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FORMULATION AND EVALUATION OF FAMOTIDINE FLOATING MATRIX TABLETS

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ABSTRACT

The aim of this research studies was to formulate a drug delivery system for Famotidine. This study examined the usage of a 3-factor, 3-level BoxBehnken project and efficacy of a floating pill for the famotidine pill with five-point center facts. The value of HPMC K4 (Hydroxy Propyl Methyl cellulose), the quantity of HPMCK15 and the quantity of HPMCK100 were designated as self-governing variables and the floating time (TFT), half-life,% 10 hours drug release, and distribution coefficients (n) selected as the dependent variant. Prepared tablets for famotidine were tested for a complete elimination study and were obtained following zero order kinetic release. Responses were analyzed using ANOVA and separate reply limits were assessed using an F test and a polynomial equation designed for each response using the MLRA. The amount of HPMC K4 and the amount of HPMCK15 were found to have a significant effect on all selected response fractions and the amount of HPMCK100 had a significant effect on TFT. A moderate amount of HPMC K4, HPMCK100, and HPMCK15 are essential for achieving a good float time and a small amount of floating cell. It's clear from the scatter profiles that the batches F_3, F_7, and F_8 showed the first stage of the explosion in the first hour of completion. The explosion phase was followed by a limited drug release all the time. The pills produced showed a good time floating and controlled drug release for a period of 12.

KEYWORDS: Famotidine, Gastro retentive floating tablet, Box-Behnken Design, Hydroxy Propyl Methyl Cellulose.

INTRODUCTION

The goal of the present study is to develop a single drug delivery system for Famotidine. Famotidine is an antagonist of the histamine H2 receptor. That is commonly recommended for active duodenal ulcers, abdominal ulcers, Zollinger Ellison syndrome, Gastro Esophageal Reflux Disease (GERD) and erosive Esophagitis. Its minimum half-life is 2.5-4.0 hours. The recommended current oral dose of famotidine is 20mg two times in a day or 40mg one time daily. Low bioavailability (40-45%) and short half-life 2.5 to 4.0 hours of Famotidine following oral taken favoritisms the expansion of continuous strength formation. The intestinal remedy delivery system is stored into the abdominal and supports to increase oral drug delivery. The purpose of the investigation work is to develop, analyze a floating release pill for Famotidine in order to improve availability as well as treatment.

Specific objectives of the study include

Composition of FamDidine-containing GRDDS, which can stay into the abdominal and longer to release the release drug in the upper part of the GIT. Renting BoxBehnken make for GRDDS construction. Examination the structure in their hardness, softness, drug content, floating time, total float time, in vitro dissolving studies, in vitro buoyancy studies, in vivo buoyancy study and solidity studies. The scientific usefulness of structural flexibility is used in their response and testing methodology to obtain a reliable and fulfilling product. Comparison of visual effects of prepared construction with predicted values.

MATERIAL AND METHOD

Evaluations of mouth dissolving tablets famotidine

Preformulation study

The angle of repose

It is measured through funnel technique. Funnel is set on a flask stand at a specific peak. A chart wrapper is put under the funnel on a table. The crush is passing slowly across the funnel, until if form a mound. The blend residue is stop when the mound traces the tip of the funnel. Circumference of the mound of residue mixture is strained through the pencil lacking troubling the mound. The area of the pile 'r' is marked. The repose of angle was determined using the equation.

Ten h = h / r

Therefore, θ = ten-1 h / r

Where, θ = rest angle
h = lump height
r = lump base radius

Bulk density
Mass thickness is the average weight of the residue to maximum dose of powder. It is evaluated via taken the weigh amount of blend crush beginning every preparation in a fifty ml test tube moreover the original quantity of the residue to calculate was written. The mass density of crush is obtained through the formula.
$P_b = M/ V_b$
Where.
ρ_b = mass density
m= Total mass of residue
v_b = mass volume of residue

Tapped density
It is defined as whole mass of the dust is separated by tapped quantity of dust. It is calculated by taken the grind in measuring cylinder and tapping the dust with seven thundered fifty count. The tapped level is marked. The difference b/w tow tapping less than two present, if the difference > 2%, the tapping continued with 1250 times and the tapped volume is marked. The drumming regular when the difference b/w two tapping successive volume is less than 2%. It is calculate by the following formula, (table no. 3.7).
$p_t = m/ v_t$
Pt = Witched quantity
M = total powder weight
IVt = powder volume

Compression index
Grinding pressure was calculated according to Carr's Index.

Carr's pressure index (%) = [(TBD-LBD) X 100] / TBD
Or it can be defined as Carr's Index associates the taxable density of an object in a person with a tap and is calculated using the following relationship:
Compressibility Index = Compressed quantity - density X 100
The quantity is captured

Hausner'sratio: this is a measure of density that is taped to density. Calculated in the following formula.
Hausner rate = tap density / volume density.

Preparation of famotidine tablets
Sieving: Exactly weigh amount of Famotidine was sieved from mesh no. 80 then, HPMC K4M, HPMC K15M; HPMC K100 was sieved mesh no. 80.

Melting: White wax melted in china dish.

Mixing: Add the drug famotidine to the melted mass and mix well. Then add the HPMC polymers, sodium bicarbonate and lactose and mix well.

Granulation: prepare a mixture that is allowed to cool at room temperature and then removed from china dish. Weight passed through filter 20.

Moisture: The lead granule was mixed with talc and magnesium Stearate.

Concentration: compressed granules pressed into tablets with a standard concave punch and a 10 rotary proton mini channel machine with a storage capacity of 200 mg.

Table no. 1: Composition of famotidine tablets with different batches.

Ingredients(mg/tab)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
Famotidine	40	40	40	40	40	40	40	40
HPMCK4M	0	30	0	0	30	30	0	30
HPMCK15M	0	0	30	0	30	0	30	30
HPMCK100	0	0	0	30	0	30	30	30
$NaHCO_3$	20	20	20	20	20	20	20	20
Bee wax	30	30	30	30	30	30	30	30
Lactose	98	68	68	68	38	38	38	8
Magnesium sterate	6	6	6	6	6	6	6	6
Talc	6	6	6	6	6	6	6	6
Total weight	200	200	200	200	200	200	200	200

Evaluations of post formulation studies of tablets
Psycho-Chemical studies of formulated tablets
Thickness
The thickness of the tablets was determined using a venire caliper. There were five to eight pills in each group used, and average values were calculated. The size was indicated in millimeters.

Weight variation test
A study of the weight variation of 20 tablets in each construction was taken and first measured for each tablet, after which a total of 20 tablets are weigh up using an electric balance (AW-220 shimadzu), deviations not exceeding + 7% and tests performed on a formal basis (Table 3.9).

Drug content
The four pills contained fine powder; an amount equal to 50mg of famotidine is properly measured and moved toward a 100ml volumetric bottle having 50ml of methanol. It is allowed to stand for six hours to ensure the complete dissolution of the drug. Responses were made in bulk, filtered, and clean accordingly, and the gratified of famotidine was expected to be 248 nm; the use of UV signal methanol use was negligible.

Hardness
For each six-tablet complex construction is resolute with a Monsanto hardness tester (cadaman). The pills were kept next to their axong axis between the two testers' jaws at this point; the reading should be zero kg / cm2. After that the applied force circulates the information until the pills break.

Friability
It is a form of energy pills. It has to do with the capabilities of both moving tablets and the disintegration of packaging during product management, packaging and consumer use.

Buoyancy lag time
Determined to test the time taken by the float measurement form at the upper of the dispersion area, later this one has been located in the center. These constraints is be determined as part of the completion examination. The outcomes were tabularized.

Floating time
Strength tests are commonly achieved on SGF-Simulated Stomach Fluid stored at 37^0C. The time when the volume form continues to float in the termination sources is termed the floating time.

***In-vitro* test of finished formulated tablets of famotidine**
Determination of swelling index
The swelling index of drugs have been decided to the phosphate buffer (ph 6.8), at room temperature up to 8 hrs. The bloated burden of this tablet has been ascertained via as soon as intervals15. The swelling equation may be determined without difficulty through using this equation:
Percentage of water uptake polymer swelling

$$= \frac{(Ws - Wi)}{WI} \times 100$$

Ws define the Wight of matrix at time t, W is the primary mass of the Matrix.

***In-Vitro* drug release studies (Dissolution study)**
Preparation of buffer solution: 8.5ml was measured in 1000 milliliter volumetric bottle and makeup the volume 1000 mi with distilled water.

Requirements
Medium: 0.1N Hcl
Volume: 900 ml
Apparatus: SUP II (paddle)
RPM: 100
Time: up to 12 hrs
Temperature: 37ºc ± 0.5 ºC
λmax: 266nm

Performed the experiment, six pills were located in six tubes each having 900ml of 0.1N Hcl stored at 37ºc ± 0.5 ºC for some time the obligatory quantity of taster was withdrawn and the similar quantity was added to 0.1N HCL (keep basin status). The pattern solution was modified to 266 nm of Pharmotidine using a UV-spectrophotometer to determine its additional drug release% or cash gift within the pattern.

Assay: Crush 20 tablets and weigh 20 mg famotidine and dilute to 0.1N HCl and mark a volume of 100ml. After there, remove 10 ml and dilute to 100ml with 0.1N HCl. Learn to absorb 266 nm from a UV spectrophotometer.

Statistics study (Curve fitting examination)
To decide the action of medicine issue charge kinetics of pills and records acquired was plotted as:
The vs. of time and cumulative percentage of drug launch (*in vitro* drug launched plots). The vs of rectangular root of time and log cumulative percentage drug launch (Higuchi, splots). The vs of time of the log cumulative percent drug remained (first-order plots). The vs. of time of the loge percent drug launch (Pappas plots).

***In vitro* dispersion time**
Take 10 ml of distilled water in a measuring cylinder. Five tablets were taken from each formulation and Tablets are added in distilled water at 37 $\pm$ 0.5^0C. Determined the tablets for completes dispersion at time require.

Ratio of wetting Time and Absorption
Taken 5 cm petridish. Two-piece of tissue paper is placed in a petridish. Water solvable eosin dye is additional to petridish. The pills are placed on the floor of tissue paper. After some time, the purple or pink shade is produced at the surface of tablet, the time is cited. It is a wetting time. The identical technique is accompanied by the water absorption ratio. It's far determined by using the subsequent eq^n,

$$R = \frac{W_b - W_a}{W_a} x\ 100$$

Where,
W_b = water absorption after wetting of tablets
W_a = Water absorption before wetting of tablets

Stability studies
The selected formulation became examined for three months at the storage conditions at room temperature and 40°c at 75%RH was examined for their drug content. The residual drug contents of formulations had been located to be in the permissible limits, as shown in the desk. The tablets showed excellent bodily stability at

room temperature and 40°c at 75% RH. No appreciable changes were determined in any of the formulations. The drugs were additionally subjected to IR studies to determine well matched the drug with the recipients used within the tablets. Their studies confirmed it here are not any interactions amongst the medicine and inactive ingredients.

RESULT AND DISCUSSIONS

Ft-ir spectral studies

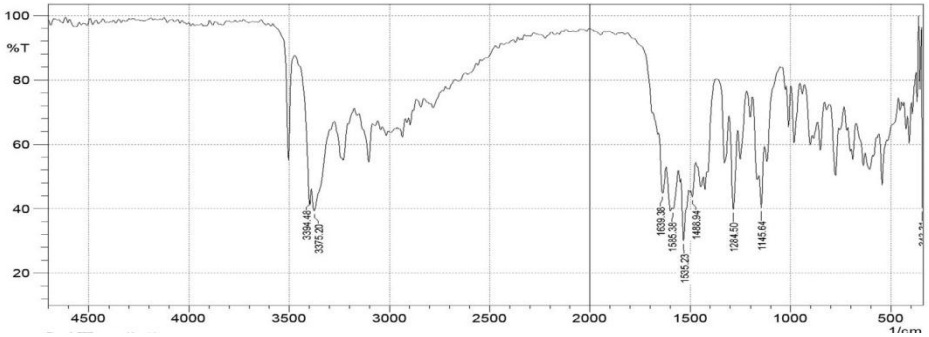

Fig. 1: FT-IR Spectra of famotidine.

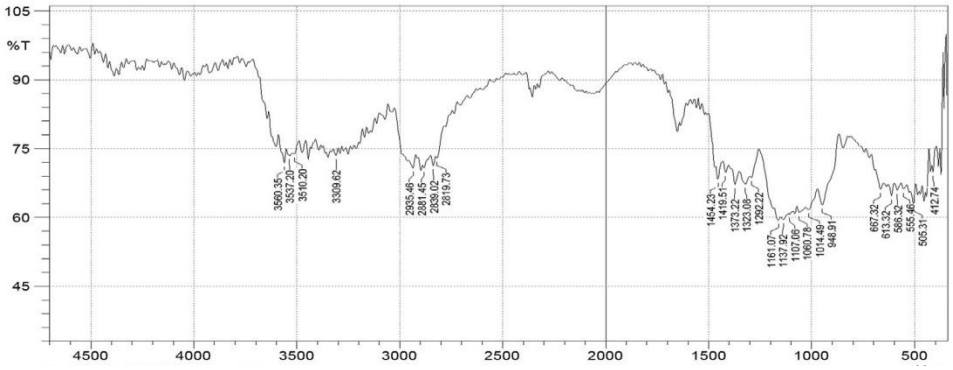

Fig. 2: IR spectra of HPMC.

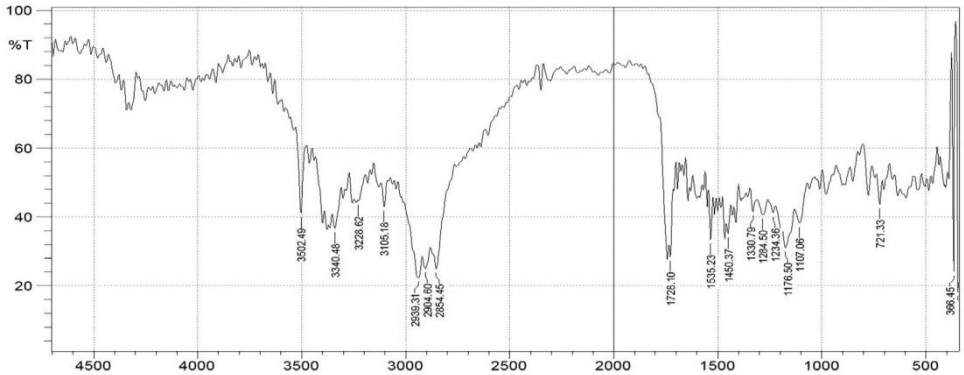

Fig. 3: IR spectra of Drug + excipients.

Evaluation of preformulation studies

Table 2: Evaluation of precompression parameters of all preparation.

Formulation	Angle of repose (θ)	Bulk density (g/cm^1)	Tapped density (g/cm^1)	Compressibility Index (%)	Hausner's ratio
F_1	$27^0.10'$	0.2955	0.3601	14.05	1.21
F_2	$25^0.22'$	0.2945	0.3488	15.77	1.23
F_3	$28^0.60'$	0.2918	0.3435	12.85	1.14
F_4	$27^0.96'$	0.2815	0.3395	13.66	1.13
F_5	$24^0.44'$	0.2762	0.3365	15.25	1.15
F_6	$24.^0.75'$	0.2665	0.3285	12.95	1.18
F_7	$27^0.22'$	0.2910	0.3195	12.22	1.12
F_8	$26^0.22'$	0.2710	0.3166	12.06	1.10

Evaluation of post compression parameters

Table 3: Evaluation of physical properties of all formulation.

Formulations	Weight variant (mg)	Friability (%)	Content uniformity	Thickness(mm)	Hardness (kg/cm^2)
F_1	3.29±0.038	0.24	99.75	5.3 ± 0.02	3.25
F_2	3.24±0.07	0.35	99.69	5.1 ± 0.03	3.75
F_3	3.35±0.020	0.19	98.55	5.4 ± 0.01	3.95
F_4	3.55±0.010	0.28	99.56	5.1 ± 0.02	3.56
F_5	3.36±0.013	0.17	99.98	5.3 ± 0.01	3.48
F_6	3.33±0.044	0.32	99.97	5.2± 0.01	4.00
F_7	3.28±0.012	0.30	99.44	5.5± 0.04	3.98
F_8	2.99±0.005	0.20	99.25	3.2± 0.01	3.24

Buoyancy lag Time and Total floating time

Table no. 4: Showing buoyancy lag Time and Total floating time.

Batch no.	Buoyancylag time	Totalbuoyancy time(hrs)
F_1	635	16
F_2	97	4
F_3	89	5
F_4	79	13
F_5	181	6
F_6	64	9
F_7	45	16
F_8	40	15

***Invitro* drug release profile**

Table 4: *Invitro* release profile of drug.

Time (hrs)	F_1	F_2	F_3	F_4	F_5	F_6	F_7	F_8
1	9.45	25.80	16.23	8.06	22.13	14.10	6.19	13.05
2	14.09	59.03	35.55	11.95	44.02	25.15	12.15	17.80
3	18.25	96.30	47.10	18.12	66.95	31.16	18.02	23.17
4	26.23		64.12	24.02	96.36	40.44	23.96	27.76
5	30.03		77.09	32.95		45.25	28.99	31.65
6	33.26		97.10	40.13		54.70	32.02	38.77
7	40.10			48.24		68.22	35.94	44.45
8	48.22			56.02		79.95	41.70	50.20
9	54.88			65.55		90.03	47.14	55.66
10	57.95			74.02		98.32	54.72	61.25
11	60.95			83.96			58.93	69.59
12	68.66			97.18			63.22	73.20

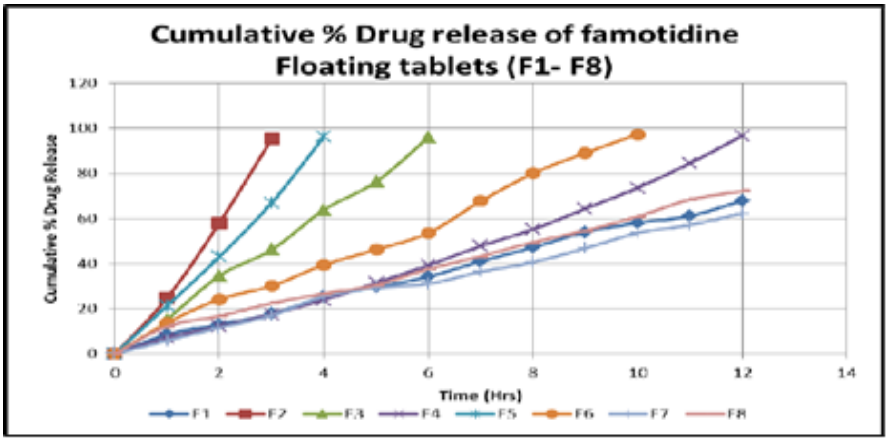

Fig. 4: *in vitro* profile of drug release for formulation F_1 to F_8.

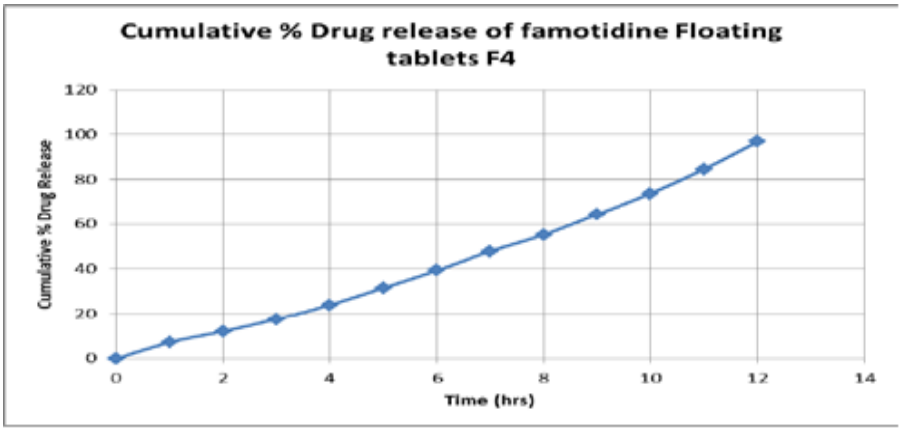

Fig. 5: Showing in vitro drug release profile of best formulation F_4.

Drug release kinetic

Time (Hr)	Cumulativ% drug released	%drug remaining	Square roottime	logCumu% drug remainining	log time	Log Cumu %drug released	%Drug released
0	0	100.	0.000	2.000	0.000	0.000	100
1	8.25	93.03	2.000	1.666	0.000	0.952	8.35
2	13.01	88.23	1.526	1.855	0.421	1.093	5.22
3	18.05	83.96	1.843	1.896	0.566	1.342	6.12
4	24.36	77.25	2.000	1.971	0.598	1.492	6.42
5	32.12	67.98	2.458	1.795	0.701	1.501	7.66
6	40.05	59.95	2.551	1.783	0.812	1.612	7.73
7	48.54	51.23	2.757	1.828	0.945	1.765	8.66
8	54.95	43.98	2.913	1.772	0.898	1.822	7.34
9	65.12	36.65	3.000	1.662	0.966	1.799	9.20
10	74.05	25.66	3.273	1.532	1.201	1.798	9.33
11	83.96	16.01	3.402	1.193	1.052	1.933	10.96
12	97.23	4.32	3.554	0.601	1.080	1.992	12.35

Stability studies

Table 3.16: Solidity statistics of famotidine tablets keep at 40±2^{0}C/75%±5% RH.

S. no.	Storage circumstances: 40±2^{0}C/75%±5% Relative Humidity				
	Test	original period	30 days	60 days	90 days
1	Physical appearance	Not change	Not change	Not change	Not change
2	Weight variation	3.55	3.45	3.29	3.27
3	Thickness (mm)	5.1	5.0	4.99	4.95
4	Hardness (kg/cm^1)	3.56	3.54	3.45	3.30
5	Fariability (%)	0.28	0.25	0.22	0.21
6	Content uniformity	99.56	99.50	99.35	99.30
7	Buoyancy lag time	79	75	70	68
8	excellence of dispersion	God	Good	Good	Good

CONCLUSION

According to previous work, Famotidine floating tablets were developed with polymers such as HPMC K4M, HPMC K15M, and HPMC K100 tablet prepared by granulation technique.

Large dispersions such as crospovidone and Croscarmellose sodium and compounds reduce the dispersion time of the tablets. Next: Floating pills with continuous issue features proposal critical benefits such as site specification with advanced installation and efficiency.

This machinery is incorporated into a variety of stomach medications as a major absorbent area. Moreover, the floating method does not require sophisticated technology and therefore, it is easy to accept.

Therefore, it can be employed in various development courses according to need. Drugs with meager bioavailability due to their partial absorption in the superior intestine can be successfully sent to FDDS. Thus it increases their absorption and improves their full availability.

The floating model is used in construction to treat several ailments. Buoyant delivery program is considered a beneficial strategy for the treatment of stomach and intestinal cancer.

REFERENCES

1. Al-Aiden FA, Mc Elnay JC, Scott MG, et al. Management of H. pylori eradicate on the influence of structured counselling and follow-up. Br J Pharmacol, 2002; 53: 163–171.
2. Ali MA, Albert JM, Haridas S et al. High prevalence and level of resistance to metronidazole, but lack of resistance to other antimicrobials in H. pylori, isolated from a multiracial population in Kuwait. Aliment Pharmacol & Thera, 2006; 24(9): 1359-1366.
3. Amir E, Ali M, Nader A, Ardeshir L. Detection of H. pylori using PCR in dental plague of patients with and without gastritis. Med Oral Patol Oral Buccal, 2010; (15): 28-31.
4. Aulton ME, Wells TI. Pharmaceutics: The Science of Dosage Form Design, 1998; 2: 397.
5. Churchill Livingstone, London, England. Streubel B, G Seitz, M Stolte, et al. MALT lymphoma associated genetic aberrations occur at different frequencies in primary and secondary intestinal MALT lymphomas. Gut, 2006; 55(11): 1581–1585.
6. Badhan AC, Mashru RC, Shah PP et al., Development and evaluation of sustained release gastroretentive minimatrices for effective treatment of H. pylori Infection. AAPS Pharm Sci Tech, 2009; 10(2): 459-67.
7. Bamba, M. and F. Puisieusx. Release mechanisms in gel forming sustained release preparation. Int. J. Pharm, 1979; 2: 307-315.
8. Banker GS, Anderson LR. Tablets. In: Lachman L, Liberman HA, Kanig JL, Eds. The theory and practice of industrial pharmacy. Mumbai, India: Varghese Publishing House, 1987.
9. Barakat NS, Elbagory IM, Almurshedi AS. Controlled-release carbamazepine matrix granules and tablets comprising lipophilic and hydrophilic components. Drug Deliv, 2009; 16: 57.
10. Bardonneta P, Faivrea V, Pughc W etal. Gastroretentive dosage forms: Overview and special case of H. pylori. J Control Release, 2006; 111: 1–18.