Research Paper

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Formulation and Evaluation of Omeprazole Gastroretentive Floating Tablets for the Treatment of Peptic Ulcer.

Pharmaceutical Science

KEYWORDS : Gastro retentive floating tablet, Omeprozole, HPMC

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ABSTRACT

This investigation describes the preparation and in vitro evaluation of gastroretentive floating tablet of Omeprazole by direct compression technique using varying concentrations of different grades of polymers (HPMC K4 M and HPMC K15 M) with sodium bicarbonate and citric acid were evaluated for their gel forming and release controlling properties. Sodium bicarbonate and citric acid were incorporated as gas generating agents. Omeprazole having short biological half life (2-3.5 h), absorption in the initial part of the small intestine and 50% absolute bioavailability of drug favor development of sustained release floating formulation. The effects of soluble components (sodium bicarbonate and citric acid), gel forming agents and amount of Omeprazole on drug release profile and floating properties were investigated. Tablets were prepared by direct compression technique. The tablets were characterized by lag time, floating time, weight variation, swelling index, drug content and dissolution profile. The results indicated that a high amount of floating agent and combination of HPMC K4 M and HPMC K15 M polymer favored the sustained release of Omeprazole from gastroretentive tablet formulations. Drug release study was evaluated for 7 hours using USP XXII paddle-type dissolution apparatus using 0.1N HCl as dissolution medium drug release of 94% of F6 formulation.

INTRODUCTION

Omeprazole (Fig.1) Suppresses gastric acid secretion by blocking "acid (proton) pump" within gastric parietal cell [Basak SC, IJPS, 2004]. It is commonly used in treatment of peptic ulcer disease (PUD) and gastro esophageal reflux disease (GERD). Omeprazole is also used alongside Fexofenadine and other antihistamines for the treatment of skin conditions such as hives[Shabaraya AR, IJPS, 2000]. Omeprazole, the model drug for this study, is a histamine H2-receptor antagonist. It is widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, gastroesophageal reflux disease, and erosive esophagitis [Shirwaikar AA, IJPS, 2005].

OBJECTIVE

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. It is also reported that oral treatment of gastric disorders with an H2-receptor antagonist like Omeprazole used in combination with antacids promotes local delivery of these drugs to the receptor of the parietal cell wall. Local delivery also increases the stomach wall receptor site bioavailability and increases the drugs' ability to reduce acid secretion.

EXPERIMENTAL METHODS

Preparation of Floating Tablets

Effervescent Floating tablets containing Omeprazole were prepared by direct compression technique using varying concentrations of different grades of polymers (HPMC K4 M and HPMC K15 M) with sodium bicarbonate and citric acid. All the ingredients were accurately weighed as show in Table -1 and passed through different mesh sieves accordingly. Then, except Magnesium stearate and talc all other ingredients were blended uniformly in glass mortar After sufficient mixing of drug as well as other components, Magnesium stearate and talc was added, as post lubricant, and further mixed for additional 2-3 minutes. The blend was characterized for the different physical parameters such as bulk density, Tapped density. The tablets were compressed using rotary tablet machine. The weights of the tablets were kept constant for all formulation. Tablets were compressed at 200 mg weight on an 8-station mini rotary tableting machine.

Table 1: Composition of different floating tablet formulations of Omeprozole

S. No.	Ingredients	F1	F2	F3	F4	F5	F6	
1	Omeprazole	30	30	30	30	30	30	
2	HPMC K 4 M	90	90	--	--	45	45	
3	HPMC K 15 M	--	--	90	90	45	45	
4	Sodium Bicarbonate	20	10	20	10	20	10	
5	Citric Acid	10	20	10	20	10	20	
6	PVP K-30	20	20	20	20	20	20	
7	Lactose	30	30	30	30	30	30	
8	Magnesium Stearate	2	2	2	2	2	2	
9	Talc	2	2	2	2	2	2	

RESULTS AND DISCUSSION

The physical characteristics of tablets (F1 to F6) such as hardness, friability and weight variation, swelling index were determined and the results are shown in Table-2.

Table 2: Hardness, Friability, Weight variation, Drug content and Thickness of tablets of different formulation F1 to F6 Formulation

Batch	Hardness Test (Kg/cm2)	Friability (%)	Weight variation	Drug content (%)	Swelling index
F1	4.5	0.46		91.33	
F2	4.0	0.51		90.66	
F3	4.0	0.31		96.00	
F4	4.0	0.41		96.66	
F5	4.5	0.36		91.33	
F6	4.2	0.31		95.33	

Buoyancy lag time and duration of floating were determined using 100 ml beaker containing 0.1N HCl medium are shown in Table-3 and the results it can be concluded that the batch containing only HPMC K4M and HPMC K15M showed good Buoyancy lag time is 60 t0 84 sec and Total floating time is 12h.

Table No. 3: Batch Buoyancy Lag Total Floating

Batch	Time (seconds)	Time (hrs)
F1	68	>12
F2	84	>10
F3	62	>12

F4	78	>10
F5	60	>12
F6	81	>10

The floating formulations F1 to F6 were subjected for the dissolution studies using USP dissolution apparatus 2 (paddle) in 900 ml of 0.1N HCl medium. The effervescent floating tablets of Omeprozole were formulated in seven different batches F1 to F6 by using hydrophilic polymers HPMC K 4 M and HPMC K 15M along with effervescing agent sodium bicarbonate and citric acid as showing in table 4. The drug release obtained was 30 % in first two hours, 94 % of the drug were found to be released in subsequent 7 hours respectively (table 4). Among these formulations, the release rate was increased in the following order: F6 > F1 > F2 > F3 > F5 > F4. The released the drug 94 % in 7 hours (fig. 2). It is thus concluded that effervescent floating tablet containing Omeprazole gave slow and complete drug release spread over 7 hours.

Table 4: Cumulative % drug released of F1 to F7 (0.1N HCl) Formulation

	% drug release						
Batch	**1hr**	**2hr**	**3hr**	**4hr**	**5hr**	**6hr**	**7hr**
F1	17.94	23.92	38.87	48.83	61.79	86.91	91.69
F2	23.92	28.90	35.88	48.85	65.78	83.72	90.69
F3	15.94	25.91	43.85	55.81	61.69	72.75	88.70
F4	21.92	37.87	43.80	62.69	68.77	76.74	83.72
F5	23.82	30.89	41.86	58.80	63.78	80.73	85.71
F6	19.93	31.89	53.82	58.80	62.79	73.75	94.68

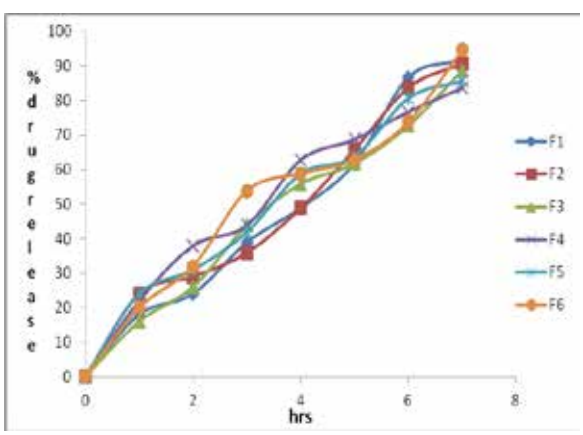

Fig 2 : Graph of In vitro drug release profile

CONCLUSIONS

This study discusses the preparation of floating tablets of Omeprazole The effervescent-based floating drug delivery was a promising approach to achieve The addition of gel-forming polymer HPMC K4 M and HPMC K15 M and gas-generating agent sodium bicarbonate and Citric acid was essential to achieve *in vitro* buoyancy. The results indicated that a high amount of floating agent and combination of HPMC K4 M and HPMC K15 M polymer favored the sustained release of Omeprazole from gastroretentive tablet formulations. Addition of citric acid, to achieve buoyancy under the elevated pH of the stomach, caused an enhancement in drug release. In all cases the increase of the floating agent content caused a lowering of the magnitude of release exponent indicating the shifting of release mechanism from non- fickian. All these results indicated that a low amount of floating agent and high amount of hydrophilic polymer favored the sustained release of Omeprazole from gastro retentive tablet formulations. A lesser FLT and a prolonged floating duration could be achieved by varying the amount of effervescent and using different polymer combinations. The *in vitro* drug release profiles obtained for tablets (F6) made with combinations of HPMC K4 M and HPMC K15 M showed FLT (81s) and a prolonged floating duration(> 10hrs) which was a sustain release characteristic (94%) for 7 hrs.

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