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ORIGINAL RESEARCH PAPER

ANALYSES OF LIPIDS RELEASE FROM ALGINATE CAPSULES WITHIN THE SIMULATED GASTROINTESTINAL ENVIRONMENT

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This work aims to assess the behaviour of alginate capsules with essential lipids and to characterise their transport rates under simulated gastrointestinal conditions. The maximum encapsulation efficiency can be attained in the alginate capsules with oil loadings up to 40% (w/w). The results on the emulsion efficiency of sodium alginate – oil containing capsules at different oil loading capacity show that our preparations are able to hold the encapsulated oil and therefore deliver in a certaine place of a model human digestive system. Changes in mechanical properties reflected changes in the gel microstructure with the capsules becoming stronger in gastric phase (values of Young's modulus of about 7×10^4 Pa) and weaker in intestinal conditions (Young's modulus $\approx 1 \times 10^4$ Pa). Results on the swelling behaviour showed that all capsules shrink in gastric and swell in intestinal conditions. The amount of oil encapsulated in the capsules remains stable during the gastric stage, whereas the residual amount of oil was released from the alginate capsules at the intestinal phase. Mathematical modelling using Fick's low of diffusion was applied to the rates of lipids release revealing that changes in mechanical properties under media conditions governs the diffusional mobility of lipids in the encapsulated matrix.
Keywords: alginate, capsules, release, in vitro hydrolysis, mechanical properties, mathematical modelling

Introduction

Nowadays, more and more consumers prefer foods that provide various benefits for their personal health. In the food industry, the encapsulation process greatly contributed to the development of functional foods. Encapsulation enables the isolation, protection, transport and release of the active components, such as: flavors, vitamins, peptides, minerals, fatty acids, poly-unsaturated fatty acids, antioxidants, enzymes and living cells. Out of the numerous compounds used as encapsulating material, the sodium alginate are the most important food ingredient

in the encapsulation process (Lopez-Rubio *et al.*, 2006; Fang and Bhandari, 2010; Patel and Velikov, 2011). There are many researches on microencapsulation of essential lipids using several methods including spray-drying (Lazko *et al.*, 2004), simple and complex coacervation (Chang *et al.*, 2006), emulsion extrusion (Yuliani *et. al.*, 2006) and supercritical fluid precipitation (Martín *et al.*, 2010). Emulsion extrusion is considered as the most common approach of microencapsulation and might be achieved by emulsifying or dispersing the hydrophobic components in an aqueous solution where gelation occurs (ionotropic or thermal) (Yuliani *et al.*, 2006).

By using emulsion extrusion for microencapsulation, a broad selection of polymer coatings ("shell") has been established. The sodium alginate is a linear polysaccharide, soluble in water, formed out of α-l-guluronic and β-d-mannuronic acids residues. The aqueous solution of sodium alginate is transformed in gel under the action of calcium ions which form the intermolecular cross-links with the carboxyl groups of guluronate leading to the well-known "egg-box" structure (Goh *et al.*, 2012).

Literature reveals that physico-chemical properties of alginate gel utilized as carrier for the encapsulation of bioactive compounds in simulated gastro-intestinal conditions were in a wide interest recently (Wichchukit *et al.*, 2013; Chan, 2011). In a view of the actual problem of modern nutrition, various functional foods enriched with micronutrients have been developed over the years (Yoshizawa, 2004; Gorbunova *et al.*, 2016; Bannikova and Evdokimov, 2016). And yet, the desire to improve the stability and quality of processed foods, where chemical reaction pathways and enzymatic processes are critical considerations, is remained under researched worldwide.

Many essential oils have been shown potential benefits for a human health, such as reduction of the risk of coronary heart disease, hypertension, thrombosis, symptoms of allergies, some types of cancer and the rate of aging (Na *et al.*, 2011). However, the application of oil in the food system has limitations because the oil is unstable against oxidation during storage. Also, the unpleasant taste and odor of several oils can cause deterioration in the quality of food products. Therefore, encapsulation techniques of oil have been widely recognized as an effective tool to deliver the active ingredients and protecting them from the external environment (Yoshizawa, 2004). The overall aim of this study was to investigate the efficiency of oil encapsulation in Ca-alginate beads in order to produce capsules with a maximum oil content. An alginate-oil emulsion was prepared and dropped into a gelling bath to produce oil loaded Ca-alginate capsules. The influence of oil volume fraction on the emulsion stability and the encapsulation efficiency was studied. Further, the purpose of this study was to provide an understanding on the kinetics release of oil during *in-vitro* digestion from capsules with different oil content. The rates of transport of lipids from the capsules with different lipid content were carried out thus confirming the control delivery of bioactive in a model small intestine of a human digestive system. Last, the Fickian diffusion

modeling was applied to the release profile of lipid thus arguing for the controlled transport governed by the media and mechanical properties of the capsules.

Materials and methods

Materials

Sodium alginate was in the form of powder from Sigma Aldrich (St. Louis, Missouri, USA). According to the specification sheet, viscosity of 1% (w/w) sodium alginate in distilled water was 0.02 Pa·s.

Orange oil (Citrus Sinensis (L.) Pers) with a purity of 100% was obtained from "Botanika" company, Russia. Essential oils are natural Botanically and Biochemically Defined.

Analytical reagents, such as calcium chloride, sodium chloride, hydrochloric acid, monobasic potassium phosphate were obtained from BDH Chemicals (Poole, United Kingdom). All reagents were used without further purification. Bile salts, pancreatin (6000 U) and pepsin (3600 U) were purchased from Aventis Farma (Mumbai, India). n-Hexane of 97% purity was purchased from Acros Organics, New Jersey, USA.

Sample preparation

For the alginate capsules preparation, all the capsules were prepared at room temperature. There were two different ways to prepare the alginate capsules by incorporating 20% and 40% of oil inside the bead. Overall, 1.5% (w/w) sodium alginate and 20 or 40% oil (w/w) by weight to alginate solution were dissolved in deionized water with continuous stirring for 2 h at 22 °C following the homogenization at a pressure 5 Bar. The solution was left to stand for a further 30 min to allow any bubbles to surface before preparing the alginate capsules. 100 ml of the emulsion was dripped into 200 ml solution containing 12 mmol·l^{-1} calcium chloride and using a 250-ml funnel to create a stream of droplets. The capsules were remained in calcium chloride bath for 30 min, then sieved and rinsed with deionized water. The capsules were stored in container with fresh 12 mmol·l^{-1} calcium chloride solution at 5 °C for 22 h before characterization (Gorbunova *et al.*, 2016).

Experimental analysis

Determination of emulsion efficiency (ES)

The oil-loaded, Ca-alginate capsules were separated from the gelling solution using a sieve. The capsules were rinsed with distilled water to remove excessive surface oil. The non-encapsulated oil was determined by measuring the weight of free oil left on the surface of gelling solution as well as the surface on the wet capsules. Filter paper was used to absorb the surface oil on the wet capsules. The difference between the initial amount of oil used (W_1) and the non-encapsulated oil (W_2) gives the amount of oil encapsulated (W_3), as shown in Eq. (1). The Encapsulation Efficiency (*EE*) was expressed as the percentage of oil encapsulated with respect to

the initial amount of oil used, as shown in equation 2 (Huang, Kakuda, Cui, 2001; Soliman et al., 2013):

$$W_3 = W_1 - W_2 \quad (1)$$

$$EE(\%) = 100 \cdot \frac{W_2}{W_1} \quad (2)$$

In vitro digestion

A digestion protocol that simulates the gastric and intestinal digestion in the gastrointestinal tract was designed and adapted to the systems studied in order to take into account the structural characteristics of the alginate capsules and release kinetics of model essential fatty acids.

In the gastric stage, the simulated gastric fluid (SGF) which contains 2.0% NaCl solution in Millipore water (Millipore, Billerica, Massachusetts, USA) and pH adjusted to 2 with 1 mol·l^{-1} HCl and pepsin 3600 U·ml^{-1} was used. To 25 g of gel capsules 500 ml of pre-warmed (37 °C) SGF was added. Samples were incubated in a water bath under constant shaking (37 °C, 100 horizontal strokes per minute) for a set length of time. After 15, 30, 45, 60, 75, 90, 105 and 120 min the samples were washed with deionized water. 200 mg of alginate capsules were taken at each stage of simulated gastric digestion and analyzed for the fatty acids content.

For the *in-vitro* intestinal digestion, initial digestion of the encapsulated micro-gel particles in SGF was conducted for 2 h at 37 °C. Then, to 20±2 g of microgel particles, being digested in simulated gastric conditions, 400 ml of prewarmed (37 °C) simulated intestinal fluid (0.7% monobasic potassium phosphate; 0.1% bile salts; 0.4% pancreatin) was added. The pH was adjusted to 7.5 with 0.5 mol·l^{-1} NaOH (~40 ml). The entire sample was incubated at 37 °C under constant shaking (100 horizontal strokes per minute) for a set interval of time (up to 20 min). At the end of the set time interval, the 200 mg of digested sample were washed with Millipore water and analyzed for the oil concentration (Gorbunova *et al*., 2016).

Determination of oil concentration

The kinetics of release of essential lipids from the alginate capsules were monitored using UV-VIS-spectroscopy. This method is based on the determination of the optical density of essential lipids dissolved in hexane at 260 - 300 nm (Fuentes *et al*., 2012). The results on the concentration of lipid in hexane were monitored at λ_{max} = 280.5 nm at 20 ° C within the experimental range of 0.4-1.2 mg/ml in hexane which has a linear relationship of R^2 = 0.999 (Lambert-Beer law). A=f(C)

Swelling ratio

The capsules were tested for their swelling characteristics in gastric and intestinal conditions *in vitro*. The swell ratio was determined using the following equation:

$$S = 100\frac{m_f - m_i}{m_i} \quad (3)$$

where S is the swell ratio; m_f is final bead mass (in grams); m_i is initial bead mass (in grams) (Gorbunova *et al*., 2016).

Texture Profile Analysis

Uniaxial compressing of single alginate capsules digested within certain amount of time was made by using Brookfield CT3 Texture Analyzer with a load cell of 5 kg (Brookfield Engineering Laboratories, Middleboro, Massachusetts, USA). Capsules were immersed in water and placed onto a flat platform. The measuring geometry consisted of a cylindrical aluminum probe (6 mm diameter) which was driven to compress the sample. Tests were carried out at 1.5 mm·s^{-1} with a trigger load of 0.067 N and a compressive deformation up to 30% of the original height. The probe was set to return to its original position immediately after compression. Thirty capsules from each sample were compressed in order to give statically representative results. All experiments were conducted at room temperature (22 ± 1°C).

Young's modulus **E** (in Pascal's) was calculated using the following equation:

$$\overline{E} = \frac{3 \cdot \left(1 - \nu^2\right) \cdot \overline{F}}{\sqrt{d \cdot H^3}} \qquad (4)$$

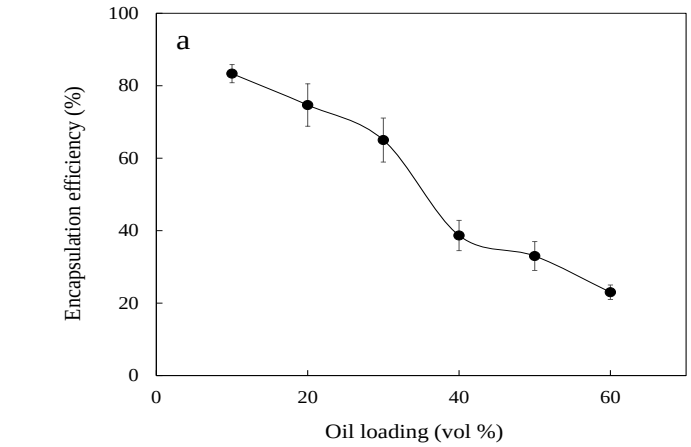
where *d* is the diameter of a bead (in meters), **F** is the force applied to bead (in newton's), *H* is the displacement (in meters) and *v* is the Poisson ratio (Gorbunova *et al.*, 2016).

All experiments were performed in triplicate with data statistical testing on ANOVA (one way, $p > 0.05$).

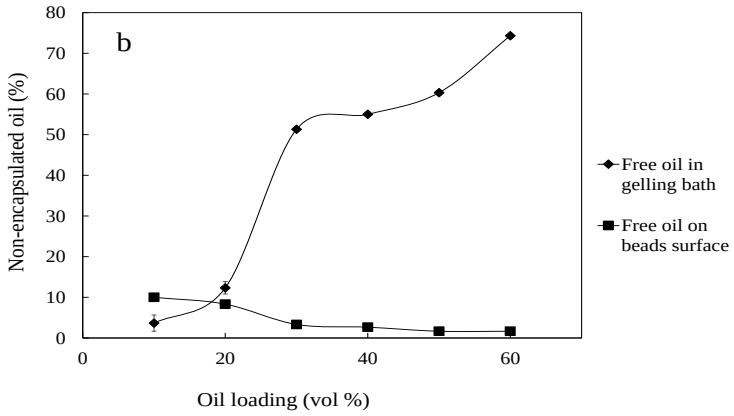
Results and discussion

Effect of oil loading on the encapsulation efficiency and non-encapsulated oil

The effect of oil loading on the encapsulation efficiency (EE) is shown in Figure 1a. The oil loading ranged from 10 to 60 % (w/w). The EE remained relatively constant (at about 85–90%) for oil loading up to 50% (w/w), but it decreased drastically (to 30%) when oil loading was increased to 60% (w/w). We also determined the fraction of non-encapsulated oil found in the gelation bath and on the surface of wet capsules, and the results are presented in Fig. 1b. Generally, the fraction of non-encapsulated oil found on the bead surface was in the range of 4–10% of total oil used. Interestingly, the surface oil fraction at lower oil loading was higher than that of higher oil loading. It is worth mentioning that the amount of surface oil found in all samples was about the same (i.e., 0.3–0.6 mL) despite the variation in oil loading. This is logical because the number of capsules and the bead size were found to be relatively constant, and the amount of surface oil should be dependent on the total surface area of the capsules. Therefore, the higher surface oil fraction obtained was a result of dividing the value with a lower oil volume. The data verifies that the non-encapsulated oil leaked into the gelation bath. The extent of leakage depended on the oil loading as well as on the type of alginate used.



(a)



(b)

Figure 1 Encapsulation efficiency (**a**) and non-encapsulated oil (**b**) of alginate capsules depending on oil loading

In this study, the maximum encapsulation efficiency that can be attained in the alginate capsules with oil loadings up to 40% (w/w). Increasing the oil loading higher than 40% (w/w) decreased the encapsulation efficiency. Literature reveals that encapsulation efficiency depends on the degree of cross-linking at the surface of the extruded emulsion droplet (Chang and Dobashi, 2003; Drusch and Berg, 2008). If there was a high amount of oil in the system of alginate, once the emulsion droplet dropped into the gelling bath, there was insufficient cross-linking between the alginate and calcium ions at the droplet surface, which resulted in formation of loose Ca-alginate hydrogel wall barriers. These results are in good agreement with those of Chan (2011), who reported an encapsulation efficiency of about 90% at an oil loading of 20 vol %.

The results on the emulsion efficiency of sodium alginate – oil containing capsules at different oil loading capacity show that our preparations are able to hold the

encapsulated oil and therefore deliver in a certain place of a model human digestive system. Hence, further work deals with the characterization of alginate capsules with different oil loading capacity during gastric and intestinal phase of the *in vitro* digestion.

Physicochemical properties of alginate capsules with oil during in vitro digestion

The swelling behaviour of the alginate capsules in simulated gastrointestinal fluid is displayed in Table 1. Both types of capsules followed the same trend, shrinking in gastric solution, most notably when the pH was reduced to 2. It has been proposed that shrinking occurs due to a decrease in the repulsive charge due to protonation of free carboxylate groups on the alginate. Furthermore, due to dissociation of calcium ions at low pH, an acid gel can be formed where COO^- groups become protonated, allowing the alginate chains to come closer together and form hydrogen bonds. Once placed in the intestinal solution, all capsules began to swell to varying degrees presumably due to an increase in the electrostatic repulsive forces at a pH above the constant acidity (pK_a) of the uronic acid groups on the alginate (Draget *et al.*, 1997). It was observed that the capsules with different amount of oil shrink and swell similar to each other. Over the time, disintegration of the capsules was observed, presumably as a result of the increased concentration of monovalent ions which occurs in intestinal conditions.

The mechanical properties of the capsules were determined as a Young's modulus as described in Materials and methods section (Table 1). The strength of the capsules under applied experimental protocol differs not considerably depending on the amount of oil loaded. The Young's modulus of the alginate capsules was determined using a compression method corresponding to the 30% deformation of the material. Figure 3 shows that the value of Young's modulus of alginate capsules decreases with increasing of oil concentration: for the oil concentration at 20% the Young's modulus were up to 7×10^4 Pa, whereas at 40% they were up to 6×10^4 Pa.

In general, the Young's modulus of alginate capsules may be considered to depend on the degree of cross-linking. It has been clearly demonstrated from the literature that the Young's modulus of alginate capsules can be increased by the use of different types of gelling ions and the addition of a larger amount of cations (Chan *et al.*, 2011; Peniche *et al.*, 2004). Thus, it was found that chemical properties of cations such as atomic number, ionic radius, ionic strength, association constant and chemical affinity influence alginate bead stiffness. Also reports from the literature show that higher cations concentration increases the bead stiffness due to a maximum crosslinking, whereas low cations concentration gives alginate more time to diffuse to the bead surface as the driving force of ions toward the gelling zone is reduced (Skjak-Bræk *et al.*, 1989). However, Soliman *et al*. (2013) has found that the best formulation for the encapsulation of essential oil in sodium alginate capsules was 2% (w/v) of alginate, 0.5% (w/v) calcium chloride, and 20 min for the cross-linking time. This gives a maximum loading capacity and maximum encapsulation efficiency for three types of oil.

Table 1. Mechanical properties and swelling ration of capsules with different oil loading

Time, min	Oil 20%		Oil 40%	
	Young's modulus, $\times 10^4$ Pa	Swelling ratio, %	Young's modulus, $\times 10^4$ Pa	Swelling ratio, %
0	3.9 ± 0.5	-	2.9 ± 0.2	-
15	4.4 ± 0.4	-19.0 ± 6.9	3.6 ± 0.3	-28.1 ± 6.1
30	5.2 ± 0.4	-26.3 ± 6.5	4.2 ± 0.2	-28.5 ± 7.1
45	5.8 ± 0.4	-27.8 ± 7.1	4.8 ± 0.1	-29.0 ± 6.5
60	6.3 ± 0.3	-29.1 ± 8.5	5.4 ± 0.3	-31.6 ± 7.1
75	6.5 ± 0.5	-26.4 ± 7.1	5.8 ± 0.3	-30.2 ± 6.1
90	6.5 ± 0.3	-22.4 ± 7.3	5.9 ± 0.2	-29.6 ± 6.9
105	6.5 ± 0.3	24.9 ± 6.5	6.0 ± 0.3	8.6 ± 7.1
120	6.7 ± 0.3	72.6 ± 8.5	6.4 ± 0.3	16.6 ± 6.5
125	3.9 ± 0.4	80.8 ± 7.1	3.7 ± 0.4	56.1 ± 5.9
130	2.5 ± 0.4	93.7 ± 6.5	2.3 ± 0.5	70.2 ± 7.1
135	1.2 ± 0.6	100.2 ± 7.1	1.0 ± 0.5	80.8 ± 7.1
140	1.0 ± 0.5	110.2 ± 7.5	0.6 ± 0.5	95.8 ± 6.5
150	0.8 ± 0.5	124.3 ± 6.8	0.6 ± 0.5	109.1 ± 7.3
160	Not determined	138.1 ± 6.9	Not determined	118.2 ± 7.1

During the gastric phase, the capsules are increased in strength as compared to their network strength during the intestinal stage. The initial decrease in modulus as depicted in Table 1 may be due to the dissociation of calcium ions from the gel network and the formation of an acid gel stabilized by weaker hydrogen bonding. All types of bead exhibit a decrease in network strength during the intestinal phase which correlates with the formation of a more open, porous gel network as the capsules swell during this period. During the intestinal phase, the Young's modulus of all capsules with different oil loading was not statistically different due to swelling and disintegration of polymer network.

The formulation and processing variables involved in the preparation of oil loaded alginate capsules were so far investigated. Using the mechanical analysis, it was found that the structure of the capsules at the end of the gastric phase had denser gel network than the network properties observed at the intestinal conditions. However, the aim of this work was to prepare the beads with the essential oil for their successful utilization as functional carriers for the release in the gastro-intestinal tract, where the bioactive is protected by the gel carrier. It is visible that in the intestinal phase the beads are eventually disintegrated which results in a control delivery of the bioactive. So, at the next stage of the current investigation the rate of oil transport from the capsules during enzymatic hydrolysis *in vitro* was characterized. Further the mathematical modelling on the kinetics release of essentials was performed thus combining the physics of diffusion law and bioactivity of encapsulated materials.

Kinetics of lipid transport from alginate capsules

As discussed, alginate is readily processable for applicable three-dimensional scaffolding materials such as hydrogels, microspheres, microcapsules, sponges, foams and fibers. Alginate-based biomaterials can be utilized as drug delivery systems and cell carriers for tissue engineering (Gorbunova *et al.*, 2016; Soliman *et al.*, 2013). The choice of encapsulation of bioactives is governed by criteria of advanced application, economics and safety (Rayment *et al.*, 2009). However, behavior of the capsules in simulated gastro-intestinal conditions remains in the area of research interest.

Kinetics release of essential lipids from the alginate capsules were monitored using UV-VIS-spectroscopy. This method is based on the determination of the optical density of essential lipids dissolved in hexane at 260 - 300 nm. Observations of essential lipids release were carried out for 180 min in simulated gastric and intestinal conditions. Smooth absorbance curves are illustrated with the maximum release of oil from the capsules to be at the intestinal conditions, i.e. after 120 min. Results indicate that the amount of oil encapsulated in the capsules remains stable during the gastric stage, whereas the residual amount of oil was released from the alginate capsules at the intestinal phase, as shown in Figure 2.

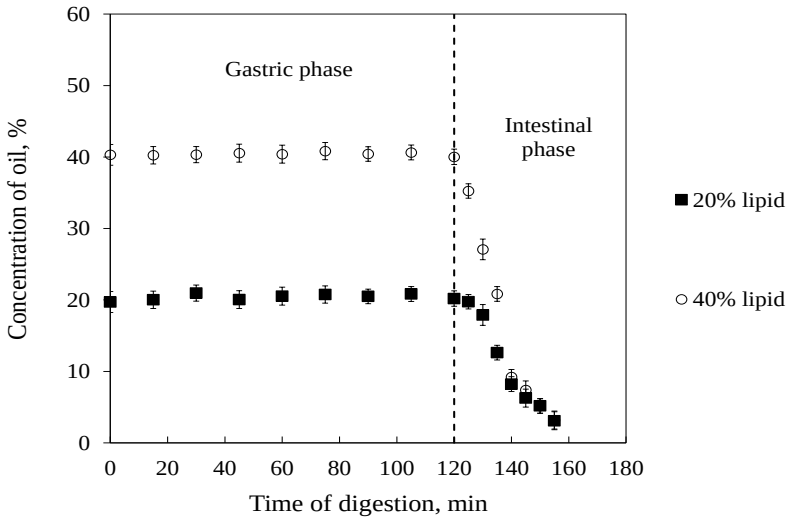


Figure 2 Concentration of lipid in alginate capsules in simulated gastro-intestinal conditions as a function of time

Figure 3 depicts changes in Young's modulus (Young's modulus$_i$ / Young's modulus$_0$) and changes in the release profile (equation. 5) of essential oil from the alginate capsules in simulated gastro-intestinal conditions as a function of time.

$$c = 100 - \left(\frac{100 \cdot c_i}{c_0} \right) \qquad (5)$$

where c is the release of oil (in percent), c_i is the concentration of oil at particular time of measurement (in percent) and c_0 is an initial concentration of oil (in percent).

The results reveal a significant increase in values of Young's modulus at the simulated gastric conditions and their considerable decrease at the intestinal conditions. It is shown that the release of essentials remains relatively constant up to 120 min of the applied experimental protocol. Further, in simulated small intestine there had been a sharp rise in transport rates arguing for a delivery of bioactive compound. Is has been proven that the release of bioactive is governed by nature of the capsules and environment conditions where the mechanical properties of capsules are considered to be a basis of the optimal utilization of delivery with the maximum rates at the intestine phase.

To identify the transport rate of the lipid in the medium of this investigation, we consider the mathematical modeling of release from advanced delivery systems which has two major benefits: (i) the elucidation of the underlying transport mechanisms; and (ii) the possibility to predict the resulting release kinetics as a function of the design (geometry and composition) of the device.

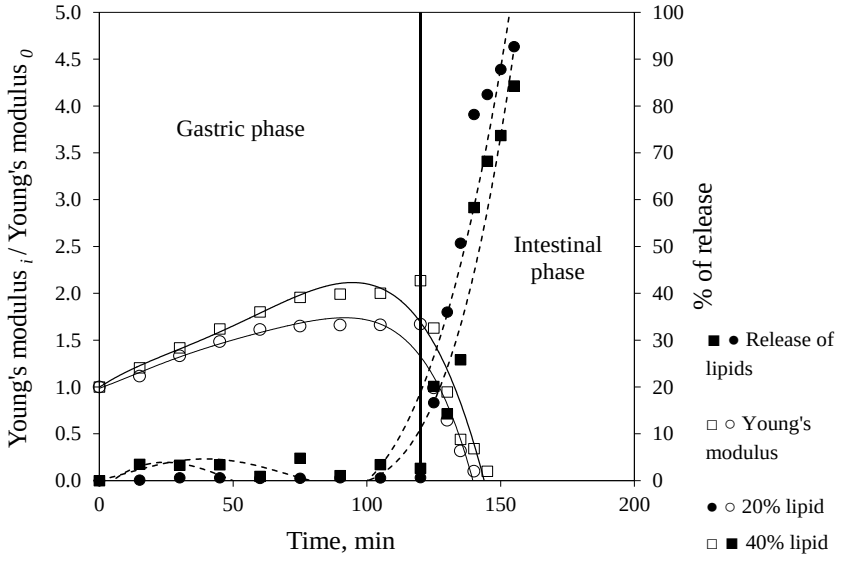


Figure 3 Changes in Young's modulus and in release profile of lipid in simulated gastro-intestinal conditions

Depending on the type of polymer, size, shape and composition of the system and different sink conditions, homogeneous mass transport phenomena have to be taken into initial bioactive distribution or constant diffusivity (diffusional processes, polymer swelling and considering bioactive diffusion only). Therefore, the equation 6 can be proposed. his model is suitable for solved analytically for a cylinder of radius R and routine use a mathematical model should be easy to height

H, yielding handle and require only short calculation times. Thus, it is important to identify the dominating mass transport phenomena and to simplify the model as much as possible. When the cylindrical tablet or capsule is placed in bulk of liquid solution two opposite processes begin to occur. Solution components like water molecule penetrate into the bulk of tablet/capsules, and active substance from the tablets/capsules will release into the bulk solution. Both of these processes are called diffusion and diffusion in tablets can be described by Eq. 6, taking in consideration axial and radial transport (Siepmann *et al.*, 1998):

$$\frac{\partial C_k}{\partial t} = \frac{1}{r}\left\{\frac{\partial}{\partial r}\left(r \cdot D_k \frac{\partial C_k}{\partial r}\right) + \frac{\partial}{\partial \theta}\left(\frac{D_k}{r} \cdot \frac{\partial C_k}{\partial \theta}\right) + \frac{\partial}{\partial z}\left(r \cdot D_k \frac{\partial C_k}{\partial z}\right)\right\}, \quad (6)$$

where C_k and D_k are concentration and diffusion coefficient of the diffusing species (k=1 for water, k=2 for active component), respectively; r denotes radial coordinate, z is the axial coordinate, θ is the angular coordinate, and t represents time.

This partial differential equation (6) can be solved under various conditions, e.g. constant or non-constant diffusivities, and using stationary or moving boundary conditions. For the investigated controlled drug delivery systems, two cases are relevant: (i) constant diffusion coefficients and stationary boundary conditions; and (ii) non-constant diffusion coefficients and moving boundary conditions. Assuming perfect sink conditions, homogeneous initial drug distribution, constant diffusivity and considering drug diffusion only, equation 6 can be solved analytically for spheres of radius R, yielding:

$$\frac{M_t}{M_\infty} = 1 - \frac{6}{\pi^2}\sum_{n=1}^{\infty}\frac{1}{n^2}\exp\left(-\frac{D \cdot n^2 \cdot \pi^2 \cdot t}{R_s^2}\right) \quad (7)$$

where M_t and M_∞ are the amount of drug released at time t and $t = \infty$, respectively, D_k is the diffusion coefficient and a_n are the roots of the Bessel function of the first kind of order zero:

$$J_0(\alpha_n) = 0 \quad (8)$$

As instantaneous and complete drug dissolution are assumed, values for the diffusion coefficients obtained (D_{eff}=9×10^{-6} cm^2/c for 20% lipid and D_{eff}=1.5×10^{-5} cm^2/c for 40% lipid) from curve fitting to experimental drug release data do not represent true, but apparent diffusion coefficients. The equation 7 was programmed in Microsoft Visual Basic and the apparent diffusion constants and correlation coefficients were calculated (data not shown). To minimize the resulting error certain minimum number of sequential layers has to be considered (in our case n=50 has been chosen). Using the presented mathematical model of the lipid release profile from the alginate matrix in gastric in intestinal conditions, the theoretical predictions of such function in Figure 6 have been depicted. As can be seen, theoretical function can be verified by the independent release experiments (R^2=0.98-0.99).

Figures 3 and 4 illustrate the outcome of employing equation 6 in the prediction of diffusion rates for the system of this investigation undergoing model gastrointestinal conditions. It combines Fickian kinetics with the mechanical properties within the time of investigation (up to 180 min). The values of lipid release are stable in gastric environment, whereas there is a sharp increase in values in alkaline conditions. Clearly, changes in mechanical properties under media conditions govern the diffusional mobility of lipids in the encapsulated matrix.

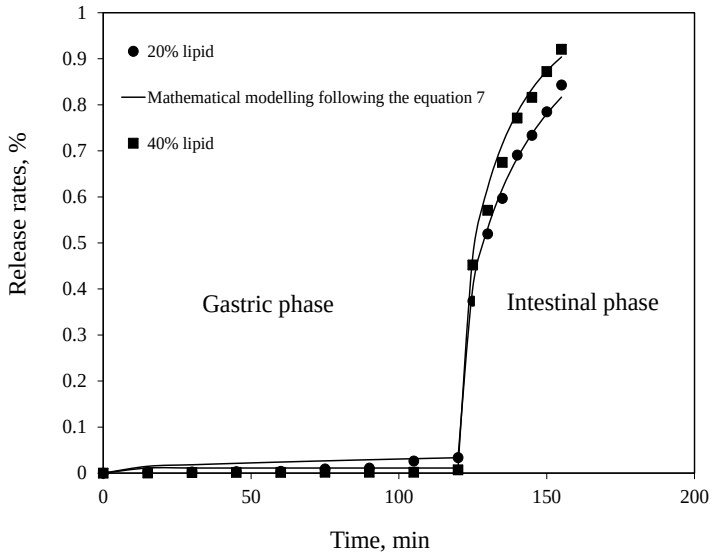


Figure 4 Release rates of lipids in simulated gastro-intestinal conditions

Conclusions

The present work addresses the release patterns of lipids in alginate capsules under simulated gastrointestinal conditions. The mechanical transformations of capsules led to an increase in strength in acidic environment which has a profound effect on the delivery of bioactive compounds through the harsh gastric environment. Operational kinetics comply with Fickian modelling, an outcome that makes sense considering the diffusion mobility of lipid within the environment of this investigation for 180 min. The instrumental techniques of this study show that alginate capsules display shrinkage in gastric conditions as a result of reduction of electrostatic repulsive forces at low pH and the dissociation of calcium ions, whereas in intestinal phase all capsules increasingly swell. It is quite remarkable that comprehensive relationships between Young's modulus and release rates of lipid in relation to simulated gastro-intestinal conditions confirming the controlled delivery of bioactive compound. This investigation is significant in relation to the formulation of "functional foods" such as infant and sports nutrition formulae, health bars, breakfast cereals, dairy products as well as in ingredient powders and

concentrates. Future work will consider the present findings thus continue using enhanced in vivo models to ascertain trends in controlled delivery.

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