

The Use of Alginates in Anti-Reflux Suspensions

Reflux of gastric acid into the esophagus may lead to heartburn and – in chronic cases – to gastro-esophageal reflux disease. The symptoms of heartburn are a sour/bitter taste in the back of the throat and mouth as well as a burning pain in the esophagus that can radiate into the chest and is reminiscent of cardiac events.^[1]

Chronic reflux can lead to more severe conditions, such as the gastroesophageal reflux disease (GERD) which affects up to 30 % of adults in the western world.^[2]

Long-term reflux of gastric juice can damage the mucous membrane of the esophagus, leading to inflammation, preliminary stages of cancer (Barrett's esophagus), ulcers and bleeding, as well as esophagus strictures due to scarred tissue.

Physiological Background

The gastric juice mainly contains water, hydrochloric acid, pepsinogen, mucus and bicarbonate. The components of the gastric juice break down, denature and disinfect the ingested food. Due to its content in hydrochloric acid, the pH of the gastric juice under fasted conditions, lies in the range of 1 to 1.5.^[3]

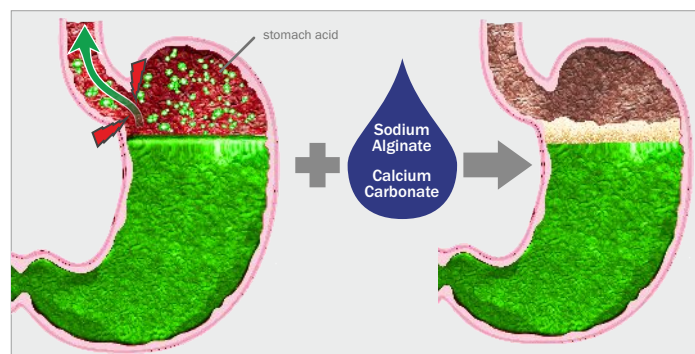
In healthy people, the lower esophageal sphincter muscle prevents the reflux of acidic gastric content into the esophagus. However, certain functional disorders may lead to a failure of the closure mechanism. Organic causes, as well as nutritional and lifestyle habits (for example: excessive consumption of alcohol, nicotine or caffeine, severe obesity, and psychological stress), can trigger or aggravate the reflux-related health issues.^{[1], [4], [5]}

Medical Treatment

The acidity of the gastric fluid can be reduced by proton-pump inhibitors (PPIs) or administration of mild basic substances. The latter have a very rapid, but short-term action. In fact, the strong reduction in stomach acidity often leads to a rebound effect, thus aggravating the situation. PPIs, on the other hand, enable a mild, long-term adjustment of the pH. There is, however, increasing concern about the possible side effects of PPIs.^[6]

Alginate-based anti-reflux preparations, by contrast, act by forming a protective layer in the stomach, and form a mechanical barrier preventing reflux into the esophagus. Over-the-counter medicine containing alginates have been in use for the symptomatic treatment of heartburn for over 50 years and have a positive track record in terms of efficacy and safety.^[7]

Pic 1 shows untreated, irritated esophagus (left) and healthy, protected esophagus (right) due to raft formation in the stomach.

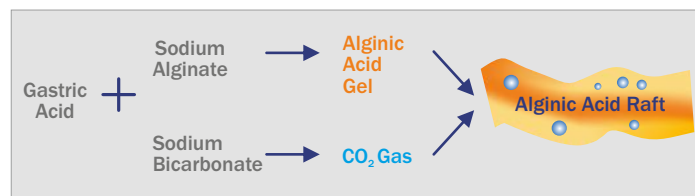


Pic 1 Calcium Alginate Raft Prevents Reflux of Gastric Acid into the Esophagus

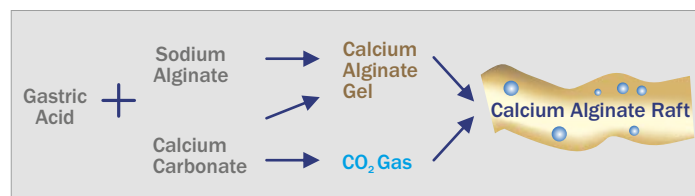
How Does it Work?

Alginates are salts of the naturally occurring alginic acid, which is a major structural component in the cell walls of brown algae. While sodium alginate is water-soluble, calcium alginate and alginic acid form gels in water. These gels are used to form protective layers in the stomach. Another element of action of these formulations is the flotation of the gel layers in the form of a protective raft. Flotation is achieved by embedding carbon dioxide bubbles in the gel layer.

Both, alginic acid and calcium alginate are able to form protective rafts (Pic 2 and 3):



Pic 2 Alginic Acid Raft Formation



Pic 3 Calcium Alginate Raft Formation

The Effect of Calcium on the Gel-Raft Strength

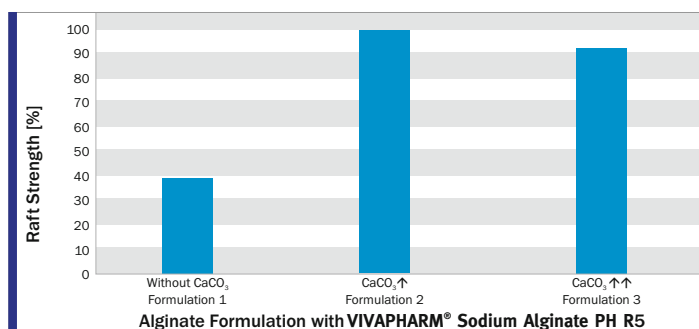
Calcium-induced cross-linking is known to have a strengthening effect on alginate gels.^{[6],[7]} In order to understand the influence of calcium on the robustness of the formed raft, a study was carried out, comparing the raft strengths for three different anti-reflux formulations based on **VIVAPHARM® Sodium Alginate PH R5**. Formulation 1 was done without calcium, only using sodium carbonate as source of CO₂. Formulation 2 contained calcium in a concentration commonly found in commercial anti-reflux products based on alginates. Formulation 3 was prepared using twice the regular calcium content.

The appearance of the resulting rafts in 0.1 M HCl is shown in Pic 4.



Pic 4 Gel Raft in 0.1 M HCl Without Calcium Carbonate (Left), With a Usual Amount of Calcium Carbonate (Middle) and With an Elevated Amount of Calcium Carbonate (right)

The formulation without calcium produced the thinnest (Pic 4) and weakest (Graph 1) gel raft layers. Formulation 3, containing an elevated amount of calcium carbonate, developed the thickest gel raft (Pic 4). Compared to Formulation 2, considered as the standard, Formulation 3 showed a lower raft strength (Graph 1). This may be a result of the inclusion of more and larger gas bubbles into the raft, thus reducing its overall robustness.



Graph 1 Raft Strengths of Gels in 0.1 M HCl Without Calcium Carbonate, With a Usual Amount of Calcium Carbonate and With an Elevated Amount of Calcium Carbonate

Formulation Guidance

As demonstrated by the results, the raft strength and thickness is affected by the concentration of calcium carbonate.

Table 1 shows the basic outline of a corresponding formulation.

Example Formulation

Ingredient	[g/100 mL]
VIVAPHARM® Sodium Alginate PH R5	5
Water (deionized) for dissolving the Alginate	70
Sodium bicarbonate	2.13
Calcium carbonate	3.25
Flavor	q.s.
Preservative	q.s.
Water (deionized) for pre-dissolving further ingredients and volume adjustment	q.s.

Tab.1 Example for an Anti-Reflux-Formulation with **VIVAPHARM® Sodium Alginate PH R5**

References

- [1] Gastroesophageal Reflux Disease (GERD), Missouri Medicine, 115 (3), 214-218 (2018).
- [2] Ness-Jensen, E. et al.: Lifestyle Intervention in Gastroesophageal Reflux Disease, Clinical Gastroenterology and Hepatology, 14 (2), 175-182 (2016)
- [3] <https://flexikon.doccheck.com/de/Magensaft>
- [4] Marburger, Anke: Alginate und Carrageenane – Eigenschaften, Gewinnung und Anwendungen in Schule und Hochschule, Philipps-Universität Marburg 2003.
- [5] Diagnosis and treatment of gastroesophageal reflux disease, World Journal of Gastrointestinal Pharmacology and Therapeutics, 5 (3), 105-112 (2014).
- [6] Fossmark, R. et al.: Adverse Effects of Proton Pump Inhibitors—Evidence and Plausibility, International Journal of Molecular Sciences, 20 (20), (2019).
- [7] Mandel, K. G. et al.: Review Article: Alginate-Raft Formulations in the Treatment of Heartburn and Acid Reflux, Alimentary Pharmacology & Therapeutics, 14 (6), 669– 690 (2000).

Disclaimer:

The information provided in this brochure is based on thorough research and is believed to be completely reliable. Application suggestions are given to assist our customers, but are for guidance only. Circumstances in which our material is used vary and are beyond our control. Therefore, we cannot assume any responsibility for risks or liabilities, which may result from the use of this technical advice.

www.jrspharma.com

JRS PHARMA GMBH & CO. KG

Business Unit Excipients
73494 Rosenberg (Germany)
Phone: +49 7967 152-312

ExcipientsService@JRSPharma.de