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1 Dr. R.L Kalyani, 2 T. Rajini, 3 G.Swapna, 4 P.Goutham

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EFFERVESCENT FLOATING TABLETS OF CIPROFLOXACIN HYDROCHLORIDE: FORMULATION AND IN VITRO EVALUATION

[1] Dr. R.L Kalyani, [2] T. Rajini, [3] G.Swapna, [4] P.Goutham
[1]Professor,[234]Assistant Professor
Vaagdevi College of Pharmacy, Warangal, Telangana

ABSTRACT:

Ciprofloxacin hydrochloride is a broad-spectrum antibiotic used to treat various bacterial infections. However, its short half-life and the need for frequent dosing can limit its therapeutic effectiveness. Effervescent floating tablets offer a promising solution by providing controlled drug release and prolonged gastric retention, thus improving bioavailability and patient compliance. This study focuses on the formulation and in vitro evaluation of effervescent floating tablets of ciprofloxacin hydrochloride.

To formulate effervescent floating tablets of ciprofloxacin hydrochloride and evaluate their in vitro performance, including buoyancy, drug release, and stability.

Effervescent floating tablets of ciprofloxacin hydrochloride were formulated using different polymers, such as hydroxypropyl methylcellulose (HPMC) and sodium alginate, along with effervescent agents (sodium bicarbonate and citric acid). The tablets were evaluated for various physicochemical properties, including weight variation, hardness, friability, and drug content. The buoyancy characteristics were determined by measuring the floating lag time and the duration of floating. In vitro drug release studies were conducted using a USP dissolution apparatus in simulated gastric fluid (SGF). The release kinetics were analyzed using mathematical models such as zero-order, first-order, and Higuchi models. Stability studies were also carried out to assess the long-term storage conditions of the tablets.

The effervescent floating tablets exhibited good physicochemical properties, with a floating lag time of less than 2 minutes and sustained buoyancy for up to 8 hours. The drug release studies showed a controlled release profile over 8 hours, following Higuchi's diffusion model. The tablets provided a steady release of ciprofloxacin hydrochloride, with no initial burst effect. The formulation also demonstrated good stability, with no significant changes in drug content or

release characteristics during stability testing.
Effervescent floating tablets of ciprofloxacin hydrochloride were successfully formulated with favorable characteristics, including prolonged floating, controlled drug release, and stability. This formulation offers an effective approach for improving the therapeutic efficacy of ciprofloxacin hydrochloride by enhancing its bioavailability and reducing dosing frequency, thereby improving patient compliance.

Keywords:
Ciprofloxacin hydrochloride, effervescent floating tablets, formulation, controlled release, in vitro evaluation, drug release, bioavailability.

1. INTRODUCTION:

When compared to alternative drug delivery methods, the oral route is often chosen because it is simple to administer, patient compliance is high, formulation flexibility is available, and manufacturing costs are low1.
Multiple doses are used in traditional oral dosage forms to preserve the drug's therapeutic window; however, this formulation strategy did not significantly slow the drug's fluctuating plasma levels, which were caused by the fast gastrointestinal transit and thus contributed to the early drug loss2.This restriction necessitates the creation of a unique drug delivery method that might guarantee improved site specificity, less side effects, and regulated release characteristics. Compared to traditional daily multi-doses, the gastro-retentive delivery system is expected to offer a safer and more effective treatment with fewer systemic side effects, a lower dosage, a shorter treatment duration, and better patient compliance because of the ease of drug administration. In particular, this strategy may be used to increase the effectiveness of medications used to treat peptic ulcers and other upper gastrointestinal tract infections. Reducing the carrier density (floating systems), enhancing mucoadhesive qualities, and creating expandable or modified-shape systems all aid in the creation of gastric retention systems5,6. For medications that are primarily absorbed in an acidic medium and unstable in an intestinal or colonic environment, these systems are especially helpful in treating stomach diseases. According to reports, medications such as famotidine and clarithromycin may be delivered via a gastro-retentive system7. This is explained by the fact that, despite its quick absorption throughout the gastrointestinal system, large amounts of clarithromycin are required in the stomach to guarantee the efficient eradication of H. pylori. Furthermore, famotidine's short half-life (2.5–4 hours) and limited bioavailability (40%) support its use in sustained release system formulation.

With qualities including compactness and ease of manufacture, increased dosage flexibility, affordability, and ease of self-administration, the tablet dosage form is the most practical medication delivery method.9. It is thought that controlled release dosage forms provide an additional benefit over the daily multiple-doses needed to sustain the therapeutic levels of medications10,11. Systemic drug availability in oral drug administration may be influenced by a number of variables, including pH, gastrointestinal motility, enzymes, and ions12. These elements change absorption levels via influencing medication stability, ionisation, and solubility13. As a carrier that improves medication bioavailability and therapeutic efficacy after oral delivery, gastro-retentive systems show promise in overcoming the aforementioned challenges.14, 15. Such systems' comparatively low density enables them to float and extend the medication's

retention period in the stomach, negating the length and pace of normal gastric emptying. This raises the degree of drug absorption and eventually improves the therapeutic result.16, 17.

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Through the use of the direct compression method, hydroxypropyl methylcellulose (HPMC) K100M, HPMC K4M, and sodium bicarbonate were admixed as swelling and floating agents, respectively, in order to create and assess effervescent floating bilayer-controlled release tablets loaded with clarithromycin and famotidine. To guarantee the quality of the created tablets, the prepared formulations were evaluated according to their thickness, hardness, weight fluctuation, friability, and content homogeneity.

2. MATERIALS AND METHODS:

Materials: Clarithromycin and famotidine were the preferred medications provided by Ferozsons Laboratories Limited (Nowshera, Pakistan). HPMC K4M and HPMC K100M (BDH Chemical Limited, Pool, England) were used as swelling agents and retardants, respectively. Sodium bicarbonate (Sigma, Germany) served as the gassing agent, magnesium stearate (Sigma, Germany) functioned as the release rate retardant, and talc (BDH Chemical Limited, Pool, England) acted as the lubricant. Lactose (Sigma, Germany) was used as a release rate accelerator. All compounds were of analytical quality and used without additional purification.

Calibration curves: Famotidine and clarithromycin, each at 100 mg, were individually dissolved in 0.1N HCl to provide clear solutions at a concentration of 1 mg/ml. The stock solution was diluted with 0.1N HCl to achieve the necessary dilutions. The dilutions and stock solutions were analysed spectrophotometrically at their respective lambda maxima of 210 nm for clarithromycin and 265 nm for famotidine. The corresponding concentrations were graphed against their relative absorbencies, and the resulting standard curves were used for drug release calculations.

The formulation and fabrication of effervescent controlled-release bilayer tablets: Table 1 presents the compositions of both bilayer and plain effervescent floating controlled release tablets. A prototype batch of 120 pills was made. Both bilayer and single-layer tablets were manufactured using the

direct compression technique. Regarding bilayer pills, the contents were combined with the clarithromycin layer during 15 minutes of trituration and thereafter passed through a 60-mesh screen. Subsequently, a lubricant was included into the sieved bulk, enabling the tablets to be produced by direct compression. The same process was used for the famotidine layer, which was formed by compressing its formulation above the clarithromycin layer. For the uncoated tablets, the lubricated materials were immediately crushed using a tableting machine (Erweka-Apparatebau compression machine type T B 24), maintaining a hardness value of 6.6 Kg/cm. All the pills were manufactured by hand.

Table 1: Formulation of effervescent floating controlled release bilayer and plain tablets.

Bilayer tablets					Plain tablets	
Drugs	Chemicals	Formula 1	Formula 2	Formula 3	Formulation 4	Formulation 5
Clarithromycin layer	Clarithromycin	250 mg	250 mg	250 mg	250 mg	250 mg
	HPMC K100M	77.5 mg	155 mg	———	165.49 mg	———
	HPMC K4M	77.5 mg	———	155 mg	———	165.49 mg
	Talc	10.8 mg	10.8 mg	10.8 mg	13.4 mg	13.4 mg
	Mg Stearate	5.4 mg	5.4 mg	5.4 mg	6.7 mg	6.7 mg
	Lactose	57.8 mg	57.8 mg	57.8 mg	46.9 mg	46.9 mg
	$NaHCO_3$	81 mg	81 mg	81 mg	167.5 mg	167.5 mg
Famotidine layer	Famotidine	20 mg	20 mg	20 mg	20 mg	20 mg
	HPMC K100M	32.5 mg	65 mg	———		
	HPMC K4M	32.5 mg	———	65 mg		
	Talc	2.6 mg	2.6 mg	2.6 mg		
	Mg Stearate	1.3 mg	1.3 mg	1.3 mg		
	Lactose	9.1 mg	9.1 mg	9.1 mg		
	$NaHCO_3$	32 mg	32 mg	32 mg		

Characterisation: Flow properties, including the angle of repose, Hausner's ratio, and compressibility index of the powder mixes, were assessed using established protocols.

Compatibility analysis of drug and excipients: To ascertain potential interactions between the drug and excipient, FTIR analyses were performed with a Fourier Transform Infrared Spectrophotometer (LI600300 spectrum Two Lita, Liantrisant, UK) throughout a wavelength range of 4000-400 cm-1.

Form and measurements of the manufactured tablets: Magnifying lenses were used to ascertain the configuration of tablets. The thickness and diameter were measured using a clean and calibrated vernier calliper (Erweka, Germany). Five tablets from each formulation were randomly picked, and their thicknesses and diameters were measured separately. The data were presented as mean ± standard deviation.

Hardness: The hardness of the tablets indicates their capacity to endure mechanical force during manipulation. The hardness was determined using the Erweka Model TB 24 apparatus (Germany), given in kg/cm^2. Five pills from each formulation were randomly chosen, and their hardness was assessed.

Weight variation and friability assessment: Ten tablets were randomly chosen from each formulation and weighed separately using a precision balance (AX120, Shimadzu, Japan). The mean weight of the pills was presented as mean ± SD and assessed against permissible pharmacopoeial standards. The friability of each tablet batch was assessed using a standard laboratory friabilator (Erweka, Germany) on a randomly chosen sample of 20 tablets. This was executed in line with usual protocol, and the findings were

Tablet density: Density is a crucial element for floating tablets. Tablets will float only if their density is less than that of stomach fluid, namely below 1.004 g/cm^3. The tablet density was determined using the previously indicated equation25.

Where "ρ" denotes density, "m" represents the mass of the tablet (g), and "v" signifies the volume of the tablet (cm^3). The volume may be determined using equation 2:

Where "r" denotes the radius of the tablet (cm), and "h" represents the crown thickness of the tablet (cm).

Investigation of Oedema The weight increase or water absorption, indicative of the tablet's swelling tendency, was assessed using a previously established technique with minor modifications. The tablets were introduced into the 0.1N HCl solution, maintaining a temperature of 37±0.5ºC with a constant stirring rate of 25 rpm. The tablets were extracted and re-weighed after the removal of surface moisture using filter paper at designated time intervals. The water absorption/swelling index was calculated using the following equation:

$$\text{Water uptake} = \frac{Wt - Wo}{Wo} X\ 100 \ldots\ldots(3)$$

Wt represents the weight of the tablet at a certain time "t," whereas W0 denotes the starting weight of the tablet at time zero.

The floating behaviour was assessed via a USP type II dissolving device (paddle type). The containers contained 900ml of 0.1N HCl, with the paddle's rotation speed maintained at a constant 50rpm. The temperature was maintained at 37±0.5°C for a period of 12 hours. The buoyancy lag time and total floating duration for each tablet formulation were documented individually (El-Zahaby et al., 2014).

The powdered tablets (10 from each batch) and corresponding weights of each medication were immersed in 100 cc of 0.1N HCl at a pH of 1.2 and dissolved at a temperature of 37 ± 0.5°C. The pure drug and powdered tablet mass were appropriately diluted prior to spectrophotometric examination at 210 nm and 265 nm for clarithromycin and famotidine, respectively. The drug release was assessed using the USP paddle technique in 900 ml of 0.1N HCl as the dissolving medium. The paddle rotation was sustained at 50 rpm, and the temperature was regulated at 37±0.5°C. Aliquots of 5 ml were extracted at specified time intervals.

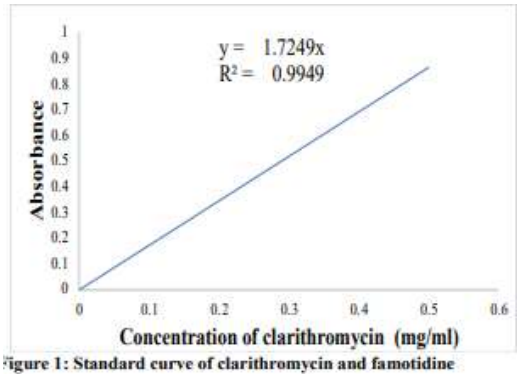


Figure 1: Standard curve of clarithromycin and famotidine

Filtered and evaluated spectrophotometrically at the corresponding lambda maximum of the pharmaceuticals. The percentage of drug release was documented, with the data presented as triplicate measurements in the format of mean ± SD31. The drug release mechanism was ascertained utilising the power law formula (Power Law; Mt/M∞ = K t n) using Microsoft Excel 32,33.

3. RESULTS AND DISCUSSIONS:

Standard calibration curves: Standard curves were established, yielding linear relationships between concentration and absorbance, as seen in Figure 1. The derived regression equation for the clarithromycin standard curve is y = 1.7249x, with a R^2 value of 0.9949. The regression equation for the famotidine standard curve was y = 25.825 x, with a R^2 value of 0.999.

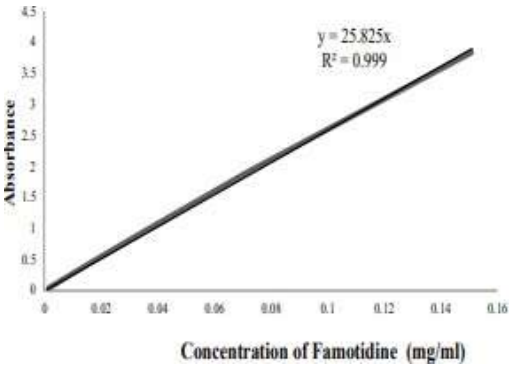


Table 2: Standard (A) and determined (B) values of flow characteristics

A. Standard values			
Flow characteristics	Hausner's ratio	Compressibility index (%)	Angle of repose
Excellent	1.00-1.11	<10	25-30
Good	1.12-1.18	11-15	31-35
Fair	1.19-1.25	16-20	36-40
Passable	1.26-1.34	21-25	40-45
Poor	1.35-1.45	26-31	46-55
Very poor	1.46-1.59	32-37	56-65
Very, very poor	>1.60s	>38	>66

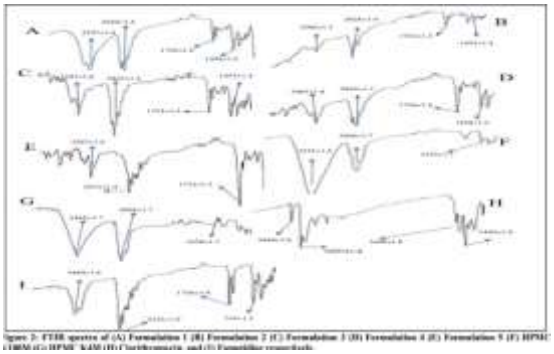
B. Determined values					
Code	Angle of repose	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's ratio	Compressibility index (%)
F1	27.3 ± 0.03	0.443 ± 0.06	0.58059 ± 0.09	1.140	12.20
F2	27.6 ± 0.08	0.442 ± 0.12	0.49504 ± 0.11	1.147	12.81
F3	27.9 ±0.06	0.439 ±0.10	0.50405 ±0.12	1.150	13.04
F4	28.6 ± 0.04	0.430 ± 0.11	0.49494 ± 0.9	1.160	13.79
F5	27.7 ± 0.05	0.441 ± 0.09	0.50715 ± 0.14	1.157	13.56

Flow characteristics: The assessment of flow qualities is crucial for the formulation of a refined product. The flow properties, including angle of repose, compressibility index, and Hausner's ratio, conformed to the established standards (USP.org: harmonisation).

As shown in Table 2 (2004). The compressibility index, Hausner's ratio, and angle of repose values ranged from 12.30% to 16.70%, 1.12 to 1.18, and 26.7° to 29.4°, respectively, for the formulation mixtures, indicating favourable flow properties and their appropriateness for direct compression, as noted in prior studies (Table 2 A and B).

FTIR results: The distinctive peaks of the active compounds, famotidine and clarithromycin, were mostly unchanged in the formulations35 (Figure 2). The polymer bands of HPMC K100M and HPMC K4M adhere to earlier findings without any alteration in location or intensity. Consequently, the chemical interactions were eliminated in the formulation components of the generated tablet formulations.

The controlled release floating tablets had an exquisite physical look. The thickness of the five formulations varied from 3.55 to 3.57 mm, whereas the diameter of all formulations was between 15.15 and 15.17 mm. The hardness of the tablets varied between 6.5 and 6.8 kg/cm². The findings indicated that all the tablets could endure the challenges associated with handling, owing to an appropriate hardness range of 5-10 kg/cm². 25. The friability of the produced tablets was < 1.0%, indicating the mechanical stability of both plain and double-layered tablets. The weights of all tablet formulations were within the permitted USP range of ± 5%. The theoretical weight of the tablet was maintained at a constant amount of 670 mg for each of the five formulations. The inter-batch weight variance was maintained at a low level. The results of the physical examinations of the tablets are shown in Table 3.



The swelling index and floating behaviour: The tablet density must be less than that of stomach contents (1.004 g/cm³) to demonstrate floating capability. All developed formulations remain buoyant on the surface of fluids that simulate gastrointestinal contents, so confirming the appropriateness of their density. The water uptake/swelling ratio signifies the volume of water absorbed by the employed polymers. The swelling arises from the functional network topology and the ionisation of functional groups. The test was conducted on all formulations for 4 hours, demonstrating that the tablet expands to 90% of its original size. The

tablets' swelling intensified with time owing to the hydrophilic properties of the used polymers (HMPC K100M and HPMC K4M). The swelling profile of tablets formulated with HPMC K4M was substantially greater than that of floating tablets formulated with HPMC K100M (Student t-test: $p < 0.05$; Figure 3; F2 Vs F3; F4 Vs F5). Initially, the outermost layer of the polymer expanded, forming a gel barrier layer. As the outer gel barrier layer gradually eroded, a new layer expanded owing to water absorption, and this process was repeated towards newly exposed surfaces. This preserved the integrity of the dosage form and facilitated the regulation of the medication release profile. The viscosity of polymers directly affects the swelling ratio, tablet integrity, and floating ability. Figure 3 illustrates the swelling index of the formulated tablets.

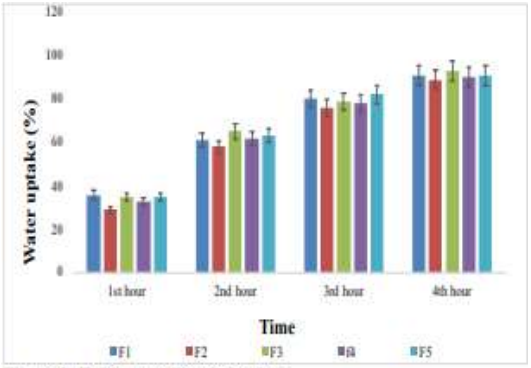


Figure 3: Tablets swelling behaviour

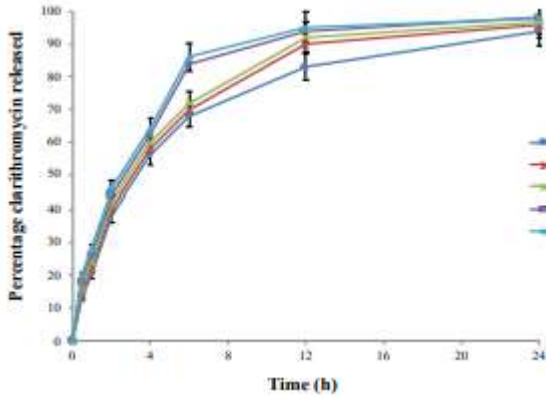
All formulations also included a gas sourcing agent, namely sodium bicarbonate, in addition to polymers. Upon contact with a medium of 0.1 N HCl at pH 1.2 and a temperature of 37 ± 0.5°C, the sodium bicarbonate-containing tablets began to float and maintained this buoyant state for many hours. Table 4 displays the total lag and total floating time for various produced formulations. Among bilayered floating tablets, F3 containing HPMC K4M has markedly extended the lag and floating duration to over 12 hours ($p<0.05$). A similar tendency was seen in plain tablets, where F5 attained a floating duration over 10 hours, in contrast to less than 7 hours for F4 formulated with HPMC K100 ($p<0.05$). This may be attributed to the low density and suboptimal compression properties in F3 and F5 due to the usage of HPMC K4M in comparison to other formulations. The formulations using HPMC K 100M (F) exhibit superior compressibility and hence delayed floating behaviour in comparison to those containing the polymer HPMC K4M. These results align with earlier documented studies that examined the flow characteristics and compaction of various grades of HPMC. Previous investigations have shown that HPMC K100M yielded superior compaction relative to HPMC K4M, while HPMC K4M

Table 4: Tablet floating characteristics

Code	Tablet density (g/cm^3)	Floating lag time (sec)	Total float time (hours)
F1	0.95 ± 0.070	15.9 ± 3.72	> 12
F2	0.97 ± 0.070	20.8 ± 7.66	< 7
F3	0.92 ± 0.069	14.3 ± 3.34	> 12
F4	0.96 ± 0.071	15.75 ± 4.95	< 7
F5	0.93 ± 0.070	18.9 ± 8.5	> 10

The dissolving behaviour of clarithromycin from bilayered floating tablets exhibited prolonged release characteristics. The medication release from the tablets was effectively maintained for up to 24 hours (Figure 4). The formulation based on HPMC K100M (F2) exhibits considerably superior sustained drug release capabilities relative to F3 (containing HPMC K4M) due to the enhanced compaction of HPMC K100M. Similar effects of HPLC grades on the release profile were seen in the case of plain tablets (Figure 4). The impact is more significant in the case of famotidine release from the aforementioned formulations (Figure 4). The findings indicate that medication release rates were extended by the use of either a single polymer or a mixture thereof.42, 43. The medicines were released from the polymeric tablets by non-Fickian

diffusion, as shown by n values above 0.5 and falling below 1 (Table 5).44.45.



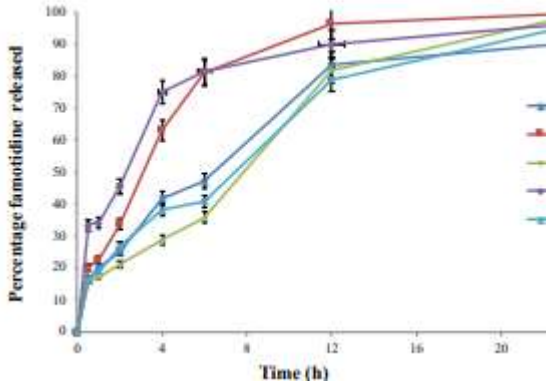


Table 5: Drugs release kinetics for prepared floating tablets

Code	Power law			
	K±SD	R^2	n	Release Mechanism
Clarithromycin				
F1	0.0029±0.0023	0.9865	0.6215	Anomalous non-Fickian Diffusion
F2	0.0025±0.0±0062	0.9756	0.6126	Anomalous non-Fickian Diffusion
F3	0.0025±0.0003	0.9801	0.6231	Anomalous non-Fickian Diffusion
F4	0.0065±0.0±0017	0.9698	0.5301	Anomalous non-Fickian Diffusion
F5	0.0013±0.0016	0.9588	0.5592	Anomalous non-Fickian Diffusion
Famotidine				
F1	0.002±0.005	0.965	0.515	Anomalous non-Fickian Diffusion
F2	0.001±0.0.0024	0.957	0.530	Anomalous non-Fickian Diffusion
F3	0.006±0.0014	0.962	0.605	Anomalous non-Fickian Diffusion
F4	0.001±0.0.0029	0.961	0.500	Anomalous non-Fickian Diffusion
F5	0.005±0.006	0.958	0.555	Anomalous non-Fickian Diffusion

4. CONCLUSION:

This research has effectively developed plain and bilayer sustained-release floating pills of clarithromycin and famotidine. The formulated tablets met the requisite physicochemical qualities according to pharmacopeial standards. The in-vitro investigations demonstrated that all formulations exhibited sustained release characteristics influenced by hydrophilic polymers such as HPMC K4M and HPMC K100M. The buoyancy and release characteristics of these pharmaceuticals from formulated tablets were markedly affected by the incorporation of a gas-forming agent such as sodium bicarbonate. HPMC K100M has superior compressibility characteristics that reduce water absorption. The release of the medication from HPMC K100M was substantially slower compared to HPMC K4M.

REFERENCES:

1. Bhoi GS, Pimpodkar N V. Medicated Chewing Gum: An Innovative approach for Oral Drug Delivery System. Asian J Pharm Technol. 2015; 5(1): 50-55.

2. Kumar R, Philip A. Gastroretentive Dosage Forms for Prolonging Gastric Residence Time. Int J Pharm Med. 2007; 21: 157-171. doi:10.2165/00124363-200721020-00005

3. Firke S, Roge A, Ghiware N, Dhoot SB, Vadwalkar SM. Floating Microspheres as Gastro-Retentive Drug Delivery System: A Review. Res J Pharm Technol. 2013; 6(12): 1452-1458.

4. Nayakulu BR, Kumar NR, Kumar CK, Abhilash PR. Formulation and evaluation of floating matrix tablet of Losartan for gastroretentive drug delivery. Asian J Pharm Technol. 2016; 6(2): 85-90.

5. Jadhav RP, Kumbhar SB, Kengar MD. Design and In-vitro Evaluation expandable Gastro retentive tablets of Diltiazem Hydrochloride. Asian J Pharm Technol. 2020; 10(2): 53-59.

6. Bahri-Najafi R, Mostafavi A, Tavakoli N, Taymouri S, Shahraki M-M. Preparation and in vitro-in vivo evaluation of acyclovir floating tablets. Res Pharm Sci. 2017; 12(2): 128-136. doi:10.4103/1735-5362.202451

7. Hardikar S, Bhosale A. Formulation and evaluation of gastro retentive tablets of clarithromycin prepared by using novel polymer blend. Bull Fac Pharmacy, Cairo Univ. 2018; 56(2): 147- 157. doi:https://doi.org/10.1016/j.bfopcu.2018.07.001

8. Muzib YI, Malleswari K. Formulation and Evaluation of Floating Drug

Delivery Systems of Famotidine Tablets. Res J Pharm Technol. 2010; 3(4): 1109-1113.
9. Ilić I, Govedarica B, Šibanc R, Dreu R, Srčič S. Deformation properties of pharmaceutical excipients determined using an in-die and out-die method. Int J Pharm. 2013; 446(1): 6-15. doi:https://doi.org/10.1016/j.ijpharm.2013.02.001
10. Mathew M, Madathil S, Govind A, Swamy VB. Formulation and Evaluation of Cinitapride Controlled Release Tablets. Asian J Pharm Res. 2016; 6(2): 87-94.
11. Gulen B, Demircivi P. Synthesis and characterization of montmorillonite/ciprofloxacin/TiO2 porous structure for controlled drug release of ciprofloxacin tablet with oral administration. Appl Clay Sci. 2020; 197: 105768. doi:https://doi.org/10.1016/j.clay.2020.105768
12. Abrahamsson B, Albery T, Eriksson A, Gustafsson I, Sjöberg M. Food effects on tablet disintegration. Eur J Pharm Sci. 2004; 22(2): 165-172. doi:https://doi.org/10.1016/j.ejps.2004.03.004
13. Adkin D, Davis S, Sparrow RA, Huckle P, Wilding I. The effect of mannitol on the oral bioavailability of cimetidine. J Pharm Sci. 1995; 84 12: 1405-1409.
14. Souza MPC de, Sábio RM, Ribeiro T de C, Santos AM dos, Meneguin AB, Chorilli M. Highlighting the impact of chitosan on the development of gastroretentive drug delivery systems. Int J Biol Macromol. 2020; 159: 804-822.doi:https://doi.org/10.1016/j.ijbiomac.2020.05.104
15. Sneha SW, Trupti VK, Darekar AB, Saudagar RB. A review: Floatable gastroretentive drug delivery system. Asian J Pharm Res. 2015; 5(1): 51-60.

16. Zhang P, Shadambikar G, Almutairi M, Bandari S, Repka MA. Approaches for developing acyclovir gastro-retentive formulations using hot melt extrusion technology. J Drug Deliv Sci Technol. 2020:102002.doi:https://doi.org/10.1016/j.jddst.2020.102002

17. Pawar V, Kansal S, Asthana S, Chourasia M. Industrial perspective of gastroretentive drug delivery systems: Physicochemical, biopharmaceutical, technological and regulatory consideration. Expert Opin Drug Deliv. 2012; 9: 551-565. doi:10.1517/17425247.2012.677431

18. Elsamaligy S, Bodmeier R. Development of extended release multiple unit effervescent floating drug delivery systems for drugs with different solubilities. J Drug Deliv Sci Technol. 2015; 30: 467-477. doi:https://doi.org/10.1016/j.jddst.2015.05.008

19. Prajapati VD, Jani GK, Khutliwala TA, Zala BS. Raft forming system—An upcoming approach of gastroretentive drug delivery system. J Control Release. 2013; 168(2): 151-165. doi:https://doi.org/10.1016/j.jconrel.2013.02.028

20. Reddy YK, Kumar KS. Formulation and Evaluation of Effervescent Floating Tablets of Domperidone. Asian J Res Pharm Sci. 2020; 10(1): 1-5.

21. El Nashar NF, Donia AA, Mady OY, El Maghraby GM. Formulation of clarithromycin floating microspheres for eradication of Helicobacter pylori. J Drug Deliv Sci Technol. 2017; 41: 213-221. doi:https://doi.org/10.1016/j.jddst.2017.07.016