Research Article

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FABRICATION AND *IN-VITRO* EVALUATION OF INTRAGASTRIC DRUG DELIVERY SYSTEM OF CEFUROXIME AXETIL

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ABSTRACT

The aim of the present work was to design and develop hydrodynamically balanced tablets of Cefuroxime axetil to enhance the bioavailability of the drug. Cefuroxime axetil is classified as a second-generation cephalosporin antibiotic and β-lactum antibiotics based on spectrum of activity. Floating tablets were prepared by the wet granulation technique by using carbopol as retarding agent and sodium bicarbonate as gas generating agent. The effects of gel forming agent carbopol on drug release profile and floating properties were investigated. It has been observed that release characteristics were decreased with increase in polymer concentration due to increased tortuosity and length of drug diffusion path. Formulations are evaluated for *in-vitro* buoyancy and drug release profile using dissolution apparatus using 0.1N HCl as a medium. The results showed that floating tablets of Cefuroxime axetil containing carbopol 90mg/tablet controlled the drug release up to 12hrs and improved bioavailability.

Keywords: *In-vitro* buoyancy, retarding agent, gel forming agent, solubility, Bioavailability, Drug release.

1. INTRODUCTION

Rapid gastrointestinal transit could result in incomplete drug release from the dosage form above the absorption region, leading to diminished efficacy of the administered dose. Cefuroxime axetil is widely used in the therapy; it is a semi-synthetic cephalosporin obtained from the 7-cephalosporanic acid nucleus of cephalosporin. In humans, gastrointestinal absorption of cefuroxime is negligible[1] whereas the acetoxyethyl ester of cefuroxime (Cefuroxime axetil), an oral prodrug[2] shows a bioavailability of 30 to 40% when taken on fasting and 50 to 60% when taken after food [3-6]. The low bioavailability[7] and short biological half life (1.5 hours) of Cefuroxime axetil following oral administration favours development of a gastro retentive formulation. Therefore different approaches have been proposed to retain the dosage form in the stomach; one of the most feasible approaches for achieving prolonged and predictable drug delivery profile in the GI tract is floating system[8]. Hydrodynamically balanced systems can remain in the gastric region for several hours and hence significantly prolong the gastric residence time[9] of drugs. Prolonged gastric retention improves bioavailability, reduces drug waste, and improves solubility for drugs that are less soluble in a high pH environment of small intestine. Cefuroxime axetil is the commercially available second generation cephalosporin[10] which is active against a wide range of Gram-positive and Gram-negative organisms[11] and is resistant to most β-lactamases.

2. MATERIALS AND METHODS

Cefuroxime axetil was gift sample from Lupin pharma, India. Carbopol was purchased from Merck (Mumbai, India). All other chemicals used were of analytical grade and

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were procured from S.D. Fine Chemicals, Mumbai, India.

3. EXPERIMENTAL:

Preparation of floating tablets

Each floating tablets containing 200mg Cefuroxime axetil were prepared by a conventional wet granulation method using various concentration of carbopol and sodium bicarbonate. The required quantity of drug and polymers were mixed thoroughly. The wet mass was prepared by adding required quantity of starch mucilage as a wetting agent. The wet mass was passed through a #16 sieve number and the wet granules were dried in hot air oven for 30 min at 50°C. The dried granules mixed with tartaric acid, magnesium stearate and talc. The prepared blend was compressed by rotary tablet press (CADMAC, Hyderabad, India) using 8mm flat face punch into tablets. Composition of floating tablets were formulated with polymers is shown in table 1. Prior to compression, granules were evaluated for their flow property, angle of repose and compressibility characteristics such as bulk density, tapped density, Carr's Index, Hausner's ratio and the values were shown in the table 2.

Standard curve of Cefuroxime axetil

100 mg of Cefuroxime axetil was accurately weighed and transferred into 100 ml volumetric flask. It was dissolved and diluted to volume with 0.1N HCl to give stock solution containing 1000µg/ml. The absorbance of solution was measured against 0.1N HCl as blank at 280 nm using UV-Visible spectrophotometer. Coefficient of correlation was found to be 0.998 in 0.1N HCl shown in Fig 1.

Physicochemical evaluation of floating tablets

The selected batches made in bulk were subjected to evaluations as per Indian pharmacopoeia. Physical parameters of the prepared formulations were shown in table 3.

- Shape of the tablet
- Weight variation
- Hardness
- Thickness
- Friability
- Disintegration studies
- *In-vitro* buoyancy study
- *In-vitro* dissolution studies

Shape of the tablet

Macroscopic examination of tablets from F1 to F5 was found to be circular shape with no cracks.

Weight variation

Twenty tablets were selected at random, weighed and the average weight was calculated. Not more than two of the individual weights should deviate from the average weight by more than 5%.

Friability

For each formulation, preweighed tablet samples (20 tablets) were placed on the friabilator, which is then operated for 100 revolutions. The tablets were then dedusted and reweighed. Conventional compressed tablets that loose <0.5–1.0% of their weight are considered acceptable.

$$\%friability = \frac{initial\ wt - final\ wt}{initial\ wt} \times 100$$

Hardness

Tablet hardness of each formulation was determined using a Monsanto hardness tester. Results were calculated from the average results of six tablets.

Thickness

Tablet thickness is determined using Vernier calipers. Six tablets were evaluated to determine the average thickness.

***In-vitro* buoyancy study**

The In-vitro buoyancy study[12-13] was characterized by floating lag time and total floating time. The test was performed using a USP type II paddle apparatus using 900 ml of 0.1 N HCl at paddle rotation of 50 rpm at 37 ± 0.5 ^{0}C. The time required for the tablet to rise to the surface of the dissolution medium and the duration of time the tablet constantly floated on the dissolution medium were noted as floating lag time and total floating time respectively.

***In-vitro* dissolution study**

The dissolution study[14] was carried out using USP II (paddle method) apparatus in 900 ml of 0.1 N HCl (pH 1.2) for 12 hours. The temperature of the dissolution medium was kept at 37±0.5^{o}C and the paddle was set at 100 rpm. 10 ml of sample solution was withdrawn at specified interval of time and filtered through Whatman filter paper. The sample was replaced

with fresh dissolution medium (pH 1.2). The samples were diluted to a suitable concentration with 0.1 N HCl. The absorbances of the withdrawn samples were measured at λmax 280 nm using UV-Visible double beam spectrophotometer.

Swelling index

The swelling properties of carbopol matrices containing drug were determined by placing the tablet matrices in the dissolution test apparatus, in 900 ml of distilled water at 37 ± 0.5 ^{0}C paddle rotated at 50 rpm. The tablets were removed periodically from dissolution medium. After draining free from water by blotting paper, these were measured for weight gain. The swelling index[15] was calculated using following formula and the results of swelling index for all the formulations are shown in table 6 and percentage swelling index is shown in Fig 3.

$$\text{Swelling index} = \frac{W1 - W0}{W0} \times 100$$

W1=Weight of dry tablet, W0=Weight of swollen tablet

4. RESULTS AND DISCUSSION

Hydrodynamically balanced floating tablets of Cefuroxime axetil were prepared and evaluated to increase its local action & bioavailability. In the present study formulations with variable concentrations of carbopol and evaluated for physicochemical parameters & *in vitro* buoyancy studies.

***In-vitro* buoyancy studies:**

The tablets were placed in a 100 ml glass beaker containing 0.1 N HCl. Floating Lag Time: The time required for the tablet to rise to the surface of the medium and float was determined as floating lag time.

Floating Duration Time: The time for which the tablet remained floating on the surface of medium was determined as floating duration time.

From the results it can be concluded that the batch F5 showed good buoyancy lag time & total floating time, the values were shown in table 4.

***In-vitro* drug release studies:**

The dissolution study was carried out using USP II (paddle method) apparatus in 900 ml of 0.1 N HCl (pH 1.2) for 12 hours. 10 ml of sample solution was withdrawn at specified interval of time and filtered through Whatman filter paper. And the sample was replaced with fresh dissolution medium. The sample diluted to a suitable concentration with 0.1 N HCl. The absorbance of the withdrawn samples was measured at λmax 280 nm using a UV visible double beam spectrophotometer. The results of in-vitro drug release profiles obtained for all the formulations are shown in table 5 and percentage drug release is shown in Fig 2.

It was concluded that the formulation F5 containing carbopol in the concentration of 90mg/tablet controlled the drug release to 12hrs (98.91) compared to other formulations. As the concentration of carbopol increased the drug release from the formulation decreased in a controlled manner which is supported from the swelling index values. % Swelling decreased with polymer concentration because high concentration of the polymer restricts its movement.

From the above observation it was concluded that formulation F5 was the best formulation among all other formulations as it showed controlled release of drug from tablet formulations.

The drug release rate decreased in the rank order;

F5 > F4 > F3 > F2 > F1

This can probably be attributed to the different diffusion and swelling behaviour of the polymer. It was stated that a faster and greater drug release was expected for reasons with the evolution of gas, the matrix would become more relaxed allowing water penetration and diffusion of drug might be easier.

5. CONCLUSION:

The present investigation deals that formulation and evaluation of effervescent based floating tablet of Cefuroxime axetil by using carbopol as release retarding material. From the results, it could be concluded that for the development of controlled release dosage form of Cefuroxime axetil with carbopol is useful which impart hydrophilic environment and wettability to drug which leads to more uniform drug release with increased solubility.

It was concluded that the formulation F5 shows controlled pattern of drug release up to 12hr. Developed floating tablets possessed the required physico-chemical parameters such as hardness, friability, weight variation, drug content, swelling index and floating properties. All the developed floating tablets floated up to 12 hrs.

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Table 1: Formulation of floating tablets of Cefuroxime axetil

Ingredients	Quantity in mg/tablet				
	F-1	F-2	F-3	F-4	F-5
Cefuroxime axetil	200	200	200	200	200
Carbopol	50	60	70	80	90
$NaHCO_3$	110	100	90	80	70
Tartaric acid	30	30	30	30	30
Magnesium Stearate	5	5	5	5	5
Talc	5	5	5	5	5
Starch mucilage	q.s	q.s	q.s	q.s	q.s
Total	400	400	400	400	400

Table 2: [Flow properties]
Precompression parameter of floating tablets of Cefuroxime axetil

S. No	Parameters	F-1	F-2	F-3	F-4	F-5
1	Angle of repose (°)	28.8±0.55	30.5±1.08	27.4±1.21	29.98±0.85	26.4±055
2	Bulk density	0.446±0.03	0.491±0.09	0.394±0.005	0.511±0.01	0.418±0.07
3	Tapped density	0.540±0.04	0.597±0.07	0.486±0.003	0.598±0.06	0.501±0.09
4	Carr's index	17.40	17.75	18.93	14.54	16.56
5	Hausner's ratio	1.22±0.0072	1.21±0.005	1.23±0.003	1.17±0.002	1.19±0.008

Table 3: Physical parameters of floating tablets of Cefuroxime axetil

S. No	Parameter	F1	F2	F3	F4	F5
1	Hardness * (kg/cm^2)	4.7±	5.0±	4.6±	4.9±	4.7±
2	Friability*(%)	0.1129±	0.1307±	0.1605±	0.2103±	0.1901±
3	Weight variation*	400.54±0.02	401.65±0.05	400.91±0.03	399.59±0.07	400.5±0.01
4	Thickness*(mm)	2.13±0.01	2.10±0.02	2.14±0.03	2.11±0.04	2.13±0.03

*All values are expressed as mean ± SD, (n=3)

Table 4: *In-vitro* buoyancy study of floating tablets of Cefuroxime axetil

S. No	Batch Code	Floating lag time(Sec.)	Floating time(hrs)
1	F-1	30	>12
2	F-2	40	>12
3	F-3	35	>12
4	F-4	32	>12
5	F-5	28	>12

Table 5: The results of *in-vitro* drug release profiles obtained for all the formulations

S. No	Time (hr)	**% of amount of drug release** ± S.D. (n=3)				
		F1	**F2**	**F3**	**F4**	**F5**
1	1	15.41	13.23	11.21	9.86	6.34
2	2	27.67	25.77	22.87	19.94	14.67
3	3	41.42	38.26	34.67	31.26	25.87
4	4	56.98	49.46	41.86	38.98	31.90
5	5	77.33	60.34	52.28	49.35	39.49
6	6	81.01	74.29	65.69	61.63	48.88
7	7	89.92	82.55	79.11	74.59	51.26
8	8	99.93	98.43	86.88	81.02	68.84
9	9	-	-	94.56	89.42	76.14
10	10	-	-	100.01	94.78	83.91
11	11	-	-	-	99.49	91.27
12	12	-	-	-	-	98.91

Table 6: The results of % Swelling index of formulations F1 to F5

Time(hrs)	% Swelling index				
	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	73.2	69.32	68.50	67.74	54.53
2	102.22	89.64	86.18	86.63	77.80
3	124.85	118.40	106.40	102.30	92.89
4	147.40	124.79	124.90	113.87	100.78
5	151.11	134.33	132.34	122.56	107.89
6	167.48	150.00	141.76	133.74	115.00
7	176.77	154.84	143.60	137.36	122.45
8	179.43	160.53	148.78	145.68	121.67
9	182.40	172.25	153.89	154.84	116.88
10	186.90	170.15	151.70	151.63	114.78
11	189.80	166.39	152.00	148.58	104.94
12	195.9	161.84	142.15	136.63	103.67

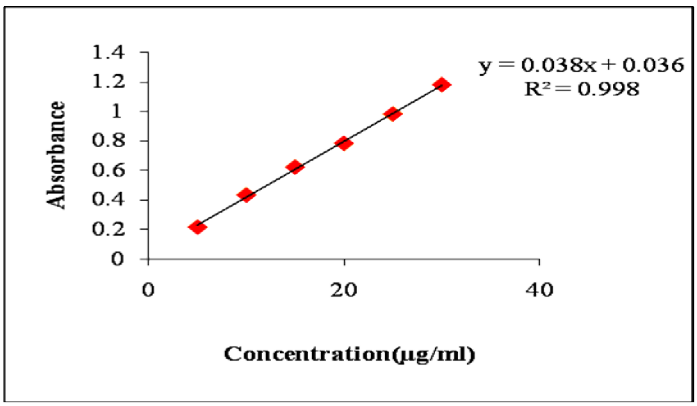

Fig: 1 Standard Curve of Cefuroxime Axetil

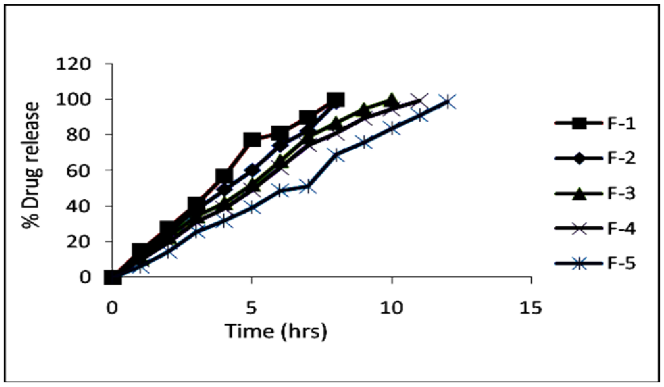

Fig 2: Percentage drug release of formulations F_1, F_2, F_3, F_4 and F_5

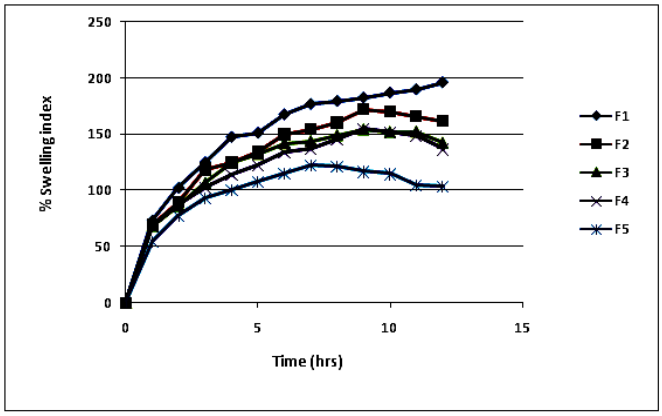

Fig 3: Relationship between swelling index and time of F1 to F5

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