Kopongpanich P, Senasuthum S, Promnim T, Hayashi T, Wada K, Suriyakriangkai P, Thitikornpong W, Titapiwatanakun V, Yotsombut K. Comparative studies on characterization and effectiveness of various alginate-based raft-forming antacid products. Pharmacy Practice 2026 Apr-Jun;24(2): 3533.
https://doi.org/10.18549/PharmPract.2026.2.3533

Original Research

Comparative studies on characterization and effectiveness of various alginate-based raft-forming antacid products

Peerawas Kopongpanich, Sarunrus Senasuthum, Tanet Promnim, Takao Hayashi, Kengo Wada, Pakorn Suriyakriangkai, Worathat Thitikornpong, Varin Titapiwatanakun, Kitiyot Yotsombut

Received (first version): 06-Nov-2025 Accepted: 02-Apr-2026 Published online: 29-May-2026

Abstract

Background: Gastroesophageal reflux disease develops from exposure of the esophagus to acidic refluxate from the stomach and duodenal bile. While a floating raft, in which calcium carbonate was the main antacid ingredient, is formed on top of the stomach fluid to provide a physical barrier against acid gastroesophageal reflux after ingesting alginate-based antacid products. **Objective:** This work aimed to test in vitro effectiveness of five alginate suspensions commercially available in the Thai market to understand their characteristics and behaviors in gastric conditions mimicking the human stomach. **Methods:** Five commercial alginate suspensions were tested under simulated gastric conditions (0.1 N HCl, 37 °C). Raft formation was assessed by recording onset time, volume, mass, and buoyancy. Raft strength was quantified using a texture analyzer with a penetration probe, while porosity was examined visually. Acid neutralization capacity (ANC) was measured by titration against 0.1 N HCl to pH 3.0, and neutralization duration was monitored over time. Correlations between raft characteristics and ANC were analyzed. **Results:** Rafts of products formed voluminously (64.9-83.8 mL, 39.8-46.4 g), porous and floating rafts within 0.4-6.3 min. Raft strength and neutralization duration was in the range of 13.3-29.9 g and 24-46 min, respectively. Marked differences were not evident in the acid neutralization capacity (ANC) values of the products (8.8-9.9 mEq). No correlation was observed between ANC and raft-forming capacity or duration of neutralization though raft structures could affect their neutralization profiles. **Conclusion:** The results demonstrated that formulation design and raw material sourcing could vary product performance. While the obtained values of in vitro effectiveness could be applied to set the specifications and characterization methods for developing new raft-forming formulations and products. Importantly, understanding raft characteristics could empower pharmacists to make informed recommendations, providing patients with improved symptom relief and management.

Key words: Gastroesophageal reflux disease, Raft-forming formulation, Alginates, Antacid, Anti-reflux

Peerawas Kopongpanich. PharmD, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. ko.peerawas@gmail.com
Sarunrus Senasuthum. Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. raweewan.s@chula.ac.th
Tanet Promnim. Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. Tanet.P@chula.ac.th
Takao Hayashi. Department of Pharmaceutical Sciences, Faculty of Pharmacy, Meiji Pharmaceutical University, Tokyo, Japan. y191238@std.my-pharm.ac.jp
Kengo Wada. Department of Pharmaceutical Sciences, Faculty of Pharmacy, Meiji Pharmaceutical University, Tokyo, Japan. y191328@alm.my-pharm.ac.jp
Pakorn Suriyakriangkai. Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. 6630068633@student.chula.ac.th
Worathat Thitikornpong. PhD, Department of Food and Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. Worathat.T@pharm.chula.ac.th
Varin Titapiwatanakun. PhD, Department of Pharmaceutics and Industrial Pharmacy, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. varin.t@pharm.chula.ac.th
Kitiyot Yotsombut*. PhD, Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Chulalongkorn University, Bangkok, Thailand. Kitiyot.y@pharm.chula.ac.th

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a prevalent chronic condition of the upper gastrointestinal system, affecting an estimated one billion individuals globally. It is the second most common gastrointestinal diagnosis, surpassed only stomach discomfort. GERD accounts for approximately 5.25 million outpatient visits and 325,000 emergency room visits annually, highlighting its significant burden on healthcare systems worldwide[1]. GERD develops from the reflux of stomach contents into the esophagus, pharynx, or oral cavity, leading to significant symptoms or complications. Common signs and symptoms of GERD include acid regurgitation, heartburn, chest pain, dysphagia, and globus sensation[2]. Fluid refluxate and aerosolized gastric acid from the stomach can travel to the larynx and even the airways, exacerbating conditions such as hoarseness, wheezing, chronic cough, and asthma, known as extraesophageal symptoms[3]. Recent epidemiological studies indicate a rising global prevalence of GERD. Estimates suggest a global prevalence ranging from 15% to 25%. Regional prevalence varies significantly, with rates in Saudi Arabia reported at 15%–45.4%, western Asia at 10%–20%, the Middle East at 8.7%–33.1%, and eastern Asia at less than 10%.

Western countries, including the United States, exhibit higher prevalence rates, estimated at 10%–30%. The high prevalence of GERD and other gastrointestinal tract disorders profoundly impacts patients' health-related quality of life, underscoring the importance of effective management and prevention strategies[4].

For over 30 years, alginate-based reflux suppressants have been utilized in the management of GERD. These treatments can be broadly categorized into two primary types: formulations that primarily contain alginate with a small amount of antacid to facilitate raft formation, and those that include a substantial amount of antacid alongside alginate. A variety of formulations are available across different countries, each incorporating unique combinations of alginate and antacid ingredients to enhance efficacy and cater to local market demands[5].

The raft-forming capability of alginates arises from their ability to create and maintain a low-density, viscous gel in the presence of an acidic environment in the stomach. This layer serves as a barrier in antireflux formulations[6]. This gel forms rapidly upon exposure to gastric acid, typically within seconds in vitro and within a few minutes post-dosing in vivo. Alginate/antacids are typically formulated with bicarbonate, which functions as a gas-generating component. In the presence of gastric acid, the reaction produces carbon dioxide (CO_2) bubbles that become trapped within the developing gel matrix. This process transforms the gel into a foam, enhancing its buoyancy and allowing it to float on the surface of gastric contents, akin to a raft on water. Additionally, the foam encapsulates acid-neutralizing capacity, contributing to its therapeutic effect[7]. Other antacids, such as calcium carbonate, facilitate gel formation and enhance gel strength by promoting interactions between calcium ions and alginate polymer chains. Calcium carbonate, in particular, contributes to alginate gelation through its dissociation under acidic conditions, which releases divalent calcium cations. These cations interact with the alginate, leading to cross-linking. Extensive research found that chelation between guluronic acid blocks creates an 'egg-box' structure, substantially increasing the viscosity of the system[7,8].

Formulation factors, including the types and quantities of antacids, their ratio to alginate, acid-neutralizing capacity, and the concentration and viscosity of the formulation, are anticipated to influence raft formation. Ideal rafts should exhibit cohesion, buoyancy, sufficient volume, resistance to reflux into the esophagus, and stability against disruption caused by gastric motility. These characteristics are clinically relevant, as they directly impact the effectiveness of alginate-based reflux suppressants in alleviating symptoms and protecting the esophagus[9,10]. Given the availability of various commercial alginate-based reflux suppressants in Thailand, understanding the physicochemical properties of these formulations is crucial. Testing and comparing these properties can provide valuable insights into their performance, enabling healthcare providers to recommend the most effective products for managing GERD.

Therefore, the objective of this study was to evaluate the characteristics of various alginate-based raft-forming antacid formulations available in Thailand. The study employed multiple physicochemical characterization methods to assess the efficacy of these pharmaceutical products.

MATERIALS AND METHODS

Materials

Five alginate-based antacid products, including the Originator product (REF) and four generic samples (labeled as S1 to S4), were acquired from accredited pharmacies in Thailand. All products contain raft-forming ingredients as indicated on the labels. Each 10 ml contains 500 mg of sodium alginate, 213 mg of sodium bicarbonate, and 325 mg of calcium carbonate. Hydrochloric (HCl) acid (37% fuming) was obtained from Honeywell™ Fluka™. All chemicals and solvents were of analytical grade and were utilized as received.

Raft forming characteristics

The five alginate-based raft-forming antacids were tested. These characteristics include 1) raft forming speed, 2) flotation, 3) floating lag time, and 4) raft coherence. To test these properties, 10 mL of each product was added to 150 mL of 0.1 M HCl acid in Apparatus 3 dissolution chambers at 37°C. Raft-forming properties were observed immediately after the products were introduced to the acid[11].

Raft forming speed was determined as "immediate" when the raft formed apparently within 10 seconds of contact with the acid. If this condition was not met, it was regarded as "non-immediate". Complete flotation was defined as the condition where a whole raft rose to the liquid surface, whereas partial flotation was identified when some insoluble materials submerged in the medium or settled at the bottom of the chamber and persisted throughout the 30-minute observation period for raft development. Floating lag time was defined as the time needed for 90% of the raft to float into the surface of the medium. Raft coherence was determined during the removal of the raft for weighing. Coherence was considered "good" if the rafts maintained a solid mass, whereas it was deemed "poor" if the rafts broke apart during handling[9].

Raft tensile strength

A maximal dose of sample (20 mL) was added to 150 mL of 0.1M HCl in a 250 mL low-form glass beaker at 37°C to create rafts. While developing each raft, an L-shaped stainless steel wire probe was maintained upright in the beaker for 30 minutes. The Stable Micro Systems TA. XT plus texture analyzer was used with a 5 kg load cell and an alginate raft hook (A/ARH). The beaker was placed on the texture analyzer table after 30 minutes of raft formation, and the wire probe was hooked onto the arm and dragged vertically up through the raft at 5 mm/s. Grams were used to quantify the force needed to pull the wire probe through the raft. Three tests were done[9].

Raft volume and raft weight

Rafts were produced using the same procedure as that employed for raft strength testing, excluding the wire probe, and were subsequently incubated for 30 minutes. Prior to raft formation, the weight of each beaker was recorded (W1).

The total weight of the beaker and its contents was recorded after raft development (W2), indicating the highest point attained by each raft outside the beaker. The raft was removed from the beaker by decanting the liquid and transferring the raft into a pre-weighed plastic weighing boat. Following a 30-second standing period, surplus liquid was removed, and the raft's weight was recorded (W3). The residual liquid in the beaker was eliminated using a paper towel, after which it was replenished with deionized water (DI) to the designated mark and subsequently weighed (W4). The calculation of each raft's volume was performed using the formula: raft volume = (W4 − W1) − (W2 − W1 − W3). The raft volume is expressed in milliliters (mL), while all weights are recorded in grams (g). This formula assumes that the density of the removed liquid (supernatant) is equivalent to that of deionized water.[9] The tests were conducted in triplicate.

Raft morphology

The morphology of the raft was assessed using a scanning electron microscope and energy dispersive X-ray spectrometer (SEM-EDS, JEOL JSM-6610LV). The constructed raft underwent drying through an automated critical point dryer (Leica EM CPD300), after which a segment of the raft was affixed to a stage and coated with gold. The morphology of the raft was examined utilizing SEM-EDS at a temperature of 25˚C. The image resolution was adjusted to x50, and x100.

Raft neutralization profile

Rafts were prepared in 250 mL glass beakers by adding 20 mL of the sample with 70 mL of 0.1 M HCl, which had been equilibrated at 37°C. The rafts were maintained at this temperature for 30 minutes to facilitate maturation. Upon development, the raft was meticulously placed into a Buchner funnel, with excess media being discarded. A filtration process was employed to eliminate excess HCl, and the raft was collected for pH measurement using a calibrated pH meter. Subsequently, 3 mL of 0.04 M HCl solution was added to the raft and allowed to settle for 5 minutes prior to a 3-minute filtration process. The filtrate was collected, and the pH was measured. The process was continuously conducted until the pH of the filtrate was not further neutralized (pH < 4) by the raft. The pH cutoff of 4.0 was selected due to its established recognition in clinical practice as the transition point from acid to nonacid reflux, signifying the clinical importance of the change from acidic gastric conditions to weak acidity at a pH greater than 4.0. The tests were conducted in five replicates.

Acid neutralizing capacity of the products

The acid neutralizing capacity (ANC) is a critical parameter for assessing a formulation's ability to neutralize gastric acid effectively[6]. The sample preparation and testing procedure adhered to the USP General Chapter <301> on Acid-Neutralizing Capacity[6]. For suspension dosage forms, the samples were agitated thoroughly until achieving uniformity. A sample amount equivalent to the minimum dosage was weighed into a 250 mL beaker then diluted with water to a total volume of 70 mL and stirred at approximately 300 rpm for 1 minute while maintaining the temperature at 37°C. Subsequently, 30.0 mL of 1.0 N HCl was added to the test preparation under continuous stirring with a magnetic stirrer. The mixture was stirred precisely for 15 minutes following the acid addition. Immediately afterward, the excess hydrochloric acid was titrated with 0.5 N sodium hydroxide within 5 minutes, targeting a stable pH of 3.5, which was held for 10–15 seconds.

The milliequivalents (mEq) were calculated using the formula:

Total mEq = $(30 \times N_{HCl}) - (V_{NaOH} \times N_{NaOH})$

Where: N_{HCl} = normality of the hydrochloric acid VS

V_{NaOH} = volume of sodium hydroxide VS used during titration

N_{NaOH} = normality of the sodium hydroxide VS

If the sample's acid-neutralizing capacity exceeds 25 mEq, the procedure requires 60.0 mL of 1.0 N HCl, with the calculations adjusted accordingly.

Statistical analyses

Statistical analyses were performed using GraphPad Prism software, version 9. Group comparisons were assessed via one-way analysis of variance (ANOVA) with a significance level of $\alpha = 0.05$. Tukey's post hoc test was used to identify differences between groups, facilitating the detection of statistically significant variations while accounting for multiple comparisons.

RESULTS AND DISCUSSION

Raft forming characteristics

The ability of a raft-forming formulation to rapidly develop a stable, cohesive raft structure is a critical performance attribute. Raft forming characteristics refer to the ability of certain substances to create a gelatinous layer on the surface of gastric contents, thereby relieving symptoms such as heartburn and acid reflux. This mechanism is primarily utilized in alginate-based antacid formulations designed to alleviate gastrointestinal discomfort. The process involves the dissolution of calcium carbonate and the subsequent release of calcium ion and carbon dioxide gas into the gastric fluid. The calcium ions interact with alginate to form a cross-linked gel, while the carbon dioxide becomes entrapped within the gel matrix. When the formulation encounters an acidic environment, the mixture initially sinks to the bottom of the medium; as carbon dioxide is generated, the gel becomes buoyant and rises to the surface, forming a floating raft.[12, 13] The characteristics of raft formation, including raft-forming pattern and speed, flotation, floating lag time, and coherence, are summarized in Table 1. The raft formation speed of REF, S1, and S2 was immediate, whereas S3 and S4 exhibited a non-immediate formation rate. Complete flotation to the surface was observed for REF, S1, and S4, while S2 and S3 demonstrated only partial flotation. Compared to REF (0.40 min), S1, S2, and S3 exhibited significantly longer floating lag times ($p < 0.05$), while S4 showed the longest lag time (6.30 min, $p < 0.01$). Good coherence was observed in REF, S1, and S2, whereas S3 and

Table 1. Raft forming characteristics of five commercially available alginate-based antacid products in Thailand

Sample	Raft-forming pattern	Raft formation speed	Raft floatation	Floating lag time	Coherence	Palatability attribute
REF	The raft dispersed into a medium-sized gel, forming a fast raft that floated onto the surface of the media.	**Immediate**	**Complete**	**0.40 min**	**Good**	Peppermint Flavor, mild salty taste, moderately viscous
S1	The raft swiftly dispersed into fine-to-medium sized gel, forming the fastest raft that floated onto the surface of the media.	**Immediate**	**Complete**	**1.30 min**	**Good**	Raspberry Flavor, mild salty taste, moderately viscous
S2	The raft dispersed into fine-to-medium sized gel, forming fast raft that floated onto the surface of the media.	**Immediate**	Partial	**1.01 min**	**Good**	Peppermint Flavor, mild salty, moderately viscous
S3	The raft swiftly dispersed into a fine gel, then aggregated at the bottom to form raft. The formed raft floated as a whole onto the surface.	Non-immediate	Partial	1.26 min, 17.30 min*	Poor	Mint Flavor, mild salty, moderately viscous
S4	The product was difficult to disperse into the media and forms large gel particles at a medium rate, creating a raft that floats onto the surface of the media.	Non-immediate	**Complete**	6.30 min	Poor	Mint Flavor, mild salty, highly viscous

Note: *At 1.26 minutes, all rafts floated; however, the floated raft showed instability, resulting in the gel leg dripping down to the container bottom. At 17.30 minutes, the dropped gel leg re-formed the raft and floated to the media surface.

S4 displayed visibly weaker cohesion and poorer raft integrity. Formulations containing higher alginate content and calcium-based antacids tend to exhibit faster raft formation and better raft integrity. Conversely, Takbirgou reported that sodium alginate and sodium bicarbonate concentrations play crucial roles in determining floating lag time; an increased amount of alginate results in a heavier gel, which requires more time to achieve buoyancy[14].

The observed differences among products may be attributed to variations in raft-forming patterns. REF, S1, and S2 rapidly dispersed into fine- to medium-sized gels that immediately floated to the surface, forming aggregated rafts with good coherence and complete flotation. In contrast, S3 dispersed into very fine-sized gels, that likely trapped insufficient air, causing the gel to initially sink before eventually floating. S4, due to its higher viscosity, dispersed less readily, leading to incomplete gel formation and a delayed flotation time. A uniform and well-formed raft enhances the barrier against acid reflux and ensures prolonged contact with the gastric mucosa for sustained protection.

The present findings align with prior work on commercial alginate–antacid products, which demonstrated that rapid raft formation and adequate raft strength are crucial for neutralizing the acid pocket and preventing reflux[15,16]. From a clinical perspective, these differences in raft-forming characteristics are meaningful. Products exhibiting faster raft formation, complete flotation, and strong coherence are more likely to effectively cover the acid pocket, a key site implicated in GERD symptoms[15,16]. Rapid raft formation and stable flotation enable timely symptom relief, while strong raft integrity enhance resistance to gastric motility, maintaining the raft's position for prolonged therapeutic action. Larger raft volume ensures wider gastric coverage and more effective protection of the esophageal mucosa. Consequently, formulations such as REF, S1, and S2, which demonstrated favorable raft-forming profiles, may provide superior clinical efficacy in managing GERD compared with S3 and S4.

Raft tensile strength

Raft strength is a key parameter used in quality control to ensure batch-to-batch consistency of raft-forming products. It reflects the ability of a raft to resist disintegration in the acidic gastric environment and to withstand gastric motility and reflux forces, thereby maintaining adherence to the stomach lining for sustained symptom relief. In essence, this property mimics the in vivo resistance of raft systems to mechanical deformation. The measured tensile strength depends not only on the mechanical strength of the gel but also on its viscosity and the surface tension of the surrounding medium[6]. The inherent raft strength is produced by the crosslink between calcium ion and alginate carboxylate salt to form a typical eggbox structure that stabilizes the raft network[11,17,18]. The raft strength results for all five formulations, based on three replications, are presented in Table 2 and illustrated in Figure 1. Among the tested products, S3 exhibited significantly higher raft tensile strength than all other formulations ($p < 0.001$) while other products were comparable with REF (15.79 ± 2.70 g) ($p > 0.05$). However, the notably high raft strength of S3 was attributed to the L-shaped wire probe lifting the entire raft rather than passing through it, resulting in disproportionately high raft strength reading that are not directly comparable to other formulations. The issue with S3 product likely stemmed from inadequate adhesion to the container surface, which may translate clinically to reduced adherence to the gastric or esophageal mucosa and consequently diminished anti-reflux efficacy.

When S3 was excluded, the raft strength of the remaining formulations ranged from 13.335 ± 0.760 g for S4 to 18.041

Table 2. Raft tensile strength of five commercially available alginate-based antacid products in Thailand.

Raft tensile strength (g)				
Sample	**Replication 1**	**Replication 2**	**Replication 3**	**Average (SD)**
REF	18.827	13.667	14.877	15.790 (2.699)
S1	15.9	21.105	17.117	18.041 (2.723)
S2	15.559	12.533	16.418	14.837 (2.041)
S3	29.735	30.612	29.213	29.876 (0.677)
S4	14.206	12.808	12.992	13.335 (0.760)

± 2.723 g for S1, which no statistically significant differences observed between these formulations and REF ($p > 0.05$), indicating comparable mechanical performance. A correlation exists between raft tensile strength and raft resilience, defined as the ability to resist break-up due to stomach and esophageal motility. Accordingly, S1, which demonstrated the highest tensile strength among comparable products, may offer a longer-lasting acid barrier and greater clinical benefit in reducing reflux frequency. Importantly, all formulations exceeded the minimum raft strength requirement of 7.5 g specified by the British Pharmacopoeia (BP)[19]. Hampson et al. reported that raft strength varies by alginate source, ranging from 4.0 g in *Durvillaea antarctica* to 12.1 g in *Laminaria hyperborea*[9]. Higher concentrations and molecular weights of polymers used generally result in stronger rafts that can withstand the peristaltic forces of the stomach. A higher proportion of guluronic acid (G-block) units in sodium alginate and greater calcium carbonate content enhance strength by promoting denser cross-linking within the alginate network[12,20,21]. Conversely, the inclusion of aluminum ions or HPMC may disrupt gel structure and reduce strength[22]. Additionally, raft components, meal components and media pH also influence raft properties[8]. Clinically, greater raft tensile strength indicates a more stable barrier capable of resisting disruption by gastric contractions and reflux pressure, , maintaining continuous protection at the gastroesophageal junction. Consequently, patients using formulations with stronger rafts may experience longer-lasting symptom relief and improved esophageal protection.

Raft volume and raft weight

Raft volume and weight are important parameters for formulation optimization, reflecting the physical characteristics and potential performance of alginate raft systems. Both properties can influence the product's clinical efficacy, as a larger raft volume provides broader coverage of the gastric mucosa and a more stable floating barrier against reflux. Raft volume and weight could also have an influence on raft strength[9,23]. The results for all samples are presented in Table 3 and illustrated in Figure 2. Compared with REF (45.42 ± 3.61 g), the raft weights of S1–S4 did not differ significantly ($p > 0.05$). Raft volumes, calculated using the previously described formula, ranged from

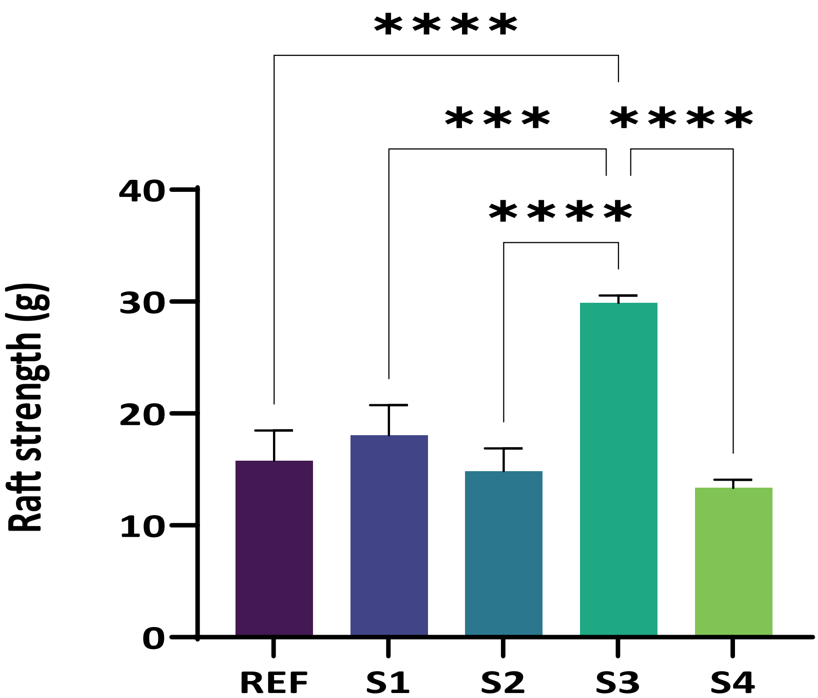


Figure 1. Raft tensile strength (g) of five commercially available alginate-based antacid products in Thailand
*(*** p < 0.001, **** p < 0.0001)*

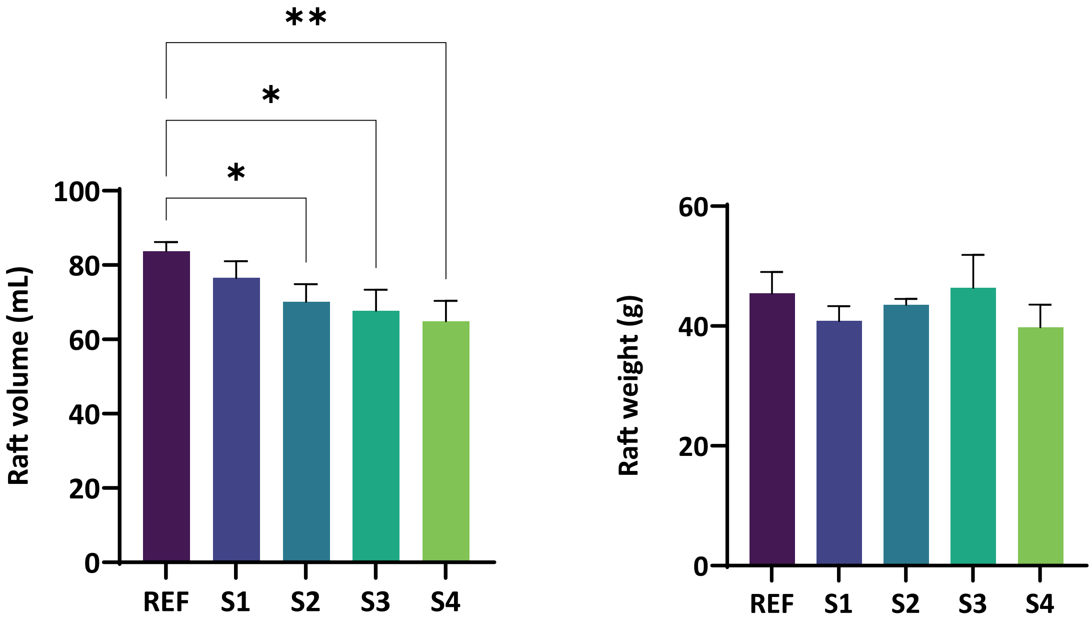


Figure 2. Raft volume and raft weight of five commercially available alginate-based antacid products in Thailand *(* $p < 0.05$, ** $p < 0.005$)*

Table 3. Raft volume and raft weight of five commercially available alginate-based antacid products in Thailand

Sample	Replication	W1 (g)	W2 (g)	W3 (g)	W4 (g)	Calculated raft volume (mL)	Average raft volume (SD) (mL)	Average raft weight (SD) (g)
REF	1	106.59	272.67	49.57	309.46	86.36	83.76 (2.41)	45.42 (3.61)
	2	109.17	278.25	43.69	316.17	81.61		
	3	109.22	279.71	43.01	320.01	83.31		
S1	1	109.51	270.68	41.78	301.54	72.64	76.56 (4.49)	40.82 (2.53)
	2	103.29	275.69	42.72	308.56	75.59		
	3	107.02	272.98	37.95	316.49	81.46		
S2	1	112.51	290.96	42.76	319.03	70.83	70.14 (4.73)	43.51 (1.04)
	2	106.9	273.27	44.69	303.06	74.48		
	3	107.01	278.72	43.07	300.75	65.1		
S3	1	105.56	274.15	49.42	297.49	72.76	67.71 (5.64)	46.39 (5.47)
	2	106.89	271.44	40.08	300.1	68.74		
	3	112.24	285.28	49.67	297.23	61.62		
S4	1	112.5	279.99	37.95	300.68	58.64	64.85 (5.55)	39.78 (3.81)
	2	112.73	283.03	37.22	312.41	66.6		
	3	107.02	279.42	44.16	304.58	69.32		

64.85 ± 5.55 mL to 83.76 ± 2.41 mL. Compared with REF (83.76 ± 2.41 mL), S2–S4 showed significantly smaller volumes ($p < 0.05$), whereas S1 showed no significant difference ($p > 0.05$).

An increase in raft weight and volume generally correlates with improved floatability[23]. The superior flotation performance of REF and S1, which demonstrated both higher raft weights and volumes. Interestingly, despite S4 exhibiting the lowest raft weight and volume, it still achieved complete flotation, suggesting that other factors, such as viscosity, bubble entrapment, or gel elasticity, may also influence buoyancy. Larger and heavier rafts tend to provide better coverage of gastric contents, promoting the formation of a continuous floating layer that minimizes reflux exposure. This feature likely enhances clinical efficacy in suppressing heartburn and regurgitation. However, excessive raft density may delay flotation and the onset of symptom relief, emphasizing the importance of achieving an optimal balance between raft strength and buoyancy during formulation design.

Raft morphology

Raft morphology, characterized by its uniformity and porosity, determines its ability to maintain structural integrity under acidic conditions. The generation and entrapment of CO_2 during formation create hollow regions within the raft structure, producing distinct morphological characteristics for each product[24,25]. The SEM images of all samples revealed structural differences, as illustrated in Figure 3, with notably higher levels of porosity observed in REF and S1, which corresponded to their excellent flotation profiles.

These variations in morphology may also influence the buoyancy and stability of the rafts, potentially affecting their clinical performance in managing reflux. The porous and absorbent nature of rafts could play a role in retaining their ANC probably due to release of trapped antacids. Further investigation is warranted to better understand the impact of these morphological differences on therapeutic efficacy.

Raft neutralization profile

Evaluating the raft acid neutralization capacity demonstrates how effectively the rafts maintain their antacid barrier properties within their structure and prevent further damage to the esophagus[18]. Figure 5 and Table 5 illustrate the raft neutralization duration of various products, defined as the time during which the raft maintains pH > 4 in the test. The REF formulation exhibited a neutralization duration of 24.00 ± 8 minutes, which served as the reference standard. The rafts of the other formulations showed longer neutralization durations, suggesting comparable or enhanced buffering capacity and acid neutralizing potential. However, the differences in average neutralization durations among all five formulations were not statistically significant when compared to REF ($p > 0.05$).

Despite containing common antacid ingredients in identical amounts, the variations in alginate source, alginate specifications, and unique additional components in each formulation influence the neutralization profiles. These differences arise due to variations in the raft microstructure, which affect liquid permeability, diffusion, and the rate of acid penetration. When acidic environments interact with the raft, they engage with entrapped antacid components, altering the duration and consistency of neutralization[11,25]. These findings highlight the interplay between raft composition and structure in determining the effectiveness of acid neutralization. Clinically, a formulation capable of maintaining pH > 4 for a prolonged period offers extended mucosal protection and symptom relief, even in the presence of ongoing gastric acid secretion

Acid neutralizing capacity (ANC) of the products

Each product possesses an intrinsic acid neutralizing capacity (ANC) determined by its antacid content, which acts immediately upon ingestion to neutralize the acid pocket at the gastroesophageal junction. A portion of the antacid, however, becomes entrapped within the raft matrix during formation, contributing to sustained neutralization over time[25,26]. The ANC values for all formulations are summarized in Table 4. Compared with REF (9.56 ± 0.23 mEq), S1 exhibited a slightly lower ANC (8.76 ± 0.12 mEq, $p < 0.05$), whereas S2–S4 showed comparable or marginally higher ANC values ($p > 0.05$). Despite these variations (Figure 4), all samples met the minimum ANC requirement of no less than 5 mEq per dose, as specified by the U.S. FDA, confirming compliance with regulatory standards for antacid efficacy[27].

While ANC reflects a formulation's ability to neutralize gastric acid, its clinical significance in alginate-based antireflux therapies is limited. In these systems, pH neutralization plays a supportive rather than a primary role, as the dominant therapeutic mechanism arises from the formation of a cohesive raft that prevents reflux of gastric contents into the esophagus[6,7]. This is particularly important because GERD in some patients may not always be associated with highly acidic gastric contents. Additionally, other causes, such as bile or nonacidic reflux, have been implicated in the pathophysiology of GERD[28,29].

Nevertheless, adequate ANC remains important for rapid pH normalization in the acid pocket, particularly in patients with acid-sensitive esophageal mucosa. Maintaining pH above 4.0 enhances mucosal protection and provides symptomatic relief. Therefore, ANC and raft integrity act synergistically—the buffering effect offers immediate acid suppression, while the raft structure provides sustained mechanical protection, together achieving comprehensive reflux control.

CONCLUSION

This study evaluated the characteristics of five alginate-based raft-forming antacid products available on the market. Although each product label specifies the same doses of core raft-forming components—sodium alginate, sodium bicarbonate, and calcium carbonate—these alone do not reliably predict product performance. The results indicate that additional excipients play a substantial role in influencing raft structure and stability, leading to observed differences among products. Formulation variations, raw material sourcing, and batch-to-batch inconsistencies likely also impact performance. While this study focused on products available in Thailand, similar variability may be present internationally. The methods used here aim to stimulate further research into product effectiveness and offer valuable testing protocols for future studies on alginate-based raft-forming antacids. Standardizing testing methods for these products would enhance understanding of their performance and support consistent quality across different formulations and brands. Understanding raft characteristics and ANC profiles could empower pharmacists to make informed recommendations, providing patients with improved symptom relief and management.

AUTHORS' CONTRIBUTIONS

Peerawas Kopongpanich-methodology, formal analysis, investigation, data curation, validation, writing (original draft preparation), writing (review and editing), visualization ;

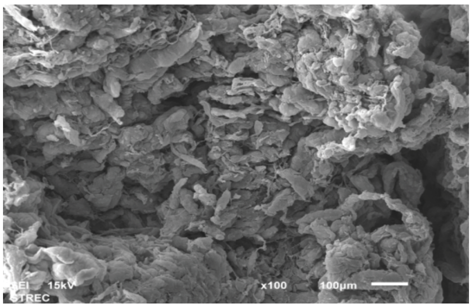
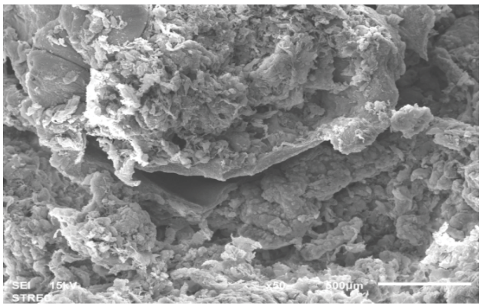
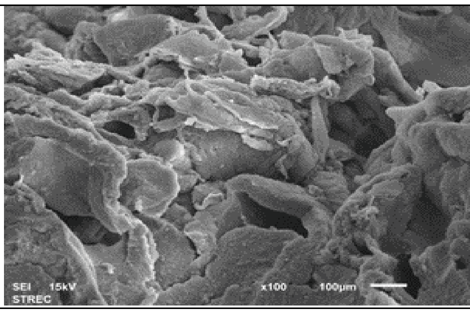
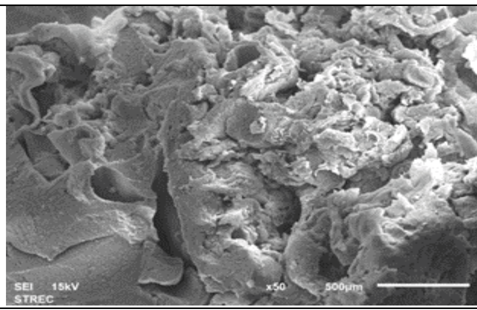
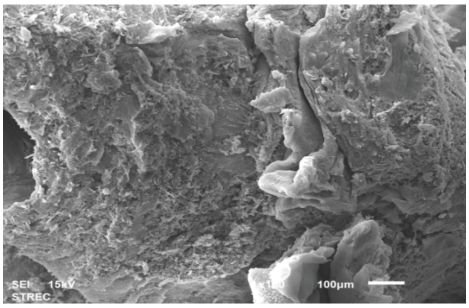
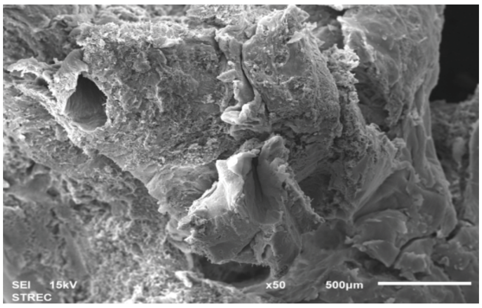
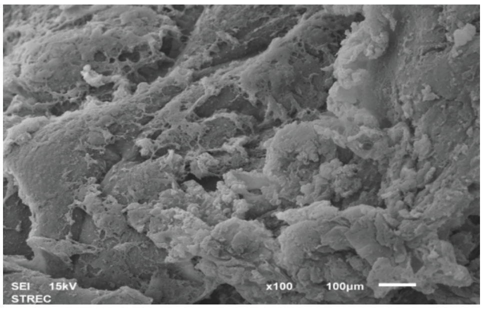
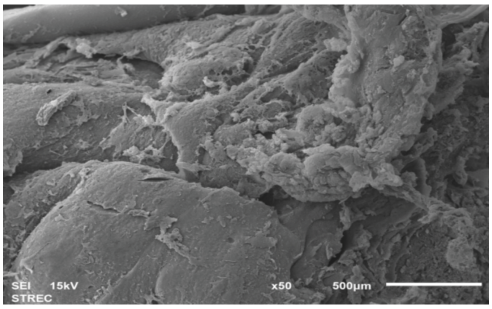
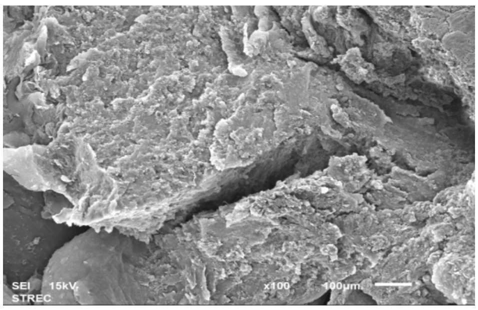
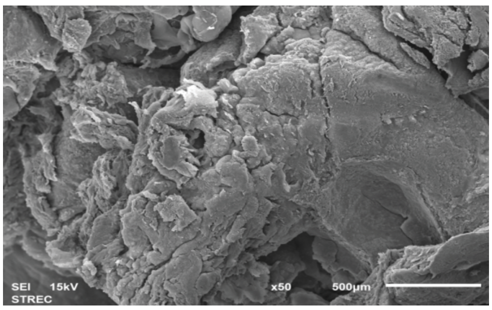
Sample	**x100**	**x50**
REF		
S1		
S2		
S3		
S4		

Figure 3. SEM images of rafts of five commercially available alginate-based antacid products in Thailand.

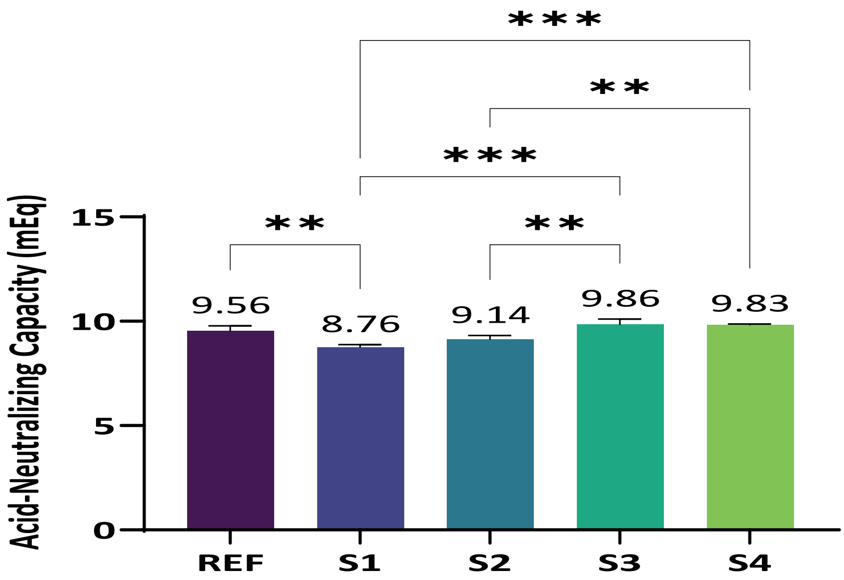


Figure 4. Acid neutralizing capacity (ANC) of five commercially available alginate-based antacid products in Thailand.
*(** p < 0.005, *** p < 0.001)*

Table 4. Acid Neutralizing Capacity (ANC) of five commercially available alginate-based antacid products in Thailand

Acid neutralizing capacity (mEq)				
Sample	**Replication 1**	**Replication 1**	**Replication 1**	**Average (SD)**
REF	9.4	9.82	9.45	9.56 (0.23)
S1	8.9	8.66	8.73	8.76 (0.12)
S2	8.94	9.22	9.27	9.14 (0.18)
S3	9.71	9.73	10.15	9.86 (0.25)
S4	9.82	9.87	9.8	9.83 (0.04)

Table 5. Raft neutralization duration of five commercially available alginate-based antacid products in Thailand

Sample	**Average duration of raft neutralization (SD) (min)**
REF	24 (8)
S1	32 (14.97)
S2	41.6 (18.24)
S3	46.4 (15.39)
S4	41.6 (14.31)

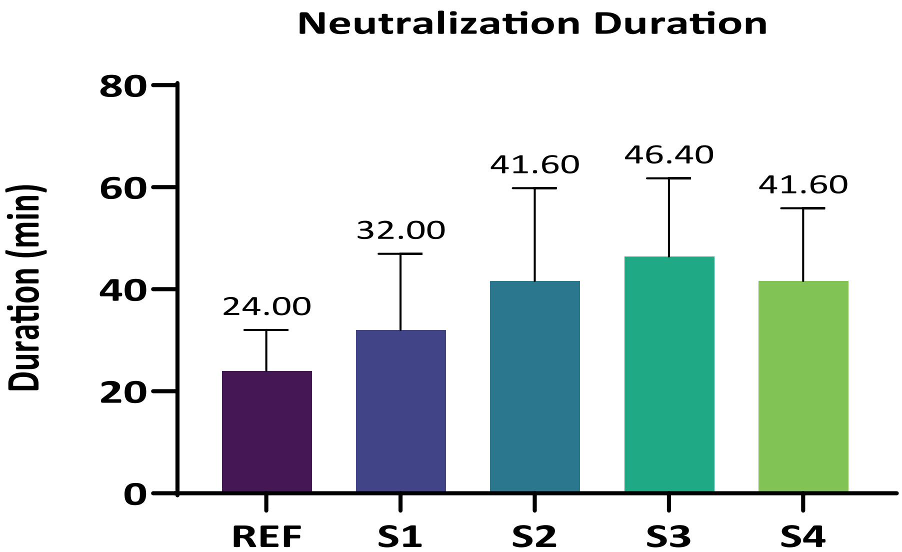


Figure 5. Raft neutralization duration of five commercially available alginate-based antacid products in Thailand.

Sarunrus Senasuthum-formal analysis, investigation, resources, writing (review and editing); Tanet Promnim-formal analysis, investigation; Takao Hayashi-formal analysis, investigation, data curation; Kengo Wada-formal analysis, investigation, data curation; Pakorn Suriyakriangkai-investigation, writing (original draft preparation); Worathat Thitikornpong-investigation, validation, writing (review and editing), supervision; Varin Titapiwatanakun-conceptualization, methodology, resources, writing (original draft preparation), writing (review and editing), supervision, project administration; Kitiyot Yotsombut-conceptualization, methodology, validation, resources, writing (original draft preparation), writing (review and editing), supervision, project administration, funding acquisition

All authors have read and agreed to the published version of the manuscript.

CONFLICTS OF INTERESTS

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

References

1. Kazakova T, Danoff R, Esteva I, Shchurin A. Gastro-esophageal reflux disease in primary care practice: a narrative review. Ann Esophagus. 2023;6(25):1-11. doi: 10.21037/aoe-21-62.
2. Belete M, Tesfaye W, Akalu Y, Adane A, Yeshaw Y. Gastroesophageal reflux disease symptoms and associated factors among university students in Amhara region, Ethiopia, 2021: a cross-sectional study. BMC Gastroenterol. 2023;23(1):130. doi: 10.1186/s12876-023-02758-8.
3. Maret-Ouda J, Markar SR, Lagergren J. Gastroesophageal reflux disease: a review. JAMA. 2020;324(24):2536-47. doi: 10.1001/jama.2020.21360.
4. Fass R, Frazier R. The role of dexlansoprazole modified-release in the management of gastroesophageal reflux disease. Therap Adv Gastroenterol. 2017;10(2):243-51. doi: 10.1177/1756283x16681701.
5. Hampson FC, Jolliffe IG, Bakhtyari A, Taylor G, Sykes J, Johnstone LM, et al. Alginate–antacid combinations: raft formation and gastric retention studies. Drug Dev Ind Pharm. 2010;36(5):614-23. doi: 10.3109/03639040903388290.
6. Kapadia CJ, Mane VB. Raft-forming agents: antireflux formulations. Drug Dev Ind Pharm. 2007;33(12):1350-61. doi: 10.1080/03639040701385691.
7. Mandel KG, Daggy BP, Brodie DA, Jacoby HI. Review article: alginate-raft formulations in the treatment of heartburn and acid reflux. Aliment Pharmacol Ther. 2000;14(6):669-90. doi: 10.1046/j.1365-2036.2000.00759.x.
8. Keppler S, Mannara G, Marra F, Bornhorst GM. Characterization of raft-forming alginate suspensions formed in HCl or model food systems at varying pH levels to better simulate gastric postprandial conditions. Drug Dev Ind Pharm. 2021;47(7):1079-89. doi: 10.1080/03639045.2021.1954940.
9. 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. doi: 10.1016/j.ijpharm.2005.01.036.
10. Yousaf M, Nirwan JS, Smith AM, Timmins P, Conway BR, Ghori MU. Raft-forming polysaccharides for the treatment of gastroesophageal reflux disease (GORD): Systematic review. J Appl Polym Sci. 2019;136(40):48012. doi: 10.1002/app.48012.
11. Savla HM, Naik IV, Gargote C, Shashidhar N, Nair S, Menon MD. Physicochemical properties of various alginate-based raft-forming antacid products: a comparative study. Int J Basic Clin Pharmacol. 2021;10(12):1330-41. doi: 10.18203/2319-2003.ijbcp20214449.
12. Kerdsakundee N, Mahattanadul S, Wiwattanapatapee R. Development and evaluation of gastroretentive raft forming systems incorporating curcumin-Eudragit® EPO solid dispersions for gastric ulcer treatment. Eur J Pharm Biopharm. 2015;94:513-20. doi: 10.1016/j.ejpb.2015.06.024.
13. Munusamy R, Shanmugasundharam S. Enhanced gastric residence time of acyclovir by floating raft formulation using box-behnken design. Heliyon. 2024;10(2):e24301. doi: 10.1016/j.heliyon.2024.e24301.
14. 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. doi: 10.1016/j.ijbiomac.2023.128686.
15. Rohof WO, Bennink RJ, Smout AJ, Thomas E, Boeckxstaens GE. An alginate-antacid formulation localizes to the acid pocket to reduce acid reflux in patients with gastroesophageal reflux disease. Clin Gastroenterol Hepatol. 2013;11(12):1585-91; quiz e90. doi: 10.1016/j.cgh.2013.04.046.
16. Kwiatek MA, Roman S, Fareeduddin A, Pandolfino JE, Kahrilas PJ. An alginate-antacid formulation (Gaviscon Double Action Liquid) can eliminate or displace the postprandial 'acid pocket' in symptomatic GERD patients. Aliment Pharmacol Ther. 2011;34(1):59-66. doi: 10.1111/j.1365-2036.2011.04678.x.
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. doi: 10.1016/j.heliyon.2024.e31803.
18. Kamandloo F, Salami M, Ghamari F, Ghaffari S-B, EmamDjomeh Z, Ghasemi A, et al. Development and evaluation of anti-reflux functional-oral suspension raft composed of sodium alginate-mung bean protein complex. Int J Biol Macromol.

2024;256:128490. doi: 10.1016/j.ijbiomac.2023.128490.
19. British Pharmacopoeia Commission. Alginate Raft-forming Oral Suspension. British Pharmacopoeia 2023: volume III. London: TSO; 2023.
20. Darwish MKM, Abu El-Enin ASM, Mohammed KHA. Formulation, optimization, and evaluation of raft-forming formulations containing Nizatidine. Drug Dev Ind Pharm. 2019;45(4):651-63. doi: 10.1080/03639045.2019.1569033.
21. Wannasarit S, Mahattanadul S, Issarachot O, Puttarak P, Wiwattanapatapee R. Raft-forming gastro-retentive formulations based on Centella asiatica extract-solid dispersions for gastric ulcer treatment. Eur J Pharm Sci. 2020;143:105204. doi: 10.1016/j.ejps.2019.105204.
22. 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. doi: 10.1016/j.jsps.2021.08.005.
23. Malivindi R, Patitucci F, Prete S, Dattilo M, Leonetti AE, Scigliano N, et al. Efficacy and safety assessment of PIMIN050 raft-forming system as medical device based on Citrus sinensis and Crassostrea gigas for the management of gastroesophageal reflux disease. J Drug Deliv Sci Technol. 2022;78:103986. doi: 10.1016/j.jddst.2022.103986.
24. Abbas G, Hanif M, Khan MA. pH responsive alginate polymeric rafts for controlled drug release by using box behnken response surface design. Des Monomers Polym. 2017;20(1):1-9. doi: 10.1080/15685551.2016.1231046.
25. Moazen M, Shafaghi A, Ebrahimi-Najafabadi H, Ghasemi S, Ashoobi MT, Manoochehri S. Optimization of pH-sensitive ingredients and characterization of raft-forming alginate-based oral suspensions as reflux suppressant. J Drug Deliv Sci Technol. 2022;68:103124. doi: 10.1016/j.jddst.2022.103124.
26. Dettmar PW, Gil-Gonzalez D, Fisher J, Flint L, Rainforth D, Moreno-Herrera A, et al. A comparative study on the raft chemical properties of various alginate antacid raft-forming products. Drug Dev Ind Pharm. 2018;44(1):30-9. Epub 20170913. doi: 10.1080/03639045.2017.1371737.
27. Ayensu I, Bekoe SO, Adu JK, Brobbey AA, Appiah E. Evaluation of acid neutralizing and buffering capacities of selected antacids in Ghana. Sci Afr. 2020;8:e00347. doi: 10.1016/j.sciaf.2020.e00347.
28. Richter JE. Role of the gastric refluxate in gastroesophageal reflux disease: acid, weak acid and bile. Am J Med Sci. 2009;338(2):89-95. doi: 10.1097/MAJ.0b013e3181ad584a.
29. Storr MA. What is nonacid reflux disease? Can J Gastroenterol. 2011;25(1):35-8. doi: 10.1155/2011/626752.