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DESIGN AND CHARACTERIZATION OF FLOATING TABLET OF CEFPODOXIME PROXETIL

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ABSTRACT: The present study in the development of Hydrodynamically Balanced Systems (HBS) of Cefpodoxime proxetil, third generation antibiotic drug which are designed to increase the gastric residence time, thus prolonging the drug release. Hydroxy propyl methyl cellulose (HPMC) of different viscosity grades at three different drug to polymer ratios were used to prepare HBS by direct compression technique. The prepared HBS tablets were evaluated in terms of their pre-compression parameters, physical characteristics like hardness, friability, uniformity of weight, uniformity of drug content, swelling index , invitro floating studies, invitro drug release and short term stability studies. The drug polymer ratio, viscosity grades of HPMC, different diluents and gas generating agents were found to influence the drug release and floating properties of the prepared HBS. The floating properties and drug release characteristics were determined for the prepared HBS in 0.1 N HCl dissolution media. All the HBs formulations showed good invitro floating properties with an optimum concentration of gas generating agents sodium bicarbonate and citric acid. The rate of drug release decreased with increased polymer concentration. It was found that HPMC viscosity had significant impact on the drug release from the prepared HBS. Among the three viscosity grades of HPMC (K4M, K15M, K100M), HPMC K4M along with lactose as diluents was found to be beneficial in improving the drug release rate and floating properties .

Introduction:

The real issue in the development of oral controlled release dosage forms is not just to prolong the delivery of drugs for more than 12 hours, but to prolong the presence of the dosage forms in the stomach or upper gastrointestinal (GI) tract until all the drug is released for the desire period of time (1). Novel oral controlled dosage form that is retained in the stomach for prolonged and predictable period is of major interest among academic and industrial research groups. One of the most feasible approaches for achieving

prolonged and predictable drug delivery profile in the GI tract is to control gastric residence time (GRT).

Dosage form with prolonged GRT or gastro-retentive dosage form (GRDF) provides an important therapeutic option (2). Dosage forms that can be retained in the stomach are called gastroretentive drug delivery systems (GRDDS) (3). The gastroretentive drug delivery systems can be retained in the stomach and assist in improving the oral sustained delivery of drugs that have an absorption window in a particular region of the gastrointestinal tract. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability (4). Various gastroretentive techniques were used, including floating, swelling, high density, and bioadhesive system, have been explored to increase the gastroretention of dosage forms (5,6). Floating systems having 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. (7,8). The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site of the body, to achieve promptly and then maintain the desired therapeutic drug concentration that elicits the pharmacological action and to minimize the incidence and the severity of unwanted adverse effects. To achieve this goal, it would be advantageous and more convenient to maintain a dosing frequency to once, or at most, a twice-daily regimen. An appropriately designed extended-release dosage form can be a major advance in this direction (9)

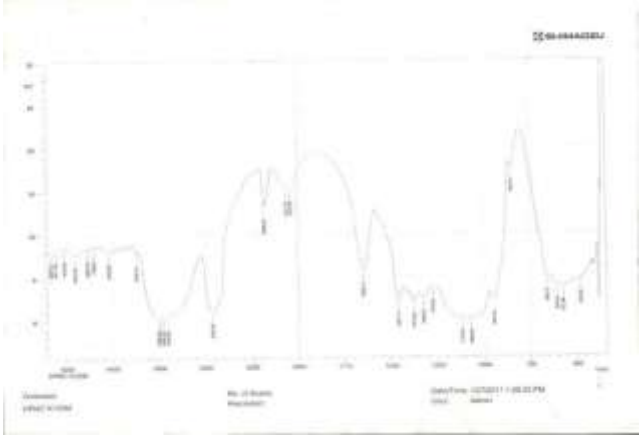
Cefpodoxime proxitel is a oral third generation cephalosporin antibiotic.It is active against gram Positive and gram negative bacteria.It is commonly used to treat acute otitis media, Pharyngitis,Uncomplicated Urinary tract infection.Cefpodoxime proxetil is a prodrug that is absorbed from the gastrointestinal tract ,half-life (2hrs) ,Bioavailability (50%) (10).Cefpodoxime proxitel is the ideal candidate for the floating drug delivery system. The purpose of this work was to develop novel sustained release of Cefpodoxime proxitel floating tablets to increase gastric residence time of Cefpodoxime proxitel.

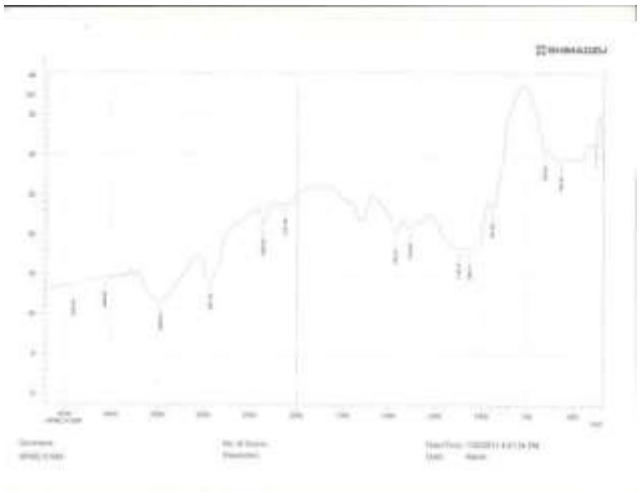
Materials and methods

Cefpodoxime proxitel was received as a gift sample from Panacea biotech (Mohali), Hydroxy propyl Methyl Cellulose K4M, K15M, K100M were received as a gift sample from CIPLA (Poanta sahib), Microcrystalline cellulose were received as a gift sample from Panacea biotech. Sodium bicarbonate, citric acid,Talc and Magnesium stearate were procured from (Glennmark).

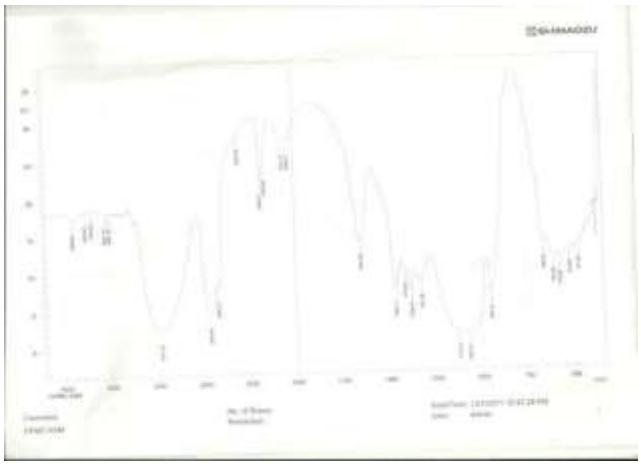
Identification of drug: -

IR Studies: - HPME K 100M

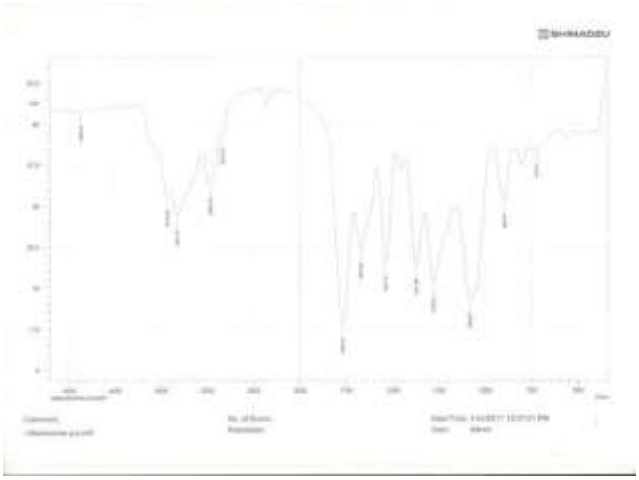




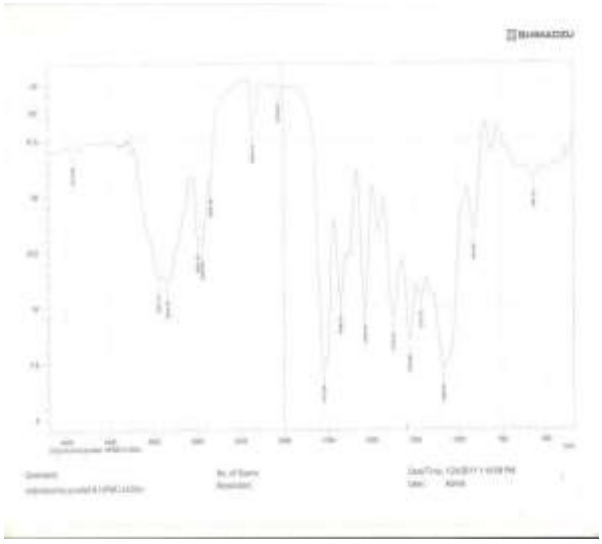
HPME K 4M



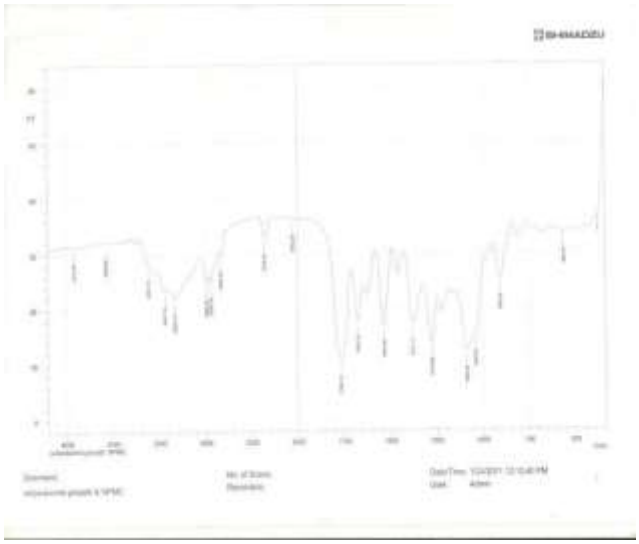
HPME K 15M



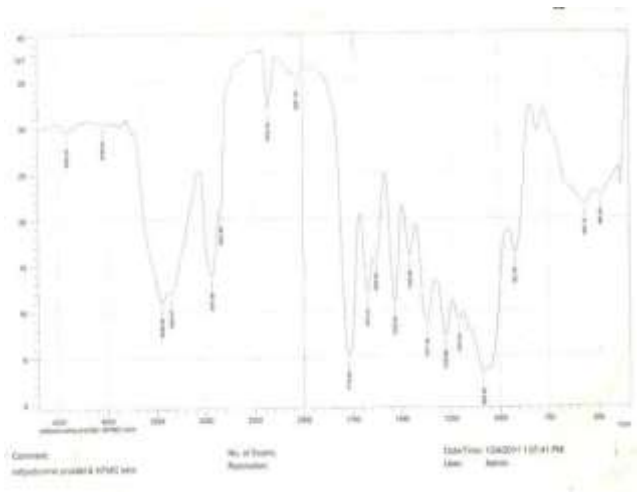
CEFPODOXIME PROXETIL



CEFPODOXIME PROXETIL & K100M

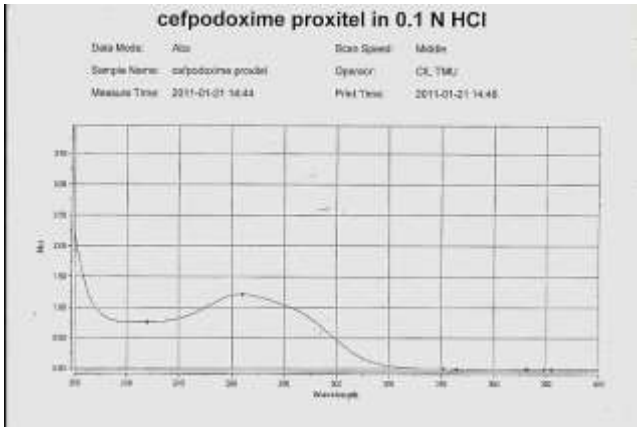


CEFPODOXIME PROXETIL & K15M



CEFPODOXIME PROXETIL & K4M

UV STUDIES



Standard curve of cefpodoxime proxetil

CONC.	ABSORPTION
5	0.312
10	0.643
15	0.923
20	1.192
25	1.504

Procedures for preparation of Floating tablet of cefpodoxime proxitel

Floating tablet of cefpodoxime proxitel were prepared by direct compression method.All the ingredients were accurately weighed.In order to mix the ingredients properly drug and polymer were blend in mortar followed by the addition of Sodium bicarbonate , Citric Acid, Microcrystalline cellulose ,Talc and Magnesium stearate
, After thoroughly mixing the ingredients, Tablets were compressed in rotary punching machine

Evaluations

Flow properties of powder blend

The flow properties of granules (before compression) were characterized in terms of angle of repose, Carr index and Hausner ratio (11)

Physical Evaluation of floating tablet of cefpodoxime proxitel

1) Hardness test
   The crushing strength (Kg/cm²) of tablets was determined by using Monsanto hardness tester

2) Friability test
   This was determined by weighing 10 tablets after dusting, placing them in the friabilator and rotating the plastic cylinder vertically at 25 rpm for 4 min. After dusting, the total remaining weight of the tablets was recorded and the percent friability was calculated

3) Uniformity of weight
   This test is performed to maintain the uniformity of weight of each tablet which should be in the prescribed range, this is done by sampling and weighing 20 tablets at random and average weight is calculated.

4) Content Uniformity
   5 tablets were weighed from each formulation, powdered and equivalent to 130 mg of Cefpodoxime Proxitel were weighed and dissolved in sufficient quantity of methanol and make up to 100 ml with methanol. The solutions were suitably diluted with buffer solution pH 1.2 and the content of Cefpodoxime Proxitel was estimated spectrophotometrically at 263 nm using pH 1.2 as a blank.

5) Thickness and Diameter
   Five tablets were randomly selected for the determination of thickness and diameter with the help of vernier caliper

6) Swelling Index
   The swelling index of tablets was determined in 0.1N HCl (pH 1.2) at room temperature. The swollen weight of the tablet was determined at predefined time intervals over a period of 24 h. The swelling index (SI), expressed as a percentage, and was calculated from the following equation

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

Formulation: -

INGREDIENTS (MG)	F1	F2	F3	F4	F5	F6	F7	F8	F9
DRUG	130	130	130	130	130	130	130	130	130
HPME K4M	100	—	—	50	50	—	60	—	60
HPME K15M	—	100	—	—	50	50	40	60	—
HPMEK100M	—	—	100	50	—	50	—	40	40
SODIUM BICARBONATE	30	30	30	30	30	30	30	30	30
CITRIC ACID	5	5	5	5	5	5	5	5	5
MCC	25	25	25	25	25	25	25	25	25
MAGNESIUM STERATE	5	5	5	5	5	5	5	5	5
TALC	5	5	5	5	5	5	5	5	5
TOTAL	300	300	300	300	300	300	300	300	300

RESULTS AND DISCUSSION In the present study, Hydrodynamically Balanced Systems of Cefpodoxime proxetil were prepared by using different viscosity grades of Hydroxy propyl methyl cellulose (HPMC), viz, K4M, K15M and K100M(4,000, 15,000 and 1,00,000cps respectively) at different drug to polymer ratio with or

without gas generating agent like sodium bicarbonate and citric acid. Two different diluents used are lactose and MCC.

The weighed quantities of drug and polymers were mixed thoroughly in different ratios and HBS tablets were prepared by direct compression method. The prepared HBS tablets were evaluated The prepared tablets of all the formulations were evaluated for precompression parameters like angle of repose, bulk and tapped density and compressibility index and physical characters like tablet hardness, friability, weight variation, buoyancy lag time, total floating time, Swelling index, in-vitro drug release.

FORMULATION CODE	BULK DENSITY	TAP DENSITY	FRIABILITY	HARDNESS	DRUG CONTENT
F1	0.320	0.40	0.323	5.5	298
F2	0.322	0.40	0.666	6.5	300.2
F3	0.325	0.404	0.66	6.0	300.8
F4	0.321	0.398	0.671	5.0	298.7
F5	0.320	0.40	0.334	6.5	299.6
F6	0.323	0.398	0.668	6.0	301.4
F7	0.318	0.396	0.331	5.5	299.3
F8	0.321	0.40	0.333	5.0	301.8
F9	0.321	0.398	0.666	6.5	304.3

FORMULATION CODE	FLOATING LAG TIME(SEC	FLOATING TIME(HRS)
F1	45	24
F2	37	24
F3	43	24
F4	51	24
F5	57	24
F6	69	24
F7	53	24
F8	51	24
F9	59	24

FORMULATION CODE	ANGLE OF RESPONSE	WEIGHT VARIATION
F1	22°	300.5
F2	24°	299.25
F3	21°	300.75
F4	21°	299
F5	23°	299.85
F6	22°	299.15
F7	20°	286.25
F8	23°	301
F9	22°s	285

time	log time	Root time	abs	con µg	Conc*1	con *5	cor*100	cum	%	log cumu re
60	1.778151	7.745967	0.02	3.448276	0.0034482759	0.017241	3.103448	3.103448	3.103448	0.491845
120	2.079181	10.95445	0.051	8.793103	0.0087931034	0.043966	7.913793	7.931034	7.931034	0.89933
180	2.255273	13.41641	0.083	14.31034	0.0143103448	0.071552	12.87931	12.94052	12.94052	1.111952
240	2.380211	15.49193	0.11	18.96552	0.0189655172	0.094828	17.06897	17.20172	17.20172	1.235572
300	2.477121	17.32051	0.142	24.48276	0.0244827586	0.122414	22.03448	22.26207	22.26207	1.347566
360	2.556303	18.97367	0.188	32.41379	0.0324137931	0.162069	29.17241	29.52241	29.52241	1.470152
420	2.623249	20.4939	0.234	40.34483	0.0403448276	0.201724	36.31034	36.89397	36.89397	1.566955
480	2.681241	21.9089	0.281	48.44828	0.0484482759	0.242241	43.60345	44.41207	44.41207	1.647501
540	2.732394	23.2379	0.322	55.51724	0.0555172414	0.277586	49.96552	51.04397	51.04397	1.707944
600	2.778151	24.4949	0.383	66.03448	0.0660344828	0.330172	59.43103	60.82672	60.82672	1.784094
660	2.819544	25.69047	0.425	73.27586	0.0732758621	0.366379	65.94828	67.71379	67.71379	1.830677
720	2.857332	26.83282	0.471	81.2069	0.0812068966	0.406034	73.08621	75.25862	75.25862	1.876556

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