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Alginates: A solution for Non-Cardiac Heartburn

Abstract

Heartburn is the most common symptom presented by patients in clinical practice. Causes of heartburn ranging from cardiac origin (heart attack) to acid reflux. Different acid suppressing agents like antacids, H2 blockers, PPIs (Proton pump inhibitors) are commonly used. Alginate-based raft-forming products have been used for many years in the management of heartburn and acid reflux disorders and are widely available worldwide. They are commonly used to alleviate symptoms of acid reflux disorders, working through a mechanism distinct from conventional antacids. In the presence of stomach acid, alginates form a gel. These formulations typically include sodium or potassium bicarbonate, which, when exposed to gastric acid, produces carbon dioxide. This gas is trapped within the gel, transforming it into a foam that floats on the stomach contents, much like a raft on water. The strength of the alginate raft depends on various factors, including the amount of carbon dioxide produced and trapped, the molecular structure of the alginate, and the presence of aluminium or calcium in the antacid components. Raft formation happens quickly, usually within seconds of ingestion and offer longer-lasting relief compared to traditional antacids. Optimal benefit of alginate is achieved when taken following a meal. Alginate-based raft-forming products are also used to manage reflux symptoms in infants, children, pregnant and breast-feeding women. Their unique, non-systemic mode of action provides both fast and long-lasting relief from heartburn, ensuring their continued role in treating such conditions.

Keywords: Acid reflux, Alginate, GERD, heartburn.

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Introduction

The term "heartburn" is frequently used by patients and healthcare professionals. It is often used incorrectly to indicate any of a variety of symptoms thought to originate from the upper gastrointestinal (GI) tract. Heartburn, when accurately described, refers to a burning sensation behind the breastbone that radiates upward toward the neck. It occurs when stomach acid refluxes into the esophagus.[1] Reflux symptoms are very common, and general practitioners are likely to see many individuals who experience heartburn, but these symptoms typically wax and wane. Heartburn may become more common with increasing age and during pregnancy. In India, heartburn affects 22.2% of the population, with the prevalence of gastroesophageal reflux disease (GERD) ranging between 7.6% and 30%. Less than 10% of GERD patients in the country progress to develop erosive esophagitis.[2]

Risk factors for heartburn

Certain foods and beverages, such as coffee, tea, chocolate, spicy food and citrus, along with regular use of aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs), stress, and tobacco smoking, are commonly known to trigger heartburn.[3] Eating relatively large portions of food, meals rich in fat, spicy food and recumbence after meals also predispose to heartburn. Some prescription medicines (eg, calcium-channel blockers, nitrates) may reduce lower oesophageal sphincter pressure and predispose to heartburn. The quality of life is significantly affected due to Frequent heartburn. Self-medication like usage of antacids, PPIs, H2-blockers for symptoms of GERD (heartburn, acid regurgitation) is very common. A lack of adequate response is most likely to occur with antacids, histamine 2 receptor antagonists (H_2RAs).Frequent heartburn is defined as heartburn that occurs on at least 2 days a week; estimates are that >50 million.[4]

Heartburn occurs with about equal frequency in men and women and affects all racial and ethnic groups.

Most conditions associated with Acid reflux: a common cause of heartburn in clinical settings

A. Gastroesophageal reflux disease (GERD) and acid reflux.

Gastroesophageal reflux disease (GERD) usually presents with symptoms like heartburn and regurgitation, but it can also occur atypically, manifesting as laryngitis, cough, or non-cardiac chest pain.[5] According to the Montreal definition, "*GERD is a condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications*".[6] The prevalence of GERD's major symptom i.e heartburn ranging from 10% to 48% in population-based studies.[7] GERD affects the daily lives of individuals, disrupting physical activities, hindering social interactions, disturbing sleep, and decreasing work productivity.

Pregnancy and acid reflux

Acid reflux is more commonly found in pregnancy. Pregnant women are more prone to experiencing GERD symptoms as their pregnancy advances, with around 72% reporting symptoms in the third trimester. This condition often results in heartburn, characterized by a burning sensation in the chest and throat, particularly after meals or at night. Providing safest solution is the need of an hour.[8]

B. Laryngopharyngeal Reflux (LPR) and acid reflux

A backflow of stomach contents into the throat can lead to laryngeal inflammation and symptoms such as chronic cough, frequent throat clearing, a sensation of tightness, sore throat, and voice changes (dysphonia). Approximately 4–10% of patients experience symptoms and/or signs associated with laryngopharyngeal reflux disease (LPRD). Additionally, reflux is a contributing factor in 40–60% of patients with various voice and swallowing disorders.[9]

Acid pocket and acid reflux

This phenomenon occurs in both healthy individuals and those with esophageal hypersensitivity after eating. Acid pockets are unbuffered acidic areas that form near the gastroesophageal junction during the postprandial period. This region avoids the buffering effect of meals, maintaining a highly acidic environment (median pH of 1.6) compared to the stomach body (pH of 4.7), and is referred to as an acid pocket. It significantly contributes to acid reflux by reducing the pressure of the lower esophageal sphincter after a meal or during transient hiatal hernias (Figure 1). Larger or heavy meals typically lead to increased acid secretion, resulting in a more substantial acid pocket. Any factors that enhance acid production will also contribute to a larger acid pocket. This acid pocket is a significant contributor to postprandial heartburn and, consequently, gastroesophageal reflux disease (GERD).[10]

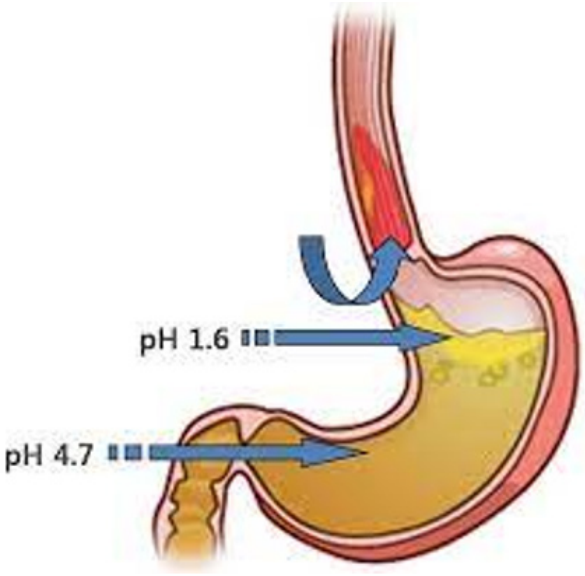

Figure 1 Acid pocket and acid reflux.

Treatment for Heart burn and acid reflux[11]

Various types of medications are commonly used in management of acid reflux disorders including antacids of different formulations (tablets & liquids), numerous liquid and tablet antacid formulations, antacid/alginates, histamine H2-receptor blockers, proton pump inhibitors (PPIs) etc (Table 1). Antacids offer rapid relief from symptoms and have a quick onset of action, but their duration of effectiveness is relatively short.

Table 1 Treatment for Heart burn and acid reflux

Type of treatment	subtype
Lifestyle and dietary changes	Head position in bed
	Avoid meals within 3 hours before bedtime
	Losing weight
Medical management	Antacids
	Alginates
	PPIs
	H2 receptor antagonist
	Prokinetics
	Baclofen
	Sucralfate

Alginates: A Novel treatment option for heart burn

Alginates are naturally occurring structural polysaccharides found in brown algae (seaweed). There are various types of alginates, each with distinct chemical structures and properties. The specific function of an alginate determines its application and the final product in which it is utilized. Alginate is found in both brown algae and certain bacteria, classifying it as both a phycocolloid and a microbial polysaccharide.[12] Alginates have been used in food, cosmetics, and pharmaceutical products for more than a century.[13] Alginates produced from different seaweeds have different chemical compositions and physical properties. Only specific types of alginates possess the necessary characteristics to be used in the production of effective reflux-suppressant products. The mechanism of action for these products is primarily physical rather than pharmacological.[12]

Experience in manufacturing alginate products has shown that the specific type of alginate used is essential for producing buoyant, voluminous, strong, and cohesive rafts. Only alginates with low molecular weight and high gel strength are effective in creating reflux-suppressant products. The product made with sodium alginate extracted from the stems of *Laminaria hyperborea* was able to form strong, cohesive, voluminous, and highly buoyant rafts. Additionally, this product exhibited greater raft thickness and a higher acid neutralization capacity.[12] Research and clinical studies have shown that 40% to 60% of Western populations can benefit from alginate-based products, and this advantage is rapidly expanding in other regions where reflux disease is increasingly acknowledged as a significant and growing issue.[12]

Mechanism of action of alginate

Alginates operate through a unique, non-systemic, physical mechanism rather than a pharmacological one (Figure 2). Viscous alginates, often combined with an antacid, form a protective barrier on top of gastric contents, thereby reducing acid exposure to the esophagus (Figure 3). Alginates, in reaction with other components like Sodium Bicarbonate and Calcium Carbonate, form a raft that is responsible for suppressing reflux and relieving heartburn symptoms.[13,14]

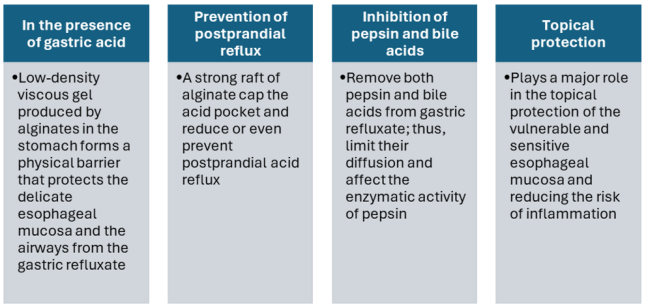

Figure 2 Mechanism of action of alginate.

Alginate-containing anti-reflux medications have a quick onset of action, comparable to that of antacids, but they also offer a significantly longer duration of effectiveness—lasting up to 4 hours, in contrast to the 30 to 40 minutes typically provided by conventional antacids.[14] The chemical compositions and physical properties of alginates differ as per the source of production (Various seaweeds). Only certain alginates have effective reflux-suppressant characteristics.[12,14]

Alginates produced from different species of seaweed and different parts of the same seaweed can determine whether raft formation is possible or not. Effective reflux suppressant products can only be produced using alginates that have a very low molecular weight and high gel strength.

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Calcium increases raft strength

Extrinsic factors that affect raft strength include the presence or absence of specific cations. Calcium enhances raft strength in vitro, whereas the addition of aluminum, commonly found in many antacid formulations, diminishes raft strength. Calcium enhances raft strength by cross-linking alginic acid polymers, which enables the formation of an "eggbox" structure that possesses significant inherent strength.[13] Alginate can be administered on its own or, more commonly, in combination with antacids, referred to as alginate-based products. Optimal benefit of alginate is achieved when taken following a meal (Figure 4).[12] The adverse events of alginate-antacid formulations are infrequent and is considered to be safe.

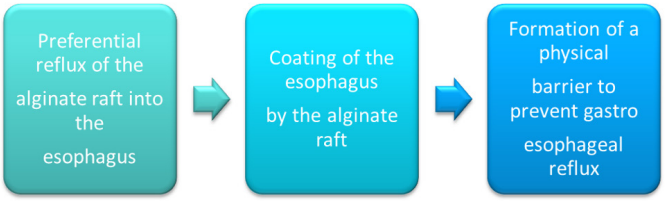

Figure 3 Mechanism of action of Alginate in GERD.

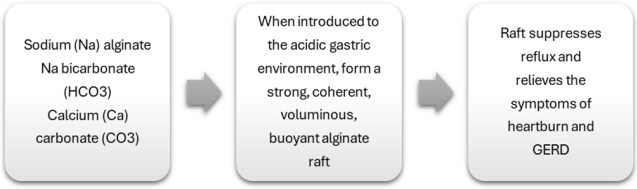

Figure 4 Action of sodium alginate in combination with Na bicarbonate and Calcium carbonate.

Usage of alginates in different clinical scenarios

Large controlled clinical trials, small uncontrolled studies, expert opinion, and patient's opinion suggest efficacy of alginates for the treatment in the following conditions (Figure 5).

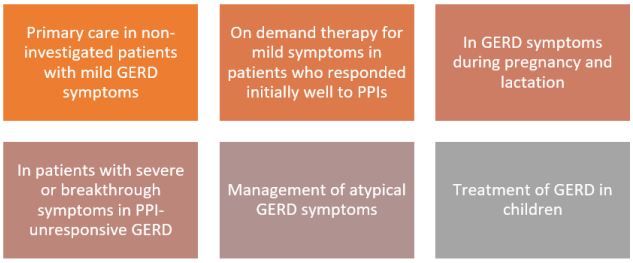

Figure 5 Usage of Alginates in Different Clinical Scenarios.

Alginates during pregnancy:

Alginate-based formulations have been successfully studied for pregnancy-related heartburn, showing effectiveness and no safety concerns. The onset of action for alginates is faster than that of proton pump inhibitors (PPIs), with alginates taking 30-60 minutes to work compared to 6-12 hours for PPIs. However, the duration of action is longer for PPIs, providing a 24-hour symptom-free interval, which is typically shorter with alginates.[15]

Role of alginates in the management of postprandial reflux:

Effect of alginate antacid formulation on postprandial acid pocket

Most patients (8 out of 10) showed an acidified segment extending from the proximal stomach into the esophagogastric junction (EGJ) while fasting, and this condition persisted after eating. Alginate-Antacid formulation neutralized the acidified segment in 6 of the 8 subjects shifting the pH transition point significantly away from the EGJ. Alginate-antacid formulations effectively neutralize the acidified segment, successfully eliminating the "acid pocket" in most patients with GERD, making it a well-targeted therapy for postprandial GERD management.[16]

Role of Alginates in the management of Nocturnal GERD

Heartburn and regurgitation are the most common manifestations of nighttime GERD. Patient with significant night-time GERD tend to have increased regurgitation. Alginates reduce regurgitation more effectively compared with placebo and antacids. Additionally, it is comparable to PPIs.

Alginate along with PPI in NERD

A study showed that sodium alginate combined with omeprazole provided better complete symptom resolution than omeprazole alone in patients with NERD (Figure 6 &7).

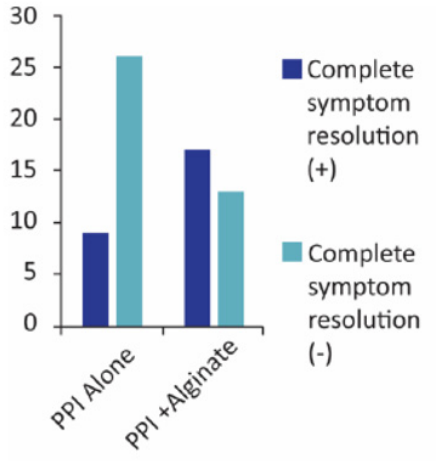

Figure 6 The rate of the complete resolution of heartburn for 7 consecutive days.[14]

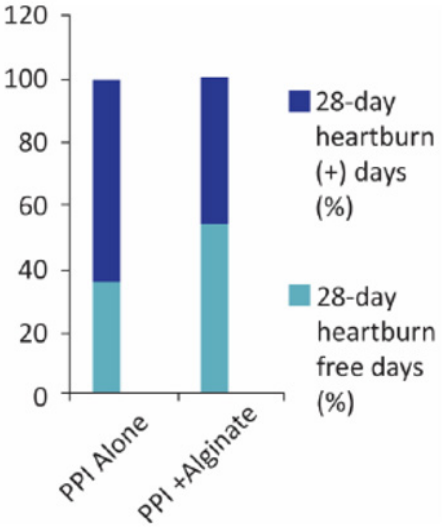

Figure 7 Heartburn-free days (%) during the 28-day observation period.[14]

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Regulatory status

Sodium alginate in combination with Sodium Bicarbonate, Calcium Carbonate as well as with Potassium Hydrogen Carbonate are approved by DCGI for the treatment of heartburn and indigestion and available in suspension and tablet form. Various formulation of alginate with other ingredients are also available in US and UK in liquid as well as tablet formulations.

Alginate in GERD: What guidelines say[17]

Alginate is recommended by various international guidelines in management of GERD (Figure 8).

Guidelines for GERD diagnosis and management	Recommendations for treatment
WGO 2015 Guidelines	Alginate and antacid therapy after dietary changes in patients with less than 2 episodes of reflux/week
NICE 2014 Guidelines	PPIs + alginate/ antacid as self-treatment
Japanese Gastroenterological Society 2016 Guidelines	PPIs for 8 weeks ± alginate and antacid therapy for symptoms relief
Consensus of Gastroesophageal Reflux Disease in Taiwan 2015	Double dosage of PPIs Prokinetics and alginate therapy as additional drugs for patients with nonerosive esophagitis

Figure 8 Guideline recommendations for Alginate.

Algorithm for management of mild moderate GERD: Role of Alginate[18] from consensus statement for South-East Asian region (Figure 9)

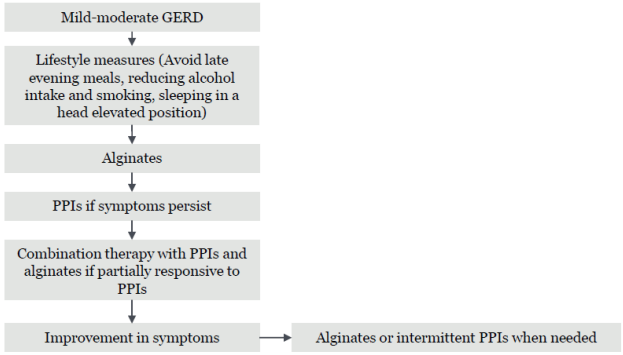

Figure 9 Algorithm for Management of mild or moderate/ mild to moderate GERD.

Place of Alginates in management of heartburn and acid reflux in clinical settings[12]

1. Alginate features a distinct mode of action that leads to the formation of rafts, which is not there with other antacids.
2. Alginate-containing anti-reflux medications have a rapid onset, comparable to that of antacids, but they also offer a significantly longer duration of action—lasting up to 4 hours, in contrast to the 30 to 40 minutes typical for conventional antacids.[13]
3. Sodium alginate solution adhered to the esophageal mucosa for a significantly longer duration compared to placebo. Which provides protective coating against stomach acid in GERD.[19]
4. Alginate monotherapy is a recommended option for managing mild GERD symptoms. Should be taken after meals & at bedtime.
5. For patients with severe or breakthrough symptoms in PPI-resistant GERD, alginates can be combined with PPIs to enhance symptom relief and decrease reflux events. While more data is required, alginates may potentially be more effective in cases of regurgitation-dominant GERD.
6. Alginates play a role in the management of atypical GERD symptoms.
7. Alginate can be used for long-term management or as an on-demand therapy after discontinuing PPIs.
8. Alginates have demonstrated effective and safe treatment for GERD in children.
9. Alginates can be utilized as a first-line therapy during pregnancy and lactation. Alginic acid is classified as "generally recognized as safe" (GRAS) and is widely used in food and cosmetic products, as well as in pharmaceutical formulations.

Conclusion

Heartburn and acid reflux significantly diminish the quality of life for millions of individuals. A range of non-prescription products is currently available in India and worldwide for the symptomatic treatment of heartburn, acid indigestion, and acid reflux disorders. Alginate formulations represent a valuable option in the management of acid reflux, offering a unique physical mechanism of action that distinguishes them from traditional pharmacological treatments. Their ability to form a protective raft on top of gastric contents provides an effective barrier against acid and food reflux, alleviating symptoms such as heartburn and regurgitation. The non-systemic nature of alginate activity provides a favorable safety profile for these specific patient populations. Clinical studies have demonstrated the efficacy of alginate-based products in various populations, including children and pregnant women, where their non-systemic nature contributes to a favorable safety profile. Overall, alginate formulations are a safe, effective, and versatile option for individuals suffering from acid reflux, providing significant improvement in quality of life. Due to its favorable safety profile and absence of side effects, it should be considered for daytime protection and treatment when needed.

Conflict of interest

Dr. Abhijit Anil Trailokya, Dr. Amar Shirsat, Dr. Shaijesh Wankhede, Avinash Talware are associated with Indoco Remedies Ltd. Mumbai.

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