How to Cite: Zabolotnaya, U.N., Timergalieva, V.R., Nasibullin, Sh.F., & Moustafine, R.I. (2026). Design of Floating Tablets Based on Hydroxypropyl Cellulose and Weakly Cross-Linked Poly(acrylic acid) for Gastroretentive Drug Delivery. *Eurasian Journal of Chemistry, 31, 1(121), 73–86.* https://doi.org/10.31489/2959-0663/1-26-7

Article

Received: 1 December 2025 | Revised: 24 February 2026 | Accepted: 27 February 2026 | Published online: 10 March 2026

UDC 541.64; 615.45

https://doi.org/10.31489/2959-0663/1-26-7

Ulyana N. Zabolotnaya, Venera R. Timergalieva, Shamil F. Nasibullin, Rouslan I. Moustafine*

Institute of Pharmacy, Kazan State Medical University, Kazan, Russia
*(*Corresponding author's e-mail: ruslan.mustafin@kazangmu.ru)*

Design of Floating Tablets Based on Hydroxypropyl Cellulose and Weakly Cross-Linked Poly(acrylic acid) for Gastroretentive Drug Delivery

Floating or buoyant dosage forms are kind of gastroretentive delivery system specifically designed to achieve localized drug release in the upper gastrointestinal tract (GI). The aim of this study is to select a composition for creating a floating matrix system based on hydroxypropyl cellulose (HPC) and Carbopol® 71G (C71G) with an evaluating of the effect of sodium bicarbonate (Na-bicarbonate) on the complexation process, and to design a gastroretentive system for acyclovir delivering. The tablets are based on physical mixtures (PhMs) HPC/C71G 1:2; 1:1. All matrices containing sodium bicarbonate showed a flotation time of less than 3 minutes, with the exception of a 2:1 PhM with 10 mg of sodium bicarbonate. PhM HPC/C71G (1:1) was observed greater matrix erosion compared to a 1:2 ratio due to the lower C71G content. During the swelling process of the matrices, interaction of polymers occurs, which is confirmed by a spectral shift in the ATR-FTIR spectra and T_g by mDSC. The addition of sodium bicarbonate did not increase the release rate due to the effervescent effect. A slightly higher release rate was observed for matrices with a 1:1 polymer ratio, due to erosion of the soluble HPC polymer.

Keywords: floating tablet, gastroretentive system, sustained release, interpolymer complexes, cellulose derivatives, hydroxypropyl cellulose, Carbopol®

Introduction

Over the past decades, scientists have focused their attention on improving the key characteristics of drugs, such as controlled release, increased bioavailability, and reduced side effects [1, 2]. The development of new gastroretentive drug delivery systems is one of the relevant trends in this direction. It is an oral delivery system capable of remaining in the stomach for a specified period, providing modified release of the active pharmaceutical ingredient (API) [3–5]. Floating tablets are one of the simplest and most widely used methods for creating a gastroretentive delivery system. They possess all the advantages of tablet dosage forms: convenience of use, storage, and transportation, as well as cost-effective production [4, 6, 7].

The effectiveness of oral therapy is limited by the low bioavailability of many drugs due to their specific properties [8, 9]. Considering that the main absorption occurs in the stomach and proximal small intestine, prolonging the residence time of the drug in this area is a critical factor for increasing the effectiveness of therapy for APIs with a narrow "absorption window" (acyclovir, riboflavin, levodopa, etc.). Some of them act only in the stomach due to pH-dependent absorption (furosemide, cinnarizine, ofloxacin, etc.) or are insoluble at alkaline pH values (atenolol, diazepam, etc.); for APIs that are unstable in the intestinal media (captopril, verapamil, etc.), as well as those with a local effect in the stomach (amoxicillin, metronidazole, etc.), incorporation into a gastroretentive delivery system is also preferred [10–12].

The operating principle of this system is based on reducing the density of the dosage form, causing it to float and remain in the upper part of the stomach, like a buoy, for several hours. This effect is achieved through gas-forming components (e.g., carbonates) included in the tablet's composition, which release carbon dioxide upon contact with stomach acid. There is a study in which menthol was used as a pore-forming agent [13]. The resulting gas bubbles "lift" the tablet, while the swelling polymers form a porous gel barrier around it, maintaining buoyancy and controlling drug release. Thus, the floating mechanism physically prevents the tablet from entering the intestine prematurely, which is key to prolonging the action of drugs absorbed in the upper gastrointestinal tract [14–19].

Currently, there are many studies on the development of floating tablets based on cellulose derivatives, including 3D printing [1, 20–27]. However, the use of chemically complementary polymers to form

interpolymer complexes (IPC) is currently a developing area [28]. The result of the interaction is the formation of IPCs, the unique properties of which are different from the properties of the original polymers and can be corrected in the required direction [29–31]. There are two options for using these systems: synthesis of IPC, with its subsequent use as a matrix-forming component, or complexation between a PhM of complementary polymers, under the influence of an acidic media simulating the environment of the stomach [32].

The ability of polymers to interact increases in an acidic media (at low pH values), because the carboxyl groups of Carbopol® are in a protonated, non-ionized form. A stable IPC is formed only at a pH below a critical pH value (pH_{crit}), which is unique for each specific pair of polymers [33–40]. Thus, the acidic media of stomach acid serves as the key physiological condition for IPC formation between HPC and C71G, and also acts as an activator for flotation. This highlights the high relevance of research in the field of gastroretentive delivery systems.

The aim of this study is to select a composition for creating a floating matrix system based on HPC and C71G with an evaluating of the effect of Na-bicarbonate on the complexation process, and to design a gastroretentive system for acyclovir delivering.

Experimental

Materials

HPC (SHANDONG HEAD CO., LTD, China) and C71G (Lubrizol Advanced Materials, USA) were used as pharmaceutical polymers, from which PhMs were prepared in various molar ratios. Acyclovir (Zhejiang Zhebei Pharmaceutical Co., Ltd., China) was used as the API. Na-bicarbonate (LLC Spectr-Chem, Russia) served as the flotation agent. Indicator is methyl red (Eco Pharm, Russia). Distilled water was used for all experiments. All reagents used were of laboratory-grade purity.

Selection of the Composition

HPC and C71G were physically mixed using a mortar and pestle in various molar rations 1:2; 1:1; 2:1, respectively. Tablets with 50 mg of PhMs, 100 mg of acyclovir and appropriate amount of Na-bicarbonate 10, 15, 20 or 25 mg were made from the physical mixtures in a 9-mm die using a programmable hydraulic press PressPRO Programmable Hydraulic Pellet Press (PIKE Technologies, USA) at compression force of 5 tons with a holding time of 5 s by direct compression. The tablets were exposed to 80 ml of 0.1 M HCl using glass beakers in a water bath IKA® IC control (IKA-Werke GmbH&Co. KG., Germany) at 37 ± 0.5 °C for 24 h. The time it took for the tablet to float (Lag time) and the total time the system remained on the surface of the media (Floating time) were measured.

Determination of the Degree of Swelling

Swelling properties were investigated by incubating matrices of PhMs with and without Na-bicarbonate with different levels of Na-bicarbonate (0, 10, 15, and 20 mg per tablet) in a temperature-controlled water bath IKA® IC control (IKA-Werke GmbH&Co. KG., Germany) maintained at 37 ± 0.5 °C. The swelling study was conducted without API. The matrices, prepared as 0.15 g tablets with a 9 mm diameter, were produced by direct compression of PhMs and PhMs with Na-bicarbonate using a programmable hydraulic pellet press PressPRO Programmable Hydraulic Pellet Press (PIKE Technologies, USA) under a pressure of 5 tons with a 5-second holding time. Each matrix was placed in a tared basket, which was immersed into glass beakers with 40 ml of 0.1 M HCl media, simulating stomach acid. The samples were placed in a quiescent media without stirring. The basket was removed from the media every 30 min during 6 h and after 24 h followed by removal of residual media with a dry wipe, the matrix was carefully dried using a filter paper and weighed on an analytical balance Shinko Denshi (VIBRA, Japan). The swelling degree (*H*%) was determined according to established formulas cited in the literature [41, 42].

The degree of swelling (*H*%) was calculated by the formula:

$$H\% = \frac{m_2 - m_1}{m_1} \times 100\ \%,$$

in which m_1 is the mass of the dry sample; m_2 is mass of swollen sample.

To assess the influence of the media and impact of Na-bicarbonate on possible structural transformations of PhMs to polycomplex matrices during swelling, matrix samples were collected after 2 h, 4 h, 6 h and 24 h of exposure in an acidic media.

Determination of the Micro-Environmental pH in the Matrix During Swelling

The preparation of the matrices for this study was carried out according to the described method for determining the degree of swelling with the addition of a methyl red indicator (0.15 % w/w) [43]. Studying the penetration of the media into the matrix were performed in acidic media pH 1.2 as described above. The pH change was recorded after 2 h, 4 h, 6 h, and 24 h of exposure in an acidic media. After a certain time, a cross-section of the matrix was made and the color change of the indicator was observed throughout the entire volume of the matrix.

Sample Preparation

Samples, taken during swelling studies, were frozen in laboratory freezer and then freeze-dried in FreeZone dryer (Labconco, USA) for 12 h at –50 °C and 0.08 mbar. After lyophilization tablets were dried in a VD 23 vacuum drying oven (BINDER GmbH, Germany) at 40 ± 0.5 °C to constant weight. The samples were ground to a powder using a ball mill ShaklR (PIKE Technologies, USA). The structural properties of the matrices during swelling were studied using the Fourier Transform Infra-Red (ATR-FTIR) spectroscopy (Thermo Scientific, Waltham, MA, USA) and modulated Differential Scanning Calorimetry (mDSC) methods for evaluation the influence of the media and impact of Na-bicarbonate on possible structural transformations of PhMs to polycomplex matrices while in an acidic media, simulating the stomach acid.

Fourier-Transformed Infrared (ATR-FTIR) Spectroscopy

The structural differences were studied using ATR-FTIR Spectroscopy. ATR-FTIR spectra were recorded by a Nicolet iS5 FTIR spectrometer (Thermo Fisher Scientific, USA) with the iD5 smart single bounce ZnSe ATR crystal in the range from 1500 to 1900 cm^{-1}. The absorption bands were interpreted in accordance with literature data [35, 38, 44].

Thermal Analysis

mDSC analysis was performed on a Discovery DSC™ instrument (TA Instruments, New Castle, DE, USA) with an RCS90 refrigerated cooling attachment. The instrument was calibrated for temperature using indium and n-octadecane standards, for enthalpy using indium, and for heat capacity using a sapphire standard. Tzero® aluminum pans (TA Instruments, USA) were used in all calorimetric studies. The empty pan was used as a reference and the mass of the reference pan and of the sample pans were taken into account. A dry nitrogen purge at a flow rate of 50 mL/min was maintained through the DSC cell. Samples in the mass range from 5 mg to 6 mg were placed in Tzero® aluminum pans (TA Instruments, USA), which were then transferred into the calorimeter's thermal cell using an autosampler. The scan was performed over a temperature range from 0 to 200 °C at a heating rate of 2 °C/min in modulated mode (period 60 s, amplitude 0.6360 °C). The method employed two consecutive heating and cooling segments. First, the sample was cooled at a rate of 20 °C/min to 0 °C and held for 5 minutes. It was then heated at 2 °C/min to 160 °C in modulated mode (period 60 s, amplitude 0.6360 °C). Following this, the sample was cooled back to 0 °C and maintained at this temperature for 5 minutes. Finally, it was heated again at a rate of 2 °C/min to 200 °C in modulated mode with the same parameters: period 60 s, amplitude 0.6360 °C. Data were collected and processed using TRIOS™ software version 5.1.1.46572 (TA Instruments, USA). Glass transition temperatures (T_g) were derived from the reversing heat flow signal. All analyses were conducted in triplicate.

Tablet Preparation

Six different PM of HPC/C71G, Na-bicarbonate and acyclovir were prepared using a mortar and pestle at HPC:C71G molar ratios of 1:2; 1:1 and with different levels of Na-bicarbonate (10, 15, and 20 mg per tablet). 1 tablet contained 50 mg of PhM, 100 mg of acyclovir and 10, 15 or 20 mg of Na-bicarbonate. The total tablet weight varied from 160 to 170 mg depending on the Na-carbonate content. Floating tablets were obtained by pressing into tablets in a 9-mm die using a programmable hydraulic press PressPRO Programmable Hydraulic Pellet Press (PIKE Technologies, USA) at compression force of 5 tons with a holding time of 5 s by direct compression.

Study of Drug Release

Release was carried out using a DT 626 Dissolution tester (ERWEKA GmbH, Germany) at 37±0.5 °C using type II “paddle method” and a paddle rotation speed of 50 rpm. 0.1 M HCl was used as the dissolution media in a volume of 900 ml, simulating stomach acid. The preparation of tablets for the experiment is described above. The experiment was conducted for 6 h. Samples (5 ml) were collected for analysis every

15 minutes during the first half hour of the experiment, and then every 30 minutes with volume replacement of pure media. Experimental results were calculated by measuring the optical density of the samples using a UV/Vis-spectrophotometer Lambda 25 (PerkinElmer, USA) at a wavelength of 255 nm [33].

Statistical Analysis

Microsoft Excel Mondo 2016 (Version 2108 Build 14332.20651) was used for the statistical analysis of all data, which were obtained from experiments performed in triplicate. Mean values ± standard deviations were calculated using one-way analysis of variance (ANOVA) and t-Test (Two-Sample Assuming Equal Variances), where probability was $p < 0.05$ as a significant criterion.

Results and Discussion

Justification of the Optimal Composition

To identify the optimal composition of floating tablets and subsequently study the complexation properties between HPC and C71G, to investigate the impact of Na-bicarbonate on complexation process, three types of PhMs were selected. PhMs HPC:C71G 1:2 and 2:1 contained an excess of each polymers and a 1:1 molar ratio, respectively. Each tablet consists of 50 mg of the corresponding PhM, 100 mg of acyclovir and different amounts of Na-bicarbonate (0 mg, 10 mg, 15 mg, 20 mg, 25 mg). After immersing the tablets of different compositions in a media, simulating stomach acid, the time to float (lag time) and the duration of flotation on the media surface (floating time) were measured. Upon contact with the acidic media, Na-bicarbonate generates carbon dioxide. The resulting CO_2 bubbles, trapped within the swollen gel layer surrounding the matrix, facilitate rapid flotation and an extended floating duration by reducing the density below 1 g/cm^3 [13–19, 32]. Tablets without Na-bicarbonate did not exhibit buoyancy. All matrices, containing Na-bicarbonate, except one (PhM 2:1 with 10 mg of Na-bicarbonate), demonstrated an optimal lag time (less than 3 minutes). The floating results for the different matrices are reported in Table 1.

After 24 hours of testing, all samples based on the PhM 2:1 (with an excess of HPC) disintegrated regardless of their Na-bicarbonate content. This is likely due to the solubility of HPC in the media and its inability to withstand the disruptive effect. Other samples with the highest Na-bicarbonate content (25 mg) were also destroyed. In large quantities, Na-bicarbonate exerts a disintegrating effect on matrices in an acidic media [11, 32]. Tablet samples of PhM 1:2 and PhM 1:1 containing 10 mg, 15 mg and 20 mg of Na-bicarbonate, exhibited all necessary floating parameters (lag time — less than 3 min, floating time — over 24 h) [11, 45, 46]. These samples were selected as optimal for further investigation.

Table 1

Effect of Na-bicarbonate level on floating parameters of matrices made of HPC/C71G at different molar ratios

HPC:C71G molar ratio	Na-bicarbonate, mg	Lag time	Floating time
1:2	0	–	No floatation observed
1:2	10	17 s	24 h
1:2	15	12 s	24 h
1:2	20	9 s	24 h
1:2	25	10 s	Disintegrated within 24 hours
1:1	0	–	No floatation observed
1:1	10	29 s	24 h
1:1	15	17 s	24 h
1:1	20	10 s	24 h
1:1	25	10 s	Disintegrated within 24 hours
2:1	0	–	No floatation observed
2:1	10	> 3 min	Disintegrated within 24 hours
2:1	15	37 s	Disintegrated within 24 hours
2:1	20	37 s	Disintegrated within 24 hours
2:1	25	37 s	Disintegrated within 24 hours

Determination of the Degree of Swelling of Matrices

Evaluating the behavior of matrices based on PhMs without API is necessary for prediction of the possibility of application of tablets as carriers for drug delivery systems (DDS). In addition, it was necessary to assess the complexation between the two polymers, as well as the influence of Na-bicarbonate on this process in acidic media, simulating fasted stomach, for the development of gastroretentive DDS. It was noted that matrices based on PhMs of both ratios retained their shape, increased in size and surface layer of matrices transformed into a hydrogel structure (Figure 1). The PhM with an excess of C71G (PhM 1:2) exhibited a higher swelling degree than the PhM 1:1. Furthermore, by the end of the experiment, the swelling degree of the PhM 1:1 began to decrease, which may indicate the erosion of HPC from the matrix (Figures 2-3) by reducing the mass. The influence of Na-bicarbonate on the swelling degree is more pronounced for PhM 1:1. As the Na-bicarbonate content increases, a decrease in the swelling degree is observed, which may also potentiate its disruptive effect on the matrix by facilitating the erosion of the HPC.

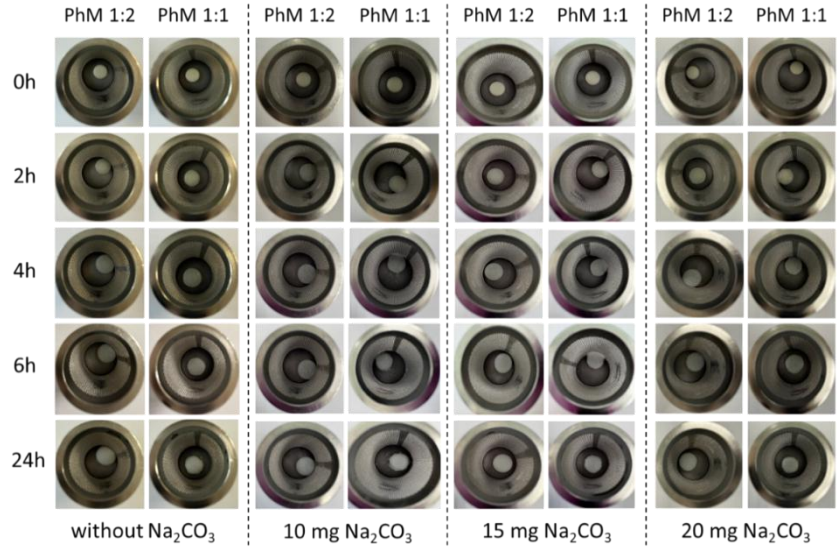


Figure 1. External appearance of PhM matrices during the swelling test

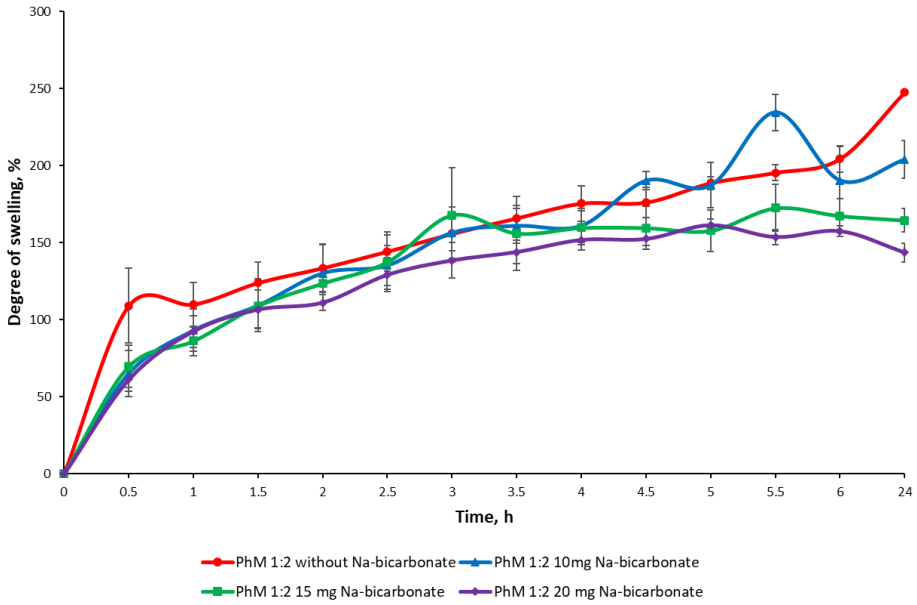


Figure 2. Swelling profiles of PhM 1:2 matrices with and without Na-bicarbonate in mimicking fasted stomach media (0.1 M HCl) (n = 3, mean ± SD)

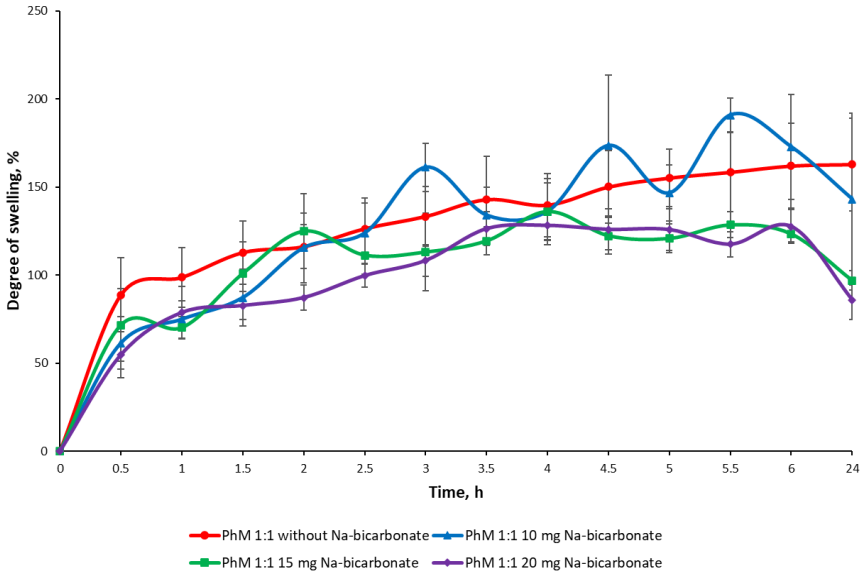


Figure 3. Swelling profiles of PhM 1:1 matrices with and without Na-bicarbonate in mimicking fasted stomach media (0.1 M HCl) (n = 3, mean ± SD)

Carbopol® as a weakly crossed-linked PAA, has a weak solubility in an acidic environment. Carbopol® polymers are bearing very good sorption property and they are capable of swelling to form a gel layer [47]. The thickening effect arises from the formation of hydrogen bonds between the carboxyl group and one or more hydroxyl donors [48, 49]. They provide gelation, viscosity, and mechanical strength necessary for structural integrity, resulting in denser, more robust matrices. HPC also is necessary for raft formation and stability. However, due to its reduced amount following erosion from the matrix, this led to the gel layer surrounding the tablet core becoming less viscous. Furthermore, the presence of the Na-bicarbonate increased the tablet's porosity, which disrupted the continuous gel structure of the soluble polymer, allowing a greater amount of water to penetrate into the swelling matrix [20, 50]. We have previously studied the swelling behavior of matrices based on these polymers, which is consistent with our assumptions [33].

Determination of the pH in the Matrix

To further investigate the micro-environmental pH, the pH indicator methyl red (0.15 % w/w) was added to the matrix to visually monitor the pH within the matrices during the penetration of media. This indicator is red at acidic pH and yellow at pH values >5.8 [43]. The appearance of the matrices during the experiment is shown in the Figure 4.

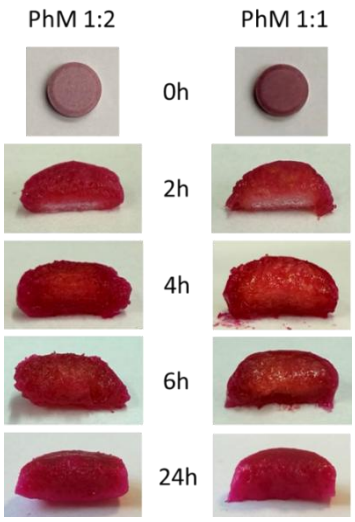


Figure 4. External appearance of PhM matrices during the media penetration

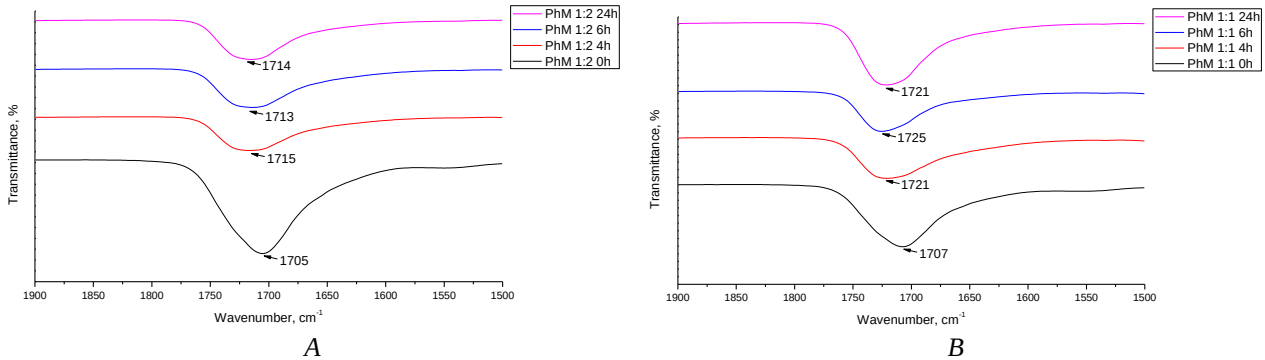
When the matrices were immersed in an acidic medium with a pH 1.2, a bright red staining of the matrix surface was observed. The Na-bicarbonate solution has an alkaline pH value [51, 52]. Since the matrix contains Na-bicarbonate, when interacting with the media, it will change the pH inside the matrix. By changing the color of the indicator, it is possible to monitor the change in the pH value during the penetration of the media into the matrix and identify the equilibrium of the reaction. The experiments showed that the outer hydrogel layer of the matrix remained red (low pH), whereas the core color of the slowly turned to yellow (high pH), from the edge towards the center. Thus, the pH within the core of the matrix turned yellow under the action of Na-bicarbonate during the penetration. 2 hours of exposure in the media showed its incomplete penetration into the entire volume of the matrix. With deeper penetration, a more pronounced change in the color of the indicator was observed (4 h, 6 h). After 24 hours of the experiment, the matrix turned red, which indicates that the reaction has completely passed and reached equilibrium in the system.

Evaluation of IPC. ATR-FTIR Spectroscopy

To assess possible structural changes in the PhM matrices, occurring under the influence of an media with a low pH value and also to evaluate the influence of Na-bicarbonate on the complexation between polymers, samples were collected after exposure to an acidic media, simulating stomach acid. The samples were specially prepared for further analysis using the method described above (Sample preparation).

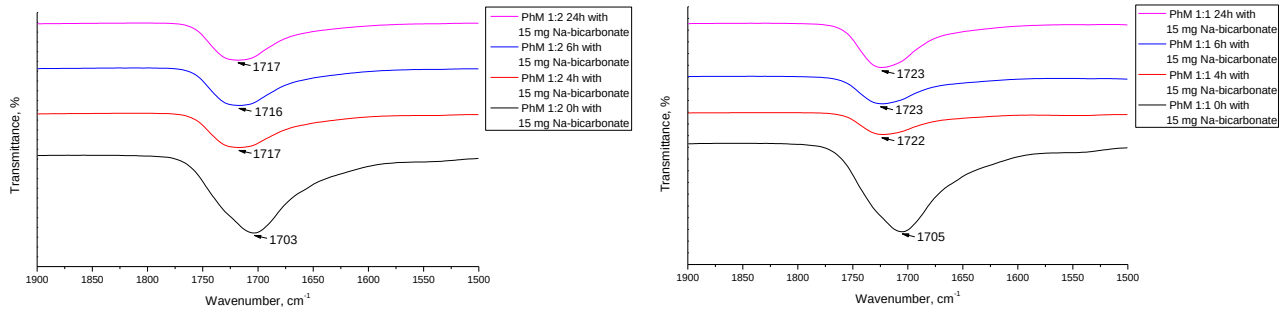
ATR-FTIR spectroscopy can be used to analyze hydrogen-bonded complexation between C71G and HPC by monitoring the shift of the characteristic absorbance band. Hydrogen bonding primarily occurs between the hydroxyl (–OH) or ester (–O–) groups of HPC and the carboxylic (–COOH) groups of C71G. In pure C71G powder, the carbonyl peak is usually located at 1700~1710 cm^{-1}. The hydrogen bonding between hydroxyl or ether groups and the carboxylic groups disrupts the existing hydrogen bonding network among the –COOH groups of C71G. Consequently, compared to pure C71G powder, the C=O stretching vibration in the FT-IR spectra exhibits shift. This spectral shift is an indicator of the extent of hydrogen bonding between HPC and C71G, it was investigated by us earlier [33]. A greater degree of hydrogen bond formation between C71G and HPC results in a higher shift of the C=O band relative to pure C71G [35, 38, 44]. This shift is also typical for IPCs with similar structures [53].

The ATR-FTIR spectra of the samples are presented in Figures 5-6. In the ATR-FTIR spectra of the individual polymers, the C71G exhibits an absorption band in the region of 1703–1707 cm^{-1}. This characteristic band confirms the stretching vibrations of the carboxyl groups in their structure. No absorption bands in this region were observed for the HPC. The ATR-FTIR spectra, obtained after different periods of matrix residence (2 h, 4 h, 6 h, 24 h) in the acidic media, confirmed that with increased residence time, the shift of the characteristic band increases. Since the PhM 1:1 is stoichiometric, more pronounced shifts are observed compared to the PhM 1:2 for both compositions with and without Na-bicarbonate. This is indicative of complex formation associated with a greater number of hydrogen bonds.



A — PhM 1:2; *B* — PhM 1:1 (ordinate — transmission, %; abscissa — wavenumber, cm^{-1})

Figure 5. IR-spectra of PhMs without Na-bicarbonate



A *B*

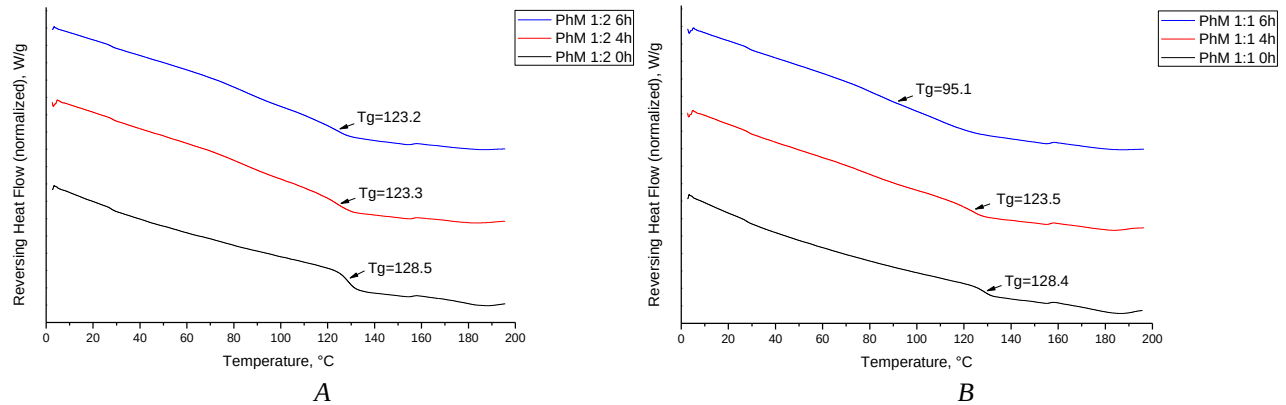
A — PhM 1:2; *B* — PhM 1:1 (ordinate — transmission, %; abscissa — wavenumber, cm^{-1})

Figure 6. IR-spectra of PhMs with Na-bicarbonate

Thermal Analysis

The procedure for preparing the samples is detailed in the Sample preparation.

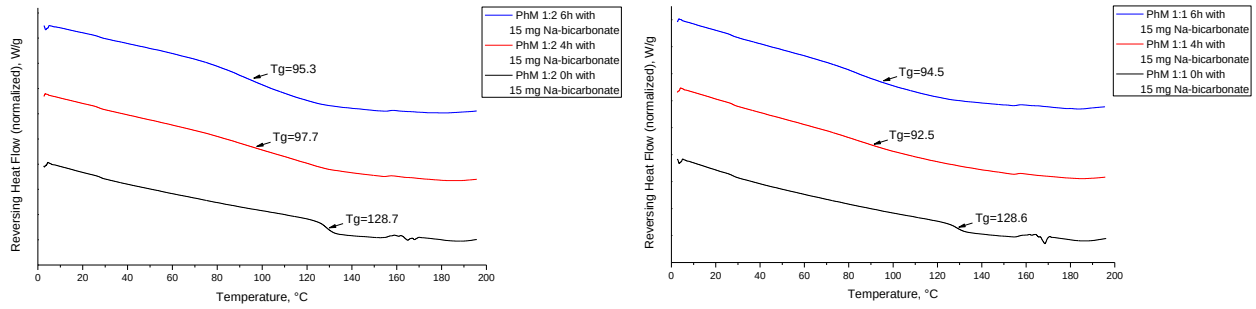
Figures 7-8 show the mDSC thermograms of the analyzed samples: PhMs without Na-bicarbonate, PhMs with Na-bicarbonate before swelling and after being in an acidic media for 4 h and 6 h. PhMs until swelling (0 h) have glass transition temperature (T_g) in the region 128.4–128.7 °C. This is typical for a pure C71G [33, 54]. A 4-hour exposure of the PhMs leads to a reduction in its T_g, which is likely due to the formation of hydrogen bonds. Extended exposure to the acidic media resulted in a more substantial lowering of the T_g. For PhMs without Na-bicarbonate, this is most pronounced for the 1:1 composition, which is probably due to the stoichiometric interaction T_g = 95.1 °C. In the case of mDSC-thermograms with Na-bicarbonate, the formation of IPC during swelling occurs in the case of both 1:1 and 1:2 formulations. At the same time, regardless of the time (4 or 6 h), a more intense shift in T_g was observed (T_g = 92.5–97.7 °C). According to literature data, the T_g of HPC is recorded in the range of 40 to 45 °C [55]. Based on literature findings, the T_g of polycomplex lies in the range between the T_g's of the initial components. The resulting T_g's for IPCs are recorded precisely in this range (T_g = 92.5–97.7 °C) [53]. This is a result of the formation of a cooperative system of intermolecular hydrogen bonds, which is consistent with our previous studies [33]. Observation of a non-classical (broadened) T_g in the swollen PhMs suggests the possible formation of a limited number of hydrogen bonds during complexation. The obtained mDSC results correlate with the ATR-FTIR results. As can be observed, the shifts of characteristic bands for the PhM 1:1 are more pronounced (1721–1725 cm^{-1}) than for the PhM 1:2 (1713–1715 cm^{-1}) without carbonate, as well as with Na-bicarbonate: PhM 1:1 (1722–1723 cm^{-1}), PhM 1:2 (1716–1717 cm^{-1}), which also indicates a IPC formation process between the polymers.



A *B*

A — PhM 1:2; *B* — PhM 1:1 (ordinate — reversing heat flow, W/g; abscissa — temperature, °C)

Figure 7. mDSC thermograms of PhMs without Na-bicarbonate



A *B*

A — PhM 1:2; *B* — PhM 1:1 (ordinate — reversing heat flow, W/g; abscissa — temperature, °C)

Figure 8. mDSC thermograms of PhMs with Na-bicarbonate

The observed changes in the DSC-thermograms of both PhMs before swelling, in the range of 150–170 °C, are associated with the decomposition of Na-bicarbonate in the mixture [56, 57]. As a result of swelling in an acidic media, the formation of two T_g characteristic of the individual polymers is not observed, which confirms the interaction between the polymers in the PhM. A single resultant T_g indicates the formation of a IPC.

Study of Drug Release

Acyclovir release in 0.1 M HCl was studied from floating tablets. The composition of the floating tablets is reported in Table 2. This is done in order to illustrate the effect of Na-bicarbonate as well as combination of HPC and C71G in matrices on the drug release of acyclovir.

Table 2

Composition of floating tablet matrices

HPC:C71G molar ratio	Mass of PhM for 1 tablet, mg	Mass of acyclovir for 1 tablet, mg	Na-bicarbonate mg	Total mass of 1 tablet, mg
1:2	50	100	10	160
1:2	50	100	15	165
1:2	50	100	20	170
1:1	50	100	10	160
1:1	50	100	15	165
1:1	50	100	20	170

Incorporation of Na-bicarbonate did not significantly affect the rapid drug release from PhMs matrices. This did not lead to acceleration of drug release by the effervescent action. However, it is worth noting that the drug release from matrices based on a PhM 1:1 is slightly higher than from a PhM 1:2 (Figures 9-10).

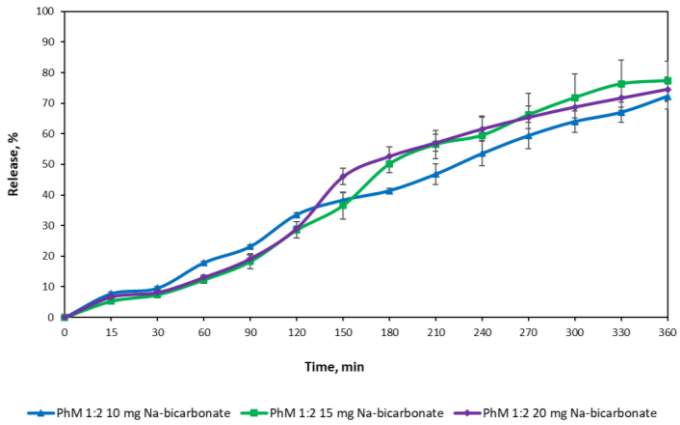


Figure 9. Effect of Na-bicarbonate level (mg/tablet) on Acyclovir release in 0.1 M HCl from PhM 1:2 tablet matrices (n = 3, mean ± SD)

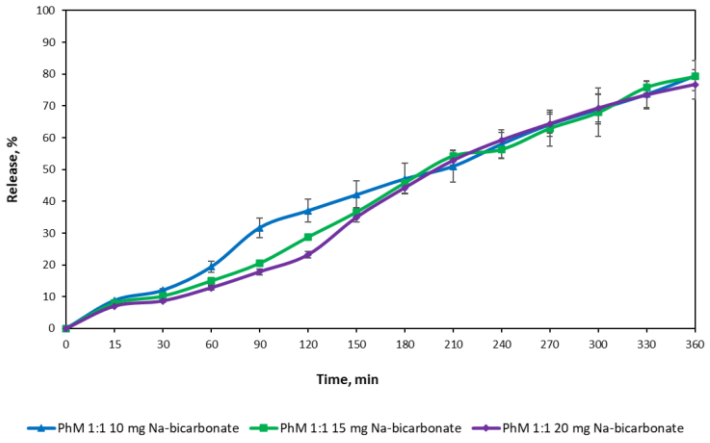


Figure 10. Effect of Na-bicarbonate level (mg/tablet) on Acyclovir release in 0.1 M HCl from PhM 1:1 tablet matrices (n = 3, mean ± SD)

This may be attributed to the erosion of the matrices due to existence of a soluble polymer (HPC) in them. The proportion of HPC in the PhM 1:2 is lower, which results in a reduced disruptive effect on the matrix. Conversely, the higher content of C71G allows the matrix to maintain its structure for a longer period due to the formation of a surface gel layer [47]. All compositions demonstrated a slower drug release, as no more than 85 % of the acyclovir was released within 6 hours. Release profile of acyclovir from all matrices, regardless of the concentration of Na-bicarbonate, can be characterized as prolonged with gradual drug release over 6 h.

Conclusions

Thus, according to the conducted studies, floating tablets based on a physical mixture of HPC and C71G were obtained. All matrices containing sodium bicarbonate showed a flotation time of less than 3 minutes, with the exception of a 2:1 PhM with 10 mg of sodium bicarbonate. The tablet matrices retained their shape during swelling and increased in size due to the swelling of Carbopol®. It is worth noting that with a polymer ratio in the PhM HPC/C71G (1:1 ratio) related to weight loss, greater matrix erosion was observed compared to a 1:2 due to the lower C71G content. Studies with methyl red indicator showed gradual penetration of the acidic media into the matrix and a color change from red to yellow. According to ATR-FTIR spectroscopy, a spectral shift is observed during matrix swelling, indicating the degree of hydrogen bonding between HPC and C71G in the samples. Thermal analysis revealed a somehow decrease in the glass transition temperatures in the DSC-thermograms, which is due to the formation of a polycomplex structure stabilized by an intermacromolecular hydrogen bonds.

The addition of sodium bicarbonate did not increase the release rate due to the effervescent effect. A slightly higher release rate was observed for matrices with a 1:1 polymer ratio, due to erosion of the soluble HPC polymer, while the higher C71G content maintains the structure due to the formation of a hydrogel layer. Thus, a PhMs of HPC/C71G with the addition of sodium bicarbonate can be used to produce floating tablets for the gastroretentive delivery of acyclovir.

Funding

The study was supported by a grant from the Russian Science Foundation (No. 23-15-00263, "Development polycomplex drug delivery systems for preparation of innovative dosage forms with modified release", https://rscf.ru/en/project/23-15-00263/).

*Author Information**

**The authors' names are presented in the following order: First Name, Middle Name and Last Name*

Ulyana Nikolaevna Zabolotnaya — 3d year PhD Student, Institute of Pharmacy, Kazan State Medical University, Fatykha Amirkhan str., 16, Kazan, Republic of Tatarstan, 420126, Russia; e-mail: ulyana.zabolotnaya@kazangmu.ru, https://orcid.org/0009-0004-8058-8007

Venera Rasimovna Timergalieva — PhD, Institute of Pharmacy, Kazan State Medical University, Fatykha Amirkhan str., 16, Kazan, Republic of Tatarstan, 420126, Russia; e-mail: venera.timergalieva@kazangmu.ru, https://orcid.org/0000-0002-3690-8905

Shamil Flurovich Nasibullin — Lecturer, Institute of Pharmacy, Kazan State Medical University, Fatykha Amirkhan str., 16, Kazan, Republic of Tatarstan, 420126, Russia; e-mail: shamil.nasibullin@kazangmu.ru, https://orcid.org/0000-0002-7255-8041

Rouslan Ibragimovich Moustafine (*corresponding author*) — PhD, Director of Institute of Pharmacy, Institute of Pharmacy, Kazan State Medical University, Fatykha Amirkhan str., 16, Kazan, Republic of Tatarstan, 420126, Russia; e-mail: ruslan.mustafin@kazangmu.ru, https://orcid.org/0000-0002-0916-2853

Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript. CRediT: **Ulyana Nikolaevna Zabolotnaya** conceptualization, data curation, investigation, methodology, visualization, writing-original draft; **Venera Rasimovna Timergalieva** conceptualization, methodology, visualization, writing-original draft; **Shamil Flurovich Nasibullin** assisted with thermal methods and advised on the experimental results; **Rouslan Ibragimovich Moustafine** conceptualization, data curation, formal analysis, funding acquisition, resources, supervision, validation, writing-original draft, writing-review & editing.

Conflicts of Interest

The authors declare no conflict of interest.

References

1 Vo, A. Q., Zhang, J., Nyavanandi, D., Bandari, S., & Repka, M. A. (2020). Hot melt extrusion paired fused deposition modeling 3D printing to develop hydroxypropyl cellulose based floating tablets of cinnarizine. *Carbohydrate Polymers*, *246*, 116519. https://doi.org/10.1016/J.CARBPOL.2020.116519

2 Alekseyev, K. V., Blynskaya, E. V., Karbusheva, E. Yu., Sedova, M. K., Tikhonova, N. V., & Uvarov, N. A. (2012). Production of Floating Medicinal Forms. *Pharmacy*, (6), 35–38 [in Russian].

3 Lin, X., Fu, H., Hou, Z., Si, Y., Shan, W., & Yang, Y. (2021). Three-dimensional printing of gastro-floating tablets using polyethylene glycol diacrylate-based photocurable printing material. *International Journal of Pharmaceutics*, *603*, 120674. https://doi.org/10.1016/j.ijpharm.2021.120674

4 Lopes, C. M., Bettencourt, C., Rossi, A., Buttini, F., & Barata, P. (2016). Overview on gastroretentive drug delivery systems for improving drug bioavailability. *International journal of pharmaceutics*, *510(1)*, 144–158. https://doi.org/10.1016/j.ijpharm.2016.05.016

5 Omidian, H. (2025). Gastroretentive drug delivery systems: A holy grail in oral delivery. *Drug Discovery Today*, 104340. https://doi.org/10.1016/j.drudis.2025.104340

6 Yuan, K. C., Chiang, Y. C., Li, P. H., & Chiang, P. Y. (2024). Physicochemical and release properties of anthocyanin gastric floating tablets colloidized with κ-carrageenan/metal ions. *Food Hydrocolloids*, *150*, 109674. https://doi.org/10.1016/j.foodhyd.2023.109674

7 Pinto, J. F. (2010). Site-specific drug delivery systems within the gastro-intestinal tract: from the mouth to the colon. *International journal of pharmaceutics*, *395(1-2)*, 44–52. https://doi.org/10.1016/j.ijpharm.2010.05.003

8 Shah, K., Singh, D., Agrawal, R., & Garg, A. (2025). Current developments in the delivery of gastro-retentive drugs. *American Association of Pharmaceutical Scientists PharmSciTech*, *26(2)*, 57. https://doi.org/10.1208/s12249-025-03052-4

9 Issarachot, O., Bunlung, S., Kaewkroek, K., & Wiwattanapatapee, R. (2023). Superporous hydrogels based on blends of chitosan and polyvinyl alcohol as a carrier for enhanced gastric delivery of resveratrol. *Saudi Pharmaceutical Journal*, *31(3)*, 335–347. https://doi.org/10.1016/j.jsps.2023.01.001

10 Charoenying, T., Opanasopit, P., Ngawhirunpat, T., Rojanarata, T., Akkaramongkolporn, P., & Patrojanasophon, P. (2023). Development of a novel tablet-shaped floating 3D-printed device with adjustable floating time as floating drug delivery systems provided zero-order release kinetics. *Journal of Drug Delivery Science and Technology*, *84*, 104506. https://doi.org/10.1016/j.jddst.2023.104506

11 Mustafin R. I., Protasova A. A., Bukhovets A. V., & Semina I. I. (2014). Issledovanie interpolymernykh sochetaniy na osnove (met)akrilatov v kachestve perspektivnykh nositeley v polikompleksnykh sistemakh dlya gastroretentivnoy dostavki [Investigation of interpolymers based on (meth)acrylates as promising carriers in multiplex gastroretentive drug delivery systems]. *Farmatsiya — Farmatsiya*, *5*, 3–5 [in Russian].

12 Blynskaya, E. V., Vinogradov, V. P., Tishkov, S. V., Suslina, S. N., & Alekseev, K. V. (2022). Modern Approaches to Obtaining Floating Drug Dosage Forms (A Review). *Pharmaceutical Chemistry Journal, 56(9)*, 1277–1284. https://doi.org/10.1007/s11094-022-02786-w

13 Raza, A., Hayat, U., Wang, H. J., & Wang, J. Y. (2020). Preparation and evaluation of captopril loaded gastro-retentive zein based porous floating tablets. *International Journal of Pharmaceutics, 579*, 119185. https://doi.org/10.1016/j.ijpharm.2020.119185

14 Tort, S., Han, D., & Steckl, A. J. (2020). Self-inflating floating nanofiber membranes for controlled drug delivery. *International Journal of Pharmaceutics, 579*, 119164. https://doi.org/10.1016/j.ijpharm.2020.119164

15 Rahim, S. A., Carter, P., & Elkordy, A. A. (2017). Influence of calcium carbonate and sodium carbonate gassing agents on pentoxifylline floating tablets properties. *Powder Technology, 322*, 65–74. https://doi.org/10.1016/j.powtec.2017.09.001

16 Yin, L., Qin, C., Chen, K., Zhu, C., Cao, H., Zhou, J., He, W., & Zhang, Q. (2013). Gastro-floating tablets of cephalexin: preparation and in vitro/in vivo evaluation. *International journal of pharmaceutics, 452(1-2)*, 241–248. https://doi.org/10.1016/j.ijpharm.2013.05.011

17 Chaudhary, S., Chandrika, A. M., Chaudhary, Y., Shahi, A., Sigdel, A., & Thapa, R. (2025). Formulation and Invitro Evaluation of Effervescent Floating Tablets of Hydrophilic Polymers Using Propranolol Hydrochloride as a Model Drug. *World Journal of Current Medical and Pharmaceutical Research, 7(1)*, 29–34. https://doi.org/10.37022/wjcmpr.v7i1.354

18 Tufail, M., Shah, K. U., Khan, I. U., Khan, K. A., Shah, S. U., Rashid, F., Khan, J., Alshammari, A., Alasmari, A. F., & Riaz, M. S. (2024). Controlled release bilayer floating effervescent and noneffervescent tablets containing levofloxacin and famotidine. *International Journal of Polymer Science, 2024(1)*, 1243321. https://doi.org/10.1155/2024/1243321

19 Siripruekpong, W., Wiwattanapatapee, R., Chambin, O., & Assifaoui, A. (2025). Structural and mechanistic exploration in the development of floating drug delivery systems using calcium-pectinate gels with sodium bicarbonate as CO_2 gas-forming agent. *Journal of Drug Delivery Science and Technology, 107*, 106729. https://doi.org/10.1016/j.jddst.2025.106729

20 Ahmad, S., Khan, J. A., Kausar, T. N., Mahnashi, M. H., Alasiri, A., Alqahtani, A. A., Alqahtani, T. S., Walbi, I. A., Alshehri, O. M., Elnoubi, O. A., Mahmood, F., & Sadiq, A. (2023). Preparation, characterization and evaluation of flavonolignan silymarin effervescent floating matrix tablets for enhanced oral bioavailability. *Molecules, 28(6)*, 2606. https://doi.org/10.3390/molecules28062606

21 Zhang, R., Shi, H., Li, S., Zhang, H., Zhang, D., Wu, A., Zhang, C., Li, C., Fu, X., Chen, S., Shi, J., Tian, Y., Wang, Y., & Liu, H. (2023). A double-layered gastric floating tablet for zero-order controlled release of dihydromyricetin: Design, development, and in vitro/in vivo evaluation. *International Journal of Pharmaceutics, 638*, 122929. https://doi.org/10.1016/j.ijpharm.2023.122929

22 Saady, M., Shoman, N. A., Teaima, M., Abdelmonem, R., El-Nabarawi, M. A., & Elhabal, S. F. (2024). Fabrication of gastro-floating sustained-release etoricoxib and famotidine tablets: design, optimization, in-vitro, and in-vivo evaluation. *Pharmaceutical Development and Technology, 29(5)*, 429–444. https://doi.org/10.1080/10837450.2024.2343320

23 Bellad, K., Nanjwade, B., Sarkar, A., Srichana, T., & Shetake, R. (2020). Development and evaluation of curcumin floating tablets. *Pharmaceutica Analytica Acta, 12*, 622. https://doi.org/10.35248/2153-2435.20.11.622

24 Bote, S., & Kolageri, S. (2022). Formulation and Evaluation of Floating Tablets of Pantoprazole. Journal of Drug Delivery and Therapeutics, 12(5), 34–45. https://doi.org/10.22270/jddt.v12i5.5577

25 Liu, H., Wang, S., Shi, H., Zhang, R., Qu, K., Hu, Y., Qu, X., Gan, C., Chen, J., Shi, X., Zhang, M., & Zeng, W. (2021). Gastric floating tablet improves the bioavailability and reduces the hypokalemia effect of gossypol in vivo. *Saudi Pharmaceutical Journal, 29(4)*, 305–314. https://doi.org/10.1016/j.jsps.2021.03.001

26 Wavhule, P., & Devarajan, P. V. (2021). Development and optimization of microballoons assisted floating tablets of Baclofen. *American Association of Pharmaceutical Scientists PharmSciTech, 22(8)*, 272. https://doi.org/10.1208/s12249-021-02139-y

27 Huh, H. W., Na, Y. G., Kang, H., Kim, M., Han, M., Pham, T. M. A., Lee, H., Baek, J. S., Lee, H. K., & Cho, C. W. (2021). Novel self-floating tablet for enhanced oral bioavailability of metformin based on cellulose. *International Journal of Pharmaceutics, 592*, 120113. https://doi.org/10.1016/j.ijpharm.2020.120113

28 Moustafine R. I., Bukhovets A. V., Protasova A. A., Shaykhramova R. N., Sitenkov A. Y., & Semina I. I. (2015). Sravnitel'noe issledovanie polikompleksnykh sistem dlya gastroretentivnoy dostavki metformina [Comparative investigation of polycomplex systems for gastroretentive metformin delivery]. *Razrabotka i registratsiya lekarstvennykh sredstv — Drug development & registration, 1(10)*, 48–50 [in Russian].

29 Khutoryanskiy, V. V., Dubolazov, A. V., & Mun, G. A. (2009). pH-and ionic strength effects on interpolymer complexation via hydrogen-bonding. *In Hydrogen-bonded interpolymer complexes: Formation, structure and applications*, 1-21. https://doi.org/10.1142/9789812709776_0001

30 Smyslov, R. Y., Gorshkova, Y. E., Nekrasova, T. N., Makhayeva, D. N., Mun, G. A., Irmukhametova, G. S., & Khutoryanskiy, V. V. (2025). Dynamic and structural insights into hydrogen-bonded interpolymer complexes of poly(2-alkyl-2-oxazolines) with poly(carboxylic acids). *Journal of Colloid and Interface Science, 699(1)*, 138185. https://doi.org/10.1016/j.jcis.2025.138185

31 Khutoryanskiy, V. V. (2007). Hydrogen-bonded interpolymer complexes as materials for pharmaceutical applications. *International Journal of Pharmaceutics, 334*(1-2), 15–26. https://doi.org/10.1016/j.ijpharm.2007.01.037

32 Bani-Jaber, A. K., Alkawareek, M. Y., Al-Gousous, J. J., & Helwa, A. Y. A. (2011). Floating and sustained-release characteristics of effervescent tablets prepared with a mixed matrix of Eudragit L-100-55 and Eudragit EPO. *Chemical and Pharmaceutical Bulletin, 59(2)*, 155–160. https://doi.org/10.1248/cpb.59.155

33 Zabolotnaya U.N., Timergalieva V.R., Nasibullin S.F., & Moustafine R.I. (2025). Development of polycomplex carriers based on hydroxypropyl cellulose and Carbopol® for gastroretentive drug delivery. *Drug development & registration, 14(4)*, 108–124 [in Russian]. https://doi.org/10.33380/2305-2066-2025-14-4-2148

34 Nurkeeva, Z. S., Mun, G. A., & Khutoryanskiy, V. V. (2003). Interpolymer complexes of water-soluble nonionic polysaccharides with polycarboxylic acids and their applications. *Macromolecular Bioscience, 3(6)*, 283–295. https://doi.org/10.1002/chin.200408305

35 Satoh, K., Takayama, K., Machida, Y., Suzuki, Y., Nakagaki, M., & Nagai, T. (1989). Factors affecting the bioadhesive property of tablets consisting of hydroxypropyl cellulose and carboxyvinyl polymer. *Chemical and pharmaceutical bulletin, 37(5)*, 1366-1368. https://doi.org/10.1248/cpb.37.1366

36 Mangazbaeva, R. A., Mun, G. A., Nurkeeva, Z. S., & Khutoryanskiy, V. V. (2006). Interpolymer complexes of hydroxypropylmethylcellulose with polycarboxylic acids in aqueous solutions. *Polymer international, 55(6)*, 668–674. https://doi.org/10.1002/pi.2012

37 Mun, G. A., Nurkeeva, Z. S., Khutoryanskiy, V., & Dubolazov, A. V. (2003). Effect of pH and ionic strength on the complex formation of poly(acrylic acid) with hydroxyethylcellulose in aqueous solutions. *Polymer Science, 45(12)*, 2091–2095.

38 Şakar-Deliormanli, A. (2012). Flow behavior of hydroxypropyl methyl cellulose/polyacrylic acid interpolymer complexes in aqueous media. *Polymer international, 61(12)*, 1751–1757. https://doi.org/10.1002/pi.4266

39 Negim, E. S. M., Nurpeissova, Z. A., Mangazbayeva, R. A., Khatib, J. M., Williams, C., & Mun, G. A. (2014). Effect of pH on the physico-mechanical properties and miscibility of methyl cellulose/poly(acrylic acid) blends. *Carbohydrate Polymers, 101*, 415–422. https://doi.org/10.1016/j.carbpol.2013.09.047

40 Fedorova, O. V., Ovchinnikova, I. G., Rusinov, G. L., Avdeeva, V. V., Zhdanov, A. P., Zhizhin, K. Yu., Kuznetsov, N. T., Zakharova, L. Ya., Kuznetsova, D. A., Razuvaeva, Yu. S., Zhiltsova, E. P., Sinyashin, O. G., Alekseeva, A. S., Vodovozova, E. L., Abdrakhmanova, I. I., Ibrahim, A., Solovyeva, V. V., Maltsev, A. V., Fisenko, V. P., Bachurin, S. O., Mikhailov, Yu. M., Aleksandrova, Yu. I., Shurpik, D. N., Stoikov, I. I., Ziganshina, A. Y., Solovieva, S. E., Antipin, I. S., Agafonov, M. A., Terekhova, I. V., Ilicheva, P. M., Pidenko, P. S., Burmistrova, N. A, Moustafine, R. I., Timergalieva, V. R., Zabolotnaya, Y. N., Khutoryanskiy, V. V., Demin, A. M., Levit, G. L., Charushin, V. N., Krasnov, V. P., Goryacheva, O. A., Mayorova, O. A., Mesheryakova, S. M., Goryacheva, I. Yu., Ayupova, A. I., Fattakhova, A. A., Rizvanov, A. A., Inozemtseva, O. A., Gusliakova, O. I., Gorin, D. A., Gerasimov, A. V., Zubaidullina, L. S., Ziganshin, M. A., Valiulin, S. V., Onischuk, A. A., Bezrukov, A. N., Galyametdinov, Yu. G., Padnya, P. L., Nazarova, A. A., Sultanova, E. D. & Burilov, V. A. (2025). Modern Strategies of Drug Therapy: Multi-Target Drug Delivery, Bioimaging, Diagnostics. *Russian Journal of General Chemistry, 95* (Suppl 1), S1-S448. https://doi.org/10.1134/S1070363225606726

41 Gordeeva D. S., Sitenkova (Bukhovets) A. V., Moustafine R. I. (2020). Interpolyelectrolyte Complexes Based On Eudragit® Copolymers As Carriers For Bioadhesive Gastroretentive Metronidazole Delivery System. *Drug development & registration, 9(2)*, 72–76 [in Russian]. https://doi.org/10.33380/2305-2066-2020-9-2-72-76

42 Viktorova A. S., Elizarova E. S., Romanova R. S., Timergalieva V. R., Khutoryanskiy V. V., Moustafine R. I. (2021). Interpolymer complexes based on Carbopol® and poly(2-ethyl-2-oxazoline) as carriers for buccal delivery of metformin. *Drug development & registration, 10(1)*, 48–55 [in Russian]. https://doi.org/10.33380/2305-2066-2021-10-1-48-55

43 Streubel, A., Siepmann, J., Dashevsky, A., & Bodmeier, R. (2000). pH-independent release of a weakly basic drug from water-insoluble and-soluble matrix tablets. *Journal of controlled release*, *67*(1), 101–110. https://doi.org/10.1016/S0168-3659(00)00200-5

44 Zhang X., Lin F., Yuan Q., Zhu L., Wang C., Yang S. (2019). Hydrogen-bonded thin films of cellulose ethers and poly(acrylic acid). *Carbohydrate Polymers, 215*, 58-62. https://doi.org/10.1016/j.carbpol.2019.03.066

45 Rao, G. K., Mandapalli, P. K., Manthri, R., & Reddy, V. P. (2013). Development and in vivo evaluation of gastroretentive delivery systems for cefuroxime axetil. *Saudi Pharmaceutical Journal, 21(1)*, 53–59. https://doi.org/10.1016/j.jsps.2012.01.003

46 Prajapati, P. H., Nakum, V. V., & Patel, C. N. (2012). Formulation and evaluation of floating matrix tablet of stavudine. *International Journal of pharmaceutical investigation, 2(2)*, 83. https://doi.org/10.4103/2230-973X.100047

47 Yusif R. M., Hashim I. I. A., Mohamed E. A., El Rakhawy M. M. (2016). Investigation and evaluation of an in situ interpolymer complex of carbopol with polyvinylpyrrolidone as a matrix for gastroretentive tablets of ranitidine hydrochloride. *Chemical and Pharmaceutical Bulletin, 64(1)*, 42–51. https://doi.org/10.1248/cpb.c15-00620

48 Priyanka, R., & Prabhu, R. (2020). Carbopol 71G-NF polymer–the next pillar of oral solid dosage form. *Magna Scientia Adv Res Rev, 1*, 010–017. https://doi.org/10.30574/msarr.2020.1.1.0018

49 Ozeki, T., Yuasa, H., & Kanaya, Y. (2000). Controlled release from solid dispersion composed of poly(ethylene oxide)–Carbopol® interpolymer complex with various cross-linking degrees of Carbopol®. *Journal of controlled release*, *63*(3), 287–295. https://doi.org/10.1016/S0168-3659(99)00202-3

50 Barman, S., Sarkar, A., Das, U., & Mandal, S. (2025). Double Target Strategy of Novel Floating Raft System Containing Metronidazole. *Journal of Pharmaceutical Innovation*, *20*(6), 1–25. https://doi.org/10.1007/s12247-025-10187-1

51 Thapa, P., & Jeong, S. H. (2018). Effects of formulation and process variables on gastroretentive floating tablets with a high-dose soluble drug and experimental design approach. *Pharmaceutics*, *10*(3), 161. https://doi.org/10.3390/pharmaceutics10030161

52 Jindal, S., Jindal, K., Gupta, G., Garg, R., & Awasthi, R. (2016). Gastroretentive floating tablets: An investigation of excipients effect on tablet properties. *Marmara Pharmaceutical Journal*, *20*(2), 100–110. https://doi.org/10.12991/mpj.20162018166

53 Moustafine, R. I., Viktorova, A. S., & Khutoryanskiy, V. V. (2019). Interpolymer complexes of carbopol® 971 and poly(2-ethyl-2-oxazoline): Physicochemical studies of complexation and formulations for oral drug delivery. *International journal of pharmaceutics*, *558*, 53–62. https://doi.org/10.1016/j.ijpharm.2019.01.002

54 Gómez-Carracedo, A., Alvarez-Lorenzo, C., Gomez-Amoza, J. L., & Concheiro, A. (2004). Glass transitions and viscoelastic properties of Carbopol® and Noveon® compacts. *International journal of pharmaceutics*, *274*(1-2), 233–243. https://doi.org/10.1016/j.ijpharm.2004.01.023

55 Khutoryanskiy, V. V., Cascone, M. G., Lazzeri, L., Barbani, N., Nurkeeva, Z. S., Mun, G. A., & Dubolazov, A. V. (2004). Morphological and thermal characterization of interpolymer complexes and blends based on poly(acrylic acid) and hydroxypropylcellulose. *Polymer International*, *53*(3), 307–311. https://doi.org/10.1002/pi.1408

56 Heda, P. K., Dollimore, D., Alexander, K. S., Chen, D., Law, E., & Bicknell, P. (1995). A method of assessing solid state reactivity illustrated by thermal decomposition experiments on sodium bicarbonate. *Thermochimica acta*, *255*, 255–272. https://doi.org/10.1016/0040-6031(94)02154-G

57 Sadik, T., Pillon, C., Carrot, C., & Ruiz, J. A. R. (2018). Dsc studies on the decomposition of chemical blowing agents based on citric acid and sodium bicarbonate. *Thermochimica Acta*, *659*, 74–81. https://doi.org/10.1016/j.tca.2017.11.007