Pharmaceutical Sciences Asia

Pharm Sci Asia 2026; 53(3), 409-418

DOI:10.29090/psa.2026.03.26.2035

Research Article

Optimization of sodium alginate concentration in a raft-forming system for the targeted gastric delivery of ginger extract

Worawut Kriangkrai [1,2], Nontakron Jaiya [1], Watcharin Meerod [1], Srisagul Sungthongjeen [1,2]*

[1] Department of Pharmaceutical Technology, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok 65000, Thailand
[2] Research and Innovation Cluster for Natural Health Products, Naresuan University, Phitsanulok 65000, Thailand

ABSTRACT

Sodium alginate concentration is a critical parameter in developing effective raft-forming systems for gastric targeting. This study evaluated concentrations of 1–5% w/w to optimize gastroretentive delivery of 6-gingerol for *Helicobacter pylori* (*H. pylori*) treatment. Increasing alginate concentration significantly enhanced viscosity (30.36–2229.11 cP) and raft strength; the 3% w/w level was identified as optimal on the basis of rheological and floating properties. Gas-generating agents (sodium bicarbonate and calcium carbonate) were incorporated with this concentration to enable raft formation and sustained buoyancy. The optimized formulation containing 4.17 % w/w ginger extract appeared as a cloudy yellowish suspension (viscosity 840.96 cP), formed a stable raft within 10 s, and remained buoyant for more than 24 h. *In vitro* dissolution demonstrated a controlled, time-dependent release profile of 6-gingerol from the floating raft matrix. Stability evaluations conducted at 45°C and 75% relative humidity for 30 days demonstrated that despite minor decreases in physical strength and viscosity, the formulation maintained a consistent 6-gingerol release profile, confirming the robustness of the optimized system. The 3% w/w sodium alginate concentration therefore provided an optimal balance of viscosity, raft-forming capability, and flotation, enabling prolonged gastric residence and sustained 6-gingerol release with potential therapeutic benefit against *H. pylori* infection.

Keywords:
Zingiber officinale; 6-gingerol; Raft-forming suspension; *Helicobacter pylori*; Gastroretentive system; Sodium alginate

1. INTRODUCTION

Helicobacter pylori (*H. pylori*) colonizes the gastric mucosa of roughly half the world's population and remains the principal driver of chronic gastritis, peptic ulcer disease, and gastric malignancy. The organism survives the acidic stomach environment by burrowing into the mucus layer, where it releases urease, cytotoxin-associated gene A (CagA), and vacuolating cytotoxin A, triggering epithelial damage and a sustained inflammatory response [1, 2]. In Thailand, seroprevalence is estimated at around 40%, placing the country among the higher-burden nations in Southeast Asia [3]. Standard eradication still relies on proton pump inhibitor–based triple therapy, but rising clarithromycin and metronidazole resistance has pushed cure rates below the 80% threshold considered acceptable in several regions [4, 5], prompting interest in adjunct or alternative agents that are less prone to resistance.

Plant-derived phenolics are one such avenue. Ginger (*Zingiber officinale* rhizome) contains gingerols and shogaols — principally 6-, 8-, and 10-gingerol and 6-shogaol — that inhibit *H. pylori in vitro*. Minimum inhibitory concentration (MIC) values range from approximately 0.78 to 300 µg/mL, depending on the specific strain, extract type, and extraction method [6-10].

***Corresponding author:**
* Srisagul Sungthongjeen Email: srisaguls@nu.ac.th

A gingerol-enriched fraction and standardized methanolic extracts have shown particularly potent activity, with MICs as low as 0.78–12.5 µg/mL against CagA+ strains and 6.25–50 µg/mL against a broader panel of clinical isolates [7]. Translating this activity into clinical benefit, however, is not simply a matter of dosing: gingerol delivered as a conventional oral solution or capsule clears the stomach within minutes, leaving too little contact time with the mucosa for meaningful local action. The bottleneck, in other words, is residence time rather than potency.

Oral delivery of liquid formulations frequently suffers from rapid gastric emptying, which severely restricts the local therapeutic window of antimicrobial agents against *H. pylori*. To overcome this limitation, raft-forming systems offer buoyancy at the surface of the gastric contents and function as a localized, sustained-release reservoir [11, 12]. On contact with gastric acid, the formulation precipitates into a coherent, low-density gel — a "raft" — that floats above the gastric contents and adheres to the mucosal surface, prolonging exposure of the entrapped drug well beyond what conventional liquids or tablets achieve [13-16]. Sodium alginate is the polymer of choice for this purpose: its guluronic acid blocks cross-link with calcium ions released from calcium carbonate in the acidic stomach, forming the structural gel, while carbon dioxide generated in the same reaction becomes entrapped within the matrix and provides buoyancy.

The performance of a raft-forming system (RFS) is critically dependent on the concentration of sodium alginate used, making formulation optimization a complex balancing act rather than a straightforward scale-up process. Low polymer concentrations produce weak rafts that disintegrate prematurely. High alginate concentrations increase formulation viscosity. Therefore, alginate concentration should be optimized to achieve sufficient raft strength while maintaining acceptable viscosity.

This study addresses that gap in two stages. First, we optimized sodium alginate concentration in a blank RFS by evaluating viscosity, floating lag time, and raft strength to identify the concentration offering the best balance among them. Second, we incorporated ginger extract into the optimized formulation and assessed its physical stability, gastroretentive behavior, and *in vitro* release profile of 6-gingerol, with the goal of establishing a raft-forming platform suited to targeted gastric delivery for *H. pylori* eradication.

2. MATERIALS AND METHODS

2.1. Materials

A standardized ethanolic extract of *Zingiber officinale*, containing 4.9662% w/w 6-gingerol, was obtained from the Thailand Institute of Scientific and Technological Research (TISTR) (Pathum Thani, Thailand). Sodium alginate, employed as the raft-forming polymer, was purchased from FMC BioPolymer (Philadelphia, PA, USA). Sodium bicarbonate, used as the gas-generating agent, was obtained from RCI Labscan Ltd. (Bangkok, Thailand), whereas calcium carbonate, serving as both the gas-generating and cross-linking agent, was purchased from LOBA Chemie Pvt. Ltd. (Mumbai, India). Carbopol 940 NF, propylene glycol, methylparaben, and propylparaben were sourced from Chemipan Corporation (Bangkok, Thailand). Saccharin sodium was obtained from Veji Chemical Co., Ltd. (Bangkok, Thailand). Sodium hydroxide was purchased from V.S. Chem House (Bangkok, Thailand), and HPLC-grade methanol was obtained from RCI Labscan Ltd. (Bangkok, Thailand). All other chemicals and reagents were of analytical grade and used as received without further purification.

2.2. Preparation of the raft-forming suspensions (RFS)

2.2.1. Blank formulations (F1–F5)

Five blank raft-forming suspensions (F1–F5) were prepared containing sodium alginate at 1, 2, 3, 4, and 5% w/w (Table 1), to evaluate the effect of polymer concentration on raft-forming performance. Sodium alginate and Carbopol 940 were dispersed in distilled water to form a mucilage, and the pH was adjusted to 6.0–7.0 with 1 N sodium hydroxide. Sodium bicarbonate and calcium carbonate were triturated in a mortar with a small portion of the mucilage to form a smooth paste, after which the remaining mucilage was incorporated gradually with continuous mixing. Saccharin sodium and the paraben stock solution were subsequently added, and the volume was adjusted to 100 mL with distilled water. The paraben stock solution was prepared by dissolving 10% w/v methylparaben and 1% w/v propylparaben in propylene glycol. The final formulations were mixed and stored at 4°C until further evaluation.

2.2.2. Ginger extract-loaded formulations (G1–G3)

Based on the physical characterization of F1–F5 (Section 3.1), the 3% w/w sodium alginate formulation (F3) was selected as the base for incorporating ginger extract. Ginger extract was added at 0.55, 4.17, and 8.33% w/w to yield formulations G1, G2, and G3, respectively. These concentrations spanned the reported MIC range for 6-gingerol against *H. pylori*. Each formulation was prepared following the procedure described for the blank formulations (Section 2.2.1). The ginger extract was first dispersed in the sodium alginate mucilage to facilitate uniform distribution before

Table 1. Composition of the blank (F1–F5) and ginger extract-loaded (G1–G3) raft-forming suspensions.

Ingredients (%)	F1	F2	F3	F4	F5	G1	G2	G3
Ginger extract	-	-	-	-	-	0.55	4.17	8.33
Sodium alginate	1.00	2.00	3.00	4.00	5.00	3.00	3.00	3.00
Sodium bicarbonate	2.67	2.67	2.67	2.67	2.67	2.67	2.67	2.67
Calcium carbonate	3.20	3.20	3.20	3.20	3.20	3.20	3.20	3.20
Carbopol 940 NF	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Paraben stock solution	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Saccharin sodium	0.10	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Distilled water up to	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00

incorporation into the final mixing stage and volume adjustment. The resulting formulations were visually inspected for physical homogeneity prior to further evaluation, and no visible phase separation or sedimentation of the extract was observed.

2.3. pH and colorimetric evaluation

The pH of each suspension was measured in triplicate at room temperature (25°C) using a digital pH meter (Eutech Instruments, Nadrazni, Czech Republic). The color of the ginger extract-loaded formulations (G1–G3) was assessed visually and classified according to the Munsell Book of Color (X-Rite Inc., Grand Rapids, MI, USA).

2.4. Viscosity measurement

The viscosity and flow behavior of the suspensions were determined using a Brookfield viscometer (AMETEK, Middleboro, MA, USA) fitted with a CP-51 spindle, at 25°C. Measurements were recorded at rotational speeds of 8, 10, 12, 14, 16, and 18 rpm, in triplicate (n = 3), and results are expressed as mean ± SD.

2.5. Evaluation of raft-forming properties

2.5.1. Floating lag time and floating duration

Floating lag time and floating duration A 45-mL aliquot of each suspension was poured into 900 mL of 0.1 N HCl maintained at 37.0 ± 0.5°C to simulate gastric fluid. The floating lag time was recorded as the time elapsed from the formulation's initial contact with the medium until the appearance of an intact raft at the surface. The floating duration was monitored visually over a 24-h period to confirm that the raft remained buoyant throughout this time. All measurements were performed in triplicate (n = 3).

2.5.2. Raft density

Raft density was determined using the graduated cylinder method with slight modifications [17]. The formulations were allowed to form rafts in 900 mL of 0.1 N HCl at 37.0 ± 0.5 °C for 24 h. The formed raft was then carefully transferred to a pre-weighed 100-mL graduated cylinder. The raft mass was determined by weighing, and its volume was measured directly from the graduated cylinder markings. Raft density was subsequently calculated as the ratio of raft mass to volume (g/mL). All measurements were performed in triplicate.

2.5.3. Raft strength

Raft strength was measured using a texture analyzer (TA.XT Plus, Stable Micro Systems, Haslemere, UK) fitted with an L-shaped wire probe. A 20 mL sample of the formulation was introduced into 250 mL of 0.1 N HCl surrounding the probe and allowed to form a raft for 30 min at 37.0 ± 0.5°C. The probe was then withdrawn vertically at 5 mm/s, and the peak force required to rupture the raft was recorded as raft strength (g). Measurements were performed in triplicate.

2.6. *In vitro* drug release study

The release of 6-gingerol from the selected formulation was evaluated using a USP Apparatus 2 (paddle) dissolution tester (UDT 804, Logan Instruments Corp., Somerset, NJ, USA) containing 900 mL of 0.1 N HCl at 37.0 ± 0.5°C, with a paddle rotation speed of 50 rpm. Aliquots (5 mL) were withdrawn at 1, 2, 4, 6, and 8 h and immediately replaced with an equal volume of fresh, pre-warmed medium to maintain sink conditions. The samples were filtered through a 0.45-µm membrane filter and analyzed via high-performance liquid chromatography (HPLC). Chromatographic separation was achieved on an Inertsil® ODS-3 column

(4.6 × 250 mm, 5 µm) using an isocratic mobile phase consisting of methanol and water (70:30, v/v) at a flow rate of 1.0 mL/min. Detection was performed at 282 nm, with 6-gingerol eluting at approximately 11.5 min. All experiments were conducted in triplicate.

2.7. Stability studies

The physical and chemical stability of the optimized ginger extract-loaded formulation (G2, containing 4.17% w/w ginger extract) was evaluated under accelerated storage conditions of 45°C/75% RH for 30 days in a controlled environmental chamber. Following the storage period, the samples were re-evaluated for changes in physical appearance, viscosity, raft strength, raft density, and *in vitro* 6-gingerol release. The results were then compared with their initial (day 0) values.

2.8. Statistical analysis

Data were analyzed using SPSS for Windows (version 29.0; IBM Corp., Armonk, NY, USA). Differences among groups were analyzed by one-way analysis of variance (ANOVA) followed by Tukey's post hoc test. Statistical significance was set at $p < 0.05$.

3. RESULTS AND DISCUSSION

The overall design and functional mechanism of the ginger extract raft-forming suspension system for targeted *H. pylori* eradication is illustrated in Figure 1. Upon oral administration, the liquid formulation undergoes rapid in situ gelation on contact with gastric acid, forming a cohesive, buoyant raft. Gelation of calcium alginate results from cross-linking of sodium alginate chains by calcium ions released as calcium carbonate reacts with hydrochloric acid in the stomach. The same reaction, together with sodium bicarbonate, liberates carbon dioxide, which becomes entrapped within the developing calcium alginate network. This trapped gas lowers the bulk density of the matrix below that of the gastric contents, allowing the raft to float at the surface rather than undergo gastric emptying with the bulk fluid. Ginger extract is entrapped within this floating raft, with 6-gingerol as its principal bioactive constituent [6]. It can then diffuse to the mucus layer, extending its residence time near the mucosal surface where *H. pylori* typically resides.

3.1. Physical characterization of blank raft-forming suspensions (F1–F5)

To determine the optimal polymer matrix for the targeted delivery system, five blank raft-forming suspensions (F1–F5) with varying sodium alginate concentrations (1% to 5% w/w) were prepared and evaluated. All formulations presented as white, homogeneous, and cloudy suspensions. The physicochemical and raft-forming properties of the raft-forming suspension (RFS) are shown in Table 2. Viscosity clearly increased with sodium alginate concentration ($p < 0.05$), rising from 30 cP (F1) to 2229 cP (F5). Increasing alginate concentration progressively intensified chain entanglement and network density [13, 14], raising viscosity from F1 through F5.

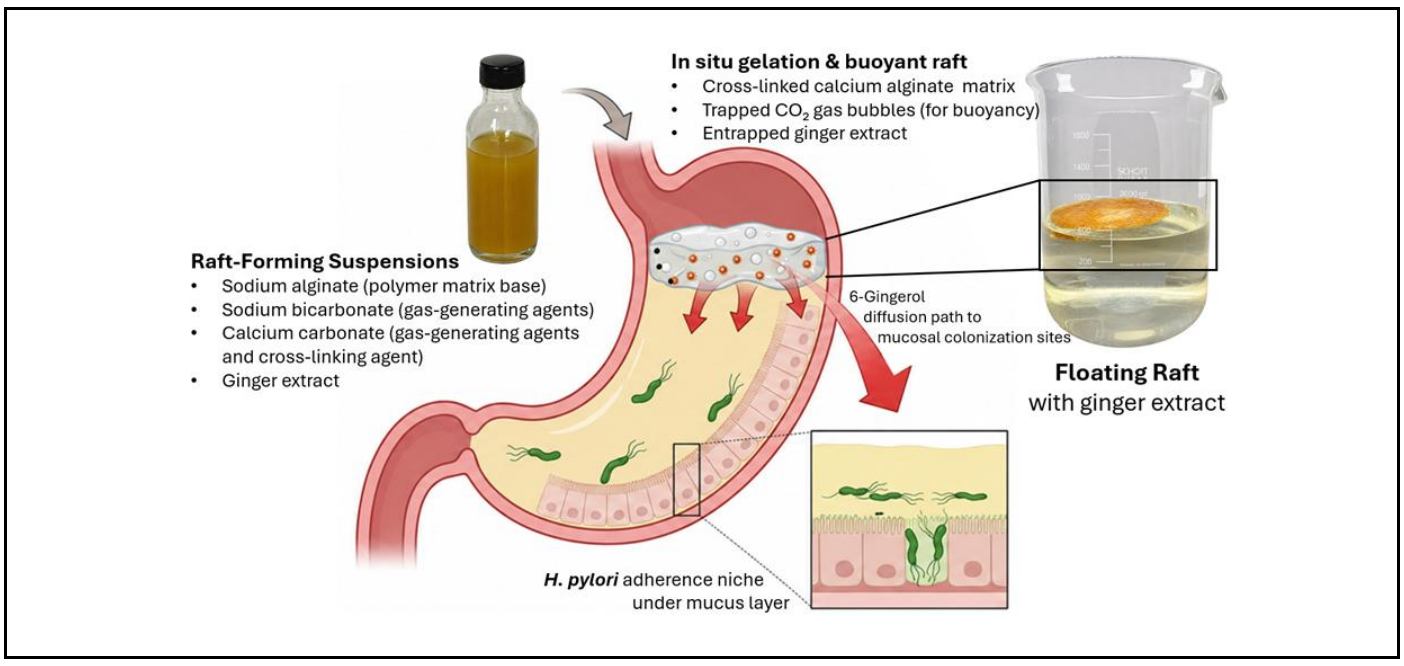

Figure 1. Overview of the ginger extract raft-forming suspension system for targeted *Helicobacter pylori* eradication, illustrating in situ raft formation, buoyancy mechanism, and controlled gingerol release to gastric mucosa.

Table 2. Physicochemical and raft-forming properties of blank formulations (F1–F5), ginger extract-loaded formulations (G1–G3), and a commercial RFS.

Properties	F1	F2	F3	F4	F5	G1	G2	G3	Commercial RFS
Viscosity (cP)	30.36 ± 3.37^{a}	154.07 ± 7.33^{b}	418.70 ± 3.99^{d}	1148.71 ± 136.60^{e}	2229.11 ± 498.02^{f}	620.78 ± 63.15^{g}	840.96 ± 69.13^{h}	864.74 ± 70.66^{h}	276.20 ± 0.00^{c}
Floating lag time (s)	4.64 ± 0.42^{a}	7.25 ± 0.12^{b}	8.62 ± 0.15^{c}	11.92 ± 0.36^{d}	16.51 ± 0.37^{e}	12.87 ± 0.26^{d}	9.89 ± 0.03^{c}	11.66 ± 0.41^{d}	6.55 ± 0.17^{b}
Raft strength (g)	5.06 ± 0.34^{a}	7.21 ± 0.40^{b}	10.13 ± 0.31^{c}	11.24 ± 0.51^{c}	11.90 ± 0.51^{c}	10.28 ± 1.25^{c}	10.90 ± 0.65^{c}	11.62 ± 0.07^{c}	8.88 ± 2.50^{b}
Raft density (g/ml)	0.91 ± 0.06	0.88 ± 0.02	0.93 ± 0.04	0.95 ± 0.02	0.94 ± 0.02	0.82 ± 0.04	0.86 ± 0.10	0.84 ± 0.03	0.97 ± 0.02
Floating duration (h)	>24	>24	>24	>24	>24	>24	>24	>24	>24
pH	-	-	-	-	-	9.10 ± 0.01	8.99 ± 0.02	8.98 ± 0.05	-
Color	-	-	-	-	-	8Y4	4Y6	3Y6	-

Note: Values are presented as mean ± SD (n = 3). Different superscript letters within the same row indicate significant differences between formulations ($p < 0.05$, one-way ANOVA followed by Tukey's post hoc test).

The commercial RFS (Gaviscon®) exhibited a viscosity of 276.20 cP. F4 and F5 exhibited very high viscosity. According to the International Dysphagia Diet Standardisation Initiative, fluids exceeding 1750 cP are classified as extremely thick, making the product difficult to pour from the bottle and unpleasant for the patient to swallow [18]. Thus, these formulations were not carried forward.

Floating lag time was the time interval between contact with gastric fluid and the formulation's rise to the surface. Floating lag time increased significantly with increasing alginate concentration, with significant differences observed among F1–F5 ($p < 0.05$, Table 2). This was consistent with higher viscosity slowing acid penetration and delaying the CO_2-generating reaction. The commercial RFS showed a lag time of 6.55 s; F3 (3% w/w) was close to this at 8.62 s. This behavior is directly attributableto the higher bulk viscosity of the pre-gel mucilage, which creates a denser transport barrier that retards the inward diffusion of hydronium ions and delays the chemical activation of the gas-generating agents [11]. However, all blank formulations exhibited rapid buoyancy well within the critical window required to escape premature gastric emptying [12].

Raft strength also increased with alginate concentration, from 5.06 g to 11.90 g (Table 2). This increase could be explained by the higher density of calcium-mediated cross-links formed at greater polymer content. This yielded a more mechanically resistant gel network [11, 19]. Formulation F3 achieved a raft strength of 10.13 g, which notably exceeded that of the commercial RFS (8.88 g) under the same testing conditions. Raft density, in contrast, remained relatively constant across formulations (0.88–0.95 g/mL) and consistently below that of simulated gastric fluid (1.06 g/mL) [12], indicating that buoyancy in this system arises primarily from CO_2 entrapment during gelation rather than from bulk polymer concentration. All formulations remained buoyant for over 24 h, indicating that the calcium alginate gel network retained sufficient structural integrity to sustain flotation regardless of alginate concentration.

F3 (3% w/w) fell within the viscosity range suitable for oral administration. F1 and F2 were too fluid to be expected to form a mechanically robust raft, while F4 and F5 were too viscous for convenient oral dosing. F3 achieved raft strength above the commercial RFS and was therefore selected as the base formulation for the incorporation of ginger extract in subsequent studies.

3.2. Effect of ginger extract raft-forming suspensions (G1–G3)

To evaluate the impact of the herbal extract on the RFS, ginger extract was incorporated into the F3 base at three concentrations (0.55, 4.17, and 8.33 % w/w, corresponding to G1–G3 in Table 1). Incorporation of the extract changed the formulation from a white suspension to a cloudy yellowish dispersion. All formulations remained physically homogeneous prior to raft formation, with no visible phase separation, or sedimentation observed during visual inspection. In Table 2, the color intensity increased with extract concentration (Munsell values 8Y4, 4Y6 and 3Y6 for G1, G2 and G3, respectively), consistent with the natural pigmentation of the ginger extract itself. The pH of the extract-loaded formulations ranged from 8.98 to 9.10, remaining within an alkaline range. The mildly alkaline pH is critical for maintaining the stability of the suspension vehicle, as it prevents premature effervescent reaction of the carbonates prior to gastric administration [11]. Although chemical stability of 6-gingerol and shogaol exhibited optimal degradation kinetics in acidic conditions around pH 3–4 [20], short-term formulation handling within this alkaline vehicle did not compromise its preliminary integrity, provided the system is kept away from elevated temperatures.

Relative to the blank F3 formulation, viscosity increased significantly with extract loading, from 620.78 to 864.74 cP. This higher viscosity was attributed to the additional macromolecular constituents present in the crude ginger extract, which contribute to the overall hydrodynamic volume and intermolecular entanglement within the aqueous vehicle [21, 22]. Despite this increase, the viscosities of all loaded formulations remained well within the acceptable range for oral liquid administration, ensuring adequate pourability, dose uniformity, and patient compliance [18].

Floating lag time varied modestly between 9.89 ± 0.03 s and 12.87 ± 0.26 s; these differences were unlikely to be clinically meaningful given that all values remained well below typical gastric-emptying times [12]. Importantly, the remaining raft-forming parameters - floating duration (>24 h), raft density (0.82–0.86 g/mL), and raft strength (10.28–11.62 g) - did not differ significantly from blank F3. This finding indicated that the incorporation of ginger extract, even at the highest tested concentration, did not compromise the structural and gastroretentive properties established during polymer optimization, supporting the compatibility of the extract with the raft-forming matrix.

On the basis of these physicochemical and raft-forming data, G2 (intermediate extract loading, viscosity 840.96 ± 69.13 cP, floating lag time 9.89 ± 0.03 s, raft strength 10.90 ± 0.65 g) was selected for subsequent *in vitro* release and stability studies. This intermediate concentration provided an acceptable balance between extract content, oral viscosity and mechanical raft integrity while remaining within the concentration range previously shown to span the reported MIC values of 6-gingerol against *H. pylori* [7, 8].

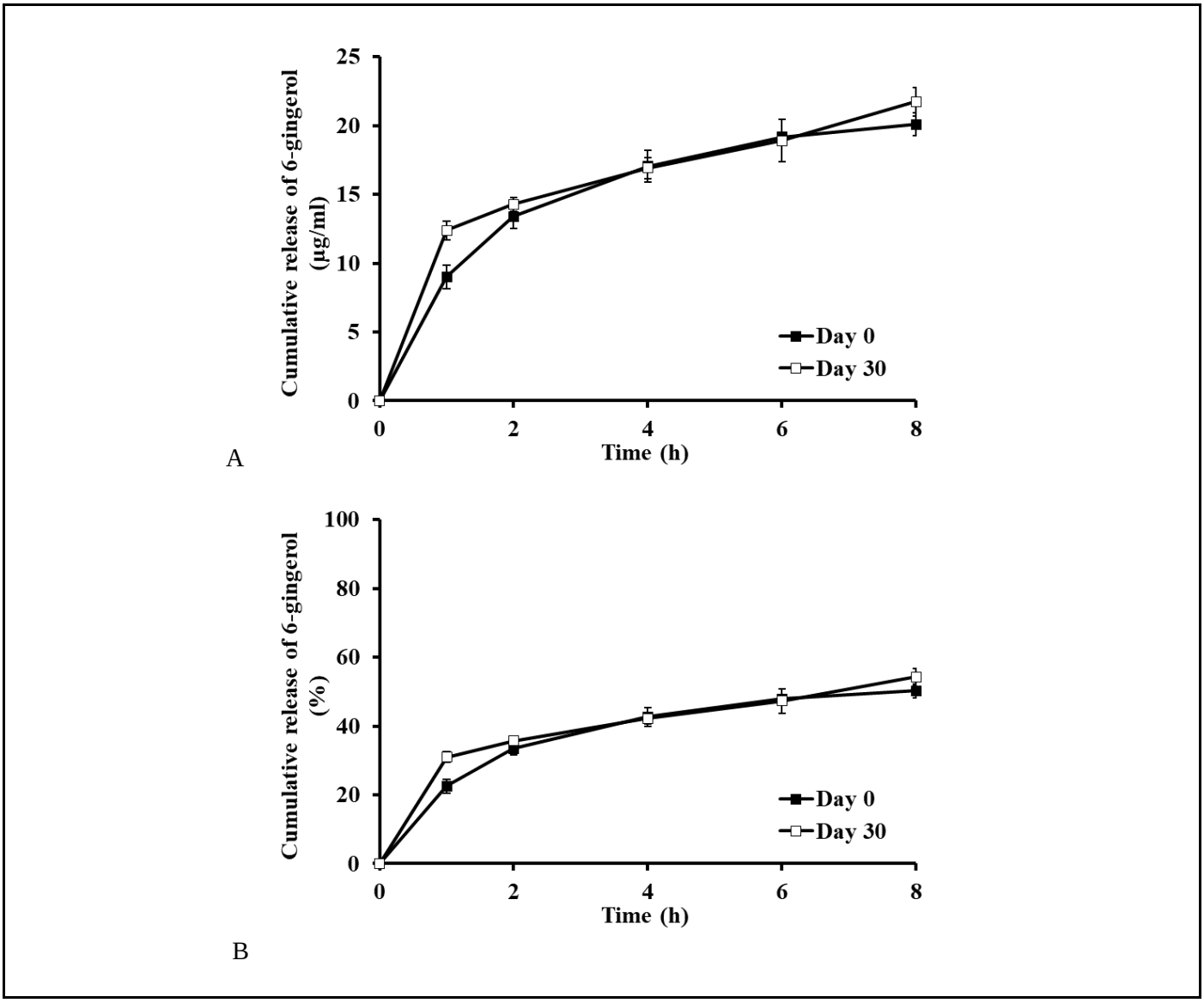

Figure 2. *In vitro* cumulative release profile of 6-gingerol from the optimized formulation (G2) in 0.1 N HCl before and after accelerated storage at 45°C/75% RH. (A) Cumulative amount of 6-gingerol released (µg/mL); (B) Cumulative percentage of 6-gingerol released relative to the total loaded 6-gingerol (%).

3.3. *In vitro* ginger extract release study

The *in vitro* dissolution profile of the ginger extract from the floating G2 raft was characterized under simulated gastric conditions (0.1 N HCl, 37.0 ± 0.5 °C), utilizing 6-gingerol as the representative active biomarker [6, 7, 20]. It was quantified by HPLC using a standard curve linear over the tested range ($y = 7834.7x - 87.5$, $R^2 = 0.9999$). Cumulative release followed a biphasic, time-dependent pattern (Figure 2A), with an initial burst phase during the first 2 h followed by a slower, decelerating release phase through 8 h. The cumulative percentage of 6-gingerol released relative to the total loaded amount is shown in Figure 2B. The optimized formulation contained approximately 40 µg of 6-gingerol per administered dose. At 8 h, 50% of the total loaded 6-gingerol was released under the initial condition (Day 0), while 54% was released after 30 days of accelerated storage. Thus, 6-gingerol was not completely released within 8 h, with approximately half of the loaded 6-gingerol remaining entrapped within the floating raft matrix. Notably, the released concentrations exceeded the reported MIC values for 6-gingerol against *H. pylori.* [8, 9]. This finding indicates that the raft-forming system can provide sustained local delivery of 6-gingerol while retaining a substantial fraction of the active ingredient within the raft matrix. The biphasic release pattern was in agreement with dissolution profiles previously reported for alternative alginate-based herbal raft systems [23, 24]. The release kinetics were explained by correlation with the Higuchi equation. The drug release was governed primarily by diffusion through the cross-linked alginate gel rather than matrix erosion.

3.4. Stability study

The physical and mechanical stability of the optimized formulation (G2) was evaluated after 30 days of storage under accelerated conditions (45 °C/75 % RH). As detailed in Figure 3A, exposure to elevated temperature and humidity induced noticeable changes in the physical appearance and performance of the formulation. Macroscopic observation revealed a distinct color change from a pale yellow suspension (Munsell value 4Y6) to a darker brownish suspension (Munsell value 4Y3). This may be attributed to thermal oxidation and/or Maillard-type degradation of phytochemical constituents during storage [25, 26]. In contrast, the pH remained unchanged, indicating that the formulation maintained its overall chemical environment despite thermal stress. However, the viscosity decreased after 30 days, suggesting partial degradation or structural relaxation of the sodium alginate polymer network under accelerated storage conditions.

Raft strength dropped precipitously from 10.90 g to 2.04 g, representing an approximately 81% reduction (Figure 3B). Takbirgou et al. reported that the alginate-based raft systems could undergo physical and mechanical changes under accelerated storage conditions [27]. This substantial loss of structural coherence confirms that thermal and hydrolytic stress impaired the ability of the alginate to form a robust, cross-linked network upon contact with acid. Conversely, the floating lag time decreased slightly to 6.62 s. While a shorter lag time might superficially appear beneficial, in this context, it likely reflects the reduced viscosity barrier, allowing acid to penetrate the suspension more rapidly, rather than an enhancement in the gas-generating efficiency [28].

The *in vitro* dissolution profile of 6-gingerol on day 30 closely mirrored the initial baseline profile (Figure 2). A statistically significant difference ($p < 0.05$) was noted only during the initial 1-h burst phase—likely facilitated by the depolymerized, less viscous matrix offering less resistance to immediate drug diffusion—while no significant deviations occurred at subsequent time points.

These stability results showed that the formulation maintained its sustained drug release and buoyancy under accelerated storage conditions. However, the mechanical strength of the alginate matrix decreased over time, indicating susceptibility to thermal degradation. To address this limitation in future commercial formulations, the incorporation of polymer stabilizers such as HPMC or polymeric solid dispersions should be investigated to reinforce the gel network and protect alginate chains from thermal cleavage. Furthermore, as the present study relied on accelerated conditions as a preliminary screening approach, long-term stability testing under standard ICH conditions (25°C ± 2°C / 60% ± 5% RH) is warranted to establish a definitive shelf-life for the suspension.

4. CONCLUSIONS

This study successfully developed and characterized a gastroretentive raft-forming suspension for the targeted gastric delivery of ginger extract, with sodium alginate concentration emerging as the key determinant of raft-forming performance. The 3% w/w

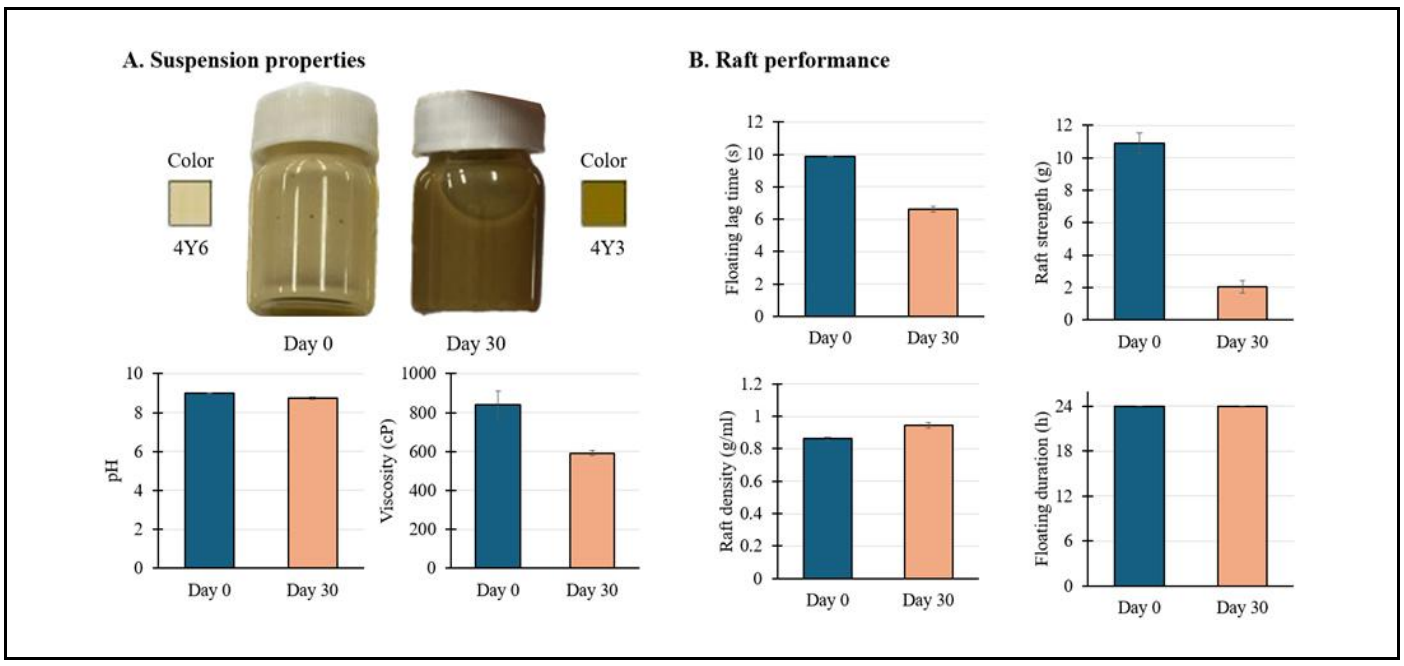

Figure 3. Stability study and physical characteristics of the optimized ginger extract-loaded formulation (G2) after 30 days of storage at 45°C/75% RH.

as the most suitable level for a raft-forming suspension intended for gastric delivery of ginger extract. At this concentration the blank formulation combined acceptable oral viscosity with superior raft strength (10.13 g) relative to a commercial reference product (8.88 g) while maintaining rapid floating lag time and buoyancy beyond 24 h. Incorporation of ginger extract at 4.17% w/w produced only modest increases in viscosity and did not compromise floating performance or raft integrity. *In vitro* dissolution profiles revealed a biphasic pattern that generated local concentrations (approximately 9–20 µg/mL of 6-gingerol) exceeding reported MIC values against *H. pylori*. However, accelerated stability evaluations (45°C and 75% relative humidity for 30 days) revealed critical limitations of the current delivery system. Thermal and hydrolytic stress induced chemical browning of the botanical phenolics and triggered a reduction in mechanical raft strength, indicating that the structural network integrity is highly sensitive to storage conditions despite maintaining a consistent drug release profile. Therefore, future studies must focus on optimizing polymer stabilizers and excipients to prevent thermal degradation, as well as conducting standard long-term shelf-life studies, to improve the long-term stability and commercial applicability of the suspension. These findings demonstrate that a The 3% w/w sodium alginate raft-forming platform can prolong gastric residence of a plant-derived antibacterial agent and sustain its local availability. Further work should focus on improving mechanical stability during storage and enhancing the extent of drug release so that the system can advance as a non-antibiotic adjunct for *H. pylori* eradication.

5. ACKNOWLEDGEMENTS

This research study was financially supported by Naresuan University (NU), and the National Science, Research and Innovation Fund (NSRF), Grant No. R2568B076. The authors also gratefully acknowledge the Faculty of Pharmaceutical Sciences at Naresuan University, Phitsanulok, Thailand.

Author contribution

Worawut Kriangkrai: Conceptualization, Methodology, Formal analysis, Supervision, Writing – review & editing. Nontakron Jaiya: Investigation, Formal analysis, Data curation, Visualization, Writing – original draft. Watcharin Meerod: Investigation, Methodology, Data curation. Srisagul Sungthongjeen: Conceptualization, Funding acquisition, Project administration, Supervision, Writing – review & editing.

Funding

This research study was financially supported by Naresuan University (NU), and the National Science, Research and Innovation Fund (NSRF), Grant No. R2568B076.

Conflict of interest

None to declare

Ethics approval

None to declare

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used Gemini to improve the language, structural flow, and readability of the manuscript, as well as to ensure adherence to American English standards. The authors reviewed and edited the output as necessary and accept full responsibility for the content of the final manuscript.

Article info:

Received July 30, 2026
Received in revised form August 11, 2026
Accepted August 16, 2026

REFERENCES

1. Chmiela M, Kupcinskas J. Review: Pathogenesis of *Helicobacter pylori* infection. Helicobacter. 2019;24(S1):e12638.
2. Malfertheiner P, Camargo MC, El-Omar E, Liou J-M, Peek R, Schulz C, et al. *Helicobacter pylori* infection. Nat Rev Dis Primers. 2023;9(1):19.
3. Rattanachaisit P, Burana C, Jaroenlapnopparat A, Vongseenin S, Chaithongrat S, Rerknimitr R, et al. The prevalence and treatment outcomes of *Helicobacter pylori* infection in a tertiary hospital in Thailand, 2018–2021. JGH Open. 2023;7(6):439-44.
4. Shih C-A, Shie C-B, Hsu P-I. Update on the first-line treatment of *Helicobacter pylori* infection in areas with high and low clarithromycin resistances. Ther Adv Gastroenterol. 2022;15:17562848221138168.
5. Sukri A, Lopes BS, Hanafiah A. The emergence of multidrug-resistant *Helicobacter pylori* in Southeast Asia: A systematic review on the trends and intervention strategies using antimicrobial peptides. Antibiotics. 2021;10(9):1061.
6. Qian J, Li Z, Wang J, Lin Y, Yu Y. 6-gingerol and its derivatives inhibit *Helicobacter pylori*-induced gastric mucosal inflammation and improve gastrin and somatostatin secretion. Front Microbiol. 2024;15:1451563.
7. Mahady GB, Pendland SL, Yun GS, Lu Z-Z, Stoia A. Ginger (*Zingiber officinale* Roscoe) and the gingerols inhibit the growth of Cag A+ strains of Helicobacter pylori. Anticancer Res. 2003;23(5a):3699-702.
8. Elbestawy MKM, El-Sherbiny GM, Moghannem SA, Farghal EE. Antibacterial, antibiofilm, and anti-inflammatory activities of ginger extract against *Helicobacter pylori*. Microbiol Res. 2023;14(3):1124-38.
9. Gaus K, Huang Y, Israel DA, Pendland SL, Adeniyi BA, Mahady GB. Standardized ginger (Zingiber officinale) extract reduces bacterial load and suppresses acute and chronic

inflammation in Mongolian gerbils infected with cagA+ Helicobacter pylori. Pharm Biol. 2009;47(1):92-8.
10. Raj R, Agarwal N, Raghavan S, Chakraborti T, Poluri KM, Pande G, et al. Epigallocatechin gallate with potent anti-*Helicobacter pylori* activity binds efficiently to its histone-like DNA binding protein. ACS Omega. 2021;6(5):3548-70.
11. Prajapati VD, Jani GK, Khutliwala TA, Zala BS. Raft forming system—An upcoming approach of gastroretentive drug delivery system. J Control Release. 2013;168(2):151-65.
12. Bardonnet PL, Faivre V, Pugh WJ, Piffaretti JC, Falson F. Gastroretentive dosage forms: Overview and special case of Helicobacter pylori. J Control Release. 2006;111(1):1-18.
13. Abou Youssef NAH, Kassem AA, El-Massik MAE, Boraie NA. Development of gastroretentive metronidazole floating raft system for targeting Helicobacter pylori. Int J Pharm. 2015;486(1):297-305.
14. Kim HM. Raft formation of sodium alginate in the stomach. J Neurogastroenterol Motil. 2016;22(4):705-6.
15. Takbirgou H, Salami M, Askari G, Emam-Djomeh Z, Kennedy JF. Characterization of novel alginate-aloe vera raft systems for treatment of gastroesophageal reflux disease. Int J Biol Macromol. 2024;257:128686.
16. Negi P, Gautam S, Sharma A, Rathore C, Sharma L, Upadhyay N, et al. Gastric ulcer healing by chebulinic acid solid dispersion-loaded gastroretentive raft systems: preclinical evidence. Ther Deliv. 2022;13(2):81-93.
17. Matchimabura N, Praparatana R, Issarachot O, Oungbho K, Wiwattanapatapee R. Development of raft-forming liquid formulations loaded with ginger extract-solid dispersion for treatment of gastric ulceration. Heliyon. 2024;10(11):e31803.
18. Miele NA, Di Monaco R, Dell'Amura F, Rega MF, Picone D, Cavella S. A preliminary study on the application of natural sweet proteins in agar-based gels. J Texture Stud. 2017;48(2):103-13.
19. Johnson FA, Craig DQM, Mercer AD, Chauhan S. The effects of alginate molecular structure and formulation variables on the physical characteristics of alginate raft systems. Int J Pharm. 1997;159(1):35-42.
20. Bhattarai S, Tran VH, Duke CC. The stability of gingerol and shogaol in aqueous solutions. J Pharm Sci. 2001;90(10):1658-64.
21. Jing Y, Cheng W, Li M, Zhang Y, Pang X, Qiu X, et al. Structural characterization, rheological properties, antioxidant and anti-inflammatory activities of polysaccharides from *Zingiber officinale*. Plant Foods Hum Nutr. 2023;78(1):160-5.
22. Hu W, Yu A, Wang S, Bai Q, Tang H, Yang B, et al. Extraction, purification, structural characteristics, biological activities, and applications of the polysaccharides from *Zingiber officinale* Roscoe. (ginger): A review. Molecules. 2023;28(9):3855.
23. Siripruekpong W, Praparatana R, Issarachot O, Wiwattanapatapee R. Simultaneous delivery of curcumin and resveratrol via *in situ* gelling, raft-forming, gastroretentive formulations. Pharmaceutics. 2024;16(5):641.
24. Bunlung S, Nualnoi T, Issarachot O, Wiwattanapatapee R. Development of raft-forming liquid and chewable tablet formulations incorporating quercetin solid dispersions for treatment of gastric ulcers. Saudi Pharm J. 2021;29(10):1143-54.
25. El Hosry L, Elias V, Chamoun V, Halawi M, Cayot P, Nehme A, et al. Maillard reaction: mechanism, influencing parameters, advantages, disadvantages, and food industrial applications: A Review. Foods. 2025;14(11):1881.
26. Chaipoot S, Kulprachakarn K, Wiriyacharee P, Somjai C, Chaimueng K, Jaijoi S, et al. Temperature-driven maillard conjugation and phenolic changes in dried lychee pulp: implications for antioxidative enhancement. Foods. 2026;15(3):468.
27. Takbirgou H, Salami M, Askari G, Emam-Djomeh Z, Löbenberg R, Serpe MJ, et al. Development and evaluation of alginate-based gastroretentive raft-forming systems enabling sustained release of propolis in gastric ulcer treatment. Drug Deliv. 2026;33(1):2616887.
28. Hampson FC, Farndale A, Strugala V, Sykes J, Jolliffe IG, Dettmar PW. Alginate rafts and their characterisation. Int J Pharm. 2005;294(1):137-47.