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Formulation and Evaluation of Dicloxacillin Sodium Floating Tablets.

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Research Article

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ABSTRACT

The purpose of this research work was to develop gastroretentive drug delivery system of Dicloxacillin sodium. Floating tablets were prepared by wet granulation method using gas generating agents such as sodium bicarbonate and citric acid anhydrous, like Hydroxypropyl methylcellulose (HPMC K100M), Xanthan gum, Sodiumcarboxy methylcellulose (NaCMC) and Microcrystalline cellulose (MCC). Dicloxacillin sodium floating tablets were prepared by wet granulation method were found to be good without chipping, capping and sticking. The drug content was uniform in all the tablet formulations indicating uniform distribution of drug within the matrices. All the prepared batches showed satisfactory floating lag time and total floating time found to be more than 12 h. Formulation F14 showed desired drug release selected as a best formulation and subjected to stability studies for 3 months showed that formulation is intact without interaction. Finally optimized formulation F14 complying with all properties of floating tablets and found to be satisfactory.

INTRODUCTION

The oral route is the most preferred route of administration because of its patient compliance. Now a day's controlled systems are designed offering a number of advantages including improvement in reduced dosing frequency, therapeutic efficacy, safety and patient compliance. Gastric retention time is one of the important factors, which adversely affect the performance of these drugs when administered simply by an oral controlled drug delivery system [1].

Dicloxacillin sodium is a narrow-spectrum beta-lactam antibiotic of the penicillin class and having more acid-stable than many other penicillins and can be given orally. It is used for the treatment of pneumonia, bone, ear, skin and urinary tract infections caused by susceptible Gram-positive bacteria. It is active against β-lactamase producing organisms such as *Staphylococcus aureus*, which would otherwise be resistant to most penicillins. β-lactam antibiotics were mainly active only against Gram-positive bacteria, these will work by inhibiting cell wall biosynthesis in the bacterial organism [1].

The absorption of Dicloxacillin sodium after oral administration is rapid but incomplete. Peak blood levels are achieved in 1 - 1.5 h. It indicates variable absorption from the gastrointestinal tract. Dicloxacillin sodium has a bioavailability of 60-80 % and half-life of less than 1 h. Thus, this necessitates frequent administration of Dicloxacillin sodium. So, to overcome these problems (absorption, half-life of the drug and to reduce the dosing frequency) gastro retentive floating drug delivery system of Dicloxacillin sodium were prepared provide satisfactory drug release, maintain a constant blood levels and prolong the duration of action.

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MATERIALS AND METHODS

Formulation of Dicloxacillin sodium floating tablets

The floating tablets were prepared by wet granulation method [2], using different hydrophilic and hydrophobic polymers HPMC K100M, Xanthan gum, Na CMC and MCC different ratios of polymers is prepared as mention in Table 1. The ingredients were weighed accurately and mixed thoroughly. The granulations were done with starch paste (22 mesh). The granules were dried in conventional hot air oven at 45 °C. Drying of granules was stopped when the sample taken from the oven reached a loss on drying (LOD) value of 1 – 3%, as measured by a moisture balance at 105°C. The dried granules were sized through 40 / 60 mesh, lubricated with magnesium sterate (1% w / w) and purified talc (1% w / w) and then compressed. The tablets were prepared by using a rotary tablet compression machine (12mm diameter, Riddhi 10 stn mini tablet press RDB-10, Rimek, Ahmedabad, India).

Table 1: Composition of different formulations of Dicloxacillin sodium floating tablets

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
Dicloxacillin sod. (mg)	280	280	280	280	280	280	280	280	280	280	280	280	280	280	280
HPMC K100M (mg)	200	240	290	-	-	-	-	-	-	-	-	-	150	150	150
Xanthan gum (mg)	-	-	-	200	240	290	-	-	-	-	-	-	100	-	-
Na CMC (mg)	-	-	-	-	-	-	200	240	290	-	-	-	-	100	-
MCC (mg)	-	-	-	-	-	-	-	-	-	200	240	290	-	-	100
Lactose (mg)	100	60	10	100	60	10	100	60	10	100	60	10	50	50	50
Sod. Bicarbonate (mg)	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25	28.25
Citric acid (mg)	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19
Starch (1.5%) (mg)	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75	9.75
Mag. Sterate (1%) (mg)	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5
Talc (1%) (mg)	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5	6.5

Evaluations

Pre-compression parameters

Bulk density (D_b)

Bulk density is a ratio of mass of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles. Accurately weighed quantity of powder was carefully poured in to graduated 100 mL measuring cylinder through large funnel and volume was measured, which is called initial bulk volume. It is expressed in gm / mL and is given by [3]

$$\text{Bulk density } (D_b) = \frac{\text{Mass of powder (M)}}{\text{Bulk volume of powder } (V_0)}$$

Tapped density (D_t)

Accurately weighed quantity of powder was carefully poured in to graduated 100 mL measuring cylinder through large funnel. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. It is expressed in gm/mL and is given by [3]

$$\text{Tapped density } (D_t) = \frac{\text{Mass of powder (M)}}{\text{Tapped volume of powder } (V_t)}$$

Angle of repose (θ)

It is defined as the maximum angle possible between the surface of the pile of the powder and the horizontal plane. Fixed funnel method was used, a funnel was fixed with its tip at a given height 'h' above a flat horizontal surface to which a graph paper was placed. Powder was carefully poured through a funnel till the apex of the conical pile just touches the tip of the funnel. The angle of repose was then calculated using following equation[3].

$$\tan \theta = \frac{h}{r}$$

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$$\theta = \tan^{-1}\left(\frac{h}{r}\right)$$

Where, θ= angle of repose
h= height of the pile and
r= radius of the powder cone

Carr's consolidation index (I)

Carr's index is an indication of the compressibility of a powder. It is expressed in percentage and is given by [4]

$$\%\ \text{Compressibility index (I)} = \frac{\text{Tapped density } (D_t) - \text{Bulk density } (D_b)}{\text{Tapped density } (D_t)} \times 100$$

Hausner ratio

A small index like percentage compressibility index has been defined by Hausner. Values less than <1.25 indicates good flow, where as greater than 1.25 indicates poor flow. Added glidant normally improves flow of the material under study. Hausener's ratio can be calculated by [4],

$$\text{Hausner's ratio} = \frac{\text{Tapped density } (D_t)}{\text{Bulk density } (D_b)}$$

Post-compressional parameters

Thickness and diameter

Thickness and diameter were tested in 5 different randomly selected individual tablets from each batch. The thickness and diameter of tablets were measured by digital vernier calipers [5].

Hardness

Hardness (diametric crushing strength) is a force required to break a tablet cross the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The hardness was tested by using Monsanto hardness tester. The averages of five determinations were taken[5].

Weight variation

Weight variations were tested in 10 different randomly selected individual tablets from each batch. Weight variations were measured by digital electronic balance (Citizen D 1262, India). The averages of ten determinations were taken; weight variation can be calculated by [5],

$$PD = \frac{(W_{avg}) - (W_{initial})}{(W_{avg})} \times 100$$

Where PD= Percentage deviation,
W_{avg}= Average weight of tablet,
$W_{initial}$= Individual weight of tablet.

Friability

Friability is the loss of weight of tablet in the container/package, due to removal of fine particles from the surface. This in process quality control test is performed to ensure the ability of tablets to withstand the shocks during processing, handling, transportation, and shipment. Permitted friability limit is 1.0 %. Roche friabilator (Ketan, Mumbai) was used to measure the friability of the tablets. Ten tablets were weighed collectively and placed in the chamber of the friabilator. In the friabilator, the tablets were exposed to rolling, resulting free fall of tablets (6 inches) within the chamber of the friabilator. It was rotated at a rate of 25 rpm. After 100 rotations (4 minutes), the tablets were taken out from the friabilator and intact tablets were again weighed collectively [5].

$$F = \frac{(W_{inital}) - (W_{final})}{(W_{initial})} \times 100$$

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In vitro Buoyancy study

The *in vitro* buoyancy was characterized by floating lag time and floating duration. The test was performed using USP type II paddle type apparatus using 900 ml of 0.1 N HCl at paddle rotation of 50 rpm at 37±0.5^0. The floating lag time (time period between placing the tablet in the dissolution medium and tablet floating) and floating duration of the tablets were determined by visual observation [6].

Drug content

Ten tablets were crushed and powdered. Weighed accurately the quantity equivalent to 100 mg of drug and taken in 100 mL volumetric flask and dissolved with small quantity of 0.1N HCl (pH 1.2) and volume made up to the mark with same medium and stirred for 12 hrs. After stirring, 1 mL solution was withdrawn and filtered through 0.45 µm Whatman filter paper and volume made up to 10 mL of water. The absorbance was measured and at 263 nm using UV Spectrophotometer (Shimadzu 1800, Japan) [7].

$$\text{Drug content (mg)} = \text{concentration} \times \text{dilution factor}$$

$$\%\ \text{Drug content} = \frac{\text{drug content (mg)}}{\text{label claim } (-\text{mg})}$$

Water uptake study

The swelling behaviour of a dosage units were measured by studying its weight gain. The swelling index of tablets were determined by placing the tablets in the basket of dissolution apparatus using dissolution medium 0.1N HCl at 37 ± 0.5 ^{o}C. After 1, 2, 3, 4 and 5 h, each dissolution basket containing tablets were withdrawn and blotted with tissue paper to remove the excess water and weighed by digital electronic balance (Citizen D 1262, India). Swelling index was calculated by using following formula [7].

$$\text{WU}\ (\%) = \frac{\text{Weight of the swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}} \times 100$$

In vitro dissolution study

In vitro drug release studies were carried out using USP dissolution apparatus II (Paddle model, TDL 084, Electrolab, India). The dissolution studies were performed using 900 mL of 0.1N HCl (1.2 pH) at 37 ± 0.5 °C at 50 rpm. The sample (1 mL) was withdrawn at predetermined time intervals (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 h) and replaced with same volume of fresh dissolution medium. The withdrawn sample (1 mL) was diluted with 10 mL of distil water, filtered through 0.45 µm Whatman filter paper and assayed by using UV Spectrophotometer (Shimadzu 1800, Japan) at 263 nm. Drug release mechanism was determined by Zero order and First order plots [8].

Accelerated Stability studies

The accelerated stability studies were performed as per the ICH guidelines. Selected formulations of Dicloxacillin sodium were packed in aluminum pouch and subjected to short term stability at 25 ^{o}C / 60% RH and accelerated stability at 40 ^{o}C / 75% RH for a period of 3 months. Samples from each formulation which are kept for examination were withdrawn at definite time intervals. The withdrawn samples were tested for hardness, *in vitro* buoyancy and assayed for drug content and *in vitro* drug release [9].

RESULT AND DISCUSSION

Evaluations

In the present study, a total of 15 formulations of gastro retentive floating tablets of Dicloxacillin sodium were prepared by wet granulation technique using different polymers like HPMC K100M, Xanthan gum, Na CMC and MCC as semi synthetic and natural polymers, using sodium bicarbonate and citric acid as gas generating agents, lactose anhydrous is used as diluent, starch is used as a binding agent, and magnesium sterate and talc as lubricants. Formulations were optimized by different ratios of polymers.

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Pre-compression evaluations

Bulk density, Tapped density, Carr's index, Hausner ratio and Angle of repose

Precompression parameters of Dicloxacillin sodium are shown in Table 2. The bulk density of the formulation ranged between 0.408 ± 0.004 g/mL and 0.578 ± 0.010 g/mL. Tapped density varied between 0.456 ± 0.001 g/mL and 0.675 ± 0.026 g/mL. Carr's index value ranged between 9.23 ± 0.122% to 16.98 ± 0.274%. Hausner ratio was found between 1.10 ± 0.001 and 1.20 ± 0.003 and Angle of repose has been used as indirect method of quantifying power flow ability, and fallen between 25.67 ± 1.111 to 28.85 ± 0.439. Pre-compression parameters play an important role in improving the flow properties of pharmaceuticals especially in tablet formulation. These include bulk density, tapped density, Carr's index, Hausner ratio and Angle of repose. Before formulation of floating tablets, the drug and ingredients were evaluated for all the above said parameters and it was found that all the observations were within the prescribed limits of IP. All the formulations were fallen in good flow character based on angle of repose, compressibility index and Hausner ratio reports.

Table 2: Pre-compression parameters of prepared granules of Dicloxacillin sodium

Formulation code	Bulk density (g/cm³)*	Tap density (g/cm³)*	Carr's index*	Hausner's ratio*	Angle of repose*
F1	0.408 ± 0.004	0.456 ± 0.001	10.43 ± 1.166	1.11 ± 0.014	26.24 ± 0.571
F2	0.410 ± 0.005	0.474 ± 0.007	13.43 ± 0.174	1.15 ± 0.002	27.73 ± 0.453
F3	0.439 ± 0.005	0.484 ± 0.007	9.23 ± 0.122	1.10 ± 0.001	28.26 ± 0.439
F4	0.566 ± 0.010	0.640 ± 0.002	11.55 ± 1.629	1.13 ± 0.020	25.67 ± 1.111
F5	0.565 ± 0.009	0.649 ± 0.003	12.98 ± 1.492	1.14 ± 0.019	26.01 ± 0.771
F6	0.578 ± 0.010	0.675 ± 0.026	14.30 ± 2.059	1.16 ± 0.028	27.55 ± 1.054
F7	0.425 ± 0.008	0.057 ± 0.013	16.12 ± 1.306	1.19 ± 0.018	28.01 ± 0.553
F8	0.419 ± 0.005	0.495 ± 0.014	15.33 ± 1.518	1.18 ± 0.021	28.08 ± 0.985
F9	0.436 ± 0.004	0.489 ± 0.006	12.29 ± 0.176	1.14 ± 0.002	28.85 ± 0.439
F10	0.481 ± 0.006	0.559 ± 0.010	13.78 ± 1.393	1.16 ± 0.018	27.10 ± 0.540
F11	0.460 ± 0.006	0.528 ± 0.008	12.71 ± 0.185	1.14 ± 0.002	28.35 ± 0.325
F12	0.513 ± 0.008	0.618 ± 0.012	16.98 ± 0.274	1.20 ± 0.003	27.90 ± 0.283
F13	0.524 ± 0.015	0.625 ± 0.013	16.17 ± 1.291	1.19 ± 0.018	28.50 ± 0.279
F14	0.450 ± 0.006	0.528 ± 0.001	14.64 ± 1.285	1.17 ± 0.017	27.43 ± 0.287
F15	0.499 ± 0.014	0.568 ± 0.027	12.06 ± 1.925	1.13 0.025	27.77 ± 0.174

*Mean ± SD, n=3

Post-compression evaluations

Weight variation, Thickness and diameter, Hardness, Friability and Drug content

Post-compression parameters of Dicloxacillin floating tablets are showed in Table 3. Weight variation of floating tablets ranged from 649.6 ± 1.349 to 651.7 ± 1.567. Thickness ranged between 5.605 ± 0.036 mm and 6.127 ± 0.044 mm. The diameter varied between 12.004 ± 0.059 mm and 12.133 ± 0.032 mm. The hardness lies between 5.24 ± 0.164 and 5.91 ± 0.109. The friability of all gastro retentive floating tablets of Dicloxacillin sodium was found between 0.263 ± 0.002 and 508 ± 0.002. Drug content ranged between 96.92 ± 0.627 and 98.79 ± 0.242.

The average weights were found to be within (± 7.5) the prescribed official limits. The thickness of the floating tablet indicated that die fill was uniform. The thickness depends upon the size of the punch (12 mm) and the weight of the tablet (650 mg). Friability is needed for tablets to withstand force of compression applied during the manufacture of tablets and all the formulated floating tablets of Dicloxacillin sodium were shown the percentage friability within the official limits (i.e. not more than 1 %). Formulations showed favourable drug content which were within the limits of specifications.

In vitro Buoyancy test

The *in vitro* buoyancy properties (floating lag time and total floating time) of prepared gastro retentive floating tablets of Dicloxacillin sodium were showed in Table 4. All formulations showed floating lag time between 32.27 ± 0.510 to 96.32 ± 1.618 sec. Formulation F14 showed floating lag time of 34.09 ± 1.154. Formulations F1 – F3 were prepared using different drug to polymer ratios (Drug: HPMC K100M; 280:200, 280:240 and 280:290 mg). Formulations F4 – F6 were prepared using different drug to polymer ratios (Drug: Xanthan gum; 280:200, 280:240 and 280:290 mg). Formulations F7-F9 was prepared using different drug to polymer ratios (Drug: Na CMC; 280:200, 280:240 and 280:290 mg). Formulations F10 – F12 were prepared using different drug to polymer ratios (Drug: MCC; 280:200, 280:240 and 280:290 mg). Formulations F13 – F15 were prepared using different

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drug to polymer combination ratios (Drug : HPMC K100M : Xanthan gum; 280: 150 : 100, Drug : HPMC K100M: Na CMC; 280 : 150 : 100mg and Drug : HPMC K100M : MCC; 280 : 150 : 100 mg) all formulations were containing gas generating agent (combination of sodium bicarbonate and citric acid). Floating lag time varied by different polymers and polymer ratios. This showed that as the polymer concentration increased floating lag time decreased and total floating time increased.

Table 3: Post-compression parameters of Dicloxacillin sodium floating tablets

Formulation code	Evaluation parameters					
	Weight variation (mg)*	Thickness (mm)*	Diameter (mm)*	Hardness (Kg/cm²)**	Friability (%)*	Drug content***
F1	650.6 ± 1.505	6.041 ± 0.075	12.072 ± 0.019	5.64 ± 0.114	0.317 ± 0.005	243.76 ± 0.600
F2	651.2 ± 1.032	6.103 ± 0.058	12.113 ± 0.042	5.32 ± 0.228	0.474 ± 0.002	244.81 ± 0.541
F3	649.8 ± 1.475	6.055 ± 0.081	12.108 ± 0.046	5.24 ± 0.515	0.414 ± 0.003	246.75 ± 0.156
F4	649.7 ± 0.948	5.806 ± 0.101	12.094 ± 0.042	5.62 ± 0.192	0.424 ± 0.006	245.71 ± 0.457
F5	650.0 ± 1.054	5.605 ± 0.036	12.004 ± 0.059	5.52 ± 0.303	0.264 ± 0.044	247.77 ± 0.585
F6	649.7 ± 1.946	5.917 ± 0.067	12.116 ± 0.045	5.24 ± 0.260	0.306 ± 0.001	245.58 ± 0.457
F7	649.9 ± 1.911	5.988 ± 0.106	12.121 ± 0.032	5.86 ± 0.151	0.508 ± 0.002	246.12 ± 0.584
F8	650.2 ± 1.581	6.053 ± 0.071	12.133 ± 0.032	5.48 ± 0.238	0.459 ± 0.026	245.71 ± 0.634
F9	651.5 ± 1.499	6.033 ± 0.077	12.094 ± 0.041	5.24 ± 0.167	0.368 ± 0.001	243.79 ± 0.560
F10	650.6 ± 1.173	5.745 ± 0.109	12.045 ± 0.029	5.78 ± 0.164	0.274 ± 0.002	247.37 ± 0.390
F11	651.7 ± 1.567	5.714 ± 0.030	12.048 ± 0.020	5.82 ± 0.083	0.459 ± 0.001	244.19 ± 0.627
F12	650.8 ± 1.549	5.655 ± 0.087	12.042 ± 0.023	5.91 ± 0.109	0.438 ± 0.005	247.37 ± 0.561
F13	649.6 ± 1.349	5.915 ± 0.042	12.067 ± 0.026	5.41 ± 0.158	0.431 ± 0.007	248.11 ± 0.558
F14	650.2 ± 1.549	6.127 ± 0.044	12.101 ± 0.017	5.72 ± 0.083	0.263 ± 0.002	248.72 ± 0.242
F15	650.4 ± 1.074	6.035 ± 0.057	12.055 ± 0.021	5.52 ± 0.238	0.352 ± 0.001	245.28 ± 0.707

*Mean ± S.D, n=10,**Mean ± S.D, n=5,***Mean ± S.D, n=3

Table 4: *In vitro* buoyancy property of Dicloxacillin sodium tablets

Formulation code	Floating lag time (Sec)*	Total floating time (h)
F1	89.61 ± 0.517	12
F2	62.37 ± 1.091	12
F3	32.27 ± 0.510	>12
F4	94.33 ± 1.089	10
F5	47.18 ± 0.971	12
F6	44.75 ± 0.944	12
F7	84.12 ± 1.781	9
F8	70.43 ± 0.518	9
F9	48.38 ± 1.701	11
F10	96.32 ± 1.618	9
F11	76.56 ± 1.521	10
F12	56.18 ± 1.910	10
F13	38.66 ± 1.109	>12
F14	34.09 ± 1.154	>12
F15	51.31 ± 1.019	12

*Mean ± S.D, n=3

Water uptake study

The percentage water uptake of prepared gastro retentive floating tablets of Dicloxacillin sodium were shown in Table 5. The swelling indices were increased with increase in polymer concentration. Formulations containing HPMC K100M and Na CMC showed higher swelling indices as compared with other formulations containing the same amount of Xanthan gum and MCC. This may be due to the formulations containing variable concentrations of HPMC K100M and Na CMC formed a viscous gel layer during the dissolution. It was observed that combination of HPMC K100M and Na CMC showed maximum swelling. Swelling index values starts decreased when polymer erosion starts in medium.

In vitro drug release

The cumulative drug release of the different formulations F1 – F15 were carried out by the procedure mentioned earlier. The formulations are carried out for the release studies for about 12 h. The release rates obtained for the formulations mentioned above are 96.86 ± 0.751, 95.72 ± 0.712, 97.18 ± 0.572, 96.39 ± 0.067, 92.71 ± 0.125, 96.89 ± 0.051, 91.96 ± 0.093, 95.96 ± 0.093, 95.07 ± 1.019, 96.78 ± 0.010, 92.31 ± 0.575, 95.06 ± 0.472, 94.98 ± 0.101, 96.46 ± 0.552 and 94.81 ± 0.102 respectively. The results obtained proved that the *in vitro* release is influenced by the polymer ratios. Because as the mentioned in previously increasing polymers concentration the more gel layer will form around the tablet and sustains the release of the drug from the tablet. The release rates obtained are shown in Fig. 1 and Fig. 2. It has been concluded that formulation proposed with high polymer concentration showed sustain release of the drug up to 12 h.

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Table 5: Percentage water uptake study of Dicloxacillin sodium tablets

Time (h)	Formulation code														
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15
1	53.84	48.46	33.84	51.69	55.23	41.38	61.69	55.38	58.61	62.92	68.92	73.69	36.15	50.0	48.30
2	84.61	70.76	52.30	69.07	71.07	64.15	82.92	78.30	82.30	98.61	103.23	127.38	53.07	102.92	90.46
3	115.38	102.30	82.92	89.38	95.53	84.30	102.0	95.38	104.46	121.07	157.07	160.15	109.07	122.92	135.23
4	146.15	124.76	121.53	116.0	120.76	120.0	144.46	118.61	144.76	155.09	209.07	210.92	124.46	150.76	169.07
5	176.92	144.76	155.38	126.30	145.38	158.61	174.0	141.68	175.69	189.06	240.15	250.46	146.15	195.53	219.38
6	223.07	174.15	193.84	159.84	174.92	184.30	192.46	179.69	204.92	225.84	176.61	180.15	174.15	224.30	245.69
7	207.69	190.61	218.46	133.07	208.92	220.15	166.30	154.92	172.15	167.53	159.84	149.23	195.69	268.92	175.23
8	184.61	169.53	221.38	116.76	183.23	190.61	144.46	127.84	132.15	147.69	129.38	103.07	223.12	185.69	101.38
9	161.53	144.15	154.30	96.15	144.30	167.53	120.76	102.92	98.30	90.92	92.15	52.46	179.69	135.84	68.92
10	100.0	90.0	121.23	70.61	99.69	125.38	98.30	84.61	53.84	48.92	50.92	32.15	137.85	72.46	49.38
11	69.23	68.46	102.92	47.84	46.92	98.61	50.92	47.53	35.23	22.92	16.15	12.30	68.91	29.07	24.75
12	41.69	52.15	84.30	21.38	20.76	41.23	19.69	16.76	20.15	10.92	7.53	4.61	32.07	12.15	13.18

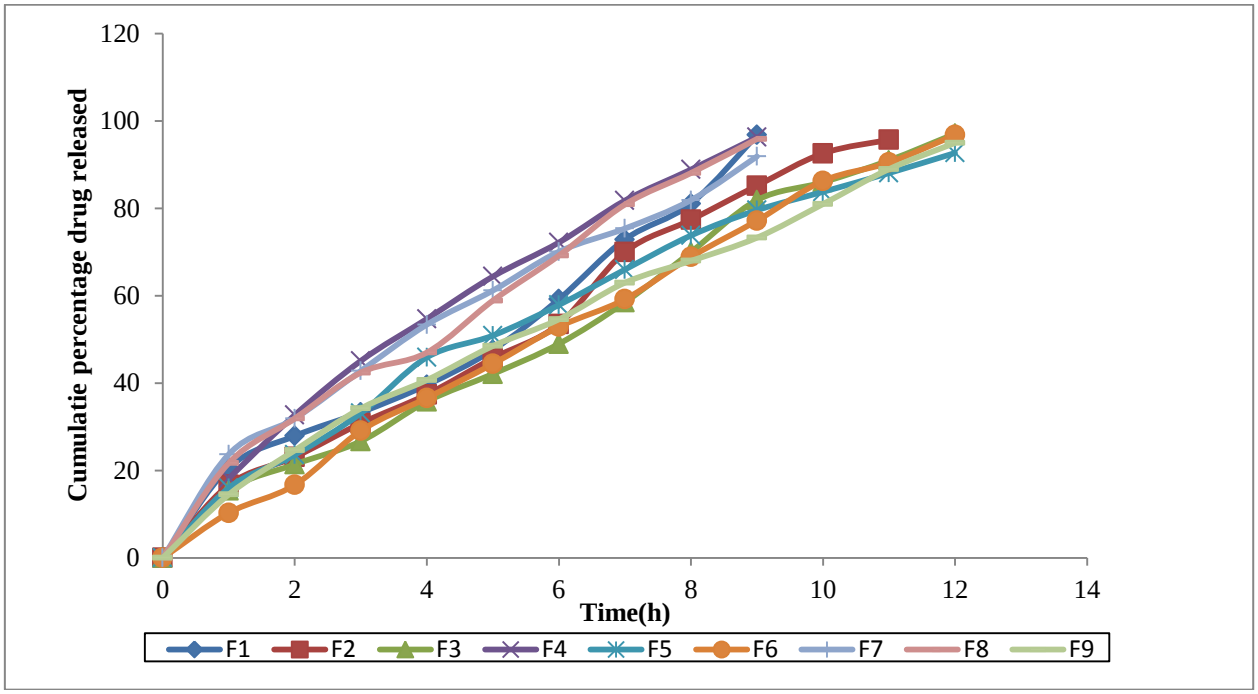

Figure 1: *In vitro* drug release of Dicloxacillin sodium tablets (F1-F9)

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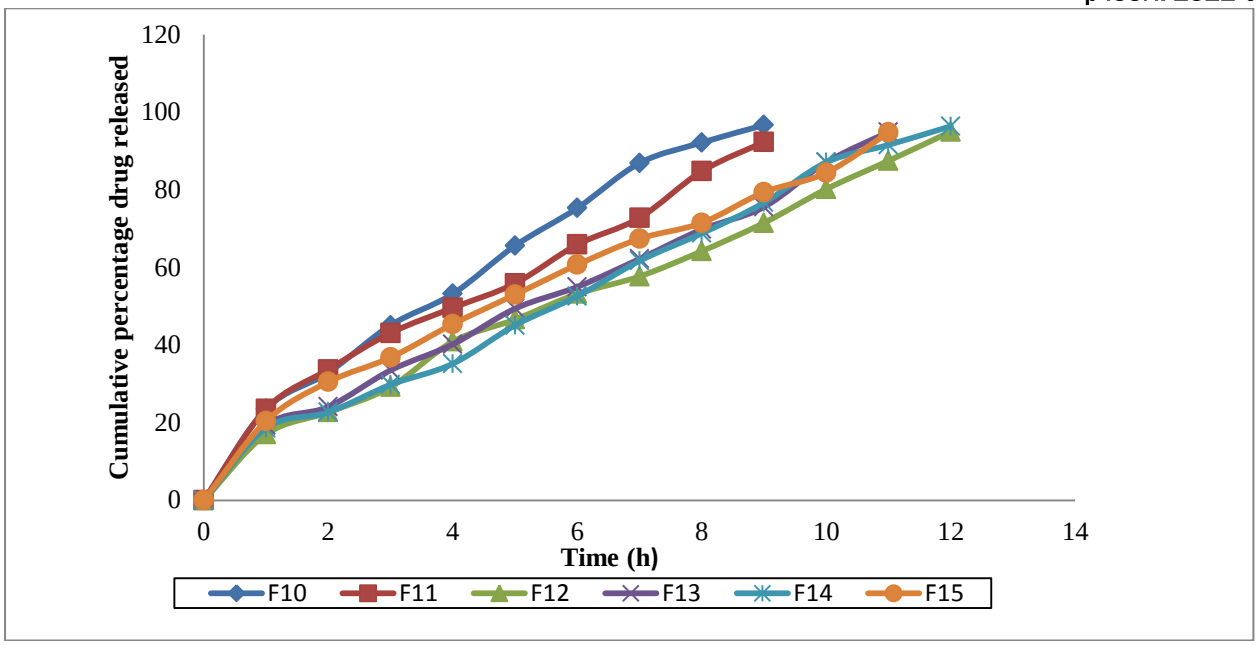

Figure 2: *In vitro* drug release of Dicloxacillin sodium tablets (F10-F15)

From the release profile formulation F4 is selected as the best formulation. The r^2 and k and n values are given in Table 6. Based on the r^2 values obtained the mechanism of drug release was determined. From the r^2 values it was fitted to zero order kinetics.

Table 6. The r^2 and k and n for selected formulation

Formulation code	Zero order		First order		Higuchi		Korsmeyer peppas		Best fit model
	r^2	k	r^2	k	r^2	k	r^2	n	
F14	0.994	7.606	0.877	0.112	0.963	34.57	0.965	0.728	Zero order

Accelerated Stability studies

During and at the end of the accelerated stability, the tested tablets showed non-significantly different drug content from that observed at the beginning of the study. They also showed satisfactory hardness and buoyancy properties during and at the end of the accelerated study period. The selected formulation of Dicloxacillin sodium floating tablets were carried out for stability studies for 3 months in different temperatures such as short term stability at 25 ± 2 °C / 60 ± 5% R.H and accelerated stability at 40 ± 2 °C / 75 ± 5% R.H for a period of 3 months and the samples were tested for hardness, *in vitro* buoyancy, drug content and *in vitro* drug release for every month and results were shown in Table 7. There was no significant change in the hardness, *in vitro* buoyancy, drug content and *in vitro* drug release of the Dicloxacillin sodium floating tablets.

Table 7: Accelerated stability studies for selected formulation F14

Temperature	Periods (month)	Evaluation parameters			
		Hardness (Kg/cm²)*	Buoyancy property (sec)**	Drug content**	Drug release (%)**
25 ± 2 °C / 60 ± 5% R.H	0	5.17 ± 0.216	38.32 ± 0.037	247.21 ± 0.871	92.181 ± 0.092
	1	5.24 ± 0.021	33.01 ± 1.013	246.18 ± 0.109	93.604 ± 0.129
	2	5.20 ± 0.425	35.73 ± 0.817	248.19 ± 0.182	93.219 ± 0.099
	3	5.22 ± 0.048	36.51 ± 0.128	247.91 ± 0.011	92.397 ± 0.103
40 ± 2 °C / 75 ± 5% R.H	0	5.19 ± 0.021	34.18 ± 0.192	247.11 ± 1.011	93.285 ± 0.121
	1	5.21 ± 0.106	35.71 ± 1.083	248.19 ± 0.911	91.91 ± 0.325
	2	5.17 ± 0.121	34.52 ± 0.871	248.28 ± 0.081	93.183 ± 0.426
	3	5.14 ± 0.091	33.34 ± 0.125	247.21 ± 0.102	92.691 ± 0.081

*Mean ± S.D, n=5, ** Mean ± S.D, n=3

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CONCLUSION

Gastroretentive floating tablets of Dicloxacillin sodium were developed to overcome the less half life and subsequent frequent dosing. *In vitro* studies and water uptake studies have shown that this is a potential drug delivery system for Dicloxacillin sodium with a good stability and sustain release profile. From *in vitro* release studies and water uptake study it was a good stability and sustains the release of drug.

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