres by Scanning Electron Microscopy (SEM)

The surface topography and internal textures of the microspheres was observed by scanning electron microscopy.

***In- Vitro* Dissolution Studies in 0.1N HCl**

The *in- vitro* dissolution studies were performed by using USP XXI V paddle type dissolution apparatus. Weighed amount of drug loaded floating microspheres was added into 900 ml 0.1N HCl, used as a dissolution medium, maintained at 37±0.5°C at a rotation speed of 100 rpm. The samples were withdrawn at predetermined time intervals. First two samples were withdrawn at 30 minutes interval and next 11 samples were withdrawn at 1 hour interval. The samples were checked spectrophotometrically at 281 nm to calculate the concentration of drug present.

RESULTS AND DISCUSSION

Percent Yield

All batches find a percentage yield of greater than 70%, whereas five batches displayed a yield of more than 80%. Percentage yield is observed to be higher with formulation of high amount of polymer. Results revealed that percentage yield increases with increase in the amount of polymer.

Entrapment Efficiency

All batches find percent entrapment more than 50 % and it is found that entrapment of drug increases with an increase in the amount of the polymer. Formulation F-6 shows maximum entrapment, whereas formulation F-7 shows minimum entrapment of the Cefuroxime Axetil.

Particle Size Analysis

Results showed that particle size of prepared microspheres was in the range of 130±20µm to 226±25µm. It was concluded that with increase in polymer concentration.

Study of Scanning Electron Microscopy (SEM)

Results showed that ethyl cellulose microspheres of Cefuroxime Axetil were predominantly spherical in shape with smooth surface. The porous nature of cephalosporin microspheres and characteristics internal structure of the microspheres, a hollow cavity inside enclosed with the rigid shell assembled with drug and polymer was clearly evident. Ethyl cellulose, Chitosan and HPMC based floating microspheres were found to be much more elongated in nature than microspheres prepared by using Chitosan and Eudragit L100. The porous nature and cavity formed in the microspheres would dictate the floating behaviour of microspheres of Cefuroxime Axetil as shown in Fig. 1.

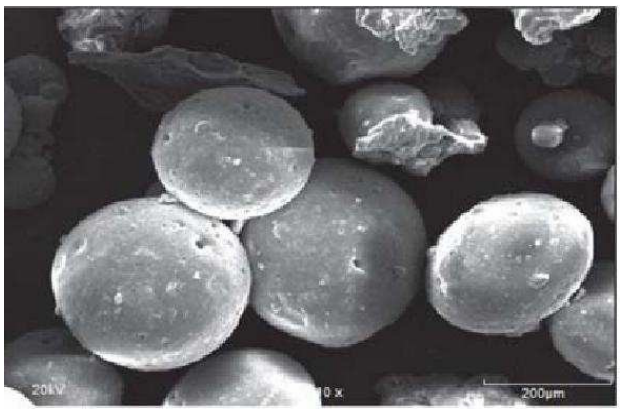

Figure 1: SEM photomicrographs of batch F-6

Floating Ability (Percent Buoyancy)

The formulated batches of floating microspheres of Cefuroxime Axetil showed average buoyancy more than 53%.Amongst the batches of prepared microspheres, batch F-6 showed highest buoyancy (72.53%). Further it was observed that in case of ethyl cellulose, Chitosan and HPMC based microspheres, buoyancy was high, as compared with only ethyl cellulose based microspheres (Table 2).

Table 2: Characterization of various batches of floating microspheres of Cefuroxime Axetil

F. code	Production yield %	Entrapment efficiency %	Buoyancy %	Mean particle size (µm)
F-1	82.8	54.12	65.75	10
F-2	84.6	66.42	62.54	17
F-3	85.9	73.12	69.45	24
F-4	77.5	63.25	60.23	30
F-5	80.8	73.67	70.22	35
F-6	82.6	80.45	72.53	41
F-7	72.3	50.64	53.86	47
F-8	75.7	60.76	55.14	53
F-9	77.6	77.61	58.65	60

Table 3: Dissolution profiles of batches of Floating microspheres of Cefuroxime Axetil

Time (mins)	F-1 (CPR)	F-2 (CPR)	F-3 (CPR)	F-4 (CPR)	F-5 (CPR)	F-6 (CPR)	F-7 (CPR)	F-8 (CPR)	F-9 (CPR)
0	0	0	0	0	0	0	0	0	0
30	14.57	11.75	10.97	10.34	7.65	6.89	15.78	14.12	11.78
60	21.50	19.20	16.76	15.67	13.45	11.67	22.54	20.67	18.98
120	29.12	27.12	24.22	25.67	21.34	17.54	31.34	29.67	26.56
180	35.16	33.47	31.97	30.77	26.55	24.65	37.16	34.78	32.76
240	41.15	39.21	37.67	36.88	32.56	30.76	43.67	41.34	38.65
300	48.30	44.12	41.34	43.45	39.56	34.67	49.56	47.45	44.87
360	54.12	48.24	46.34	50.34	44.67	39.76	55.76	53.34	50.78
420	59.45	54.32	52.34	54.76	50.78	44.74	61.56	59.65	56.45
480	64.23	61.72	59.67	60.87	55.78	50.45	65.35	63.55	60.45
540	71.22	65.43	63.23	63.45	60.67	56.34	73.23	71.45	63.78
600	75.23	69.78	67.91	67.34	65.87	60.23	76.56	73.67	67.63
660	80.23	74.26	70.67	70.67	70.65	65.45	82.56	79.67	70.45
720	86.43	78.23	74.23	74.53	75.56	70.12	89.67	82.76	74.87

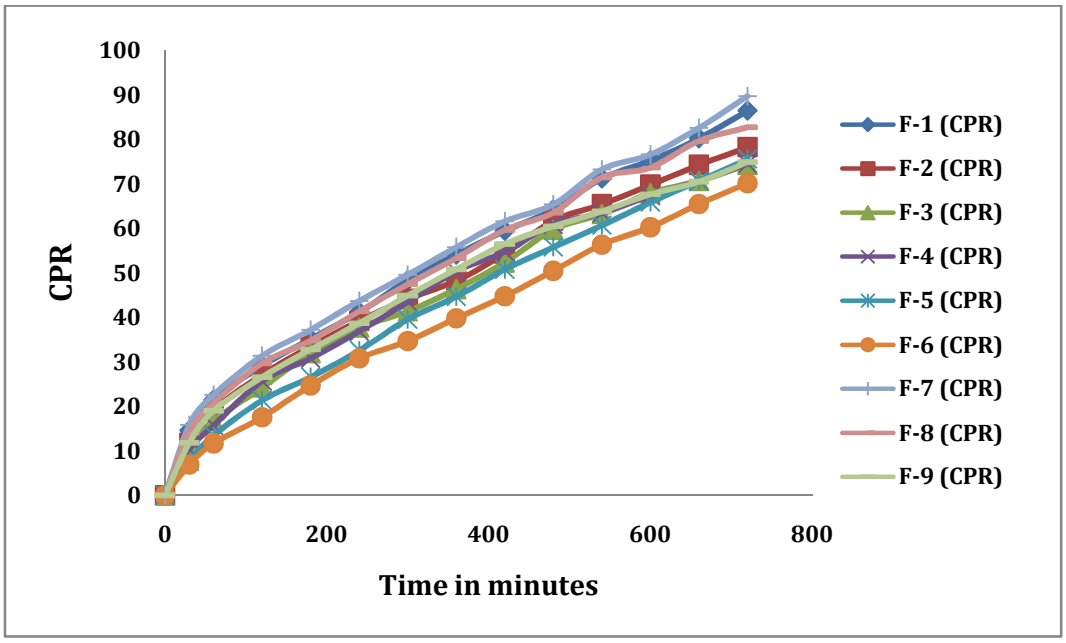

Figure 2: Dissolution profiles of batches F1 to F9

CONCLUSION

Cefuroxime Axetil floating microspheres were effectively developed by means of emulsion solvent diffusion method. The microspheres had good yield and showed high, drug entrapment efficiency. The flow properties of cephalosporin microspheres were within the acceptable range and consequently would be effortlessly packed into capsules. Release properties were satisfactory and the formulations hold promise for further development into drug delivery systems for the oral administration of Cefuroxime Axetil.

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