



UNIVERSITÀ DEGLI STUDI DI SALERNO

Department of Industrial Engineering

Master Degree in Food Engineering

**IN VITRO STUDIES OF ALGINATE RAFTS
BEHAVIOUR AGAINST
GASTROESOPHAGEAL REFLUX**

Thesis in
Transport phenomena in food processes

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Table of contents

Table of contents	IV
Table of figures.....	VI
Table of tables	IX
Abstract (Italian).....	XI
Abstract.....	XV
Introduction.....	1
1.1 Gastroesophageal reflux and possible remedies _____	2
1.2 Alginate Rafts _____	3
1.3 Characterization of rafts _____	6
1.3.1 Raft strength	7
1.3.2 Reflux resistance	7
1.3.3 Raft resilience	7
1.4 The importance of alginate on raft forming formulations _____	7
1.5 State of Art _____	8
1.6 Objectives _____	16
Materials and methods	19
2.1 Materials _____	20
2.1.1 Alginate	20
2.1.2 Calcium carbonate	21

Sommario e indici.	Pag. V
2.1.3 Sodium bicarbonate	21
2.1.4 Refalt 600	22
2.1.5 Gaviscon	22
2.2 Equipments	23
2.2.1 Viscosimeter	23
2.2.2 Texture analyzer	23
2.2.3 Drier	24
2.3 Methods	25
2.3.1 Viscosity measurement	25
2.3.2 Suspensions making	26
2.3.3 Raft formation and tension test	28
2.3.4 Extrusion	30
2.3.5 Buoyancy force evaluation	32
2.3.6 Drying	33

Results and discussion.....35

3.1 Viscosity measurements	36
3.1 Raft strength	38
3.2 Reflux resistance	41
3.3 Δ pH of acid solutions	43
3.4 Wet mass of the rafts	44
3.5 Dry mass of the rafts	46
3.6 Buoyancy force evaluation	48

Conclusions51

References55

Table of figures

Figure 1. Gastroesophageal reflux	2
Figure 2. Raft against gastroesophageal reflux [6]	4
Figure 3. Possible structures of alginate [9].....	5
Figure 4. Egg-box model [11]	6
Figure 5. Product formulation commercial products tested by Hampson et al. [14]	9
Figure 6. Strength of the alginate rafts, in grams, analyzed by Hampson et al.[14].....	10
Figure 7. Extrusion of Gaviscon Advance and Gaviscon liquid [14]	11
Figure 8. Resilience of the alginate rafts analyzed by Hampson et al. [14].....	12
Figure 9. Laboratory formulations obtained from different alginates by Hampson et al. [14]	12
Figure 10. Commercial formulations tested by Hampson et al. [12]	13
Figure 11. Raft strength of alginate rafts obtained with some commercial products [12].....	14
Figure 12. Raft resilience, in seconds, of alginate rafts obtained with some commercial products [12].	14
Figure 13. Raft strength of different formulations obtained changing calcium carbonate and sodium bicarbonate concentrations tested by Moazen et al. [18]	15
Figure 14. Reflux resistance of different raft forming formulations obtained changing calcium carbonate and sodium bicarbonate concentrations tested by Moazen et al. [18].....	16
Figure 15. Sodium alginate powder	20
Figure 16. Refalt 600.	22
Figure 17. Gaviscon liquid.	23
Figure 18. Texture Analyzer.....	24

Figure 19. Raft forming tested formulations reported in function of sodium bicarbonate/sodium alginate mass ratio on X ₁ and calcium carbonate/sodium alginate ratio on X ₂ . In blue Refalt 600 formulations are reported, in red Sigma-Aldrich alginate formulations, in green Gaviscon and in yellow Sigma-Aldrich alginate formulations with the addition of hyaluronic acid.	27
Figure 20. Tension test parameters.....	29
Figure 21. Example of tension test graphic returned by texture analyzer.....	30
Figure 22. Extrusion test parameters	31
Figure 23. Example of extrusion test graphic returned by texture analyzer	32
Figure 24. Buoyancy force settings	33
Figure 25. Values of viscosity obtained through Brookfield (scattered) and values of viscosity obtained through modelling (continuous line). On the abscissa the shear rates, expressed in 1/s. On the ordinate the viscosities, expressed in Pa*s. In blue Refalt, in dark Amazon alginate and in red Sigma-Aldrich.....	37
Figure 26. Raft strength values are contained in the labels, expressed in grams. On the abscissa there are the sodium bicarbonate over sodium alginate mass ratios. On the ordinate there are the calcium carbonate over sodium alginate mass ratios. In blue Refalt formulations are represented, in red Sigma-Aldrich ones, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid addition.....	38
Figure 27. Reflux resistance results are contained in the labels, expressed in newton. On the abscissa there are the sodium bicarbonate over sodium alginate mass ratios. On the ordinate there are the calcium carbonate over sodium alginate mass ratios. In blue Refalt formulations are represented, in red Sigma-Aldrich ones, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid addition.	41
Figure 28. pH variation results are contained in the labels. On the abscissa there are the sodium bicarbonate over sodium alginate mass ratios. On the ordinate there are the calcium carbonate over sodium alginate mass ratios. In blue Refalt formulations are represented, in red Sigma-Aldrich ones, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid addition.....	43
Figure 29. Wet mass results are contained in the labels, expressed in grams. On the abscissa there are the sodium bicarbonate over sodium alginate mass ratios. On the ordinate there are the calcium carbonate over sodium alginate mass ratios. In blue Refalt formulations are represented, in red Sigma-Aldrich ones, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid addition.	45
Figure 30- Dry mass results are contained in the labels, expressed in grams. On the abscissa there are the sodium bicarbonate over sodium alginate mass ratios. On the ordinate there are the calcium carbonate over sodium alginate mass ratios. In blue Refalt formulations are represented, in red Sigma-Aldrich ones, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid addition.	47

Figure 31. The disrupted Refalt raft during buoyancy force test 49

Table of tables

Table 1. Raft forming tested formulations. In blue Refalt 600 formulations are reported, in red Sigma-Aldrich alginate formulations, in green Gaviscon and in yellow Sigma-Aldrich alginate formulations with the addition of hyaluronic acid.	28
Table 2. Input and output variables	36
Table 3. Viscosity parameters	38
Table 4. Raft strength (Y_1) results (in blue Refalt formulations are represented, in red Sigma-Aldrich ones, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid addition)	40
Table 5. Reflux resistance results (Y_2) (in blue the Refalt, in red Sigma-Aldrich, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid).....	42
Table 6. pH variation (Y_3) results (in blue the Refalt, in red Sigma-Aldrich, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid).....	44
Table 7. Wet mass results (Y_4) in g (in blue the Refalt, in red Sigma-Aldrich, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid).....	46
Table 8. Wet mass results (Y_5) in g (in blue the Refalt, in red Sigma-Aldrich, in green Gaviscon and in yellow Sigma-Aldrich with hyaluronic acid).....	48
Table 9. Buoyancy force results	48

Abstract (Italian)

I prodotti a base di alginato di sodio vengono spesso utilizzati contro il reflusso gastroesofageo in casi di lieve entità e breve durata. Il loro funzionamento prevede la formazione di una zattera, che va a costituire un ostacolo fisico al reflusso.

In questo lavoro di tesi è stata valutata l'influenza del carbonato di calcio e del bicarbonato di sodio sulle proprietà meccaniche delle zattere in alginato di sodio, ottenute da diverse formulazioni, utilizzabili contro il reflusso gastroesofageo.

Il Refalt, prodotto disponibile in commercio, non osserva la formazione della zattera, pur contenendo alginato di sodio (40 mg/mL). Per ottenere la zattera, sono stati aggiunti carbonato di calcio e bicarbonato di sodio. Per capire in che dosi questi ultimi conferiscono le migliori proprietà meccaniche alle zattere, sono stati effettuati test a differenti concentrazioni.

In particolare, sono state testate la "forza della zattera" e la sua "resistenza al reflusso". Si tratta di due proprietà di grande rilievo per comparare le performance di preparati a base di alginato. La "forza della zattera" è stata valutata attraverso test di rottura, mediante un Texture Analyzer, nel rispetto delle indicazioni dell'appendice XVII del Volume V di Pharmacopeia. I risultati ottenuti suggeriscono che per maggiori quantità di carbonato di calcio e minori quantità di bicarbonato di sodio si ottengono le migliori performance. Ciò vuol dire che la scelta del rapporto di composizione tra carbonato e bicarbonato potrebbe rivelarsi fondamentale per ottenere una formulazione efficace. In ogni caso, le performance ottenute col Refalt

si sono rivelate al di sotto del minimo stabilito dal Pharmacopeia (7.5 g) per tutte le formulazioni testate.

La resistenza al reflusso è stata valutata mediante test di estrusione, condotti ancora tramite Texture Analyzer. I risultati ottenuti sono coerenti con quanto mostrato dalla “forza della zattera”, in quanto i valori più alti di resistenza sono stati riscontrati proprio nelle formulazioni che avevano restituito valori di forza più alti. Il più alto valore registrato è di 13.5 N.

Anche la massa delle zattere e la loro azione sul pH della soluzione in cui si sono formate sono state valutate. Per quanto riguarda il pH, si può dire che l’effetto antiacido delle formulazioni sia trascurabile al bulk. La maggiore variazione di pH registrata è di appena 0.52. La massa, d’altro canto, testimonia che le formulazioni a basso contenuto di carbonato di calcio sono poco coese, e finiscono per disgregarsi facilmente.

Gli stessi test sono stati effettuati sul Gaviscon, il prodotto a base di alginato (50 mg/mL) più conosciuto in questo ambito. I risultati ottenuti sono stati significativamente più alti per quanto riguarda le proprietà meccaniche, con una forza della zattera al di sopra del minimo stabilito da Pharmacopeia. La variazione di pH al bulk resta poco rilevante.

Altre formulazioni sono state ottenute con un alginato (33.33 mg/mL) acquistato da Sigma-Aldrich, con viscosità paragonabile a quella del Refalt. Di nuovo, aumentare la concentrazione di carbonato di calcio ha restituito forza della zattera e resistenza al reflusso maggiori. In particolare, la forza della zattera si è rivelata maggiore del minimo richiesto da Pharmacopeia per tutte le formulazioni, eccetto quella non contenente carbonato di calcio. La variazione di pH al bulk è risultata ancora poco rilevante.

L’aggiunta di acido ialuronico ad una delle formulazioni ottenute con alginato acquistato da Sigma-Aldrich, ne ha abbassato la forza alla rottura del 25%, e la resistenza al reflusso del 50%. Il valore della forza è tuttavia sufficiente a soddisfare il minimo richiesto da Pharmacopeia. L’aggiunta di acido ialuronico ha ridotto anche l’abbassamento di pH al bulk e la massa della zattera.

In conclusione, le formulazioni basate sul Refalt hanno dato le performance peggiori, insufficienti, secondo gli standard di Pharmacopeia, per i prodotti che formano zattere contro il reflusso

gastroesofageo. D'altro canto, tutte le altre formulazioni, anche quelle a minore concentrazione di alginato, hanno mostrato performance significativamente superiori, ad eccezione di quelle senza carbonato di calcio.

Si può concludere che:

- la scelta del giusto rapporto di concentrazione tra carbonato di calcio e bicarbonato di sodio può essere molto importante per le performance della zattera;
- la scelta dell'alginato sembra ugualmente importante a tale scopo.

Ulteriori studi potrebbero essere condotti per avere una caratterizzazione più completa delle zattere e per trovare una correlazione tra le performance delle stesse e il tipo di alginato utilizzato.

Abstract

Based alginate product are often used against gastroesophageal reflux for self-medication. They act forming a raft, which constitutes a physical barrier against the reflux.

In this work of thesis, the mechanical performances of different raft forming formulations have been tested in order to evaluate the effect of the calcium carbonate and sodium bicarbonate on them.

As found in commerce, Refalt does not observe raft formation. Sodium bicarbonate and calcium carbonate have been added, in order to obtain the rafts. Different percentages of these additives have been used in order to understand which could be the composition giving the best mechanical performances.

In particular, two properties have been evaluated: raft strength and reflux resistance, which are the most relevant ones in this field. Raft strength has been tested thanks to tension tests conducted through a Texture Analyzer, following the Appendix XVII of Volume V of British Pharmacopeia. Raft strength tests suggest that higher amounts of calcium carbonate give higher values of raft strength, while higher values of sodium bicarbonate bring to the opposite effect. This means that the choice of the right formulation could be done taking into account the ratio between these two components. However, even the highest value of raft strength obtained (3.93 g) is lower than 7,5 g, the minimum stated by Pharmacopeia.

Reflux resistance has been determined thanks to extrusion tests, also conducted through a Texture Analyzer. Reflux resistance tests seem to be coherent with raft strength results. In fact, the formulations showing the higher raft strength values show also the higher values of reflux resistance. The highest reflux resistance obtained is 13,85 N, from the formulation with 0 mg of sodium bicarbonate and 26 mg of calcium carbonate in 15 mL.

Also raft masses and influence on bulk pH have been observed. The variation of pH of the solutions in which rafts have formed attests that

their anti-acid action is negligible at bulk. The highest variation (obtained with a formulation containing 34 mg of sodium bicarbonate and 26 mg of calcium carbonate in 15 mL) is just 0.52. Instead, the raft mass measure attests that formulations with lower amounts of calcium carbonate show a worst coherence. In fact, rafts with low concentration of calcium carbonate were not formed, or when they were formed they were extremely fragile.

The same tests have been performed on Gaviscon, the most known alginate based raft forming product in commerce. The tests showed a value of raft strength of 11.93 g and a reflux resistance of 36.11 N. The variation of pH caused by Gaviscon is still not relevant (0.67).

Other formulations were obtained from a Sigma-Aldrich alginate, with viscosity similar to Refalt 600. Test showed that higher amounts of calcium carbonate have given higher rafts strength values and the same can be said for reflux resistance. The best formulation (with 15.33 mg of calcium carbonate in 15 mL) has given a raft strength value of 16.32 g and a reflux resistance value of 37.72 N. The pH variation induced is still not relevant at each concentration of calcium carbonate. Also the effect of hyaluronic acid on one of the Sigma-Aldrich formulations has been evaluated. The result was a decrease in performances of 25% for raft strength and 50% for reflux resistance. Its presence seems to reduce also the variation of pH and the mass of the raft. In each case, the formulations with Sigma-Aldrich alginate (included the one containing hyaluronic acid) show a raft strength higher than 7.5 g, the minimum stated from Pharmacopeia.

In conclusion, Refalt formulations have given the worst performances, not sufficient to satisfy the Pharmacopeia minimum, despite its alginate content (40 mg/mL) is higher than the Sigma-Aldrich formulation one (33 mg/mL). On the other hand, all the other formulations have returned some significant better mechanical performances, except for the ones without calcium carbonate.

After these considerations, it could be said that:

- the evaluation of the right amounts of calcium carbonate and sodium bicarbonate is important to obtain the desired performances from the rafts;
 - the choice of the alginate seems to be relevant in order to get the desired performances of the rafts.
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Further studies could be done in order to test other mechanical properties of the rafts, to obtain a complete characterization. Moreover, an investigation on the alginate structure's influence on the properties of the raft could give fundamental indications.

Chapter One

Introduction

This chapter contains an overview on alginate raft forming formulations mechanism and properties. Factors affecting their effectiveness against gastroesophageal reflux have been also evaluated. At the end of the chapter, the objectives of the work are listed, taking into account the state of art.

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