

# Sodium Alginate for Anti-reflux Suspensions – Study of Effect of Alginate Quality and Formulation Variables

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### INTRODUCTION

Each day, hundreds of our technical minds come to work at DuPont eager to tackle your toughest pharmaceutical challenges. Armed with a broad and unique portfolio and deep polymer expertise, we harness the variability of many natural materials to produce the exceptional results you need across many applications. One interesting one is in the world of anti-reflux.

GERD (gastroesophageal reflux disease/acid reflux disease) is a digestive disorder that develops from continuous exposure of the esophagus to acidic reflux from the stomach. The reflux of gastric acid leads to irritation, inflammation of esophageal linings, and many further complications. Treatment for GERD is generally targeted for gastric acid neutralization and suppression of gastric acid production and/or secretion. However, another key approach to alleviate the condition would be to minimize the exposure of esophagus to acidic refluxate. Raft-forming anti-reflux preparation is one such line of treatment wherein a viscous gel forms a physical barrier above the stomach contents and prevents it from refluxing back into the esophagus. As the viscous gel barrier floats over the stomach contents like a raft, these formulations are known as "Raft-forming anti-reflux preparations".

Amongst the potential gelling agents, alginates have been largely evaluated for their performance as raft-forming agents. Alginates being a natural polysaccharide are preferred over semisynthetic polymers in anti-reflux formulations. These formulations are generally regarded as safe among all age groups including infants, elderly and pregnant women [1, 2].

Alginates are extracted from marine brown seaweeds and are a very important structural component of their leaves and stem. DuPont's Protanal® LFR 5/60 is a high-quality Sodium Alginate manufactured from brown seaweed harvested and collected off the coast of Norway, under a very well regulated and inspected harvesting program. Sustainability and resources management being very important, DuPont works closely with the Norwegian authorities to ensure the marine ecosystem is preserved. Alginates can be found in different salt structures, such as sodium, calcium, potassium, magnesium, or in the acidic form alginic acid. The type of salt or form will mainly dictate its solubility in water at neutral pH. Alginic acid and calcium alginate are water insoluble forms, whereas sodium, potassium, and magnesium are water soluble at neutral pH. Sodium alginate is a linear copolymer composed of  $\beta$ -D-mannuronic acid (M) and  $\alpha$ -L-guluronic acid (G) linked by 1 $\rightarrow$ 4 glycosidic bonds. [3]

In anti-reflux formulations, the alginate acts as the key functional ingredient. However, the raft forming function is attributable to the complete formulation and not a single therapeutic agent. Upon contact with gastric acid, sodium alginate converts into its alginic acid form and forms an insoluble gel on interaction with other ingredients such as calcium salts and carbonates. The carbonates available in the system reacts with stomach acid and liberate free gas (CO<sub>2</sub>), which get entrapped in gel and provide buoyancy to the raft complex. The combined functionality of all ingredients creates the floating raft that acts as a temporary physical barrier to the reflux of stomach contents back to the esophagus.

This article provides an insight to the importance of sodium alginate source and optimum concentration of functional ingredients in formulation.



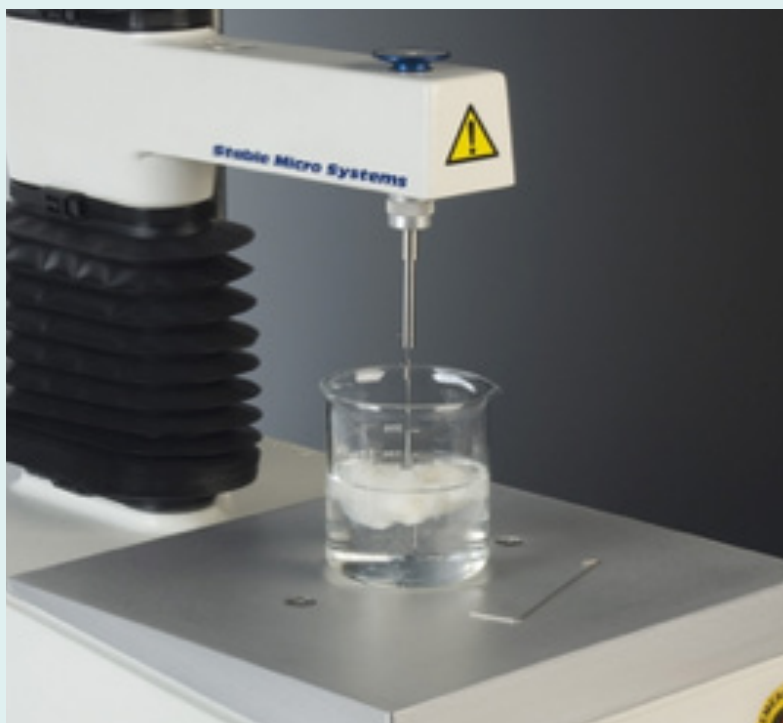
## METHODOLOGY

In the current study sodium alginate from two different commercial sources was evaluated along with Protanal®LFR5/60 for attributes of the product and its performance in formulation. The different sourced sodium alginates were tested for gel strength. A gel was prepared using sodium alginate, Calcium salts & Sodium hydroxide. The gel strength was then measured using a texture analyzer. The gel strength of polymer is an indication of its performance in formulation to form a stronger raft in stomach. The composition of suspension was further tested for different usage levels. The liquid suspension was prepared using different commercial sources of sodium alginates keeping the procedure same. The composition of prepared formulation is as indicated in table 1.0.

**Table 1.0: Anti-reflux suspension composition**

Ingredients	Amount (%)	Function
Sodium alginate	4 – 6	Gel forming agent
Sodium bicarbonate	2 – 3	Carbonate source for buoyancy
Calcium carbonate	1 – 2	Calcium source for alginate gelling
Carbomer	0.5 - 0.6	Suspending agent / Viscosity Modifier
Sodium hydroxide	0.2 - 0.3	pH Modifier
Preservatives	0.4 -0.5	Preservative
Sweetener	0.2 - 0.3	Organoleptic additives
Flavor	0.2 - 0.3	
Deionized water q.s.	100	Vehicle

**Fig 01: Texture analyzer: Raft strength measurement**



The liquid suspension was prepared by dispersing sodium alginate and calcium carbonate in deionized water. The sodium alginate solution was mixed with neutralized carbomer solution and mixed along with preservative, sweetener and flavor. Studies were conducted to understand the effect of various formulation components and the impact of suspension properties as well as raft properties.

The raft strength value is a specified characteristic of anti-reflux formulations, as described in the British Pharmacopoeia. To measure the raft strength, rafts were formed by adding the maximum dose of a specific formulation to hydrochloric acid (0.1M) at 36.5-37.5°C. An L-shaped probe was suspended down the center of the beaker before the raft formation. After 30 minutes, once the raft formed around the probe, the probe was attached to the texture analyzer to record the peak raft strength as shown in Fig. 01 [4].

**RESULTS AND DISCUSSION**

**Comparison of sodium alginate sources**

The product specifications for all 3 samples i.e. Na Alginate 1, Na Alginate 2 and Protanal® LFR 5/60 were the same. However, when tested individually, Na Alginate 2 had higher Ash content and did not fall within the specified USP/NF limits as shown in Fig. 02. This suggests the presence of additional impurities that may possibly exert effects on product stability and anti-reflux performance.

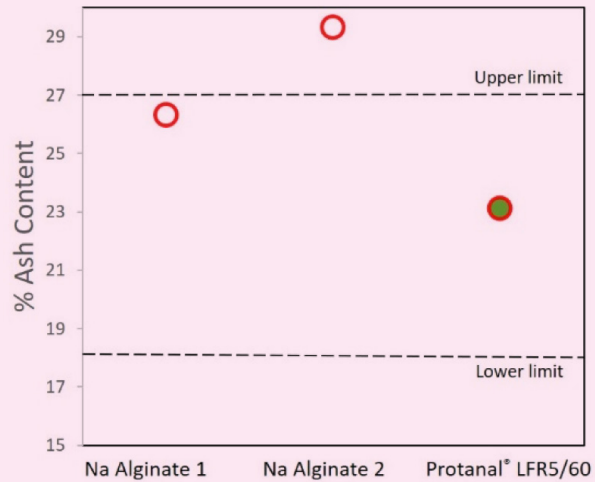
As indicated in Fig 3.0 Protanal® LFR 5/60 had the highest gel strength compared to the other two commercial alginate sources, which can potentially translate to superior raft strength in the formulation.

The formulated suspensions were evaluated for raft strength (Fig. 04) and it was observed that the suspensions formulated with Protanal® LFR 5/60 formed a much stronger raft amongst the three alginates. This further confirm the findings of gel strengths that Protanal® LFR5/60 has better gel strength as well as stronger raft than other compared source of sodium alginate.

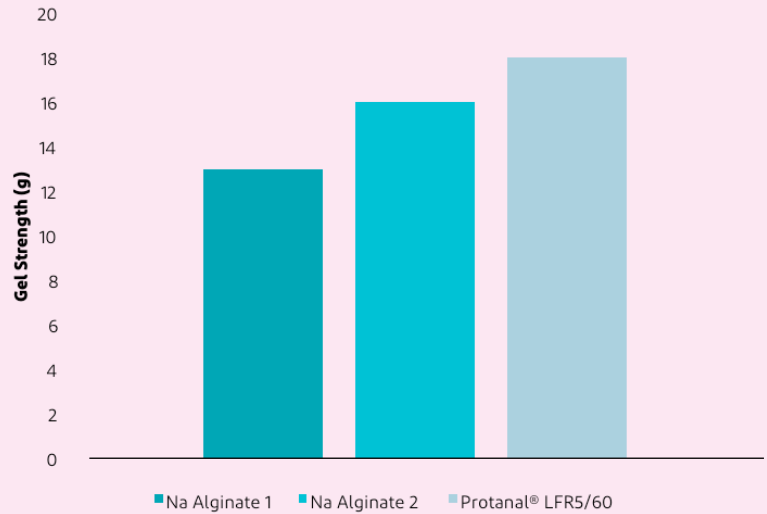


**Effect of varying different formulation components**

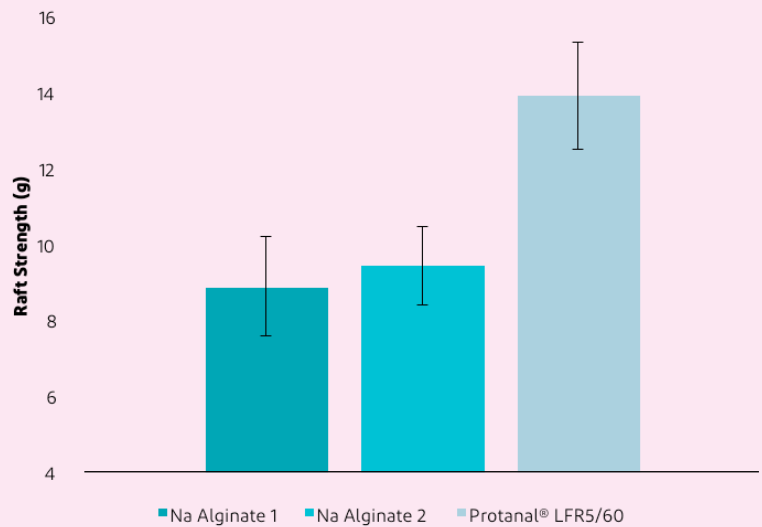
To better understand the role of the key ingredients of the anti-reflux suspension on the raft strength and raft properties, the concentration of carbomer, sodium bicarbonate, and calcium carbonate were varied. The effects of these changes on the raft strength and viscosity were evaluated.



**Fig 02: % Ash Content**



**Fig 03: Gel strength (internal procedure)**



**Fig 04: Raft Strength**

### Effect of varying concentration of Carbomer

Three concentrations of carbomer were evaluated for raft strength and viscosity. An optimum concentration was identified for robust raft formation. Too high or too low concentration results in poor raft formation (Fig. 05).

The viscosity of the formulation was also impacted by the change in carbomer concentration. It was shown that concentration of carbomer is directly proportional to formulation viscosity and same has been summarized in Fig. 06. However, higher concentration of carbomer results in slower raft formation.

### Effect of varying concentrations sodium carbonate and calcium carbonate

The concentration of sodium carbonate and calcium carbonate was varied by  $\pm 33\%$  from the reference formulation. The raft strength increased with higher concentration of calcium carbonate but formed thinner rafts (Fig. 07). This phenomenon could be linked to the larger degree of cross-linking between the alginate molecules facilitated by the higher availability of calcium, which may have created a more tightly packed network and raft. Varying the sodium bicarbonate did not have a significant impact on raft strength.

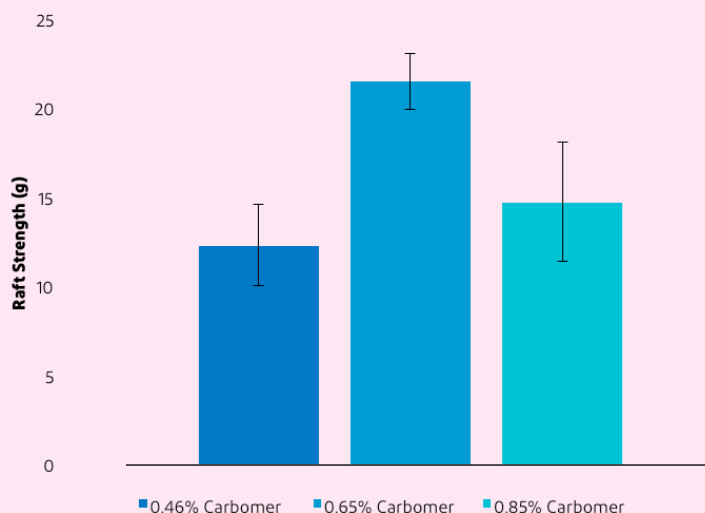


Fig 05: Effect of Carbomer on Raft strength

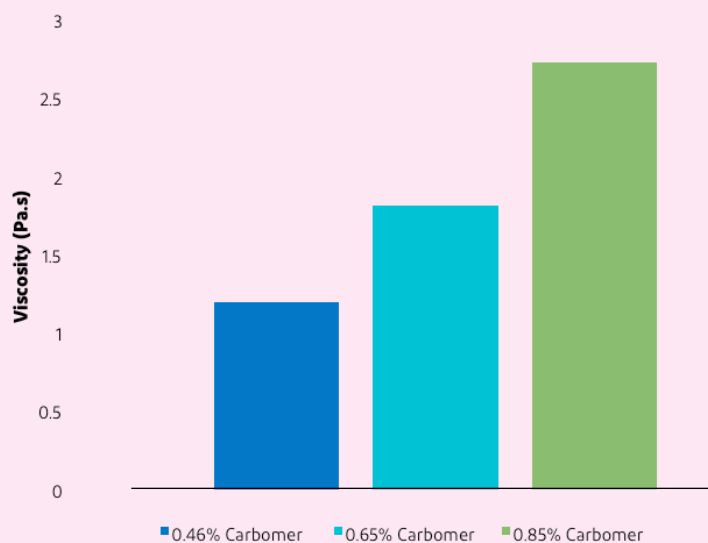


Fig 06: Effect of Carbomer on Viscosity

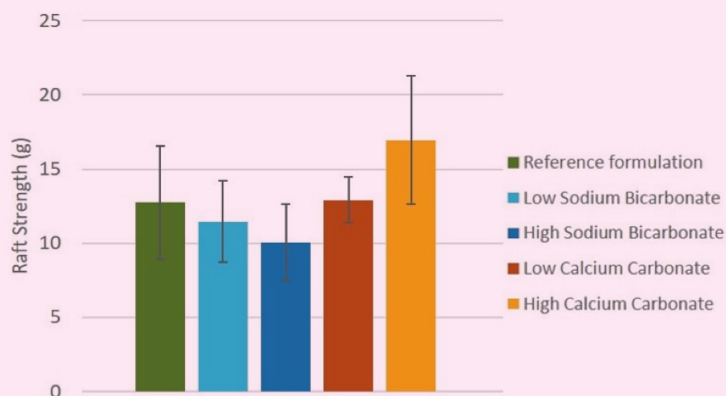
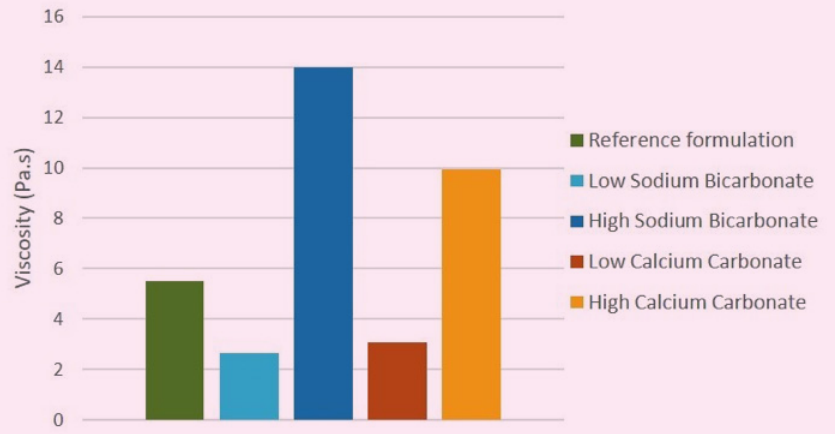


Fig 07: Effect of other ingredients on Raft strength

The viscosity of formulation was impacted by concentration of sodium bicarbonate and calcium carbonate (Fig. 08). The concentration of sodium bicarbonate and calcium carbonate is directly proportional to formulation viscosity.

The above study clearly demonstrates that the quality of the sodium alginate and the formulation variables plays vital role for best anti-reflux performance.



**Fig 08: Effect of other ingredients on Viscosity**

## CONCLUSION

Alginates are important ingredients used in anti-reflux formulations as it forms a strong physical barrier against acid reflux. The non-systemic and physical mode of action make this a safer option for pregnant women and infants. The lower impurity levels and excellent gel strength of Protanal® LFR5/60 contributes to its exceptional raft property compared to other commercial sources. The effect of different usage level of ingredient further confirms its importance in formulation for its anti-reflux performance.

This study demonstrated and confirmed that the performance of the anti-reflux formulation is highly dependent on choosing appropriate source of sodium alginate and concentration of each functional ingredients.

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