



Exploring prospective polymers for clarithromycin mucoadhesive-gastroretentive granules

Kurnia Sari Setio Putri^{1,2*}, Rayhan Akbar¹, Dave Jason Satria¹, Wisnu Widyarto¹, Raditya Iswandana^{1,2}, Baitha Palanggatan Maggadani^{3,4}, Heri Setiawan^{5,6}

¹Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia.

²Drug Delivery System Research Cluster, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia.

³Laboratory of Pharmaceutical-Medicinal Chemistry and Bioanalysis, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia.

⁴Bioanalysis in Biological Matrices Research Cluster, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia.

⁵Laboratory of Pharmacology, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia.

⁶Herbal Drug Discovery and Development Research Cluster, Universitas Indonesia, Depok, Indonesia.

ARTICLE HISTORY

Received on: 27/09/2025

Accepted on: 11/01/2026

Available Online: 05/03/2026

Key words:

Clarithromycin, mucoadhesives, gastroretentive, cellulose derivatives, carbomer, polymethacrylate.

ABSTRACT

Oral clarithromycin therapy for *Helicobacter pylori* is limited by short gastric residence and variable intragastric exposure. Formulating clarithromycin in mucoadhesive gastroretentive granules (MGG) may extend the gastric residence time, increase the concentration, and control drug release at the site of action for a longer time, and improving bioavailability and therapeutic efficacy in eradicating *H. pylori*. Polymers with certain swelling ability and mucoadhesive properties are critical to produce MGG. Therefore, this study aims to explore various polymers for their potential as carriers for mucoadhesive gastroretentive dosage forms. Clarithromycin was mixed in a ratio of 1:1 with HPMC K15M, HPC MF, HEC 250 HHX, Carbomer (Carbopol 971p), or Polymethacrylates (Eudragit RS PO), and MGG were prepared using the wet granulation method. The yield of obtained dry granules was measured, then the size, moisture content, and flow properties were characterized. Muco-/bio-adhesive properties were analyzed based on adhesion strength and MGG retained during the *ex-vivo* study. The swelling index and drug release profile of MGG in HCl 0.1 N (pH 1.2) were analyzed. The results showed that all polymers produced free-flowing granules with effective hydration and gastric tissue adhesion. Among them, the Carbopol-based granules (F4) offered the best overall balance of rapid gel formation for early attachment, good *ex-vivo* retention to 8 hours, and prolonged release maintained to 12 hours. Release profiles were best described by the Higuchi kinetic model, consistent with diffusion and dissolution-controlled drug release mechanisms from a hydrated matrix with polymer swelling. This work provides the first direct, granule-form comparison of multiple polymers for mucoadhesive gastro-retentive delivery of clarithromycin. The Carbopol 971p matrix (F4) emerges as a promising carrier to prolong gastric residence and sustain local drug availability, supporting reduced dosing frequency and improved patient convenience. Future studies will optimize polymer ratios and evaluate *in-vivo* pharmacokinetics and antibacterial performance.

1. INTRODUCTION

Helicobacter pylori (*H. pylori*) infection is a significant contributing factor to peptic ulcer disease, gastric

cancer, and other types of gastric and extra-gastric diseases in more than 50% of the world's population globally [1,2]. Clarithromycin is among the most effective antimicrobials, with a broad mechanism of action and a low minimum inhibitory concentration (MIC) for *H. pylori* [3–5]. However, the therapeutic effect through the oral route is limited by short residence time in the gastric mucosa and area, which causes challenges in maintaining high concentrations of the antibiotic at the site of action [6].

*Corresponding Author

Kurnia Sari Setio Putri, Laboratory of Pharmaceutical Technology, Faculty of Pharmacy, Universitas Indonesia, Depok, Indonesia.
E-mail: kurnia.putri@farmasi.ui.ac.id

Mucoadhesive gastroretentive dosage forms, which adhere to gastric mucosal tissues and control drug release, are among the methods with potential to address the challenges [7]. Formulating clarithromycin in mucoadhesive gastroretentive dosage forms may extend the gastric residence time, increase the concentration, and control drug release at the site of action for a longer time, and improve the bioavailability and efficacy [6,8]. Granule dosage forms were selected in this study due to several notable advantages in a larger effective surface area for adhesion and drug release, easier in formulation, process, and scale up, while allowing flexible dosing and better flow characteristics for capsule filling or sachet packaging [9].

Polymers with certain swelling ability and mucoadhesive properties, such as carbomer [10,11], polymethacrylate [12–15], and cellulose derivatives, including HPMC [11,16,17], HPC [11], and HEC [10,11,18] are critical for producing mucoadhesive gastroretentive dosage forms due to their capability to swell in the hydrous gastrointestinal tract and form hydrogen bonds with mucin in the gastric mucosal layer. Accordingly, we selected HPMC, HEC, HPC, and Carbomer (Carbopol 971p) to represent hydrophilic gel-formers with high swelling and adhesion capacity, and Polymethacrylates (Eudragit RS PO) as a water-insoluble, pH-independent matrix former that enables sustained release in this study. Chitosan and alginate were excluded in this study to avoid pH-dependent solubility and ionic crosslinking variability in acidic media.

This study aimed to explore the most effective polymer for mucoadhesive gastroretentive clarithromycin granules via a head-to-head comparison of five candidates, such as an approach not previously reported for clarithromycin. While HPMC and Carbopol have been widely investigated individually, comparative studies evaluating their performance alongside other cellulose derivatives (HPC, HEC) and polymethacrylate (Eudragit RS PO) in clarithromycin mucoadhesive granules have not been reported yet. This study provides novel insights into how different polymer types, at the same concentration, might influence the swelling, adhesion, and release behavior, guiding rational polymer selection for optimized *H. pylori* therapy.

Clarithromycin-containing mucoadhesive gastroretentive granules (MGGs) were prepared using the wet granulation method. Physical properties of granules, including organoleptic, particle size distribution, moisture content, flowability, and swelling properties, were characterized. In addition, *in-vitro* drug release profile and *ex-vivo* bio-adhesive properties of clarithromycin granules were also evaluated.

2. MATERIALS AND METHODS

2.1. Materials

Materials used in this study were clarithromycin (Pharmachem, India), Hydroxypropylmethyl cellulose/HPMC/Benece K15M (Ashland, USA), Hydroxypropyl cellulose/HPC/Klucel MF (Ashland, USA), and Hydroxyethyl cellulose/HEC/Natrosol 250 HHX (Ashland, USA), Carbomer/Carbopol 971p (Lubrizol, USA), Polymethacrylate/Eudragit RS PO (Evonik, Germany), and other chemicals of analytical grade.

Table 1. Formulation of clarithromycin mucoadhesive gastroretentive granules.

Materials	Formula (ratio)				
	F1	F2	F3	F4	F5
Clarithromycin	1	1	1	1	1
HPMC (Benece K15M)	1				
HPC (Klucel MF)		1			
HEC (Natrosol HHX)			1		
Carbomer (Carbopol 971P)				1	
Polymethacrylate (Eudragit RS PO)					1

2.2. Method

2.2.1. Preparation of clarithromycin granules

Clarithromycin MGG were prepared using the wet granulation method with the formulation as presented in Table 1. Clarithromycin and various polymers were mixed thoroughly in a ratio of 1:1, and then granulated with a binder solution (5% w/v) derived from the same polymers. The wet mass was sieved through a #8 mesh to obtain uniformly sized granules, which were then dried in a hot air oven at 40°C for approximately 2 hours, until the residual moisture content reached 2%–5%. The yield of obtained dry granules was measured before storage in an airtight container in a desiccator.

2.2.2. Physical characterization

Organoleptic properties of clarithromycin MGG were observed, including the shape, color, and odor. MGG size distribution was measured using the multistage sieve AS 300 Control (Retsch, Germany). In addition, the flow rate was measured using a flowmeter GTL (Erweka, Germany), and the angle of repose was calculated. Hausner's ratio was measured using a bulk density tester (Erweka, Germany) and calculated from the ratio of bulk and tapped density of granules [19,20]. Moisture content was measured with a moisture balance AMB 50 (Adam, UK) at 105°C. The swelling index of MGG was measured in HCl 0.1 N (pH 1.2) at 37°C ± 0.5°C. This measurement was performed by calculating the increased weight of granules at 15, 30, 60, 90, 120, 180, 240, 360, 480, 600, and 720 minutes.

2.2.3. Bioadhesion characterization

Bioadhesion properties were analyzed by measuring adhesion force and residence time of MGG on the gastric mucosal tissue of rats. Eight- to twelve-week-old Sprague Dawley rats (NAFDC, Indonesia) were kept in cages with 12-hour light/dark cycle and given food and water ad libitum. The study protocol was approved by the Research Ethics Committee of Dr. Cipto Mangunkusumo National Hospital, Faculty of Medicine, Universitas Indonesia, Indonesia (Approval No.: KET-145/UN2.F1/ETIK/PPM.00.02/2024).

Rats were fed only with water 24 hours before being sacrificed using a lethal dose of ketamine (91 mg/kg) and xylazine (9.1 mg/kg). Subsequently, the gastric tissues were

surgically removed, placed in a 0.9% NaCl solution, and stored in the refrigerator until ready for use, which should be carried out within 24 hours. Each adhesion strength and *ex vivo* bioadhesion study was conducted in triplicate ($n = 3$), utilizing one gastric tissue sample obtained from a single rat for each replicate. This design was adopted to ensure the generation of reliable and reproducible data while adhering to the 3R principles (replacement, reduction, and refinement) governing the ethical use of animals in research.

MGG adhesion strength was analyzed using a texture analyzer TA.XT (Stable Micro System, US). The gastric tissue was then affixed onto the lower probe plate of the with the mucosal surface facing upward using cyanoacrylate adhesive, avoiding tissue stretching. Granules (particle size $> 1180 \mu\text{m}$) of each formulation were placed onto the surface of the gastric tissues, followed by hydration with 0.1 N HCl solution (pH 1.2) maintained at $37 \pm 0.5 \text{ }^\circ\text{C}$ for a contact period of 2 minutes. The probe was set to apply pressure to granules with a force of 2 grams for 1 minute. Furthermore, the probe was lifted at a speed of 0.1 mm/second. The curve between time and force required was recorded on the device until granules were detached from the tissue surface. Each measurement was performed in triplicate ($n = 3$). Data were baseline-corrected to eliminate instrument drift and expressed as mean \pm SD.

An *ex vivo* bioadhesion study was carried out by placing 30 granules (particle size $> 1,180 \mu\text{m}$) of each formulation onto the surface of the gastric tissues, which were attached to a glass plate with the mucosal surface facing upward using cyanoacrylate adhesive, avoiding tissue stretching. Gastric tissue was then hydrated with 0.1 N HCl solution (pH 1.2) for a contact period of 2 minutes. A gastric tissue-attached glass plate was then placed in a dissolution tester (Electrolab TDT-08L, India) paddle type in 900 ml dissolution medium of 0.1 N HCl (pH 1.2) at $37 \pm 0.5^\circ\text{C}$. The dissolution tester was operated at 30 rpm to simulate mild gastric motility, and the number of granules remaining adhered to the tissue was counted at 15, 30, 60, 90, 120, 180, 240, 360, 480, 600, and 720 minutes, while detached granules were collected separately to discriminate detachment from mechanical abrasion [21]. All experiments were performed in triplicate, and results were expressed as mean \pm SD.

2.2.4. HPLC analysis

Clarithromycin assay in the granules and its dissolution were quantified by an HPLC system as follows: Shimadzu LC-20AT (Japan) equipped with UV/visible detector (Shimadzu SPD-20A), degasser (Shimadzu DGU-20A3), manual injector (Rheodyne, USA), and software (LC solution). The chromatographic analysis was performed in an isocratic separation mode by an Eclipse Plus C18 column ($4.6 \text{ mm} \times 250 \text{ mm}$, $5 \mu\text{m}$ particle size). The mobile phase was a homogenous mixture of acetonitrile and phosphate buffer in the ratio of (55:45, v/v) at pH 7.4 ± 0.02 , pumped at a flow rate of 1.0 ml/min, and the absorbance was monitored at a wavelength of 210 nm. The injection volume was 20 μl , and the run time was about 6 min, as the retention time of clarithromycin was found about 4.7 minutes [22].

Validation of analytical method based on USP guideline. For the evaluation of system suitability, the peak area, tailing factor, theoretical plate, and retention time of six replicate injections of a working standard solution of clarithromycin ($500 \mu\text{g/ml}$) were used, and % RSD values were calculated for each. For linearity, six different concentrations of standard solution ranging 100–600 $\mu\text{g/ml}$ were analyzed. A calibration curve was made, and the regression line was calculated as $Y = mX + c$, where X was the concentration of the standard and Y was the response (peak area expressed as AU). Accuracy was evaluated by a recovery study at three concentration levels (100, 300, and 600 ppm). For each level, triplicate measurements were performed on three independent days ($n = 3$ per level per day). Mean recovery (%) and %RSD were calculated inter-day. Repeatability (intra-day precision) was assessed from the triplicate measurements at each level on a given day ($n = 3$), reported as %RSD. Intermediate precision (inter-day) was assessed by comparing the daily mean recoveries for each level across three separate days, reporting the inter-day mean, SD, and %RSD. Limits of detection (LOD) and limits of quantitation (LOQ) were calculated where the peak area of the chromatograms were about 3.3 times and 10 times higher than the signal-to-noise ratio, respectively.

2.2.5. Assay

A precisely weighed quantity of clarithromycin granules, corresponding to 50 mg of clarithromycin, was transferred into a 50.0 ml volumetric flask. The sample was dissolved in 25 ml of 0.1 N HCl with gentle shaking and sonication to ensure complete dissolution, followed by volume adjustment to 50.0 ml using the same solvent. The solution was filtered through a $0.45 \mu\text{m}$ membrane filter, and a 3 ml aliquot of the filtrate was diluted to 10 ml with 0.1 N HCl. Clarithromycin assay in the granules was quantified by HPLC Shimadzu LC-20AT (Japan) equipped with UV/visible detector (Shimadzu SPD-20A), and the absorbance was monitored at wavelength 210 nm at retention time about 3.5 minutes [22]. Clarithromycin content in granules was calculated by comparing the actual concentration detected and the theoretical concentration in the formula. Assay of each granules was performed triplicate ($n = 3$).

2.2.6. In-vitro drug release profile

The drug release study on MGG (equal to 100 mg of clarithromycin) was performed in 900 ml of 0.1 N HCl (pH 1.2) at $37^\circ\text{C} \pm 0.5^\circ\text{C}$, using a dissolution tester (Electrolab TDT-08L, India) basket type with a stirring speed of 50 rpm. The basket apparatus was selected to prevent the dispersion of granules within the dissolution medium, thereby minimizing potential interference during the sampling process. A hydrochloric acid solution (pH 1.2) was utilized as a simple simulated gastric fluid, which has been widely used for dissolution test [23], to reduce analytical variability and ensure consistency in sample analysis.

Five milliliters of samples were taken at 15, 30, 60, 90, 120, 180, 240, 360, 480, 600, and 720 minutes, filtered using a $0.45 \mu\text{m}$ filter, and clarithromycin was then measured using HPLC (Shimadzu LC-20AT, Japan) at a wavelength of

210 nm [22]. Large solvent volume (900 ml) and an additional 5 ml of 0.1 N HCl (pH 1.2) into the dissolution medium for every 5 ml of samples withdrawn at each timepoint were performed to ensure sink condition. All data from each timepoints were obtained from triplicate experiments ($n = 3$). The percentage of cumulative drug release was calculated toward the total clarithromycin concentration in granules.

2.3. Statistical analysis

All data obtained from triplicate experiments were presented as AVG \pm SD. Due to a small dataset ($n = 3$), data were assumed as not normally distributed, thus nonparametric statistical analysis was performed. Multiple group comparisons were performed using a nonparametric Kruskal–Wallis test, followed by Dunn tests. A p value <0.05 was considered significant.

3. RESULTS AND DISCUSSION

3.1. Physical properties of clarithromycin MGG

Clarithromycin MGG were prepared using wet granulation followed by the oven-drying method, where granules produced a white color, specific odor, and bitter taste, with a yield of above 80% for all formulas, as shown in Figure 1a. All MGG formulas were placed in a static position and dried at 40°C for 2 hours, as selected drying conditions to maintain clarithromycin from degradation. Previous study indicated that clarithromycin remains stable under exposure to 40°C for 60 days [24].

All polymers in this study have been selected by considering their stability in drying and storage temperature, as well as their safety for oral administration. Safety assessments were performed using authoritative benchmarks (ADI) from EFSA/JECFA and, where applicable, FDA IID/GRAS documents. Modified celluloses (HPMC, HPC, HEC) are assigned a group ADI “not specified” by JECFA/EFSA, reflecting low toxicity and very high tolerated intakes; thus, the projected exposure is well within safety limits [25]. Carbomer (cross-linked polyacrylic acid) has an Acceptable Daily Intake (ADI) of 190 mg/kg bw/day (≈ 11.4 g/day for a 60-kg adult), and our maximum anticipated intake from the granules (≈ 1 g/day under a conservative 1:1 drug–polymer) is >10 -fold lower [26]. For polymethacrylate (basic methacrylate copolymer; Eudragit RS PO), toxicological reviews support an ADI of 20 mg/kg bw/day (≈ 1.2 g/day for 60 kg); our worst-case projected intake (≈ 1.0 g/day) remains below this value. Collectively, the levels used in the granules are below the established ADI, and therefore can be considered as safe [27].

The drying method successfully produced granules with a relatively homogenous moisture content of 2%–4%, as shown in Figure 1b. Moisture content is one of the important characteristics of MGG dosage form because of the capability to affect the flow rate, granule wetting, and adhesive strength toward the gastric mucous membrane [28]. The higher moisture content may increase bio-adhesive strength, but may lead to the degradation of active substances, increase the stickiness of granules, and reduce the flow rate.

Flow properties are critical characteristics of pharmaceutical granules due to their effect on the content

uniformity of the dosage form. MGG flow properties can be analyzed from the flow rate, angle of repose, and Hausner’s ratio. Various factors, such as granule size distribution, particle shape, density, moisture content, adhesiveness, and other particle surface conditions, can affect flow rate [29–31].

Granule F5 (containing polymethacrylate) had a significantly higher flow rate, compared to other formulas (Fig. 1c), while F1 (HPMC) and F3 (HEC) showed a lower angle of repose (Fig. 1d), representing better flowability of granules. However, as described in Figure 1e, all granules showed Hausner’s ratio of 1.06–1.20, which signified good and excellent flow properties of all formulas. These good flow properties may be due to low moisture content (Fig. 1b) and particle size distribution (Fig. 2a–e).

Size distribution measurement of all MGG formulas was carried out using the multistage sieve method, with Figure 2 showing the results. The test results showed that all formulas produced more than 40% of granules with a size of more than 1180 μm , which may contribute to good flow properties. F3 (HEC) contained fewer fine particles (Fig. 2c), contributing to the lower angle of repose (Fig. 1d). Meanwhile, F2 (HPC) contained more fine particles (Fig. 2b) that affected the lower flow rate (Fig. 1c) and higher angle of repose (Fig. 1d).

Granule dosage forms were selected as a platform for clarithromycin in this study due to several notable advantages over other mucoadhesive dosage forms. The granular form provides a larger effective surface area for adhesion and drug release, promoting intimate contact with the mucus layer and enhancing local drug bioavailability at the absorption or infection site. Compared with mucoadhesive films or beads, granules are easier to formulate, process, and scale up, while allowing flexible dosing and better flow characteristics for capsule filling or sachet packaging. Their multiparticulate nature also reduces inter- and intra-subject variability in gastric retention and drug release profiles, leading to improved formulation robustness [9]. Overall, mucoadhesive gastroretentive granules offer a versatile and physiologically compatible platform capable of maintaining prolonged gastric residence, site-specific drug release, and enhanced therapeutic efficacy in comparison to other gastroretentive delivery systems.

3.2. Bioadhesion properties of clarithromycin MGG

MGG is a dosage form designed to attach onto gastric mucosal tissues for a prolonged time, thereby extending the gastric residence time and maintaining higher drug concentration at the site of action [32,33]. Muco-/bio-adhesive properties of MGG are important to be characterized, leading to the analysis of two parameters, including adhesion strength and granules retained during the *ex-vivo* study.

Adhesion strength of MGG was assessed by the adhesion force (Fig. 3a) and the distance until detachment from the gastric mucosa at maximum tensile force (Fig. 3a). Based on those parameters, F1 (HPMC) and F3 (HEC) showed stronger adhesivity towards the gastric as compared to other granules. The adhesion strength might be affected by factors, including contact time, as well as the concentration, type, and structure of

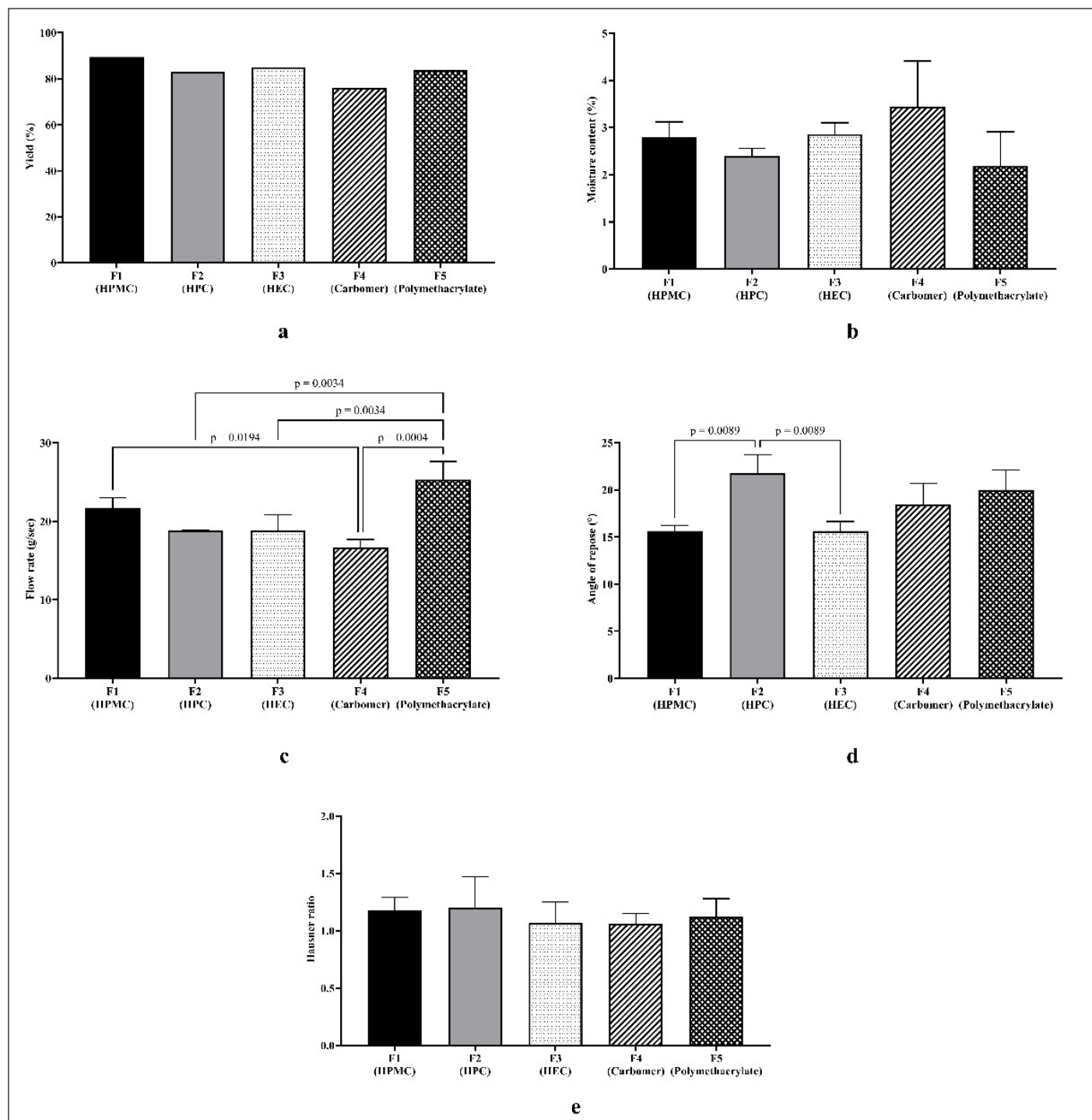


Figure 1. Physical characterization of clarithromycin mucoadhesive gastro-retentive granules, including (a) yield, (b) moisture content, (c) flow rate, (d) angle of repose, and (e) hausner ratio. Data of moisture content, flow rate, angle of repose and Hausner ratio were obtained from triplicate experiments ($n = 3$), and presented as mean \pm SD. Groups were compared using a Kruskal-Wallis, followed by Dunn tests, $p < 0.05$ was considered significant. Yield data was obtained from single batch production ($n = 1$).

polymers. Low withdrawal speed and optimal contact time can improve mucoadhesive performance [34].

Ex-vivo bio-adhesive study in Figure 3c revealed that F1 (HPMC) and F4 (Carbomer) demonstrated superior mucosal retention, maintaining adherence to the gastric mucosa for up to 12 hours, as compared to other formulas. This result is not

consistent with the data obtained from the texture analyzer, as shown in Figures 3a and 3b. The number of granules retained in the *ex-vivo* bio-adhesive study was observed visually. Gel-like layer was observed on top of the gastric mucosa attached by MGG from all formulas, even though the round-like granules were not visually detected.

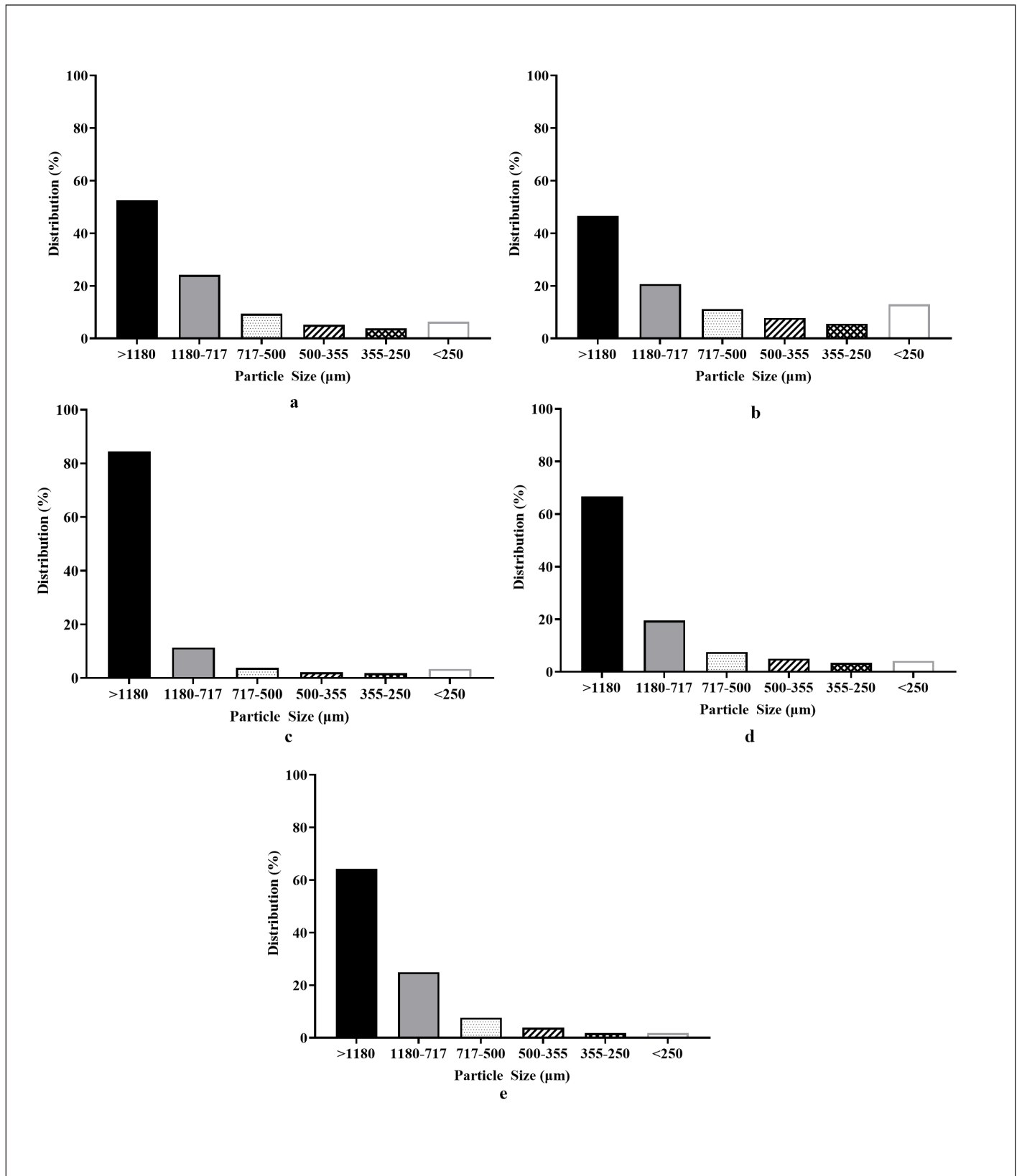


Figure 2. Particle size distribution of (a) F1/HPMC, (b) F2/HPC, (c) F3/HEC, (d) F4/Carbomer, (e) F5/Polymethacrylate-based clarithromycin mucoadhesive gastro-retentive granules. This data was obtained from single experiments ($n = 1$).

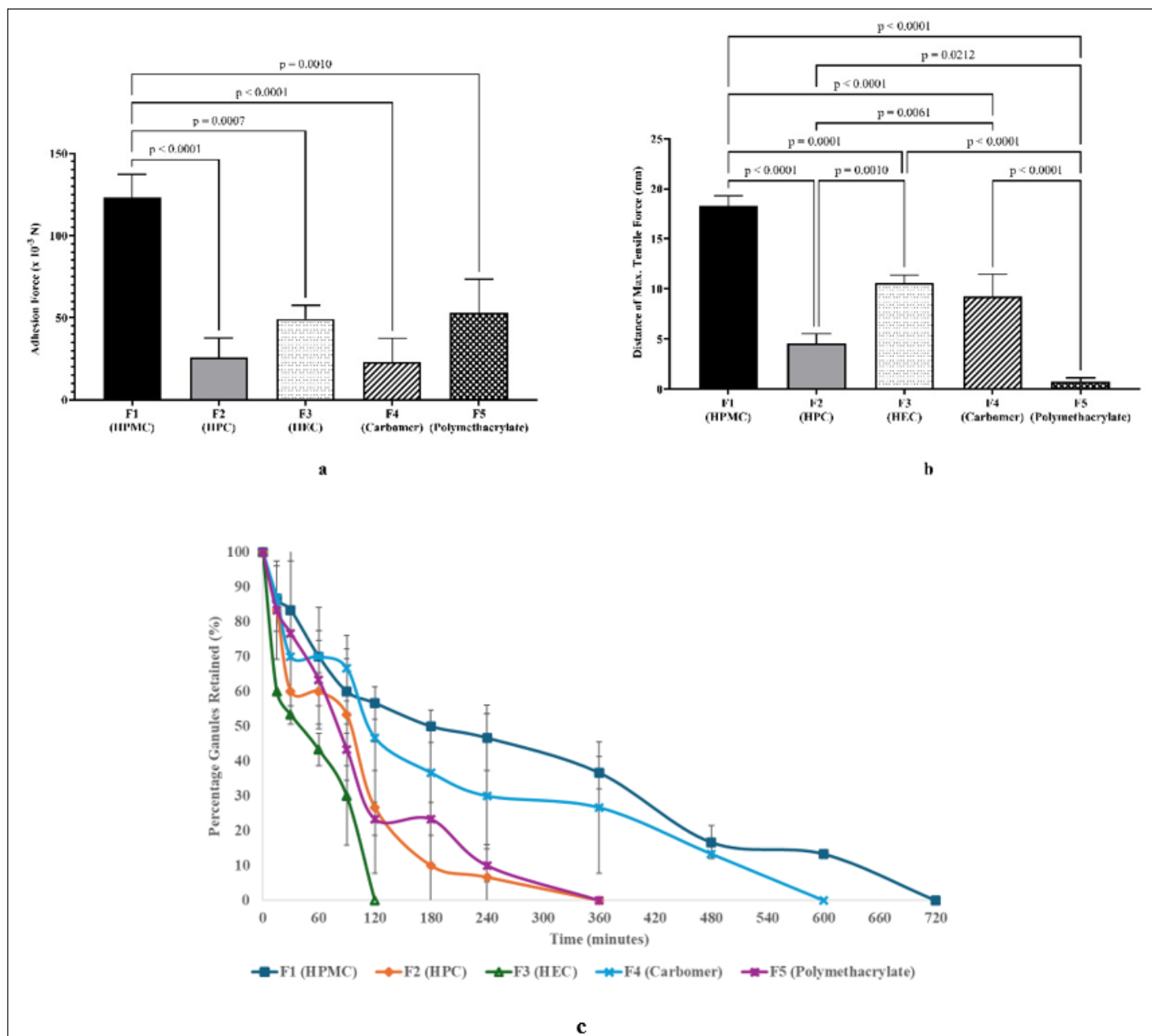


Figure 3. Bio-adhesive properties of clarithromycin mucoadhesive gastro-retentive granules, including (a) adhesion force, (b) distance at maximum tensile force and (c) percentage granules retained. All data obtained from triplicate experiments ($n = 3$) were presented as mean \pm SD. Groups were compared using a Kruskal-Wallis, followed by Dunn tests, $p < 0.05$ was considered significant.

This apparent discrepancy may be attributed to differences in the test conditions and mechanisms captured by each method. The texture analyzer primarily measures the instantaneous detachment force under controlled compression and contact time, reflecting the initial adhesive interaction between the polymer and mucin layer. In contrast, the *ex vivo* bioadhesion study evaluates dynamic retention under physiological conditions that include continuous exposure to simulated gastric fluid, tissue movement, and polymer hydration-erosion balance [35].

The stronger initial adhesion of HPMC could be related to its rapid hydration and formation of a viscous gel layer

that provides strong but relatively short-lived contact strength. Conversely, Carbomer exhibits a slower hydration profile but forms a highly swollen and cohesive network upon ionization of carboxyl groups, which may enhance long-term retention on the mucosal surface. Moreover, the extended residence time of HPMC and Carbomer granules may also result from their ability to maintain cohesive integrity and resist erosion under gastric fluid flow, allowing sustained contact even when initial detachment forces are lower. These observations suggest that instantaneous adhesion strength does not necessarily predict long-term mucoadhesive performance, highlighting the importance of complementary *in vitro* and *ex vivo* evaluations

in assessing the overall bioadhesive behavior of gastroretentive systems [35].

All polymers used in this study possess hydroxyl groups in their structures, which contribute to hydrogen bond formation and bio-adhesive properties. The more hydroxyl groups present in the polymer, the more hydrogen bonds are formed with mucin of the mucosal layer, increasing the adhesion strength of dosage forms. Furthermore, polymer chain flexibility and hydration are important for effective mucoadhesion [36].

The selection of excipients/polymers, including hydrophilicity, molecular weight, expandability, and interfacial rheology, influences mucoadhesive properties. Polymers with hydrophilic groups improve contact with the site of action, chain flexibility, and substrate penetration. Low molecular weight facilitates penetration, while high allows bonding with the mucosa. Expandability and interfacial rheology affect adhesive bond formation, viscosity, and elasticity, which are significant for adhesiveness and residence time on mucosal surfaces [37–39].

3.3. Validation of analytical method and assay

Validation of the analytical method of clarithromycin was performed prior to the assay and dissolution test, including system suitability parameters, linearity, accuracy, precision, and sensitivity (LOD and LOQ). Results of analytical method validation of clarithromycin are presented in Table 2. Furthermore, clarithromycin in mucoadhesive gastro-retentive granules and drug release profile were determined using a validated analytical method, and the results were presented in Table 3 and Figure 4b, respectively.

The acceptance criteria for the assay of clarithromycin in the dosage form were set at 90.0%–110.0%. However, formulations containing HEC granules (F3) and Eudragit RS PO (F5) did not comply with these specifications. This deviation was attributed to issues encountered during the

wet granulation process, which produced sticky granules that were difficult to sieve. Consequently, a portion of the drug substance or excipients adhered to the sieve surface, leading to nonuniform distribution of the active pharmaceutical ingredient (API) within the granules. This resulted in assay values that were either below or above the expected concentration range.

3.4. Swelling ability and *in-vitro* drug release profile of clarithromycin MGG

MGG are designed to extend drug residence time at the site of action and prolong release during the contact period [40]. Therefore, polymers should possess the ability to control drug release from the matrix. Factors that may affect release from polymer matrix include swelling index, known as the ability of the granule to expand in response to environmental conditions. This ability significantly affects MGG release profile, allowing the active substance to be released gradually and consistently [41].

Figure 4a shows that MGG containing HPMC (F1) expanded up to 770% in 30 minutes, faster than other polymers. HPMC contains many hydroxyl groups, which can absorb water very rapidly and entrap a high amount of water in the matrix, leading to a high swelling index. After 30 minutes, the weight of HPMC slowly decreased, implying the dissolution of granules. A similar swelling pattern was observed from MGG containing HPC (F2) and Carbomer (F4), which expanded rapidly at the onset and started to decrease afterwards. HPC only expanded 131%, far lower as compared to other polymers. MGG containing HEC (F3) and Polymethacrylate (F5) showed a different swelling pattern than HPMC, HEC, and Carbomer. F3 and F5 expanded lower at the beginning but constantly increased up to 12 hours.

The swelling index of polymers influences the drug release profile from the matrix. MGG containing Clarithromycin-HPMC K15M 1:1 (F1) expanded very rapidly at the onset, followed by rapid drug release in 60 minutes (Fig. 4b). HPMC exhibited a markedly faster swelling rate compared to other polymers due to its hydrophilic nature and high water affinity, which readily absorbs dissolution medium through extensive hydrogen bonding with water molecules, forms a viscous gel layer that expands rapidly, promoting matrix swelling and potential bioadhesion [42].

Polymethacrylate (Eudragit RS PO) exhibited slower swelling and water uptake due to its hydrophobic methacrylic ester backbone and low content of hydrophilic functional groups, thus acting principally as a structurally rigid, water-permeable matrix rather than a swelling gel [43]. Despite the swelling index of MGG containing Clarithromycin-Polymethacrylate/Eudragit RS PO 1:1 (F5) being lower than HPMC, the drug was released in 60 minutes. This showed that both polymer matrix swelling and the diffusion process driven by the concentration gradient, which initiated the drug release.

MGG containing Clarithromycin-HPC/Klucel MF 1:1 (F2) showed a lower swelling index, but can control drug release up to 3 hours. Moreover, Clarithromycin-HEC/Natrosol 250 HHX 1:1 (F3) and Clarithromycin-Carbomer/Carbopol 971p 1:1 (F4) maintained the release up to 12 hours despite swelling rapidly at the onset. This might be due to the strong matrix formation of HEC and Carbomer. The swelling of

Table 2. Results of analytical method validation of clarithromycin.

Parameters	Result
Peak Area	530,650.0 ± 8,892.6; RSD 1.676%
Tailing Factor	1.844 ± 0.032; RSD 1.758%
Theoretical Plate	4,082.5 ± 52.2; RSD 1.280%
Retention Time	4.466 ± 0.025; RSD 0.566%
High Energy Transfer Plate	36.748 ± 0.473; RSD 1.287%
Calibration curve	Y = 905.68X – 91886; R ² = 0.9999
Accuracy (inter-day, mean±SD)	100 ppm 100.946 ± 0.787%
	300 ppm 97.708 ± 0.370%
	600 ppm 97.209 ± 0.257%
Precision (inter-day %RSD)	100 ppm 0.780%
	300 ppm 0.378%
	600 ppm 0.265%
LOD	8.19 µg/ml
LOQ	24.82 µg/ml

Carbomer (Carbopol 971P) granules is in accordance with its ionisable polyacrylic network and strong water uptake [44]. The gel layer formed by these polymers acts as a barrier, controlling water penetration into the granule core and dissolving the drug to allow slow diffusion into the matrix. Delayed release occurred due to various factors, affecting the rate and time of drug absorption.

Drug release profile of all MGGG was further analyzed using several kinetic models, including zero order, first order, Higuchi, and Korsmeyer-Peppas equation. According to Table 4, the *r*-value signified the fitness of the drug release profile of a formula towards one of the kinetic models. Table 4 shows that the *r*-value of all formulas correlates more with the Higuchi equation rather than other kinetic models, as signified by the *r*-value closer to 1. The Higuchi kinetic model describes a time-dependent release profile as a function of the square root of time, which is often observed from a monolithic (matrix) system controlled-release dosage form [36]. The result showed that Clarithromycin MGG was manufactured by homogenously

mixing clarithromycin and polymers to produce a matrix system that allows a Higuchi time-dependent release profile of clarithromycin from granules.

Furthermore, Table 4 shows that all formulas have an *n*-value of the Korsmeyer-Peppas equation greater than 0.5. The result suggested that clarithromycin was released from all formulas based on a non-Fickian release mechanism, as a combination of diffusion and dissolution mechanisms. This drug release mechanism is frequently observed from a hydrophilic polymer-containing matrix system, which allows the matrix to expand, dissolve, and form pores to facilitate the drug diffusion. Mechanistically, the hydration of the polymer matrix leads to gel layer formation and subsequent chain relaxation or erosion; simultaneously, drug diffusion through the swollen network proceeds. The non-Fickian behaviour likely stems from the combination of polymer swelling (which increases path-length and modifies porosity) and matrix erosion or chain relaxation (which shortens diffusion pathways and may induce drug transport) [45].

The swelling index of polymers affects the drug release profile and bio-adhesive properties. This shows that F1 (HPMC) and F4 (Carbomer), containing many hydroxyl groups and good hydration properties, can swell rapidly, form hydrogen bonds with the gastric mucosa, and bind strongly.

Based on the entire data, Clarithromycin-Carbomer/ Carbopol 971p 1:1 (F4) is considered a formula with a good swelling index (up to 747%), controlled and prolonged drug release profile (80.27% ± 9.05% in 12 hours), and sufficient bio-adhesive properties. However, this formula needs improvement to promote drug release and provide sufficient drug concentration at the onset. Further investigations on combining the prospective polymers with various drug-polymer ratios (for

Table 3. Assay of clarithromycin in mucoadhesive gastro-retentive granules.

Formula	Assay (%)
F1 (HPMC)	93.99 ± 0.23
F2 (HPC)	100.93 ± 0.56
F3 (HEC)	79.01 ± 0.15
F4 (Carbomer)	107.88 ± 0.86
F5 (Polymethacrylate)	112.11 ± 0.16

Data were obtained from triplicate experiments (*n* = 3) and presented as mean ± SD.

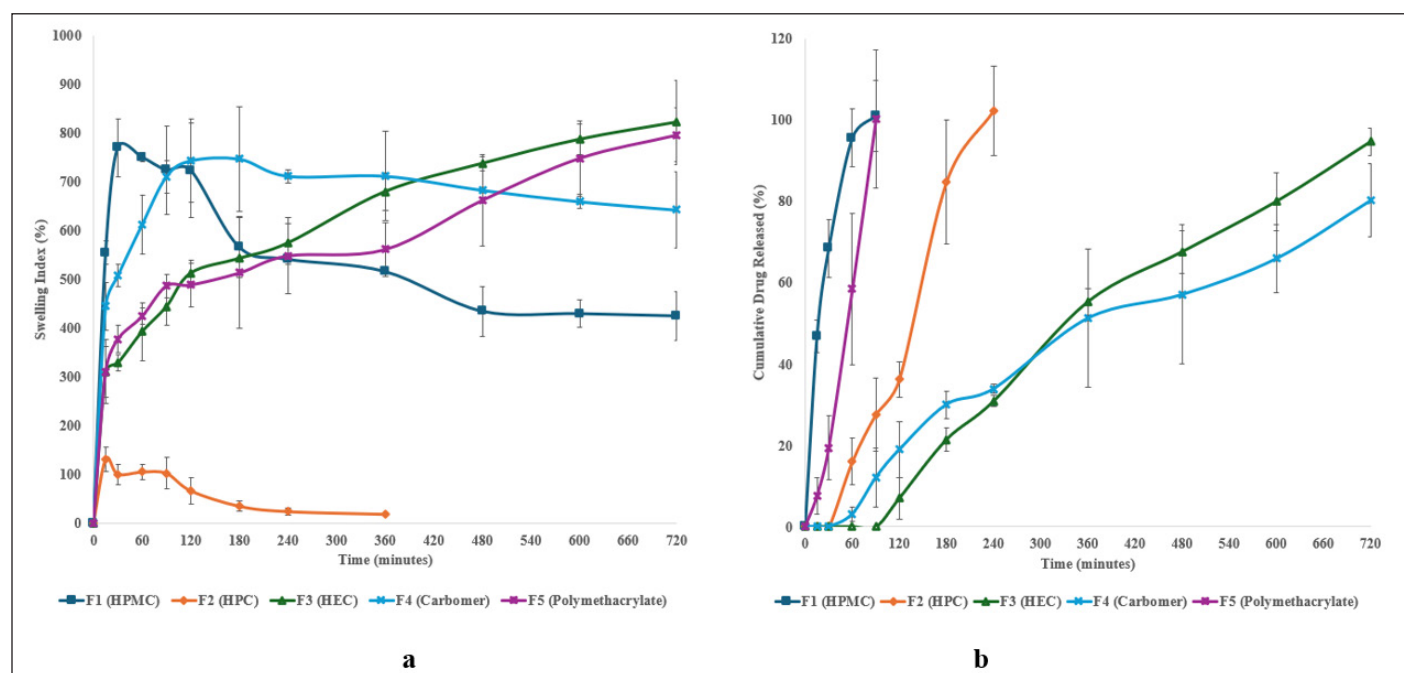


Figure 4. Swelling index (a) and drug release profile (b) of clarithromycin mucoadhesive gastro-retentive granules in HCl 0.1 N pH 1.2. All data obtained from triplicate experiments (*n* = 3) were presented as mean ± SD.

Table 4. Drug release kinetics of clarithromycin from mucoadhesive gastro-retentive granules.

Formula	Zero order	First order	Higuchi	Korsmeyer-Peppas	
	r	r	r	r	n
F1 (HPMC)	0.849	0.507	0.955	0.905	0.64
F2 (HPC)	0.953	0.633	0.998	0.966	0.73
F3 (HEC)	0.995	0.851	0.973	0.939	0.78
F4 (Carbomer)	0.975	0.751	0.996	0.994	0.66
F5 (Polymethacrylate)	0.923	0.555	0.982	0.919	0.64

r = correlation of drug release coefficient toward certain model of drug release kinetic

n = exponential value of drug release mechanism .

example, 1:2) will generate a better formula of Clarithromycin mucoadhesive granules.

Enhancing the local gastric concentration of clarithromycin through mucoadhesive gastroretentive systems represents a promising formulation strategy to mitigate clarithromycin resistance. By adhering to the gastric mucosa and prolonging residence time, mucoadhesive granules can sustain high local antibiotic concentrations in close proximity to the *H. pylori* colonization site within the mucus layer. Such localized delivery can improve the drug-to-MIC (minimum inhibitory concentration) ratio at the infection site, increasing bactericidal exposure even against moderately resistant strains. Moreover, the prolonged retention allows continuous drug diffusion into the mucus gel and the gastric epithelial microenvironment, thereby enhancing mucosal penetration and reducing bacterial regrowth between dosing intervals. Therefore, mucoadhesive gastroretentive formulations may serve as a complementary approach to conventional antibiotic regimens by improving local drug delivery efficiency and therapeutic outcomes [4].

Although the present study suggests the potential of clarithromycin mucoadhesive gastroretentive granules to improve gastric drug retention and local concentration, the therapeutic efficacy in *H. pylori* eradication has not been directly investigated in this present study. Consequently, further comprehensive pharmacokinetics and *in vivo* antimicrobial efficacy investigations are required to confirm whether this delivery approach can effectively enhance the antimicrobial outcome against *H. pylori* infection.

4. CONCLUSION

In conclusion, HPMC K15M, HPC MF, HEC 250 HHX, Carbopol 971P, and Eudragit RS PO demonstrated promising potential as matrix-forming polymers for mucoadhesive gastroretentive granule formulations. Among the tested formulas, granules containing Clarithromycin : Carbopol 971P (1:1, F4) exhibited optimal swelling capacity (up to 747%), sustained drug release (80.27 % ± 9.05% over 12 h) following Higuchi kinetics with a diffusion–dissolution mechanism, and satisfactory bioadhesive strength. These attributes suggest that the formulation could maintain therapeutic gastric concentrations for an extended period, potentially reducing dosing frequency and enhancing

patient compliance in *H. pylori* therapy. Further optimization of polymer combinations and drug-to-polymer ratios is warranted to refine the formulation for clinical translation.

5. ACKNOWLEDGMENTS

The authors would like to acknowledge Universitas Indonesia for funding this study through “Publikasi Terindeks Internasional (PUTI) Pascasarjana 2024 Universitas Indonesia” Grant with contract number NKB-36/UN2.RST/HKP.05.00/2024. The authors are also grateful to Tatarasa Primatama/Ashland Pharmaceuticals, IMCD/Evonik, and Guardian Pharmatama for providing materials to support this study.

6. AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

7. CONFLICTS OF INTEREST

The authors report no financial or any other conflicts of interest in this work.

8. ETHICAL APPROVALS

Ethical approval details are given in the ‘Materials and Methods’ section.

9. DATA AVAILABILITY

All data generated and analyzed are included in this research article.

10. PUBLISHER’S NOTE

All claims expressed in this article are solely those of the authors and do not necessarily represent those of the publisher, the editors and the reviewers. This journal remains neutral with regard to jurisdictional claims in published institutional affiliation.

11. USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declare that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

REFERENCES

- Fischbach W, Malfertheiner P. *Helicobacter pylori* infection. Dtsch Arztebl Int. 2018; 115:429–36. doi: <https://doi.org/10.3238/arztebl.2018.0429>
- Bashir SK, Khan MB. Overview of *Helicobacter pylori* infection, prevalence, risk factors, and its prevention. Adv Gut Microb Res. 2023;2023:1–9. doi: <https://doi.org/10.1155/2023/9747027>.
- Huang X, Liu Y, Lin Z, Wu B, Nong G, Chen Y, *et al.* Minimum inhibitory concentrations of commonly used antibiotics against *Helicobacter pylori*: a multicenter study in South China. PLoS

- One. 2021;16:256225. doi: <https://doi.org/10.1371/journal.pone.0256225>
4. Kowalska-Krochmal B, Dudek-Wicher R. The minimum inhibitory concentration of antibiotics: methods, interpretation, clinical relevance. *Pathogens*. 2021;10:165. doi: <https://doi.org/10.3390/pathogens10020165>
 5. Nguyen CT, Davis KA, Nisly SA, Li J. Treatment of *Helicobacter pylori* in special patient populations. *Pharmacother J Hum Pharmacol Drug Therapy*. 2019;39:1012–22. doi: <https://doi.org/10.1002/phar.2318>
 6. Grosso R, Benito E, Carbajo-Gordillo AI, Díaz MJ, García-Martín MG, De-Paz MV. Advanced interpenetrating polymer networks for innovative gastroretentive formulations targeting *Helicobacter pylori* gastric colonization. *Eur J Pharm Sci*. 2024;200: 106840. doi: <https://doi.org/10.1016/j.ejps.2024.106840>
 7. Kulkarni R, Fanse S, Burgess DJ. Mucoadhesive drug delivery systems: a promising noninvasive approach to bioavailability enhancement. Part II: formulation considerations. *Expert Opin Drug Del*. 2023;20(3):413–34. doi: <https://doi.org/10.1080/17425247.2023.2181332>
 8. Verma A, Dubey J, Hegde RR, Rastogi V, Pandit JK. *Helicobacter pylori*: past, current, and future treatment strategies with gastroretentive drug delivery systems. *J Drug Target*. 2016;24:897–915. doi: <https://doi.org/10.3109/1061186X.2016.1171326>
 9. Singh G, Kaur P. Advances in mucoadhesive gastroretentive drug delivery systems: mechanisms, materials and applications. *Int J Biol Macromol*. 2023;246:125663. doi: <https://doi.org/10.1016/j.ijbiomac.2023.125663>
 10. Waqar MA, Mubarak N, Khan AM, Khan R, Shaheen F, Shabbir A. Advanced polymers and recent advancements on gastroretentive drug delivery system: a comprehensive review. *J Drug Target*. 2024;32:655–71. doi: <https://doi.org/10.1080/1061186X.2024.2347366>
 11. Raeisi A, Farjadian F. Commercial hydrogel product for drug delivery based on route of administration. *Front Chem*. 2024;12: 1–14. doi: <https://doi.org/10.3389/fchem.2024.1336717>
 12. Chaves PDS, Frank LA, Frank AG, Pohlmann AR, Guterres SS, Beck RCR. Mucoadhesive Properties of Eudragit®RS100, Eudragit®S100, and Poly(ϵ -caprolactone) nanocapsules: influence of the vehicle and the mucosal surface. *AAPS Pharm Sci Tech*. 2018;19:1637–46. doi: <https://doi.org/10.1208/s12249-018-0968-5>
 13. Maślanka A, Szłóarczyk M, Talik P, Szafraniec-Szczęśny J, Woyna-Orlewicz K, Żmudzki P, *et al.* Study of the Effect of Eudragit RSPO on the photostability of venlafaxine in a physical mixture and in a melt form. *Processes*. 2023;11:2479. doi: <https://doi.org/10.3390/pr11082479>
 14. Sakhare S, Shinde SD, Venkatrao Yadav A, Somnath Shete A. Studies on formulation and evaluation of Eudragit RS PO based nanoparticulate system of aceclofenac for ocular delivery. *Indian J Pharm Educ Res*. 2021;55:s87–99. doi: <https://doi.org/10.5530/ijper.55.1s.40>
 15. Muter SS, Habeeb AD. Preparation and evaluation of gastroretentive floating unfolding film of baclofen. *Pharmacia*. 2025;72:1–2. doi: <https://doi.org/10.3897/pharmacia.72.e147835>
 16. Kraisit P. Impact of hydroxypropyl methylcellulose (HPMC) type and concentration on the swelling and release properties of propranolol hydrochloride matrix tablets using a simplex centroid design. *Int J Appl Pharmaceutics*. 2019; 11:143–51. doi: <https://doi.org/10.22159/ijap.2019v11i2.31127>
 17. Knarr M, Rogers TL, Petermann O, Adden R. Investigation and rank-ordering of hydroxypropyl methylcellulose (HPMC) properties impacting controlled release performance. *J Drug Deliv Sci Technol*. 2025;104:106425. doi: <https://doi.org/10.1016/j.jddst.2024.106425>
 18. Kim JH, Song SH, Joo SH, Park GH, Weon KY. Formulation of a gastroretentive *in situ* oral gel containing metformin HCl Based on DoE. *Pharmaceutics*. 2022;14(9):1777. doi: <https://doi.org/10.3390/pharmaceutics14091777>
 19. Khan NA, Khan A, Ullah R, Ullah M, Alotaibi A, Ullah R, *et al.* Preparation and characterization of hydrophilic polymer based sustained-release matrix tablets of a high dose hydrophobic drug. *Polym (Basel)*. 2022;14:1985. doi: <https://doi.org/10.3390/polym14101985>
 20. Ullah G, Nawaz A, Latif MS, Shah KU, Ahmad S, Javed F, *et al.* Clarithromycin and pantoprazole gastro-retentive floating bilayer tablet for the treatment of *Helicobacter pylori*: formulation and characterization. *Gels*. 2023;9:43. doi: <https://doi.org/10.3390/gels9010043>
 21. Schneider F, Koziol M, Weitschies W. *In vitro* and *in vivo* test methods for the evaluation of gastroretentive dosage forms. *Pharmaceutics*. 2019;11:416. doi: <https://doi.org/10.3390/pharmaceutics11080416>
 22. Alam MM, Hossain MS, Bhadra S, Kumar U, Rouf ASS. Development and validation of RP-HPLC method for quantitation of clarithromycin in matrix tablet dosage form. *Dhaka Univ J Pharm Sci*. 2017;16:69–75. doi: <https://doi.org/10.3329/dujps.v16i1.33384>
 23. Pedersen PB, Berthelsen R, Rades T, Jørgensen SA, Vilmann P, Bar-Shalom D, *et al.* Physico-chemical characterization of aspirated and simulated human gastric fluids to study their influence on the intrinsic dissolution rate of cinnarizine. *Int J Pharmaceutics*. 2022;622:121856. doi: <https://doi.org/10.1016/j.ijpharm.2022.121856>
 24. Sebt M, Schweitzer-Chaput A, Cisternino S, Hinterlang M, Ancedy D, Lam S, *et al.* Formulation and stability of a 1% clarithromycin-based topical skin cream: a new option to treat buruli ulcers?. *Pharmaceutics (Basel)*. 2024;17(6):691. doi: <https://doi.org/10.3390/ph17060691>
 25. World Health Organization, Joint FAO/WHO Expert Committee on Food Additives (JECFA). 2021. Modified celluloses (JECFA database entry). Available via <https://apps.who.int/food-additives-contaminants-jecfadatabase/Home/Chemical/3388>
 26. Younes M, Aquilina G, Engel KH, Fowler P, Frutos Fernandez MJ, Fürst P, *et al.* Safety evaluation of crosslinked polyacrylic acid polymers (carbomer) as a new food additive. *EFSA J*. 2021;19(8):6693. doi: <https://doi.org/10.2903/j.efsa.2021.6693>
 27. European Food Safety Authority (EFSA). EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS). Scientific opinion on the use of basic methacrylate copolymer as a food additive. *EFSA J*. 2021;8(2):1513. doi: <https://doi.org/10.2903/j.efsa.2010.1513>
 28. Crouter A, Briens L. The effect of moisture on the flowability of pharmaceutical excipients. *AAPS PharmSciTech*. 2014;15:65–74. doi: <https://doi.org/10.1208/s12249-013-0036-0>
 29. Kudo Y, Yasuda M, Matsusaka S. Effect of particle size distribution on flowability of granulated lactose. *Adv Powder Technol*. 2020;31:121–7. doi: <https://doi.org/10.1016/j.apt.2019.10.004>
 30. United States Pharmacopeial Convention. Powder flow. In: *United States Pharmacopeia and National Formulary (USP 47–NF 42)*. Rockville (MD): United States Pharmacopeial Convention; 2024. doi: https://doi.org/10.31003/USPNF_M99885_01_01
 31. Tharanon W, Guo Y, Peerapattana J, Sun CC. A systematic comparison of four pharmacopeial methods for measuring powder flowability. *Int J Pharm*. 2024;661:124454. doi: <https://doi.org/10.1016/j.ijpharm.2024.124454>
 32. Sahin AB, Karakurt S, Sezlev Bilecen D. Development of a mucoadhesive drug delivery system and its interaction with gastric cells. *Beilstein J Nanotechnol*. 2025;16:371–84. doi: <https://doi.org/10.3762/bjnano.16.28>
 33. Vrettos NN, Roberts CJ, Zhu Z. Gastroretentive technologies in tandem with controlled-release strategies: a potent answer to oral drug bioavailability and patient compliance implications. *Pharmaceutics*. 2021;13:1591. doi: <https://doi.org/10.3390/pharmaceutics13101591>

34. Kim D, Shin D, Koo J, Kim J, Na SJ, Bang JS, *et al.* *In vitro* Mucoadhesive properties of hydrophilic polymers: effects of contact time, disk shape, and molecular weight. *Bull Korean Chem Soc.* 2022;43:792–6. doi: <https://doi.org/10.1002/bkcs.12535>
35. Bassi da Silva J, Ferreira SBS, Reis AV, Cook MT, Bruschi ML. Assessing mucoadhesion in polymer gels: the effect of method type and instrument variables. *Polym (Basel).* 2018;10(3):254. doi: <https://doi.org/10.3390/polym10030254>
36. Bakhrushina E, Anurova M, Demina N, Kashperko A, Rastopchina O, Bardakov A, *et al.* Comparative study of the mucoadhesive properties of polymers for pharmaceutical use. *Open Access Maced J Med Sci.* 2020;8:639–45. doi: <https://doi.org/10.3889/oamjms.2020.4930>
37. Bayer IS. Recent advances in mucoadhesive interface materials, mucoadhesion characterization, and technologies. *Adv Mater Inter.* 2022;9:1–24. doi: <https://doi.org/10.1002/admi.202200211>
38. Jawadi Z, Yang C, Haidar ZS, Santa Maria PL, Massa S. Bio-inspired muco-adhesive polymers for drug delivery applications. *Polym (Basel).* 2022;14:5459. doi: <https://doi.org/10.3390/polym14245459>
39. Vasquez-Martínez N, Guillen D, Moreno-Mendieta SA, Sanchez S, Rodríguez-Sanoja R. The role of mucoadhesion and mucopenetration in the immune response induced by polymer-based mucosal adjuvants. *Polym (Basel).* 2023;15:1615. doi: <https://doi.org/10.3390/polym15071615>
40. Ainurofiq A, Putri Febrina Sari A, Mardhiyah A, Sakinatun Nisa F, Luthfiani Azka R, Kania Putri S, *et al.* Chitosan as floating-mucoadhesive polymers in gastroretentive drug delivery. *Sci Eng Health Stud.* 2023;2023:23010002. doi: <https://doi.org/10.69598/sehs.17.23010002>
41. Markl D, Zeitler JA. A review of disintegration mechanisms and measurement techniques. *Pharm Res.* 2017;34:890–917. doi: <https://doi.org/10.1007/s11095-017-2129-z>
42. Vlad RA, Pinteá A, Pinteá C, Rádai EM, Antonoaea P, Birsan M, *et al.* Hydroxypropyl methylcellulose—a key excipient in pharmaceutical drug delivery systems. *Pharmaceutics.* 2025;17(6):784. doi: <https://doi.org/10.3390/pharmaceutics17060784>
43. Esporrín-Ubieto D, Sonzogni AS, Fernández M, Acera A, Matxinandiarena E, Cadavid-Vargas JF, *et al.* The role of Eudragit® as a component of hydrogel formulations for medical devices. *J Mater Chem B.* 2023;11:9276–89. doi: <https://doi.org/10.1039/D3TB01579C>
44. Suhail M, Wu PC, Minhas MU. Using carbomer-based hydrogels for control the release rate of diclofenac sodium: preparation and *in vitro* evaluation. *Pharmaceutics.* 2020;13(11):399. doi: <https://doi.org/10.3390/ph13110399>
45. Bayer IS. Controlled drug release from nanoengineered polysaccharides. *Pharmaceutics.* 2023;15(5):1364. doi: <https://doi.org/10.3390/pharmaceutics15051364>

How to cite this article:

Putri KSS, Akbar R, Satria DJ, Widyarto W, Iswandana R, Maggadani BP, Setiawan H. Exploring prospective polymers for clarithromycin mucoadhesive-gastroretentive granules. *J Appl Pharm Sci.* 2026;16(04):221-232. DOI: 10.7324/JAPS.2026.273648