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Floating Tablets: A Single Unit Approach to Increase the Gastroretention of Cefpodoxime Proxetil

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ABSTRACT

The main objective of the present study is to develop a single unit gastric floating drug delivery system (GFDDS) of Cefpodoxime Proxet.Tablets were prepared using various proportions of polymers such as HPMCK4M and Eudragit RS 100. Direct compression method was used for the preparation of tablets. Five different formulations were developed. Tablets were evaluated for physical characterization viz. weight variation, thickness, hardness, friability, drug content, swelling index, buoyancy determination, and *in vitro* drug release study. All parameters complied with IP limits. Formulation with both the polymers (F5) showed sustained release. Formulations with hydrophilic polymer (F1, F2) showed high release of drug when compared to formulations with hydrophobic polymers (F3, F4). Polymer HPMCK4M and the combination of Eudragit RS100 were found to have optimum floating characters for a longer period. It may be concluded from whole study that the combinations of hydrophilic polymers with hydrophobic polymers are suitable to optimize sustained release formulation of Cefpodoxime Proxetil.

Keywords: : Cefpodoxime Proxetil, swelling index, floating capacity, HPMCK4M, Eudragit RS 100.

1. INTRODUCTION

Rapid gastrointestinal transit could result in incomplete drug release from the device above the absorption zone leading to diminished efficacy of the administered dose.[1] For achieving a prolonged and predictable drug delivery profile in the gastrointestinal tract, it is necessary to increase the gastric residence time. Therefore, different approaches have been proposed to retain the dosage form in the stomach. These include bioadhesive systems, swelling and expanding systems.[2-6] Floating systems are low density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach without affecting the gastric emptying rate for a prolonged period. While the system floats over the gastric contents, the drug is released slowly at the desired rate, which results in increased gastric retentive time and reduces fluctuation in plasma drug concentration.[7]

Cefpodoxime proxetil is a Beta lactum antibiotic. Its action is by binding to specific penicillin-binding proteins (PBPs) located inside the bacterial cell wall; it inhibits the bacterial cell wall synthesis. It is highly stable in the presence of beta- lactamase enzymes.[8] Cefpodoxime proxetil is a third generation cephalosporin prodrug which is administered orally. The half-life of cefpodoxime proxetil is 2.2 hours. It is incompletely absorbed from the gastrointestinal tract and has an oral bioavailability of only 50%. Floating drug delivery is able to prolong the gastric retention of drug and thereby possibly improve oral bioavailability of cefpodoxime proxetil. The gastro-retentive floating matrix tablet of Cefpodoxime proxetil were designed using HPMC K4M and Eudragit RS 100 as polymers.

2. MATERIALS AND METHODS

Cefpodoxime proxetil was procured as gift sample from Okasa Pharmaceuticals, Satara. Eudragit Rs100 was supplied from Bio - Gen extracts Pvt. Ltd., Bangalore. HPMC obtained by Colorcon Asia Ltd, Goa. Poly vinyl pyrrolidone K30 received from Jiazuoyuanha fine chemicals co., Ltd, China. Sodium lauryl sulphate and Sodium bicarbonate were obtained from Qualigens Fine Chemicals, Mumbai, India. Talc and Microcrystalline cellulose were obtained from Lobachemiepvt. Ltd. Mumbai, India. All the chemicals and reagents required for the present experimental work are of analytical grade.

2.1 Method of Preparation of Cefpodoxime Proxetil Floating Tablets

The floating tablets were prepared by blending the drug cefpodoxime proxetil, polymer (HPMCK4M /Eudragit RS 100) in different proportions respectively. This blend was triturated with sodium bicarbonate, sodium lauryl sulphate, poly vinyl pyrrolidine - K30in mortar and pestle using geometric dilution. Micro crystalline cellulose was used as diluent to make the total weight of each tablet 250 mg. The powder was passed through sieve no.100. The obtained powder was collected and retriturated. To this required amount of talc was added and compressed finally. In the present work, 5 formulations (F1 to F5) of floating tablets of were prepared using different concentrations of HPMCK4M and Eudragit RS 100 as shown in the Table No. 1.

Table No.1. Development of different formulations containing, varying proportions of polymers

Ingredients (mg)	F1	F2	F3	F4	F5
Cefpodoxime proxetil	200	200	200	200	200
HPMC K4M	80 (20%)	100 (25%)	-	-	50 (25%)
Eudragit	-	-	80 (20%)	100 (25%)	50 (25%)
Sodium bi carbonate	30	30	30	30	30
Sodium lauryl sulphate	3	3	3	3	3
Poly vinyl pyrrolidone K 30	10	10	10	10	10
Talc	5	5	5	5	5
Microcrystalline cellulose	Q.S.	Q.S.	Q.S.	Q.S.	Q.S.

2.1.1 Weight variation

To study weight variation, 20 tablets of each formulation were weighed using an electronic balance (AW-220, Shimadzu), and the test was performed according to the official method. [9,10]

2.1.2 Thickness

Thickness of tablets was determined using vernier caliper. Three tablets from each batch were used, and average values were calculated.

2.1.3 Hardness

The resistance of tablets to shipping or breakage, under conditions of storage, transportation and handling before usage depends on its hardness. The hardness of tablet of each formulation was measured by Monsanto hardness tester**.** [2,9]**.**

2.1.4 Friability

Friability is the measure of tablet strength. Roche type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined.[10]

$$\% \text{ loss} = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Initial weight of tablets}} \times 100$$

2.1.5 Drug content

Twenty tablets were crushed and powder equivalent to weight of tablet dissolved in 0.1 N HCl. Then suitable dilutions were made and absorbance at 263 nm wavelength was taken by using a UV spectrophotometer. [10]

2.1.6 Swelling Index

The swelling behavior of a dosage unit was measured by studying its weight gain. The swelling index of tablets was determined by placing the tablets in the basket of dissolution apparatus using dissolution medium pH 6.8 buffer at 37 ± 0.5^0C. After 0.5, one, two, three, four, five, six, seven and eight hours, each dissolution basket containing tablet was withdrawn and blotted with tissue paper to remove the excess water and weighed on the analytical balance (Shimadzu, AX 120).

The experiment was performed in triplicate for each time point. Swelling index was calculated by using the following formula.[11]

$$\% \text{ of Water uptake} = \frac{\text{Weight of swollen tablet} - \text{Initial weight of the tablet}}{\text{Initial weight of the tablet}} \times 100$$

2.1.7 Buoyancy determination

The buoyancy test of tablet was studied by placing them in 500 ml beaker containing 0.1 N HCl, then tablet from same batches were placed in dissolution test apparatus containing 900 ml 0.1N HCl, maintained at 37±0.5°C and agitated at 50 rpm. The floating onset time (time period between placing tablet in the medium and buoyancy beginning) and floating duration of tablet was determined by visual observation.[12]

2.1.8 In vitro drug release studies

The *in vitro* dissolution test was performed using USP type II dissolution test apparatus. The drug release study was carried out in 0.1 N HCl for 12 h in 900 ml of dissolution media, maintained at 37±0.5°C and agitated at 50 rpm. Periodically 5 ml samples were withdrawn and filtered through whatman filter paper and samples were replaced by its equivalent volume of dissolution media. The concentration of Cefpodoxime proxetil was measured spectrophotometrically at 263 nm.[13,14]

Table No.2: Data of average weight variation, thickness, diameter, hardness and friability for all the formulation of cefpodoxime proxetil

Formulation code	Weight variation (g)	Thickness (cm)	Hardness (Kg/cm^2)	Friability (%)	Drug Content (%)
	Mean ± SD*	Mean ± SD*	Mean ± SD*	Mean ± SD*	Mean ± SD*
F1	0.238 ± .007	0.38±0.031	0.84± .004	0.68± .004	96.38 ± 0.10
F2	0.232 ± .01	0.41±0.021	0.89± .001	0.59± .002	101.38 ± 0.14
F3	0.245 ± .03	0.39±0.041	0.76± .002	0.62± .001	100.38 ± 0.13
F4	0.239 ± .004	0.44±0.045	0.78± .004	0.64± .002	99.38 ± 0.15
F5	0.236 ± .005	0.42±0.035	0.84± .003	0.71± .008	101.88 ± 0.12

3. RESULT AND DISCUSSION

3.1 Evaluation of Tablets

Weight Variation, Thickness, Hardness and Friability: The results showed that weight variation, thickness were lying within limits. Because of variation in the compressional forces there is a slight variation in hardness of tablets. As the proportion of polymers increases the hardness of the tablets was found to increase in case of HPMC. Eudragit RS 100 tablets are less harder and thickest tablets. The friability loss was found to be within the limits in all the each formulation were kept in a 100ml beaker containing simulated gastric fluid, pH 1.2 as per USP. The time taken for the tablet to rise to the surface and float was taken as floating lag time (FLT). The duration of time the dosage form constantly remained on the surface of medium was determined as the total floating time (TFT).

3.2 Swelling index

The swelling index was calculated with respect to time. As time increase, the swelling index was increased because weight gain by tablet was increased proportionally with rate of hydration, later on, it decreased gradually due to dissolution of outermost gelled layer of tablet into dissolution medium. The direct relationship was observed as shown in Fig.1.

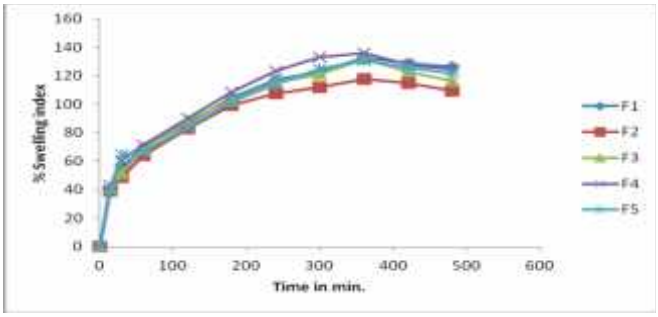

Fig. 1: Relationship between swelling index and time

3.3 *In-vitro* drug release

In-vitro drug release study for all the formulations was conducted and tabulated in Table no. 07. Formulation with both the polymers (F5) showed sustained release. Formulations with hydrophilic polymer (F1, F2) showed high release of drug when compared to formulations with hydrophobic polymer (F3, F4) as shown in the Figure 2. The hydrophilic polymer solubilised more and drug release was high. The hydrophobic polymer solubilized less which retards the drug release to a greater extent. Thus the HPMCK4M with the combination of Eudragit RS 100 provide the optimum drug release.

Table No. 3: Relationship between swelling index and time

Time (min.)	F1	F2	F3	F4	F5
0	0	0	0	0	0
15	40.2	39.2	41.2	43.2	40.2
30	55.6	48.6	51.6	60.6	64.9
60	69.4	64.4	68.4	71.4	66.4
120	86.8	82.8	88.8	90.28	83.8
180	104.6	99.6	102.6	108.6	101.9
240	117.4	107.4	115.4	123.4	114.4
300	122.9	111.9	120.9	132.9	124.9
360	132.8	117.8	131.8	135.8	130.8
420	128.8	114.8	122.8	127.8	125.8
480	126.3	109.3	116.3	124.2	121.3

Table No. 4: Data of Buoyancy lag time and total floatation time for all the formulations

Formulation code	Buoyancy lag time (min.)	Total floatation time (hrs.)
F1	2	7
F2	2.5	8
F3	4	10.5
F4	4.8	11.2
F5	3	9.5

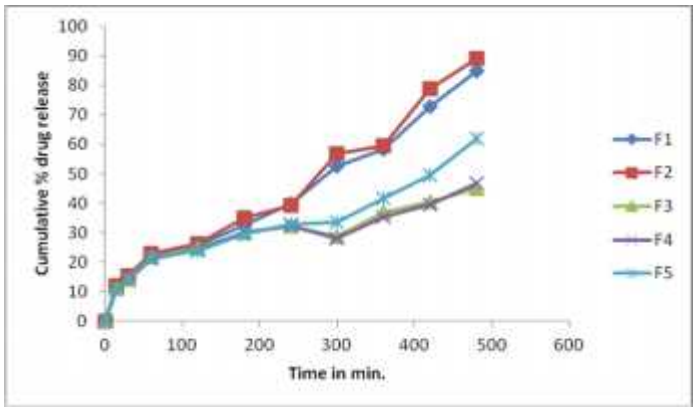

Fig. 2: Comparison of drug release from different formulations

Table No. 5: In-vitro drug release of batch F1 to F5

Time (min.)	F1	F2	F3	F4	F5
0	0	0	0	0	0
15	11.34	11.89	11.2	10.9	10.8
30	14.7	15.2	14.2	13.9	14.1
60	22.5	22.9	21.8	21.2	21.6
120	25.7	26.2	24.7	24.2	23.7
180	32.6	34.9	29.8	30.2	29.6
240	39.8	39.2	32.2	32.4	32.8
300	52.4	56.8	28.6	28.1	33.6
360	58.4	59.6	36.8	35.4	41.7
420	72.7	78.9	40.3	39.4	49.4
480	84.9	89.2	44.9	46.8	61.8

3.4 Buoyancy test

The formulations with hydrophilic polymer (F1, F2) showed less buoyancy lag time when compared to formulations with hydrophobic polymer (F3, F4). The formulation with combination of polymers (F5) showed optimum buoyancy lag time. For all the F3 and F4 formulations showed more total floating time when compared to F1 and F2 due to the presence of hydrophobic polymer which decreased the solubility. When compared in between F1 and F2, F2 showed less total floating time. Thus with an increase in the concentration of the hydrophilic polymer total floating time was found to be decreased due to increase in the solubility. In case of F3and F4, F3 showed less total floating time. Thus with an increase in the concentration of the hydrophobic polymer total floating time was found to be increased due to decrease in the solubility. Results revealed that as the concentration of the hydrophilic polymer increases, the buoyancy lagging time decreases. The increase in the concentration of the hydrophobic polymer resulted in the increase of the buoyancy lag time. Thus polymer HPMCK4M and the combination of Eudragit RS100 were found to have optimum floating characters for a longer period.

REFERENCES

1. Iannuccelli V, Coppi G, Bernabei MT, Cameroni R. Air compartment multiple-unit system for prolonged gastric residence. Part I. Formulation study. Int. J. Pharm. 1998;174:47-54.

2. Santus G, Lazzarini G, Bottoni G. An *in-vitro in-vivo* investigation of oral bioadhesive controlled release furosemide formulations. Eur. J. Pharm. Biopharm. 1997;4:39-52.

3. Deshpande AA, Rhodes CT, Shah NH, Malick AW. Controlled-release drug delivery systems for prolonged gastric residence: an overview. Drug. Dev. Ind. Pharm. 1996;22:531-539.

4. Deshpande AA, Shah NH, Rhodes CT, Malick W. Development of a novel controlled-release system for gastric retention. Pharm. Res. 1997;14:815-819.

5. Menon A, Ritschel WA, Sakr A. Development and evaluation of a monolithic floating dosage form for furosemide. J. Pharm. Sci. 1994;83:239-245.

6. Whitehead L, Fell JT, Collett JH, Sharma HL, Smith AM. Floating dosage forms: an *in-vivo* study demonstrating prolonged gastric retention. J. Control. Rel. 1998;55:3-12.

7. Khatri S, Girdhani D, Pahwa R. Recent advances in floating drug delivery system. The Indian Pharmacist. 2007;17–20.

8. Martindale, The complete drug reference; 34th edition; 178-179.

9. Indian Pharmacopoeia. Delhi (India): Controller of Publications; 1996. P. 734-36. (vol 2).

10. Banker GS, Anderson NR. Tablets. In: Lachman L, Liberman HA, Kanig JL, editors. The theory and practice of industrial pharmacy. 3rd ed. Mumbai (India): Varghese Publishing House; 1990:296-302.

11. Vendruscolo CW, Andreazza IF, Ganter JL, Ferrero C, Bresolin TM. Xanthan and galactomann matrix tablets based for oral controlled delivery of theophylline. International journal of Pharmaceutics. 2005; 296:1-11.

12. Sangekar S, Vadino WA, Chaudry I, Parr A, Behin R, Digenis G. Evaluation of effect of food and specific gravity on tablets on gastric retention time. Int J Pharm. 1987; 35:187-191.

13. Muthusamy K, Govindarajan G, Ravi TK. Preparation and evaluation of Lansoprazole Floating Micropellets. Ind. J. Pharm. Sci., 2005;67(1):75-79.

14. Shreenivas Rao B, Seshasayana A, Himasankar K, Prasana Raju Y, Ramana Murthy KV. Design and evaluation of Ethylene Vinyl Acetate Sintered Matrix tablets. Ind. J. Pharm. Sci. 2003;65(5):496-502.