RESEARCH ARTICLE

Comparative Evaluation of Raft Strength and Thickness in Calcium-Based Alginate Formulations for Gastroesophageal Reflux Disease (GERD) Management

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ABSTRACT

One common gastrointestinal ailment that has a main effect on patients' quality of life is GERD. Raft-forming alginate-based formulations provide a physical barrier against acid reflux, with their efficacy largely dependent on raft strength and thickness. This study aimed to associate raft strength and thickness of six commercially available calcium-based alginate formulations in India to assess their potential effectiveness in GERD management. The study examined six different formulations of antacids that contained sodium alginate (250 mg/5 mL), calcium carbonate (80 mg/5 mL), and sodium bicarbonate (133.5 mg/5 mL): GaviRaft®, InstaRaft®, RanRaft®, RACIRAFT™, Ranidom® RAFT, and ULGE-RAFT™. The modified balancing technique was used to evaluate the raft strength, and a calibrated Vernier caliper was used to quantify the raft thickness.Data were collected from three independent experiments. Among the tested formulations, only Ranidom® RAFT and RanRaft® met the British Pharmacopoeia (BP) standard for raft strength (≥7.5 g), indicating superior mechanical integrity. RanRaft® and GaviRaft® exhibited the highest raft thickness compared to other calcium-based alginate formulations, indicating their potential to form a strong physical barrier against reflux.All the formulations met the criteria for assay of sodium alginate as per BP (86-116%), except for Ranidom® RAFT (129.02%). The study found variations in raft strength and thickness among calcium-based alginate formulations, with RanRaft® achieving an optimal balance. These findings highlight the importance of formulation selection in GERD management. Clinical trials are desirable to authorize these *in-vitro* results and assess patient outcomes.

Keywords: Gastro Esophageal Reflux Disease, Calcium-based alginate formulations, Raft strength, Raft thickness, Acid Reflux Barrier

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INTRODUCTION

Symptoms of gastroesophageal reflux disease (GERD) contain indigestion, vomiting, chest pain, and discomfort, and the condition is defined by reflux of stomach substances into the esophagus[1]. Risk of esophageal cancer increases, and problems such as Barrett's esophagus and esophagitis can develop in cases with untreated chronic GERD. Patients' quality of life is greatly affected by GERD, even if the condition is not life-threatening[2]. It is one of the most prevalent conditions in gastroenterology, with prevalence rates in India ranging from 7.6% to 30%[3]. Among Indian states, Chennai has the highest prevalence (28.5%), while Pondicherry has the lowest (5.02%). The condition is somewhat more common in men than in women[4].

Current Treatment Approaches and Limitations

Tablets and liquid antacids, combinations of antacids and alginate, proton pump inhibitors, and histamine H2-receptor antagonists are some of the drugs used to manage acid reflux. While antacids do alleviate symptoms quickly, their effects wear off quickly[6,7]. Low magnesium and vitamin B12 levels, rebound acid production, and peril of diarrhea are some of the long-term hazards linked to proton pump inhibitors (PPIs), despite their great effectiveness.[8,9] Furthermore, PPIs might not work as well in certain people, especially those who have non-erosive reflux disease (NERD). Side effects such as lethargy, headache, and gastrointestinal issues are possible with H2RAs, despite their short-term usefulness. Moreover, regular use of H2RAs can lead to tachyphylaxis, limiting their long-term effectiveness[10]. Given these challenges, safer and more effective treatment options for GERD, particularly for PPI-refractory cases, are needed.

Raft-Forming Formulations in GERD Management

Raft-forming formulations offer a unique mechanism of action distinct from traditional antacids. The acidic contents of the stomach are able to stay out of the esophagus thanks to the protective barrier that these formulas establish a thick, gelatinous coating[11]. Some studies suggest that raft formation also eliminates acid pockets in the postprandial state[12].One of the most widely used raft-forming formulations is alginate-based, which has been available for nearly five decades. These formulations typically contain

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sodium alginate along with antacids. Upon contact by gastric acid, sodium alginate interacts with these antacids to form a buoyant, resilient raft that prevents acid reflux and protects the esophageal mucosa[13].

Clinical Evidence Supporting Alginate use

Sodium alginate has been suggested as a first-line treatment for GERD by various Asian and international guidelines[14,15]. Clinical studies have demonstrated its effectiveness across different GERD patient profiles:

Mild GERD Symptoms

Sodium alginate alone has been exposed to suggestively progress GERD symptoms, with studies indicating a fivefold increase in symptom resolution compared to placebo or traditional antacids.

GERD with Regurgitation and Heartburn

Alginate-antacid combinations have been effective in managing reflux symptoms. These formulations provide both rapid relief (due to antacid action) and prolonged symptom control (due to raft formation)[16].

PPI-Refractory GERD

Combining PPIs with alginates has shown beneficial effects in patients unresponsive to PPIs[17].

Use in Special Populations

Alginate-based formulations have been found safe for children and pregnant women[18].

Factors Affecting Raft Formation

Sodium alginate is derived from brown algae, and its raft-forming capacity depends on the species and the part of the seaweed used. Low molecular weight sodium alginates with high gel strength are considered ideal for forming effective reflux barriers. A study highlighted that interaction between sodium alginate and antacids significantly influences the physicochemical properties of the raft, impacting its efficacy in GERD management. Variations in alginate and antacid composition among different formulations lead to differences in raft formation, strength, and durability[19].

Expert Opinion and Market Insights

A recent expert opinion survey involving 48 Indian gastroenterologists emphasized raft strength as the most critical physicochemical characteristic, with 70% of respondents highlighting its role in efficacy. Additionally, raft thickness was recognized as a key marker of a strong physical barrier against reflux—thicker rafts being associated with better product performance[20].

Need for Comparative Analysis of Calcium-Based Alginate Formulations

Most *in-vitro* raft characterization studies have focused on evaluating physicochemical properties across various alginate-based formulations in India. However, while previous studies have compared alginate formulations containing aluminum- and magnesium-based antacids, there is limited literature specifically comparing calcium-based alginate formulations available in the Indian market.Given this gap, the present study aimed to assess raft strength and thickness in various calcium-based alginate formulations in India as key pointers of their *in-vivo* effectiveness.

MATERIALS AND METHODS

Materials

Table 1: Batch information and shelf life of the formulations evaluated

Product	Batch Number	Manufacturing date	Expiry date
GaviRaft®	GRS026	10/2024	09/2026
InstaRaft®	LNB0174	11/2024	10/2026
RanRaft®	ZSRF25002	01/2025	12/2026
RACIRAFT™	LNB0167	10/2024	09/2026
Ranidom® RAFT	C1APX052	10/2024	03/2026
ULGE-RAFT™	GH4921029	10/2024	09/2026

Six calcium-based alginate formulations from different brands (GaviRaft®, InstaRaft®, RanRaft®, RACIRAFT™, Ranidom® RAFT, and ULGE-RAFT™) were assessed in this study. These products were comparable in composition, with each containing sodium alginate (250 mg/5 mL), along with calcium carbonate (80 mg/5 mL) and sodium bicarbonate (133.5 mg/5 mL) as antacids. Recommended dosage for all seven products, as stated on their labels, was 10–20 mL after meals. Therefore, the maximum dose was considered to be 20 mL per product, equivalent to 1000 mg of sodium alginate, 534 mg of sodium bicarbonate, and 320 mg of calcium carbonate. All of these formulations were obtained from a local medical store. Formulation details are listed in Table 1. All reagents used were of analytical grade.

Methods

Determination of Raft Strength

In order to determine the raft's strength, the modified balancing technique was employed. During the maturation phase, the rafts were allowed to grow and mature in 250 ml glass beakers that were fitted with an L-shaped wire probe. The dimensions of the probe were 1 mm in diameter, 9 cm in length, and 2 cm in horizontal arm length. The probe was kept upright in the beaker's center axis.[21]

Next, one scale of the modified pan balance was connected to the wire probe along with the beaker and raft.. We tested the raft's stability by slowly pouring water over the other side of the balance until it sank for each parameter, the presented data are the average of three separate tests.The Raft strength of each product, as per British Pharmacopeia (BP), was expected to be atleast 7.5 grams[22].

Determination of Raft Thickness

For every product that was tested, a calibrated Vernier caliper was used to measure the raft's thickness from the top and bottom indicated spots on all four corners of the beaker. The results were recorded in millimeters (mm). Each parameter's presented data are based on three separate studies.

Sodium Alginate Content

The experiment relied on an established approach that is based on high-performance liquid chromatography (HPLC). Our HPLC system was designed with a Dionex P100 series quaternary pump, UV detector, and autosampler in mind. For chromatographic peak separation, the Hi-Qsil column (3 µm, 250 mm × 4.6 mm) was utilized. Thermo Fisher Scientific Inc. of Waltham, MA created and maintains Chromeleon, which was utilized for data analysis. The software version was 6.80. In 1000 ml of deionized water, 0.05% orthophosphoric acid was added to produce the mobile phase. After 0.1 N NaOH was used to

bring the pH level down to 7.0, a 0.45 µ membrane filter (PALL) was used to filter the solution. A volumetric flask was used to dissolve 50 mg of alginate standard in 30 ml of deionized water using sonication. The remaining capacity was filled to 50 ml by deionized water to create the working standard. Chromatograms were obtained after injecting the working standard solution and the blank mobile phase into the HPLC apparatus. 0.7 ml/minute flow rate was used to conduct isocratic elution using a 100% buffer solution. There was a 20 µl injection volume and a 200 nm detecting wavelength.

Six injections of a standard solution of alginate (500 ppm in diluent) were used to confirm that the system was suitable. All six injections were to have a relative standard deviation of no more than 2%. The linearity was confirmed by duplicate analysis of six distinct alginate standard concentrations and the plotting of an area versus concentration linearity graph. At least 0.995 was required for the correlation coefficient.

There were three separate analyses of the items' sodium alginate content. After 30 minutes of sonication, 5 ml of the raft-forming formulation was combined with 200 ml of deionized water in a 250 ml volumetric flask. The volume was raised to 250 ml with deionized water following centrifugation at 4000 rpm for 5 minutes after chilling. The supernatant was tested using the HPLC method that was previously described, following its filtration via a 0.22 µm syringe filter. Each sample's sodium alginate concentration was determined using the standard graph's linear equation (R2>0.995).

The following equation was used to determine the sodium alginate percentage for each product:

$$\% \text{ assay of sodium alginate} = [X\ (mg/ml)\ x\ 250\ ml\ x\ Dilution\ factor\ x\ 100]/LC \ldots (1)$$

The label claim is given in milligrams of sodium alginate per five milliliters of solution, and X represents the milligrams per milliliter of sodium alginate content in each sample. British Pharmacopeia (BP) estimated that, for each product, the proportion of sodium alginate would vary from 85.0% to 115% of the indicated quantity.

RESULTS

Raft Strength

At their highest dosages, Figure 1 shows the raft strengths of the six products. Only RanRaft® (7.5 g) and Ranidom® RAFT (8.9 g) rafts met BP requirement of having a mean raft strength of by least 7.5 g.

Raft Thickness

Figure 2 shows the raft thickness for each of the six products when used at their highest dosages.The raft thickness of RanRaft® (25 mm) and GaviRaft® (25 mm) was the highest among all the formulations.

Sodium Alginate Content

Figure 3 displays the sodium alginate content for each of the six items as it appears on their labels. All of the formulations with the exception of Ranidom® RAFT had sodium alginate contents that were within the specified range (84-116%).The content was found to be >116% for Ranidom® RAFT. The sodium alginate content of RanRaft® (100.24%) was closest to 100%, followed by RACIRAFT™ (102.91%) and GaviRaft® (105.73%).

DISCUSSION

There is a lot of evidence that raft-forming formulations based on alginate can alleviate GERD symptoms. The rafts' strength is determined in large part by the antacid components. In contrast to antacids made of aluminum or magnesium, the rafts created by the calcium ions in this formulation crosslink with the alginate salts to create the

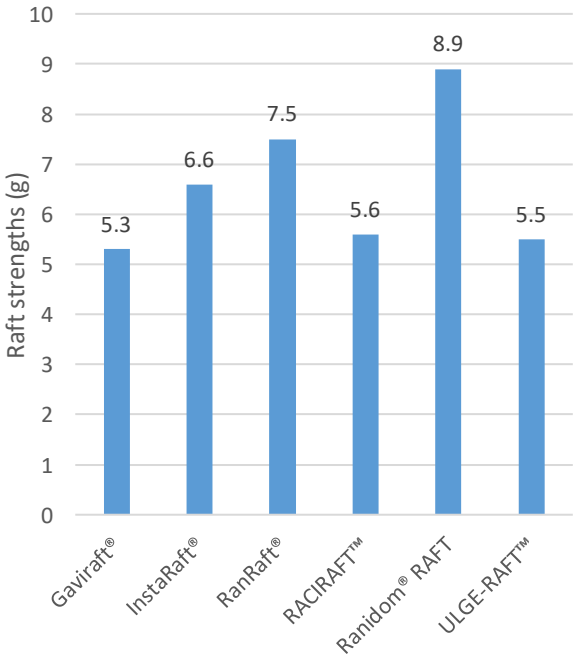

Figure 1: Raft strengths of various marketed calcium-based alginate formulations

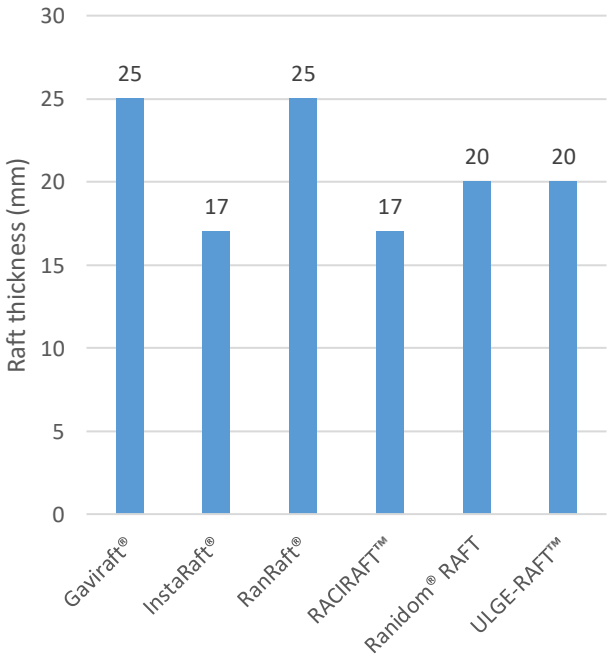

Figure 2: Raft thickness of various marketed calcium-based alginate formulations

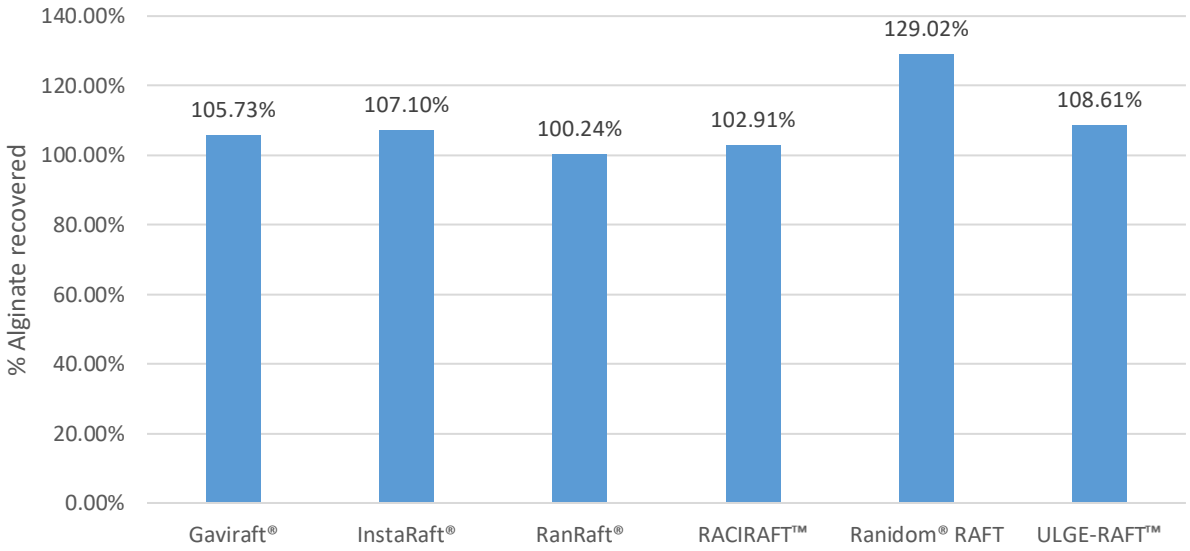

Figure 3: Sodium alginate content of various marketed calcium-based alginate

distinctive egg-box structure.[23] This study focused on the *in vitro* assessment of raft strength and thickness in various calcium-based alginate formulations available in the Indian market. These properties are key determinants of efficacy, as they influence buoyancy, durability, and acid-blocking capability, ensuring effective protection against gastric reflux.

Raft strength plays a vital role in determining mechanical integrity of barrier. A strong raft is expected to resist breakage under gastric conditions, thereby providing longer-lasting protection against reflux. The BP specification requires a minimum raft strength of 7.5 g for an effective formulation[24]. The results from this study showed that among the six tested formulations, only Ranidom® RAFT and RanRaft® met this requirement, indicating their potential superiority in sustaining raft integrity. The strength of the raft alsoplays a vital role in avoiding acid breakthroughs, particularly in patients with severe GERD. A weaker raft may disintegrate prematurely, reducing its ability to provide consistent relief from reflux symptoms. Additionally, the gel network formed by sodium alginate must be stable enough to withstand peristaltic and gastric movements, further emphasizing the importance of robust raft strength. The stability of the raft is also dependent on environmental features like gastric pH, enzymatic activity, and the presence of bile salts, all of which can influence raft cohesion and longevity[25].

Raft thickness serves as a quantitative marker of the physical blockade provided by the formulation. A thicker raft is believed to cover a larger surface area, leading to enhanced reflux prevention. The results indicated that RanRaft® and GaviRaft® exhibited the highest raft thickness compared to other formulations.Thicker rafts may also contribute to prolonged symptom relief by extending the duration of acid suppression. This can be particularly beneficial for nocturnal GERD, where reflux episodes occur during sleep, increasing the risk of Esophageal damage. Additionally, variations in raft thickness among formulations may be attributed to differences in sodium alginate molecular weight and viscosity, which affect the gelation process and overall raft expansion. The ability of a raft to maintain thickness over time is crucial, as gradual thinning may compromise its protective function. Considerable differences in the physicochemical properties of various alginate-based formulations available in market were reported in earlier study. Differences in these findings among formulations may be attributed to quality of sodium alginate used in each formulation, which depends on the seaweed species and the specific part of the seaweed from which the alginate is extracted[26].

In conclusion, the study revealed notable variations in raft strength and thickness among calcium-based alginate formulations, with RanRaft® demonstrating superiority in achieving an optimal balance between these critical parameters. These findings emphasize the importance of calcium-based alginate formulation selection in optimizing raft performance for reflux suppression. Since GERD is a chronic condition requiring long-term symptom management, selecting the right formulation is critical for clinical outcomes, as it can influence symptom relief, treatment adherence, and overall patient quality of life. More clinical trials are necessary to validate these *in-vitro* results and assess their impact on patient outcomes.

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Abbreviations

BP: British Pharmacopoeia; GERD: Gastroesophageal reflux disease; H2RAS: Histamine H2-receptor antagonists; HPLC: High-performance liquid chromatography; NERD: Non-erosive reflux disease; PPI: Proton pump inhibitors.

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