EMPRO

Current Research in Pharmaceutical Sciences

Available online at www.crpsonline.com

ISSN: 2250 – 2688

Received: 11/08/2020
Revised: 25/08/2020
Accepted: 31/08/2020
Published: 08/10/2020

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DOI: 10.24092/CRPS.2020.100303

Website: www.crpsonline.com

Quick Response Code:

Formulation and Evaluaton of Floating Tablet of Cefpodoxime Proxetil

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ABSTRACT

Ideal once daily floating drug delivery system should release the drug for 24 hours and float up to 24 hrs. Once daily floating matrix tablet of Cefpodoxime proxetil should be release the drug for 24 hours to maintain the effective plasma level. All the formulations were prepared by using two different grades of HPMC (K100 and K4), cross povidone and MCC pH 101. HPMC is a matrix forming agent. All the formulations showed buoyancy lag time of less than 5 seconds regardless of concentration of HPMC K100 M, K4 and cross povidone. It may be due to the low density of tablet. The swelling index of HPMC K100 M was found to be higher than that of HPMC K4 M. This may be due to high molecular weight and high viscosity of HPMC K100 M. The formulation F1 containing low level of HPMC K100 M (75 mg) and low level of cross povidone (75 mg) showed higher burst release and maintained drug release up to 24 hours. The tablet was remained floated for 24 hours. High level of HPMC K100 M (F2, F3, F5,F6,) results in greater amount of gel being formed. This gel increases diffusion path length of the drug and hence release rate decreases. On the same line it formulation F5 and F8 should show relatively less drug release as high level of HPMC K100 M(100 mg & 125 mg respectively) is used in these formulations. But both the formulations released more than 97% drug within 24 hours. the formulations F10,F13,F14,F16,F17 released the drug within 20 hours. The formulation F11 which contains high amount of HPMC K4 M than F10 (100mg) and low level of cross povidone (75 mg) shows drug release up to 24 hours with sufficient floating duration. The formulation F15 and F18 contains high level of HPMC K4 M (125mg) and high level of cross povidone (100mg and 125mg) respectively. Both the formulations showed sustained drug release up to 24 hrs.

Key words: formulation, floating tablet, cefpodoxime proxetil

1. INTRODUCTION

Floating drug delivery system (FDDS) or hydrodynamically balanced system (HBS) have a bulk density lower than gastric fluid and therefore remain floating in the stomach without affecting the gastric emptying rate for a prolonged period of time[1]. The drug is slowly released at a desired rate from the floating system and after the complete release, the residual system is expelled from the stomach[2]. This leads to an increase in the GRT and better control over fluctuations in plasma drug concentration[3]. Swelling type dosage forms after swallowing swell to an extent that prevents their exit from the stomach through the pylorus[4]. As a result, the dosage form is retained in the stomach for a longer period of time[5].

The concept of FDDS was described in the literature as early as 1968, when Davis discovered a method for overcoming the difficulty experienced by some peoples of gagging or choking while swallowing medicinal pills. Since then several approaches have been used to develop an ideal FDDS[6]. The various buoyant preparations include hollow microspheres or microballoons, granules, powders, capsules, tablets, pills, and laminated films[7]. Most of the floating systems reported in literature are single unit system such as HBS and floating tablets[8,9].

There are two type of FDDS one is Non-effervescent and another is effervescent. The most commonly used excipients in non-effervescent FDDS are gel forming or highly swellable cellulose type hydrocolloids, polysaccharides, and matrix forming polymers. The effervescent buoyant delivery system utilize matrices prepared with swellable polymer such as methocel or polysaccharides, e.g. chitosan, and effervescent components, e.g. sodium bicarbonate and citric or tartaric acid[10] or matrices containing chambers of liquid that gasify at body temperature[11].

Gastro retentive drug delivery systems have made it possible to deliver drugs in GIT for prolonged period of time in a controlled manner. Thus, it is envisaged to develop a floating drug delivery system, which can be retained in stomach for prolonged period of time by virtue of their floating properties. Hence it is advantageous to prepare a small sized floating microsphere which could float and simultaneous adhere to directly to the mucous network where the absorption window of H_2 receptor antagonist can exists. Floating microspheres of cefpodoxime proxetil could localize the drug within the peptic region to enhance the drug absorption process in a site-specific manner. Developed floating system of cefpodoxime proxetil increase the local drug concentration by prolonging the residence time of the formulation in the stomach.

2. MATERIALS AND METHODS

2.1 Preformulation study

2.1.1 Organoleptic properties and description

The sample of Cefpodoxime Proxetil was studied for organoleptic characters such as color, odor, and appearance.

2.1.2 Melting point

The melting point of Cefpodoxime Proxetil was done by capillary method.

2.1.3 Loss on drying

The 1.0 g sample was weighed accurately in a conditioned and tared vessel that compatible with the sample being tested. The sample containing vessel was then placed in an oven at 105ºC, typically for 4h. The sample was cooled in desiccators and weighed. Values are given in table 11S

2.1.4 Solubility

The solubility of Cefpodoxime Proxetil to be determined by adding excess amount of drug in the solvent at room temperature and kept for 24 h with occasional shaking. Equilibrium solubility was determined by taking supernatant and analyzing it on Shimadzu UV 2501, double beam spectrophotometer.

2.1.5 FTIR Spectroscopy

The FTIR spectrum of Cefpodoxime Proxetil was recorded using FTIR spectrophotometer (Shimadzu 8400S) using KBr pellet technique.

2.1.6 UV spectroscopy

Stock solution (1mg/ml) of Cefpodoxime Proxetil was prepared in Glycine Buffer (pH 3) with 1% SLS and 0.1N HCL. This solution was appropriately diluted with respective solvents to obtain a suitable concentration. The UV spectrum was recorded in the range 200-400 nm on Shimadzu 2501 PC double beam spectrophotometer as respectively. The wavelength of maximum absorption (λ max) was determined.

2.2 Construction of Beer-Lambert's plot

Stock solutions of 100 μg/ml were prepared in Glycin Buffer (pH 3) with 1% SLS and 0.1N HCL. From it standard solutions in the range 5-30 μg/ml were prepared by appropriate dilution with respective solvent. The absorbance of each standard solution was determined spectrophotometrically. Using absorbance-concentration data Beer-Lambert's plot were constructed.

2.3 Preparation of matrix tablets

2.3.1 Preparation of powder blend

Powder blend were prepared for the preparation of matrix tablet by direct compression method. All the ingredients were weighed accurately & mixed by passing through 60 no. sieve. Mixing was again done by spatulation & tumbling in glass mortar and pestle.

2.3.2 Compression of powder blend

The compression of powder blend was done by direct compression method. The compression was carried out using 12 mm flat-faced circular punches on rotary compression machine (RIMEK tablet punching machine, Minipress-I).Various ingredients and quantities used were as shown in the table 1 & 2.

2.4 Evaluation of powder blend

Prepared powder blend was evaluated for bulk density, angle of repose, compressibility index.

Table 1: Floating Matrix formulation containing HPMC K100 M

Ingredients (mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9
Cefpodoxime Proxetil	580	580	580	580	580	580	580	580	580
HPMC K100 M	75	100	125	75	125	100	100	125	75
Avicel (pH101)	100	100	100	100	100	100	100	100	100
Cross povidone	75	75	75	100	100	100	125	125	125
Total weight	830	855	880	855	905	880	905	930	880

Table 2: Floating Matrix formulation containing HPMC K4 M

Ingredients (mg)	F10	F11	F12	F13	F14	F15	F16	F17	F18
Cefpodoxime Proxetil	580	580	580	580	580	580	580	580	580
HPMC K4 M	75	100	125	75	100	125	75	100	125
Avicel (pH101)	100	100	100	100	100	100	100	100	100
Cross povidone	75	75	75	100	100	100	125	125	125
Total weight	830	855	880	855	905	880	905	930	880

2.4.1 Bulk density

Both untapped bulk density, ρ_u (often called loose or aerated bulk density) and tapped bulk density, ρ_b were determined. A amount of powder blend was introduced in a 10 ml measuring cylinder up to 9 ml volume. Then the weight of powder blend was determined by subtracting the weight of empty measuring cylinder from final weight of measuring cylinder. The cylinder was allowed to fall onto a hard surface from a height of 2.5 cm at 2 sec intervals. The tapping was continued till no volume change was noted. ρ_u and ρ_b were determined by following formulas;

$$\rho_b = \frac{M}{V_b}$$

$$\rho_u = \frac{M}{V_u}$$

2.4.2 Carr's Compressibility Index

An important measure that can be obtained from bulk density determinations is the percent compressibility C, which is defined as follows

$$C = \frac{\rho_b - \rho_u}{\rho_b} (100)$$

2.4.3 Hausner ratio

A similar index has been defined by Hausner.

$$\text{Hausner ratio} = \frac{\rho_b}{\rho_u}$$

2.4.4 Angle of repose

The angle of repose of the powder blend was determined by using funnel method. The accurately weighed powders were taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The diameter of the powder cone was measured and angle of repose was calculated by using the equation:

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

Where, h and r are the height and radius of the powder cone. Average values shown in Table 12

2.5 Evaluation of Tablets

2.5.1 Thickness

The thickness of the tablets was determined using a Vernier Caliper. Five tablets from each batch were used to calculate average values.

2.5.2 Weight Variation

Weighed accurately 20 tablets and average weight were calculated.

2.5.3 Hardness

For each formulation, the hardness of five tablets was checked using the Monsanto hardness tester (Cadmach, Ahmedabad, India).

2.5.4 Friability

For each formulation, twenty tablets were selected randomly and weighed. Tablets were then placed in friability testing apparatus i.e. Roche friabilator (Remi Electronics, Mumbai, India), which was rotated at a speed of 25 rpm for 4 minutes. Tablets were then weighed and friability values were determined which are reported.

Drug Content: Five tablets were weighed and powdered. The quantity equivalent to 550 mg of cefpodoxime Proxetil was weighed accurately and taken in 500-ml volumetric flask. 200 milliliters of 0.1N HCl was added, sonicated for 5 min, made up to 500 ml with 0.1 N HCl, and filtered. From above solution further dilution was made and the drug concentration was determined at 261.4 nm by using UV spectrophotometer.

2.5.5 Buoyancy lag time

The buoyancy lag time was determined using a USP dissolution apparatus Type II containing 900 mL of Glycin buffer solution (pH 3) at 75 rpm. The time interval between the introduction of the tablet into the dissolution medium and its buoyancy to the top of dissolution medium was taken as buoyancy lag time.

2.5.6 The duration of buoyancy

The time, for which the tablet constantly floats on the surface of the medium, duration of buoyancy, was measured. The duration of buoyancy was determined using a USP dissolution apparatus Type II containing 900 ml of Glycin buffer solution (pH 3) at 75 rpm.

2.6 Determination of Swelling Index

The swelling index of tablet was determined in 900 ml Glycin (pH 3) using USP dissolution apparatus Type II at 75 rpm. The medium was maintained at 37±0.5 ◦C throughout the study. After a selected time intervals, the tablet was withdrawn, blotted to remove excess water and weighed. Swelling characteristics of the tablet was expressed in terms of swelling index

$$\text{Swelling index} = \frac{W_t - W_0}{W_0}$$

Where, W_0 is the initial weight of tablet, & W_t is the weight of tablet at time t.

2.7 Dissolution

In-vitro drug release studies of the prepared matrix floating tablets were conducted for a period of 24 h using USP XXIV type II apparatus (Lab India Disso 2000) at 37± 0.5° C and 75 rpm speed. The dissolution studies were carried out in triplicate with Glycine buffer solution (pH 3) under sink conditions. Five milliliters of aliquot was withdrawn at predetermined time intervals of 1, 2, 4, 6, 8, 10, 12,14,18,20 and 24 hours. The medium was replenished with 5ml of Glycin buffer solution each time.

After filtration and appropriate dilution, the samples were analyzed by a UV spectrophotometer (Shimadzu UV-250 1PC double beam spectrometer) at 261.4 nm using dissolution medium in reference cell. The total amount of drug release was calculated using calibration curve.

3. RESULTS

The sample of Cefpodoxime proxetil was found to be a yellowish white to light white crystalline powder. The melting point of Cefpodoxime Proxetil was found to be in the range of 155-160°C. Loss on drying of sample was calculated and the LOD was found not more than 0.2 percent. Wavelengths of maximum absorbance (λmax) of cefpodoxime Proxetil was found to be 261.8 nm & 262.4 nm in Glycine buffer solution & 0.1N HCL respectively as in spectra in different media are given in Figure 1& 2.

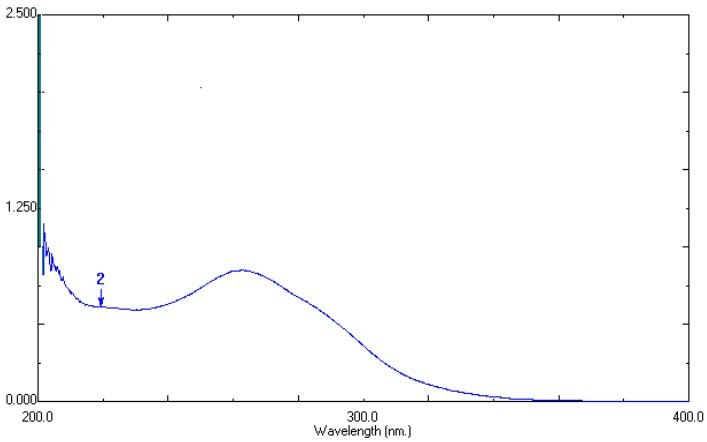

Figure 1: UV spectrum of Cefpodoxime proxetil in Glycine buffer pH 3 (peak 3=261.8 nm)

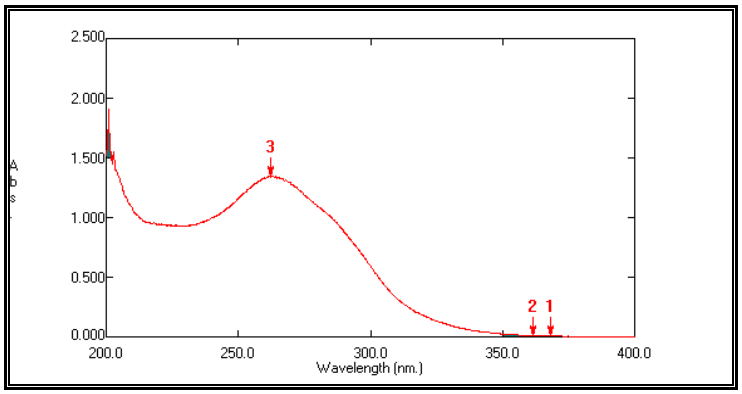

Figure 2: UV spectrum of Cefpo doxime proxetil in0.1N HCL (peak 3=262.4 nm)

Table 3: maximum wavelength (λ max) of cefpodoxime proxetil in different media

Solvent	λ max (nm)
Glycin buffer (pH 3)	261.8
0.1N HCL	262.4

The FTIR spectra are shown in Figure 3 and interpretation of FT-IR spectra are given in Table 4

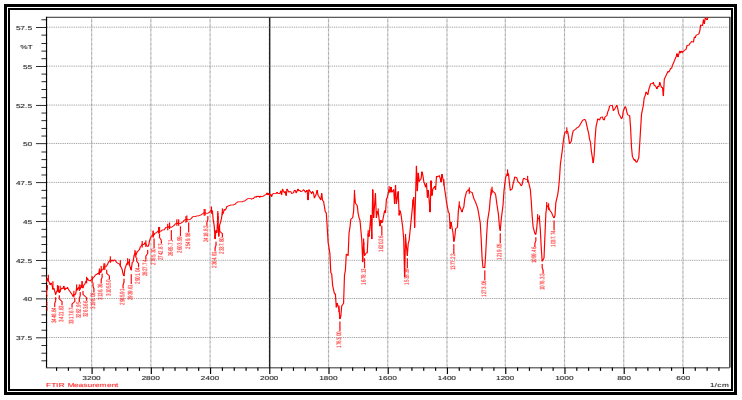

Figure 3: FTIR spectrum of Cefpodoxime proxetil

Table 4: Interpretation of FTIR spectrum of drug

Peak observed (cm-1)	Interpretation	Peak observed (cm-1)	Interpretation
2939,2901,2827	C-H str. (aliphatic)	1763	C=O stretching
2985	C-H str. (aromatic)	674	C-S-C stretching
3421	N-H str.	1640	C=C stretching
1620	N-H bend	1273	C-N stretching
1638	C=N str.	1377	C-H bending
1076,1099	C-O str.		

Table 5: Concentration and Absorbance values for Cefpodoxime proxetil in Glycine buffer (pH 3) (λ max 261.8 nm)

Concentration (mcg/ml)	5	10	15	20	25	30
Absorbance	0.130	0.270	0.419	0.562	0.695	0.869

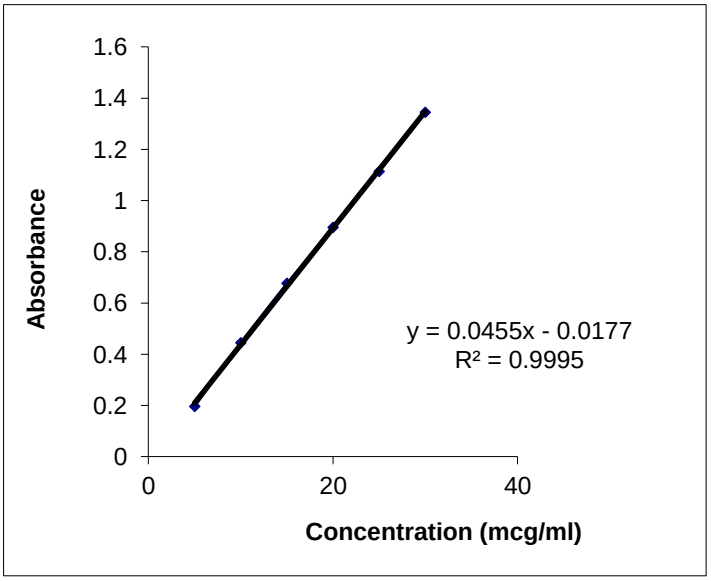

Figure 4: Beer-Lamberts plot for Cefpodoxime proxetil in Glycin buffer (pH 3)

Table 6: Concentration and Absorbance values for Cefpodoxime in 0.1N HCL (λ max-262.4 nm)

Concentration (mcg/ml)	5	10	15	20	25	30
Absorbance	0.197	0.445	0.677	0.835	1.114	1.345

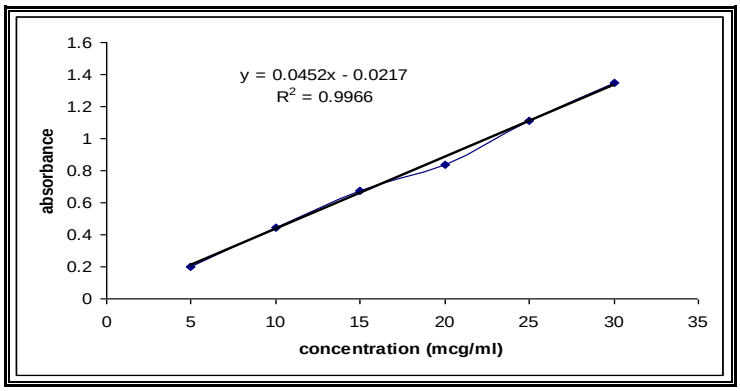

Figure 5: Beer-Lamberts plot for Cefpodoxime Proxetil in 0.1N HCL

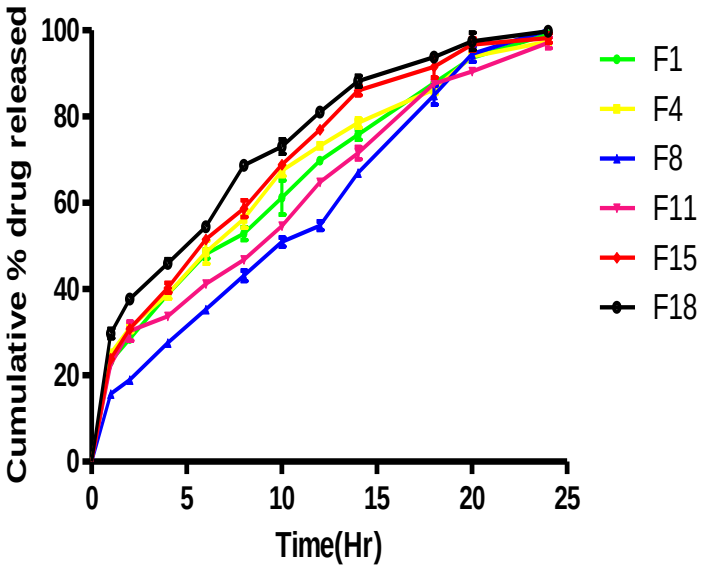

Figure 6: Cumulative % drug released profile of selected Formulation of Cefpodoxime

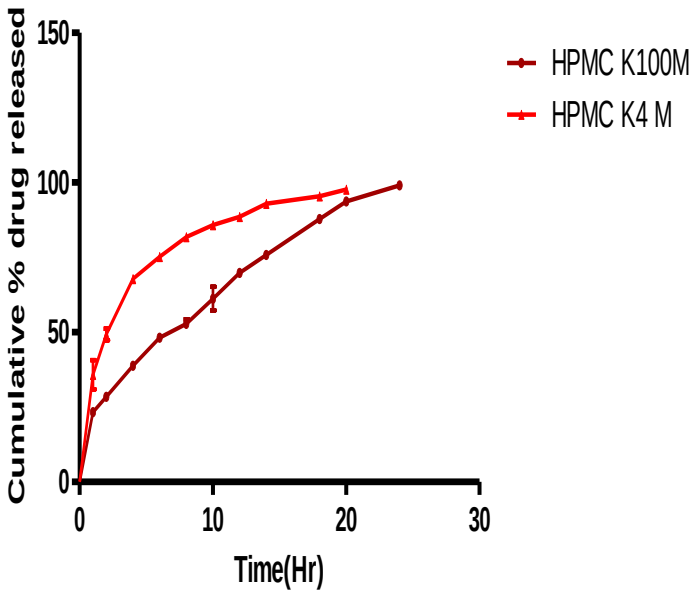

Figure 7: Effect of HPMC K100 M & K4 M on drug release

3.1 Evaluation of powder blend

Table 7: Evaluation of powder blend

Formulations	LOD (%)	Bulk Density (g/cc)	Tapped Density (g/cc)	Carr's compressibility index	Hausner's ratio	Angle of repose (degree)
F1	1.58	0.211	0.380	0.444	1.800	35.68
F2	1.52	0.221	0.387	0.428	1.751	42.30
F 3	1.59	0.214	0.378	0.433	1.766	35.68
F 4	1.64	0.229	0.370	0.381	1.615	35.68
F 5	1.60	0.22	0.367	0.400	1.668	41.34
F 6	1.71	0.218	0.390	0.441	1.788	35.68
F 7	1.72	0.207	0.385	0.462	1.859	40.69
F 8	1.64	0.219	0.381	0.425	1.739	42.61
F 9	1.63	0.211	0.379	0.443	1.796	43.53
F 10	1.58	0.211	0.381	0.446	1.805	42.61
F 11	1.65	0.218	0.385	0.433	1.766	35.68
F 12	1.57	0.223	0.382	0.416	1.713	35.68
F 13	1.62	0.229	0.379	0.395	1.655	40.03
F 14	1.70	0.210	0.376	0.441	1.790	41.34
F 15	1.71	0.222	0.388	0.427	1.747	40.03
F 16	1.79	0.230	0.368	0.375	1.600	39.69
F 17	1.69	0.224	0.368	0.391	1.642	40.69
F 18	1.59	0.219	0.387	0.434	1.767	42.30

3.2 Evaluation of tablets parameters

Table 8: Evaluation of tablets parameter

Formulation code	Thickness (mm)	Hardness (kg/cm2)	Average weight (mg)	Friability (%)	Drug content (%)
F1	5.0	6.9	828.3	0.21	98.89
F2	5.2	7.2	851.6	0.43	98.54
F3	5.2	7.3	875.9	0.28	99.23
F4	5.3	6.8	853.7	0.30	99.38
F5	5.4	7.2	903.4	0.47	98.77
F6	5.4	7.1	878.2	0.49	99.73
F7	5.3	7.3	904.1	0.51	98.23
F8	5.3	7.3	928.4	0.16	99.37
F9	5.1	8.0	879.2	0.21	100.2
F10	5.0	7.0	828.7	0.19	99.18
F11	5.0	7.2	853.9	0.24	99.47
F12	5.1	7.1	778.1	0.18	98.64
F13	5.0	6.9	854.3	0.25	97.98
F14	5.2	7.0	879.1	0.16	98.34
F15	5.2	7.3	903.7	0.14	98.58
F16	5.3	7.1	879.1	0.22	99.04
F17	5.3	7.3	904.1	0.19	98.09
F18	5.3	6.8	928.6	0.71	99.10

3.3 Dissolution profile

Table 9: Cumulative % drug released Cefpodoxime from formulation

Time (Hours)	Cumulative % release (mean ± S.D.)								
	Formulation code								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
1	23.28 ± 0.69	23.15 ±0.32	18.31 ±0.36	25.10 ±0.80	20.91 ±0.52	21.94 ±0.20	22.74 ±0.32	15.70 ±0.49	32.06 ±2.83
2	28.46 ±0.85	28.25 ±0.51	26.15 ±0.34	31.06 ±1.02	25.36 ±0.59	25.52 ±3.20	24.01 ±0.34	18.96 ±0.28	40.59 ±2.31
4	38.78 ±0.75	37.02 ±0.87	34.08 ±0.34	38.84 ±1.07	35.42 ±0.89	30.42 ±0.51	31.44 ±0.37	27.53 ±0.52	47.82 ±1.49
6	48.13 ±0.97	45.48 ±0.49	40.59 ±0.30	48.54 ±2.70	42.49 ±1.48	40.69 ±0.22	38.89 ±0.23	35.30 ±0.56	56.73 ±1.63
8	52.87 ±1.47	51.80 ±0.22	48.52 ±0.41	56.26 ±2.08	50.27 ±2.61	49.03 ±0.53	46.25 ±0.56	43.10 ±1.12	69.02 ±1.17
10	61.21 ±3.96	57.63 ±0.60	52.64 ±0.51	67.44 ±1.20	59.20 ±4.33	53.83 ±0.48	56.42 ±0.67	50.92 ±1.06	74.23 ±1.43
12	69.79 ±0.49	68.89 ±0.39	57.80 ±0.53	73.21 ±0.92	67.64 ±0.69	59.51 ±1.17	69.19 ±0.39	54.73 ±0.99	80.78 ±0.63
14	75.79 ±1.14	73.28 ±0.37	67.40 ±0.51	78.50 ±1.07	69.49 ±0.93	69.23 ±0.54	80.76 ±0.59	66.95 ±0.41	88.17 ±1.94
18	87.80 ±0.68	87.37 ±0.34	74.89 ±1.20	86.29 ±1.11	76.66 ±0.43	80.18 ±0.42	92.46 ±0.39	84.98 ±2.20	94.05 ±1.04
20	93.63 ±0.36	92.80 ±0.40	82.35 ±1.03	93.93 ±0.87	90.65 ±1.36	92.64 ±0.58	99.16 ±0.41	94.50 ±1.80	99.49 ±0.44
24	99.09 ±0.68	96.70 ±0.26	93.58 ±0.63	97.41 ±0.69	96.46 ±0.48	96.39 ±2.01		100.00 ±3.13	

Table 10: Cumulative % drug released of formulation of Cefpodoxime containing HPMC K4 M

Time (Hours)	Cumulative % release (mean ± S.D.)								
	Formulation code								
	F10	F11	F12	F13	F14	F15	F16	F17	F18
1	35.76 ±4.89	22.44 ±0.22	18.20 ±0.69	25.17 ±1.35	25.69 ±1.26	23.84 ±0.39	34.38 ±0.72	32.51 ±1.45	29.73 ±1.07
2	49.28 ±1.93	30.27 ±2.20	24.00 ±0.88	33.12 ±1.37	31.76 ±0.48	30.81 ±0.74	44.66 ±1.15	40.11 ±1.07	37.74 ±0.91
4	67.84 ±0.96	33.74 ±0.32	30.89 ±0.91	40.79 ±0.55	41.09 ±0.69	40.31 ±1.14	50.62 ±1.39	50.62 ±1.42	45.98 ±0.97
6	75.16 ±0.59	41.17 ±0.85	40.74 ±1.69	51.40 ±0.94	55.96 ±0.86	51.51 ±0.62	63.49 ±5.03	59.42 ±3.60	54.47 ±0.64
8	81.79 ±0.85	46.78 ±0.94	46.44 ±0.75	64.63 ±0.64	65.61 ±0.81	58.67 ±1.95	70.75 ±5.46	69.52 ±0.28	68.69 ±0.63
10	85.79 ±1.39	54.62 ±0.81	53.66 ±1.16	75.52 ±0.91	70.54 ±1.19	68.91 ±0.63	76.57 ±1.55	76.01 ±1.13	73.04 ±1.67
12	88.56 ±1.39	64.82 ±0.73	63.20 ±0.99	81.56 ±0.78	78.92 ±1.06	76.98 ±0.80	83.99 ±2.50	83.54 ±0.53	81.04 ±0.37
14	92.99 ±0.41	71.54 ±1.43	69.62 ±0.83	91.99 ±0.88	89.72 ±1.51	86.05 ±1.13	91.49 ±3.57	90.34 ±1.01	88.25 ±1.25
18	95.39 ±0.98	87.66 ±0.81	77.36 ±0.71	94.98 ±0.94	93.76 ±0.77	91.54 ±2.49	95.76 ±0.95	94.96 ±0.85	93.75 ±0.87
20	97.72 ±0.30	90.45 ±0.66	82.22 ±0.93	99.21 ±0.57	97.36 ±0.61	96.73 ±1.47	99.39 ±0.54	97.49 ±1.00	97.43 ±1.99
24		97.10 ±1.27	93.99 ±0.56			98.20 ±1.07			99.82 ±0.36

Table 11: Cumulative % drug release of Cefpodoxime formulation for 24 hours

Time (hours)	Cumulative % drug released (maen ± S.D.)					
	Formulation code					
	F1	F4	F8	F11	F15	F18
1	23.28 ± 0.69	25.10 ±0.80	15.70 ±0.49	22.44 ±0.22	23.84 ±0.39	29.73 ±1.07
2	28.46 ±0.85	31.06 ±1.02	18.96 ±0.28	30.27 ±2.20	30.81 ±0.74	37.74 ±0.91
4	38.78 ±0.75	38.84 ±1.07	27.53 ±0.52	33.74 ±0.32	40.31 ±1.14	45.98 ±0.97
6	48.13 ±0.97	48.54 ±2.70	35.30 ±0.56	41.17 ±0.85	51.51 ±0.62	54.47 ±0.64
8	52.87 ±1.47	56.26 ±2.08	43.10 ±1.12	46.78 ±0.94	58.67 ±1.95	68.69 ±0.63
10	61.21 ±3.96	67.44 ±1.20	50.92 ±1.06	54.62 ±0.81	68.91 ±0.63	73.04 ±1.67
12	69.79 ±0.49	73.21 ±0.92	54.73 ±0.99	64.82 ±0.73	76.98 ±0.80	81.04 ±0.37
14	75.79 ±1.14	78.50 ±1.07	66.95 ±0.41	71.54 ±1.43	86.05 ±1.13	88.25 ±1.25
18	87.80 ±0.68	86.29 ±1.11	84.98 ±2.20	87.66 ±0.81	91.54 ±2.49	93.75 ±0.87
20	93.63 ±0.36	93.93 ±0.87	94.50 ±1.80	90.45 ±0.66	96.73 ±1.47	97.43 ±1.99
24	99.09 ±0.68	97.41 ±0.69	100.00 ±3.13	97.10 ±1.27	98.20 ±1.07	99.82 ±0.36

3.4 Determination of buoyancy lag time

Table 12: Determination of buoyancy lag time of formulation containing HPMC K100 M

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Time (second)	02	01	01	01	02	02	03	02	02

Table 13: Determination of buoyancy lag time of formulation containing HPMC K100 M

Formulati code	F10	F11	F12	F13	F14	F15	F16	F17	F18
Time (second)	03	03	01	02	04	40	02	03	03

3.5 Determination of duration of buoyancy

Table 14: Determination of duration of buoyancy time of formulation having HPMC K4 M

Formulation code	F1	F2	F3	F4	F5	F6	F7	F8	F9
Time (Hours)	24	23	23	20	24	22	20	24	20

Table 15: Determination of duration of buoyancy time of formulation having HPMC K4 M

Formulation code		F10	F11	F12	F13	F14	F15	F16	F17	F18
Time (Hours)		23	24	23	24	22	22	22	22	24

3.6 Swelling study

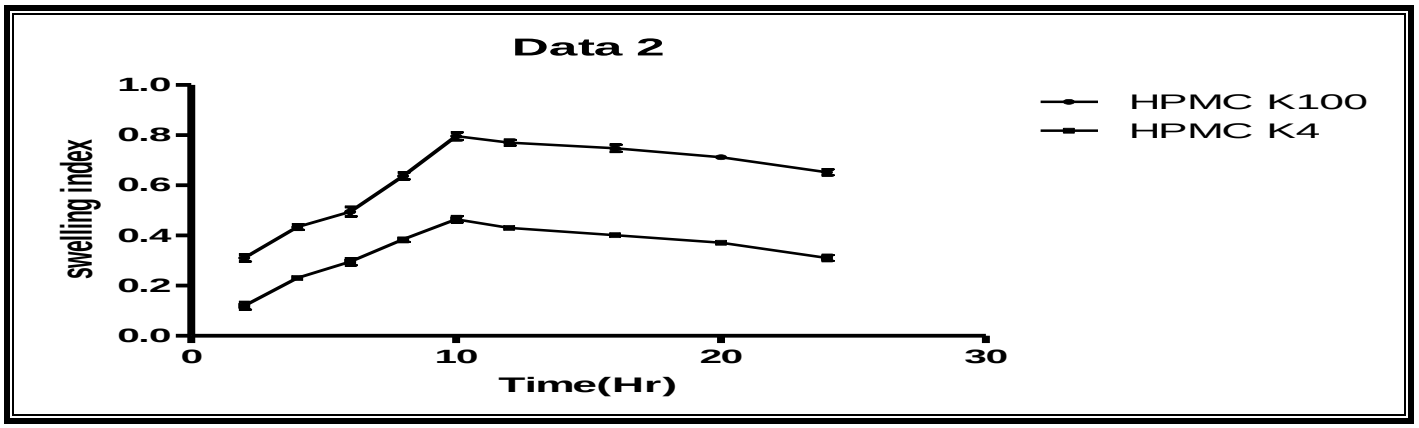

Figure 8: Swelling behavior of formulation containing HPMC K100 M & K4

4. DISCUSSION

Ideal once daily floating drug delivery system should release the drug for 24 hours and float up to 24 hrs. Once daily floating matrix tablet of Cefpodoxime proxetil should be release the drug for 24 hours to maintain the effective plasma level. All the formulations were prepared by using two different grades of HPMC (K100 and K4), cross povidone and MCC pH 101. HPMC is a matrix forming agent. All the formulations showed buoyancy lag time of less than 5 seconds regardless of concentration of HPMC K100 M, K4 and cross povidone. It may be due to the low density of tablet.

The study of swelling behavior of formulation F1 containing HPMC K100 M showed that swelling is increased up to 10 hours but after 10 hours it decreased. In first 10 hours water is absorbed by the polymer (HPMC is hydrophilic polymer which is attributed to its structure) and weight gain by tablet is seen. When water ingress from outer side to the tablet core the outer gel layer starts to erode. This erosion of polymer dominates over water sorption after 10 hours. Hence the reduction in tablet weight occurs after 10 hours because of erosion of matrix. The formulation F11 containing HPMC K4 M also shows same phenomenon but

swelling is up to less extent as compared to F1. The swelling index of HPMC K100 M was found to be higher than that of HPMC K4 M. This may be due to high molecular weight and high viscosity of HPMC K100 M.

The USP defines, among others, HPMC 2901 (Methocel E), HPMC 2906 (Methocel F) and HPMC 2208 (Methocel K). The ratios and degree of substitution vary between grades. Variations in the molecular weights of various HPMC grades are reflected in the

viscosities of aqueous solutions prepared at a standard concentration. HPMC K 100 is a high viscosity grade. The present work showed that as the concentration of HPMC K100 M increased, drug release from the matrix core decreases. HPMC swells by absorbing water and forms a swollen layer barrier for drug to diffuse through this layer. As proportion of HPMC in tablet is increased, thickness of the diffusion barrier layer increases. This results in reduced drug release. This is also supported by the results of swelling study.

The formulation F1 containing low level of HPMC K100 M (75 mg) and low level of cross povidone (75 mg) showed higher burst release and maintained drug release up to 24 hours. The tablet was remained floated for 24 hours. High level of HPMC K100 M (F2, F3, F5,F6,) results in greater amount of gel being formed. This gel increases diffusion path length of the drug and hence release rate decreases. On the same line it formulation F5 and F8 should show relatively less drug release as high level of HPMC K100 M(100 mg & 125 mg respectively) is used in these formulations. But both the formulations released more than 97% drug within 24 hours. This may be attributed to high level of cross povidone used in these formulations. As cross povidone has high water absorbing property, water uptake of tablet increases. This results in increased driving force for drug release. F1, F8 in which cross povidone was incorporated were found to be remained intact for 24 hours. The HPMC K100 M is responsible for maintaining integrity of the tablets. This was confirmed by the results of formulations F4, F6, F7, F9 in which low level of HPMC and high level of cross povidone was used. These formulations could not maintain integrity for 24 hours and resulted in less duration of floating as shown in table 15.

So it can be concluded that drug release decreases with increases in level of HPMC K100 M and increases with increasing level of cross povidone. Hence the desired drug release can be achieved by using appropriate proportions of HPMC K100 M and cross povidone.(F1, F5 and F8). HPMC K4 M is a low viscosity grade polymer as mentioned above .It was found that low concentration of HPMC K4 M with any level of cross povidone could not retard the drug release up to 24 hours. Hence the formulations F10, F13,F14,F16,F17 released the drug within 20 hours as shown in table 15.The formulation F11 which contains high amount of HPMC K4 M than F10 (100mg) and low level of cross povidone (75 mg) shows drug release up to 24 hours with sufficient floating duration. The formulation F15 and F18 contains high level of HPMC K4 M (125 mg each) and high level of cross povidone (100 mg and 125 mg) respectively. Both the formulations showed sustained drug release up to 24 hours. Again this may be due to low viscosity of HPMC K4 M and high amount of cross povidone which increases the driving forces for drug release.HPMC K100 M retards drug release more effectively as compared to HPMC K4M.

5. CONCLUSION

Floating tablets of Cefpodoxime Proxetil were prepared using HPMC K100 M, HPMC K4 M, cross povidone and MCC pH 101.HPMC K100 M and HPMC K4 M were used as release retarding agents and cross povidone as swelling agent. As the concentration of HPMC K100 M & K4 increases, drug release decreases. As the concentration of Cross povidone increases, drug release also increases. Various tablet evaluation parameters like thickness, hardness, friability, weight variation and drug content of all formulations were found to be satisfactory. All formulations were evaluated for buoyancy lag time and duration of buoyancy, they were found to be satisfactory. Dissolution study revealed that formulations F1, F4, F8, F11, F15, F18 release the drug up to 24 hours. It can be concluded that floating tablet of cefpodoxime proxetil with sustain drug delivery can be formulated by using HPMC and cross povidone in appropriate proportions (F1). Such formulation may improve bioavailability of the drug, which is mainly absorbed in upper part of GI tract.

6. CONFLICTS OF INTERESTS

There are no conflicts of interests.

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