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Rheological Investigation of the Shear Strength, Durability, and Recovery of Alginate Rafts Formed By Antacid Medication in Varying pH Environments

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Abstract

The mechanical response of alginate rafts formed by mixing liquid alginate antacid medication (Gaviscon® Extra Strength Liquid Antacid) with acidic solutions was investigated by deforming isolated rafts in a shear rheometer. As rafts were deformed to varying magnitudes of applied strain, rheological parameters were identified and related to the overall strength, durability, and recoverability of rafts formed at different pH (1.1 – 1.7) and aging conditions (0.5 – 4 hr). Rafts formed in the lowest acidity solutions (pH 1.4, 1.7) were elastically weak (G_0' = 60, 42 Pa for un-aged raft) yet maintained their elasticity during applied shear deformation to large values of strain (γ_c ~ 90%, 50%, where $G' \approx G''$), and displayed a low-to-moderate level of elastic recovery following large-strain deformation. Rafts formed in the highest acidity solution had the greatest strength (G_0' = 500 Pa for un-aged raft and 21.5 kPa for rafts after 0.5 hr of aging), reduced durability (γ_c ~ 2.5%, independent of aging), and displayed the greatest recoverability. A trade-off existed between un-aged raft strength and durability while recovery was dependent on durability, solution pH, and age. Rheometry-based evaluations of alginate rafts could be used for the informed design of future gastric retention and antacid products.

Keywords: alginate; alginate raft; mechanical properties; rheology; ionic crosslinking; acid-reflux; shear stress

1.0 Introduction

Gastroesophageal reflux disease (GERD) is the most common outpatient gastroenterological diagnosis in the United States.(Hershcovini and Fass, 2011; Mandel et al., 2000) Of the adult population in the United States, 20% experience GERD-related symptoms weekly.(Locke et al., 1997) The disease is most commonly perceived as "heartburn", caused by reflux of acidic stomach contents into the unprotected esophagus. Up to 40% of people in western countries experience heartburn after meals.(Dettmar et al., 2007)

To treat post-meal reflux, antacids and alginate-based formulations are typically used.(Hershcovini and Fass, 2011) Antacids provide rapid but transient relief, lasting only one hour on average while heartburn symptoms can continue for several hours after meals. Alginate-based formulations (*e.g.*, Gaviscon®) create a floating, gastric-retaining foam in the stomach that serves as a barrier to the penetration of stomach acid into the esophagus and upper gastrointestinal tract.(Hampson et al., 2005) Such foams can be sustained for up to four hours, resulting in immediate and lasting relief from post-meal heartburn. Antacid components are also included in alginate-based formulations, although past studies suggest that neutralization of the stomach contents is not a critical factor for the treatment of heartburn symptoms when alginate-based formulations are used to create a physical barrier to acid reflux.(Mandel et al., 2000) In addition to alginate-based antacid products, alginate materials have many applications in pharmaceutics, including drug delivery media (Florián-Algarín and Acevedo, 2010; Khutoryanskiy, 2011), slow-release would dressings (Thu et al., 2012), controlled release fibers (Wang et al., 2007), and development of retention-selective gastric foams to aid in early preclinical drug discovery (Foster et al., 2012). Additionally, alginate-based materials have found wide application in the fields of biomedical engineering and regenerative medicine.(Derby, 2012; Sun et al., 2012; Van Vlierberghe et al., 2011; Yu and Ding, 2008)

Liquid alginate antacid products for acid reflux control typically contain carbonate-based molecules as an active ingredient (*e.g.*, calcium carbonate, potassium bicarbonate, magnesium carbonate).(Hampson et al., 2005) In the presence of gastric acid, carbonates in the product react to form carbon dioxide gas. Simultaneously, free metal ions released from the antacid active ingredient (*e.g*, Ca^{2+} from calcium carbonate) diffuse through the alginate and facilitate the formation of an ionically crosslinked "egg-box" structure between α-L-guluronic acid residues in neighboring alginate molecules.(Grant et al., 1973; Lee and D. J. Mooney, 2012; Pawar and Edgar, 2012) The formation of these ionic crosslinks between alginate molecules leads to the creation of a three dimensional viscoelastic network(Johnson et al., 1997; Webber and Shull, 2004) which displays good mechanical strength when a critical concentration of ionic crosslinks is present. Carbon dioxide gas becomes trapped in the alginate network and forms an expanding, buoyant foam, commonly referred to as an alginate raft.(Mandel et al., 2000)

Basic empirical tests and clinical trials have been performed on alginate rafts to optimize the drug formulation in order to achieve rafts with good mechanical strength and durability, and effective acid suppression.(Dettmar et al., 2007; Mandel et al., 2000) To quantify the mechanical properties of alginate rafts, Hampson, *et al.*(Hampson et al., 2005) performed a controlled empirical study of rafts produced from a variety of alginate-based antacid products. The tensile force required to vertically pull an L-shaped wire through a given raft and the compressive force required to compress a given raft through an orifice were measured in addition to assessing the overall effect on the raft's structure of prolonged agitation in a tumbler mixer. From these experiments, estimations of the rafts' strength, resistance, and resilience were determined. Raft strength was found to be directly related to raft resilience, with the highest strength rafts resisting breakup during tumbling for the longest duration of time.(Hampson et al., 2005)

One challenge in characterizing the properties of alginate rafts is performing mechanical measurements which mimic the turbulent internal environment of the stomach. In addition to tensile and compressive forces, alginate rafts encounter shear forces from the churning contents of the stomach and gastric pressure waves as well as shear stresses from any adhesive interactions between the edges of the raft and the mucosal stomach walls.(Mandel et al., 2000; Richardson et al., 2004) Additionally, *in vivo* studies indicate that the rafts may be driven into the lower esophagus due to gastric pressure waves.(Malmud et al., 1979; McHardy and Balart, 1972) Penetration and extraction of the raft into the lower esophagus is expected to impart significant shear forces on the raft from frictional interactions with the esophagus and stomach wall. Thus, there is a clear need to investigate the mechanical properties of alginate rafts during exposure to shear forces.

Shear rheometers are commonly used to measure the mechanical responses of soft materials and complex fluids during exposure to controlled levels of shear stress.(Larson, 1999) Soft hydrogels formed from ionically crosslinked alginate networks swollen in aqueous fluid are frequently studied via rheometry to determine how the mechanical properties of the hydrogel change as a function of composition, aging, shear strain magnitude, and strain rate.(Florián-Algarín and Acevedo, 2010; Lin et al., 2011; Saarai et al., 2012; Storz et al., 2009; Taylor et al., 2005; Webber and Shull, 2004) Despite the extensive use of rheometry in alginate-based hydrogel research, there are almost no studies that investigate the properties of alginate-based rafts via shear rheometry. One advantage of using rheometry for investigating the mechanical properties of alginate rafts are the standardized rheometer geometries and measurement protocols from which alginate raft structure-property relationships may be defined and directly compared with existing alginate hydrogel rheometry studies.

A protocol for *in vitro* raft formation and shear rheometry testing is developed here to characterize isolated alginate rafts formed from liquid alginate antacid product. The effects of solution pH, aging, and shear deformation magnitude on the mechanical properties of the alginate rafts are evaluated in order to characterize the overall strength, durability, and recoverability.

2.0 Materials and Experimental Methods

2.1 Materials

The liquid alginate antacid product for acid reflux control investigated here was Gaviscon® Extra Strength Liquid Antacid (GlaxoSmithKline Consumer Healthcare, L.P., USA). This product was purchased from a local pharmacy and used as-received. For a 5-mL 'teaspoonful' dose, the listed active ingredients were aluminum hydroxide (254 mg) and magnesium carbonate (237.5 mg). Sodium alginate was listed as an inactive ingredient.

Aluminum hydroxide ($Al(OH)_3$) is known to react with excess acid in the stomach, reducing the overall acidity while producing Al^{3+} ions which form ionic crosslinks within the alginate network. Meanwhile, magnesium carbonate ($MgCO_3$) is an antacid ingredient that is known to react with acid in the stomach to produce carbon dioxide gas which aids in the floatation of the alginate network, forming the alginate raft. Sodium alginate is listed as an inactive ingredient in the United States and alginate products for acid reflux are classified only as "liquid antacid" although the alginate will result in an acid-blocking barrier (note: this is different from British and European pharmacopoeias, which accept alginate as an active ingredient).

To form the alginate rafts *in vitro*, deionized water (Nanopure® Infinity Barnstead water purification systems) and acetic acid (glacial, Sigma Aldrich, used as received) were mixed with the liquid alginate antacid product, described in detail in the following section. Ideally, hydrochloric acid (HCl) solutions would be used to create the alginate rafts, as HCl is a principle component of gastric secretion.(Kong and Singh, 2008; Schubert, 2012) However, most standard rheometer fixtures are fabricated from stainless steel (300 series), which is highly susceptible to pitting/crevice corrosion when exposed to HCl at any concentration or temperature.(B. D. Craig and Anderson, 1995) Chlorides penetrate and destroy the passive oxide film that is responsible for the corrosion resistance of stainless steel. Stainless steel is resistant to corrosion from acetic acid; thus, acetic acid was used in this study for the *in vitro* formation of the alginate rafts.

2.2 Alginate Raft Formation

A method was developed to form alginate rafts *in vitro*. A single dose of liquid alginate antacid product was added to aqueous solutions of acetic acid with varying pH within the typical acidity range of a fasted stomach(Kong and Singh, 2008; Schubert, 2012) (Table 1). The solution temperature was maintained at 37°C on a dual action hotplate/stirplate. A pH meter was used with buffer calibration standards to measure the pH of each solution. As the volume of the solution (~ 95 mL) represented approximately a quarter of a typical stomach volume(Ferrua and Singh, 2010), only a single dose of the antacid product (5 mL) was used instead of the maximum 24-hr dosage (16 teaspoons or ~ 80 mL). Slow stirring of the solution ensured that the antacid product mixed with the acidic solution instead of coating the bottom and sides of the glass beaker, which was found to retard raft formation. Development of the alginate network and flotation of the alginate raft to the surface of the solution occurred within five minutes. For certain experiments, the alginate raft was allowed to rest at the solution's surface for a specific duration (0.5 – 4 hr) before removal for characterization. Retrieval of the raft from the solution was accomplished by decanting excess solution followed by physically lifting the raft from the beaker with a spoon or spatula (see Fig. 1). Dimensions of the raft were approximately 50 mm in diameter (constrained by the inner diameter of the beaker) and approximately 2-3 mm in thickness.

2.3 Alginate Raft Characterization

Shear rheometry was performed to characterize the mechanical properties of the alginate rafts. An Anton Paar MCR 302 rheometer with a stainless steel parallel plate measuring system (25-mm plate diameter) was used to test the isolated rafts. A Peltier temperature control system maintained the temperature at 37°C. The following procedure was followed to load the raft sample into the rheometer: (1) the sample was placed in the center of the bottom parallel plate, (2) the top plate was moved to the measuring position (a 2-mm gap size was used) such that the raft experienced a slight normal force as detected by the rheometer force transducer, and (3) the sample was trimmed using a spatula such that the sample edge was approximately flush with the top parallel plate.

For each raft sample, oscillatory strain sweep rheometry tests were performed in which the sample's stress response was measured as a function of applied shear strain amplitude (γ, ranging from 0.1% to 100%) at a constant angular frequency (ω = 10 rad s^{-1}). The stress response of the rafts was quantified in terms of the storage shear modulus (G') and the loss shear modulus (G''). The storage modulus was a measure of the sample's elastic-like response while the loss modulus was a measure of the sample's viscous-like behavior under shear. Two strain sweep tests were performed in series for each raft sample. In the first strain sweep test, the applied strain amplitude was discretely increased from 0.1% to 100%. This test was immediately followed by a second strain sweep test in which the strain amplitude was discretely decreased from 100% to 0.1%. The coupling of increasing and decreasing strain sweep tests was designed to probe any hysteresis present in the rheological response of the samples and thus assess the ability of the samples to recover from large-strain deformation.

Alginate raft morphology did not visibly change during the rheometry testing. No evidence of wall slip between the sample and the top or bottom parallel plates was observed directly or indirectly from the resulting data. Once the desired rheometer tests were complete and the top parallel plate was raised to facilitate sample removal, samples were typically observed to stick to the top parallel plate. Additional residue from the samples was also seen on the bottom plate. The adhesion between the rafts and the parallel plate measuring system upon sample unloading also confirms a lack of wall slip. There was no evidence of significant solvent evaporation during the rheometer tests, which lasted a total of 30 minutes.

3.0 Results

The shear stress response of un-aged alginate rafts formed in solutions with varying pH is displayed in Fig. 2. The raft formed from each solution displayed unique *G’* and *G’’* curves. All *G’* and *G’’* displayed the expected linear viscoelastic plateau at small values of strain before decreasing in magnitude with increasing strain. For each *G’* curve, a limiting value of *G’* was extracted to describe the modulus of the raft when the applied strain approaches zero. This limiting value, G_0', was approximated as $G'(\gamma = 0.1\%)$, which is reported in Table 2. Additionally, the curves for each solution displayed a critical value of applied strain where *G’* and *G’* were approximately equal, reported in Table 2 as γ_c. As seen in Fig. 2 and Table 2, more acidic solutions (pH 1.1 – 1.2) resulted in rafts with greater values of G_0' and significantly reduced values of γ_c compared to rafts formed in less acidic solutions.

The strain sweep rheometer tests displayed in Fig. 2 for the five solutions were collected by varying the applied strain amplitude in discrete steps ranging from 0.1% to 100%. In all cases, this test was immediately followed by a second strain sweep that discretely varied the strain amplitude from 100% to 0.1%. Data from these increasing and decreasing strain sweeps can be displayed in one graph; the resulting hysteresis loops for *G’* are displayed in Fig. 3a-e. The relative amount of hysteresis was quantified for each data set by the difference in the values of *G’* at a strain amplitude of 1% measured from increasing and decreasing strain sweeps. This difference, termed $\Delta G'$, was determined for each raft as an absolute value and a percentage decrease from the larger value of *G’* (see Table 2), the latter allowing for direct comparison of the hysteresis magnitudes between rafts formed in the different pH solutions. While hysteresis was clearly observed in all cases, the hysteresis magnitude reached a maximum for rafts formed in Solution C (pH 1.3, Fig. 3c) before decreasing at higher (Fig. 3a,b) and lower (Fig. 3d,e) levels of acidity.

The mechanical properties of alginate rafts formed in Solution A (pH 1.1) and aged from 0.5 – 4 hr while in contact with the solution are displayed in Fig. 4. Data representing the mechanical properties of the un-aged raft is included for comparison. Similar to Fig. 2, the G' and G'' curves in Fig. 4 all displayed a linear viscoelastic plateau at small strain amplitudes which was approximated by G_0' as well as a critical value of strain, γ_c, where $G' \approx G''$ (see Table 3). The limiting storage modulus of the rafts formed and aged in Solution A increased with aging time from 30 min to 2 hr, after which the values decreased in a nonlinear fashion. Interestingly, the critical values of strain for the aged rafts displayed an average value of 2.6% ± 0.8% (95% confidence interval), very similar to the response from the un-aged raft.

In a similar manner to the pH study, data from increasing and decreasing strain sweeps was collected for rafts at each aging condition. The hysteresis loops for G' with the corresponding absolute and relative $\Delta G'$ values at 1% strain amplitude are displayed in Fig. 5a-e and Table 3. While hysteresis was observed in all cases, the hysteresis magnitudes were significantly larger for rafts aged from 0.5, 1, and 2 hr ($\Delta G'$ = -29%, -26%, and -45%, respectively) compared to rafts aged for 3 and 4 hr ($\Delta G'$ = -15% and -16%, respectively).

4.0 Discussion

The shear rheometer experiments summarized in Fig. 2 and Table 2 indicated that solution pH strongly influenced the shear mechanical strength of the alginate rafts. As described in the introduction, the two active ingredients in the liquid alginate antacid product, $Al(OH)_3$ and

$MgCO_3$, react in acidic conditions to form free Al^{3+} ions and carbon dioxide gas, both of which are necessary to form a strong, buoyant alginate raft. Conditions of low pH result in increased reaction rates between the alginate product and acidic solution. This explains the greater G_0' values observed in Table 2 for rafts formed in Solution A (pH 1.1) compared to the rafts formed in the lower acidity solutions. The elastic properties of the rafts are a function of the raft's internal structure of crosslinked alginate.(Stokke et al., 2000; Webber and Shull, 2004) Higher ionic crosslinking densities result in stiffer rafts, which act as elastic solids when exposed to shear forces. Thus, the greater concentration of free Al^{3+} ions produced within the higher acidic solution (Solution A) led to the formation of a more densely crosslinked alginate raft with subsequently increased elastic strength. In contrast, rafts formed in the lower acidity solutions are expected to have reduced crosslinking densities, which resulted in their relatively lower elastic strengths.

Interestingly, over the relatively narrow pH range that was investigated (1.1-1.7), the elastic strength of the alginate rafts decreased by an order of magnitude with increasing pH. The typical intragastric pH range for a healthy stomach in a fasted state ranges from 0.3 – 2.9 with a median fasting pH of 1.5.(Schubert, 2012) Stomach pH can increase to 4.5 – 5.8 during eating and can decrease to less than 3.1 after 1 hr following a meal.(Kong and Singh, 2008) Thus, alginate rafts formed in a typical healthy stomach following a meal may be expected to have reduced strength compared to the alginate rafts characterized in this study.

While rafts formed in more acidic solutions displayed greater initial elastic strengths (*i.e.*, G_0', the strength at low values of applied strain), rheometry results indicated that these same rafts have significantly reduced values of critical strain, γ_c, compared to rafts formed in the lower acidity solutions (see Table 2). The critical strain (where $G' \approx G''$) can be interpreted as the critical magnitude of deformation when the sample transitions from displaying a more elastic-like mechanical response ($G' > G''$) to displaying more viscous-like behavior ($G'' > G'$).(Larson, 1999) The strain-induced reduction in elasticity and transition to viscous behavior beyond γ_c indicates a deformation-induced mechanical breakdown or weakening of the alginate network, most likely due to destruction of elastically-active crosslinks within the network.(Erk and Shull, 2011) Thus, rafts formed in more acidic solutions (pH 1.1 – 1.2) mechanically degraded at lower levels of applied shear deformation than rafts formed in less acidic solutions (pH 1.4 – 1.7) which displayed greater values of γ_c and thus maintained their elastic strength to greater magnitudes of applied shear strain. These results indicate an apparent trade-off between initial elastic strength and mechanical durability during exposure to increasing magnitudes of applied shear deformation, in contrast to findings from prior studies.(Hampson et al., 2005)

The magnitude of hysteresis quantified from the increasing and decreasing strain sweeps (Fig. 3) signifies the permanent damage to the raft's internal structure due to the applied shear deformation. This difference in G' between increasing and decreasing strain sweeps, $\Delta G'$, is inversely related to the ability of the raft to recover its elastic strength following deformation to large values of applied strain. The raft formed in the highest acidity solution (Solution A, pH 1.1) displayed the smallest hysteresis (with $\Delta G'$ = -42%, Table 2) and thus appeared to have the best recoverability of all rafts which were investigated here. This finding is consistent with the expected increased concentration of Al^{3+} in rafts formed in Solution A. The ionic crosslinks facilitated by Al^{3+} are reversible so while large deformation effectively "fractured" crosslinks in the alginate network, new crosslinks formed once the deformation decreased and restored the strength of the alginate network. Thus, there appears to be a direct relationship between solution acidity and recoverability.

Rafts formed in the lowest acidity solutions (Solution D, pH 1.4 and Solution E, pH 1.7) contained relatively low concentrations of Al^{3+} and thus were expected to display the lowest levels of recovery. Instead, these rafts displayed moderate recovery following deformation ($\Delta G'$ = -70%, -59%, see Table 2), while Solution C (pH 1.3) displayed the greatest hysteresis with $\Delta G'$ = -80% and thus the worst recovery of all the rafts investigated in this study. This finding is explained by considering raft durability. Solutions D and E produced the most durable rafts, with γ_c values equal to 90% and 50%, respectively (Table 2). As these rafts maintained their elastic strength to relatively large values of applied strain, the overall magnitude of strain-induced damage to the alginate network was most likely reduced compared to the less durable rafts formed in the higher acidity solutions. Thus, substantial recovery appears to be possible for rafts formed from Solutions D and E, even with the reduced availability of Al^{3+} for network repair. The rafts formed from Solutions A and B have poor durability (γ_c = 2.5%, 4.5%) and thus significant structural damage most likely occurred during large-strain deformation. However, these rafts contained the largest concentrations of Al^{3+} available for network repair and thus recoverability was observed to be high. In contrast, the raft formed in Solution C was only moderately durable (γ_c = 39%) and due to its mid-range pH, only a moderate amount of Al^{3+} was available for network repair. Thus, rafts from Solution C displayed the overall lowest ability to recover from large-strain shear deformation.

In addition to solution pH, duration of aging was found to have a strong effect on the mechanical strength of the alginate rafts (Fig. 4). The greatest increase in strength occurred within 0.5 hr of aging, as there was a three orders of magnitude increase in G_0' with an additional 140% increase in strength from 0.5 – 2 hr (Table 3). The strengthening of the raft over time is consistent with the increased opportunity for free Al^{3+} ions from the solution to diffuse into the alginate and form ionic crosslinks. Continued crosslinking improved the strength linearly until 2 hr of aging had passed, potentially when the internal structure of the alginate reached a saturation point with respect to Al^{3+} ions. Furthermore, the hysteresis magnitudes became small and constant for 3 and 4 hr aging durations (-15% and -16%, Table 3) compared to reduced aging durations. This measure of strong recovery of the highly aged rafts agrees with the expected saturation of the alginate with Al^{3+}. Additionally, the durability of the raft (quantified by γ_c) appeared to be independent or only very weakly dependent on aging duration.

5.0 Overall Conclusions and Implications

Alginate rafts were formed *in vitro* by mixing liquid alginate antacid product (Gaviscon®) with acidic solutions ranging from pH 1.1 – 1.7. The shear mechanical response of isolated rafts was investigated by oscillatory strain amplitude sweeps in a shear rheometer to quantify specific rheological parameters related to the overall strength (G_0'), durability (γ_c), and recoverability ($\Delta G'$) of the alginate rafts.

A trade-off existed between un-aged raft strength and durability while recovery was dependent on durability, solution pH, and age. Rafts formed in the highest acidity solution (Solution A, pH 1.1) yielded the greatest initial elastic strength and the best ability to recover strength after exposure to large-strain deformation. However, these performance increases were partially offset by a corresponding decrease in durability. Rafts formed in the lowest acidity solutions (Solution D, pH 1.4 and Solution E, pH 1.7) were relatively weak but displayed the best durability and moderate levels of recoverability. Interestingly, rafts formed at mid-range pH (Solution C, pH 1.3) performed the worst of all the rafts investigated here, displaying only moderate levels of strength and durability with the lowest level of recovery following large deformation. Aging tests of the raft formed in the highest acidity solution demonstrated a three order of magnitude increase in strength within only 30 minutes and heightened recoverability after 2 hrs of aging with nominal change in durability.

Rafts formed in stomach conditions of higher acidity (pH 1.1 – 1.2) are best suited for applications where sudden impacts are expected, such as due to food and drink ingestion. However, due to the apparent trade-off between raft strength and durability, these rafts will have decreased resiliency to deformation, although strong recovery is possible when deformation is encountered and the raft becomes structurally damaged. On the other hand, rafts formed in stomach conditions of lower acidity (pH 1.4 – 1.7) are best suited for applications where constant shear stress is anticipated. These rafts will have decreased strength and recoverability but superior durability and thus are more resilient to deformation. Outcomes of this investigation illustrate the utility of shear rheometry for quantifying the mechanical response of alginate rafts under controlled shear deformation. Future studies that focus on correlating formulation composition with mechanical results from shear rheometry experiments could be utilized by alginate antacid product manufacturers to inform formulation changes for future product improvement.

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Figure Captions

Fig. 1: Photograph of an alginate raft following removal from Solution A.

Fig. 2: Storage moduli (G', filled symbols) and loss moduli (G'', open symbols) for un-aged alginate rafts formed in solutions with varying pH – Sample A, pH 1.1 (●); Sample B, pH 1.2 (♦); Sample C, pH 1.3 (▲); Sample D, pH 1.4 (■); Sample E, pH 1.7 (►) – from oscillatory strain amplitude sweep data collected at a constant angular frequency of 10 rad s^{-1} and T = 37°C.

Fig. 3: Storage moduli collected from discretely increasing (closed symbols) and decreasing (open symbols) oscillatory strain amplitude sweeps at constant angular frequency of 10 rad/s and T = 37°C for un-aged alginate rafts formed in (a) Solution A, pH 1.1; (b) Solution B, pH 1.2; (c) Solution C, pH 1.3; (d) Solution D, pH 1.4; and (e) Solution E, pH 1.7.

Fig. 4: Storage moduli (G', filled symbols) and loss moduli (G'', open symbols) for alginate rafts formed in Solution A (pH 1.1) and aged for 0 hr (un-aged, ●), 0.5 hr (►), 1 hr (■), 2 hr (♦), 3 hr (▲), and 4 hr (◄); from oscillatory strain amplitude sweep data collected at a constant angular frequency of 10 rad s^{-1} and T = 37°C.

Fig. 5: Storage moduli collected from discretely increasing (closed symbols) and decreasing (open symbols) oscillatory strain amplitude sweeps at constant angular frequency of 10 rad s^{-1} and T = 37°C for alginate rafts formed in Solution A (pH 1.1) at the following aging conditions: (a) 0.5 hr, (b) 1 hr, (c) 2 hr, (d) 3 hr, and (e) 4 hr; symbols and colors correspond with Fig. 4.

Table Captions

Table 1: Composition and pH of aqueous solutions of acetic acid used to model the acidity range of the stomach.

Table 2: The limiting storage modulus, G_0', critical value of strain, γ_c, and measure of hysteresis at γ = 1%, $\Delta G'$, for un-aged alginate rafts formed in solutions with varying pH.

Table 3: The limiting storage modulus, G_0', critical value of strain, γ_c, and measure of hysteresis at γ = 1%, $\Delta G'$, for alginate rafts formed in Solution A (pH 1.1) and aged for 0.5 – 4 hr.

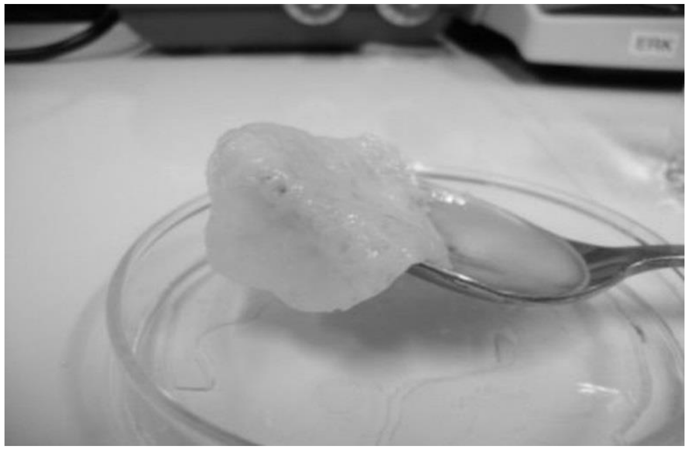


Fig. 6: Photograph of an alginate raft following removal from Solution A.

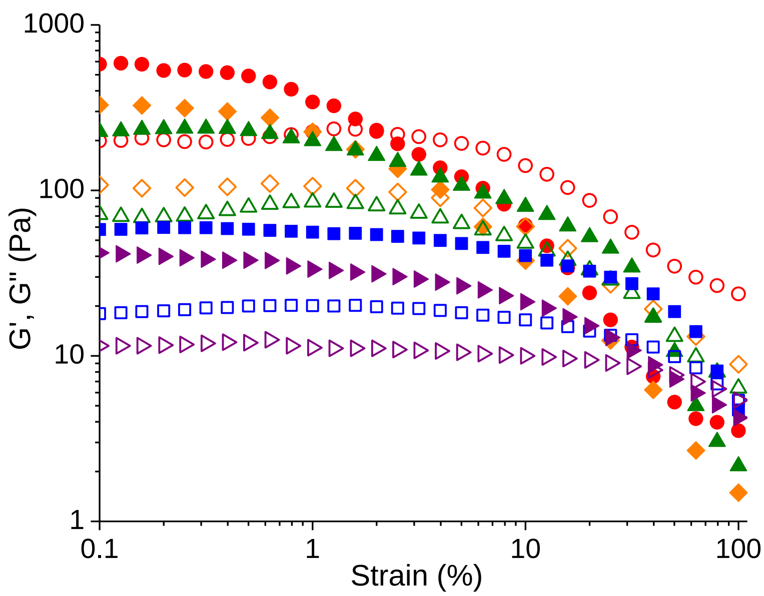


Fig. 7: Storage moduli (*G'*, filled symbols) and loss moduli (*G''*, open symbols) for un-aged alginate rafts formed in solutions with varying pH – Sample A, pH 1.1 (●); Sample B, pH 1.2 (♦); Sample C, pH 1.3 (▲); Sample D, pH 1.4 (■); Sample E, pH 1.7 (►) – from oscillatory strain amplitude sweep data collected at a constant angular frequency of 10 rad s^{-1} and T = 37°C.

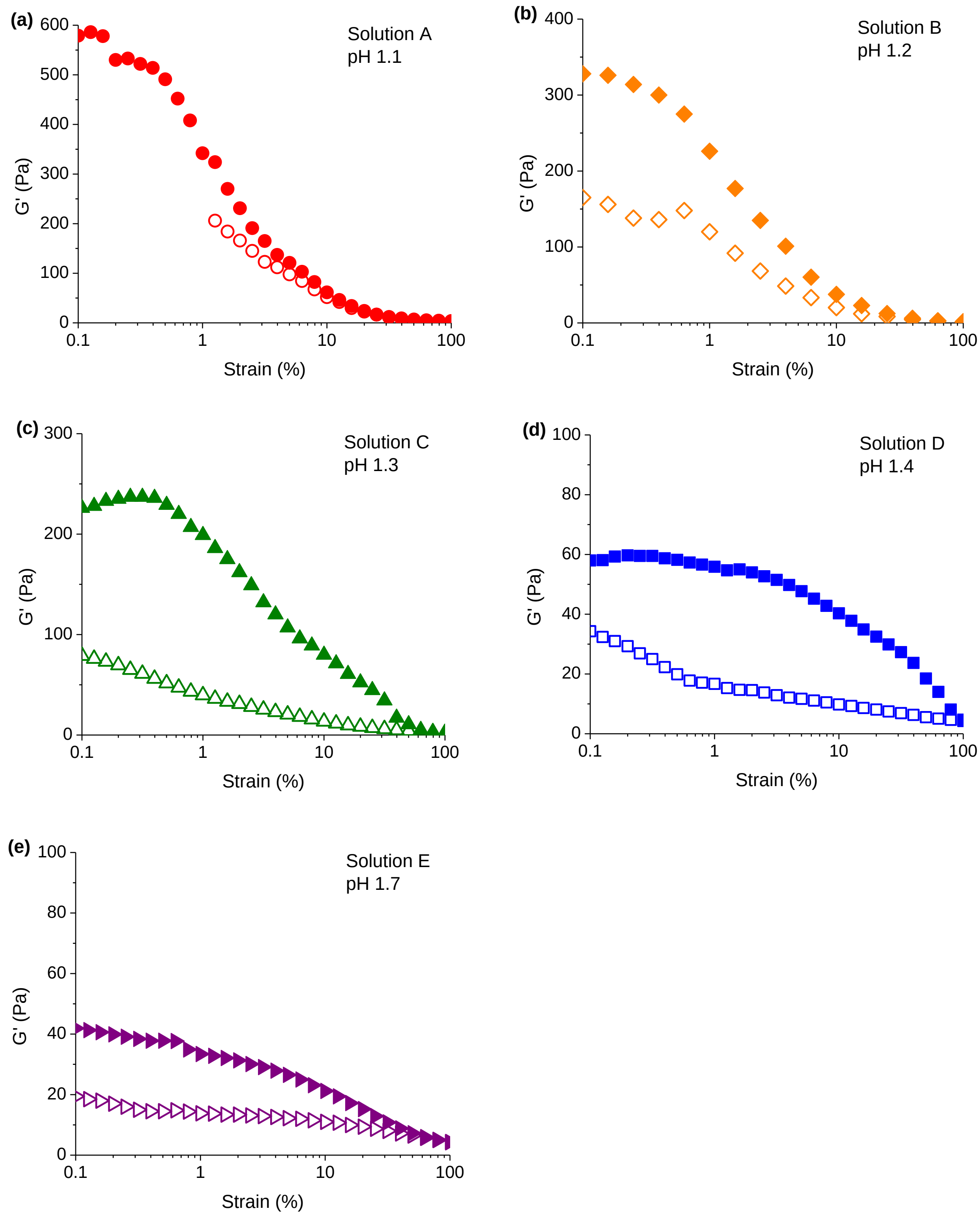


Fig. 8: Storage moduli collected from discretely increasing (closed symbols) and decreasing (open symbols) oscillatory strain amplitude sweeps at constant angular frequency of 10 rad/s and T = 37°C for un-aged alginate rafts formed in (a) Solution A, pH 1.1; (b) Solution B, pH 1.2; (c) Solution C, pH 1.3; (d) Solution D, pH 1.4; and (e) Solution E, pH 1.7.

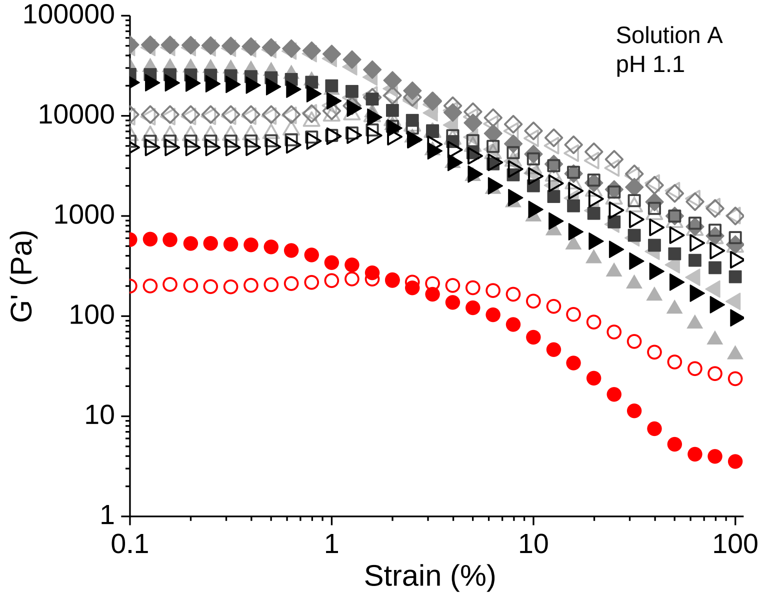


Fig. 9: Storage moduli (*G'*, filled symbols) and loss moduli (*G''*, open symbols) for alginate rafts formed in Solution A (pH 1.1) and aged for 0 hr (un-aged, ●), 0.5 hr (►), 1 hr (■), 2 hr (♦), 3 hr (▲), and 4 hr (◄); from oscillatory strain amplitude sweep data collected at a constant angular frequency of 10 rad s^{-1} and T = 37°C.

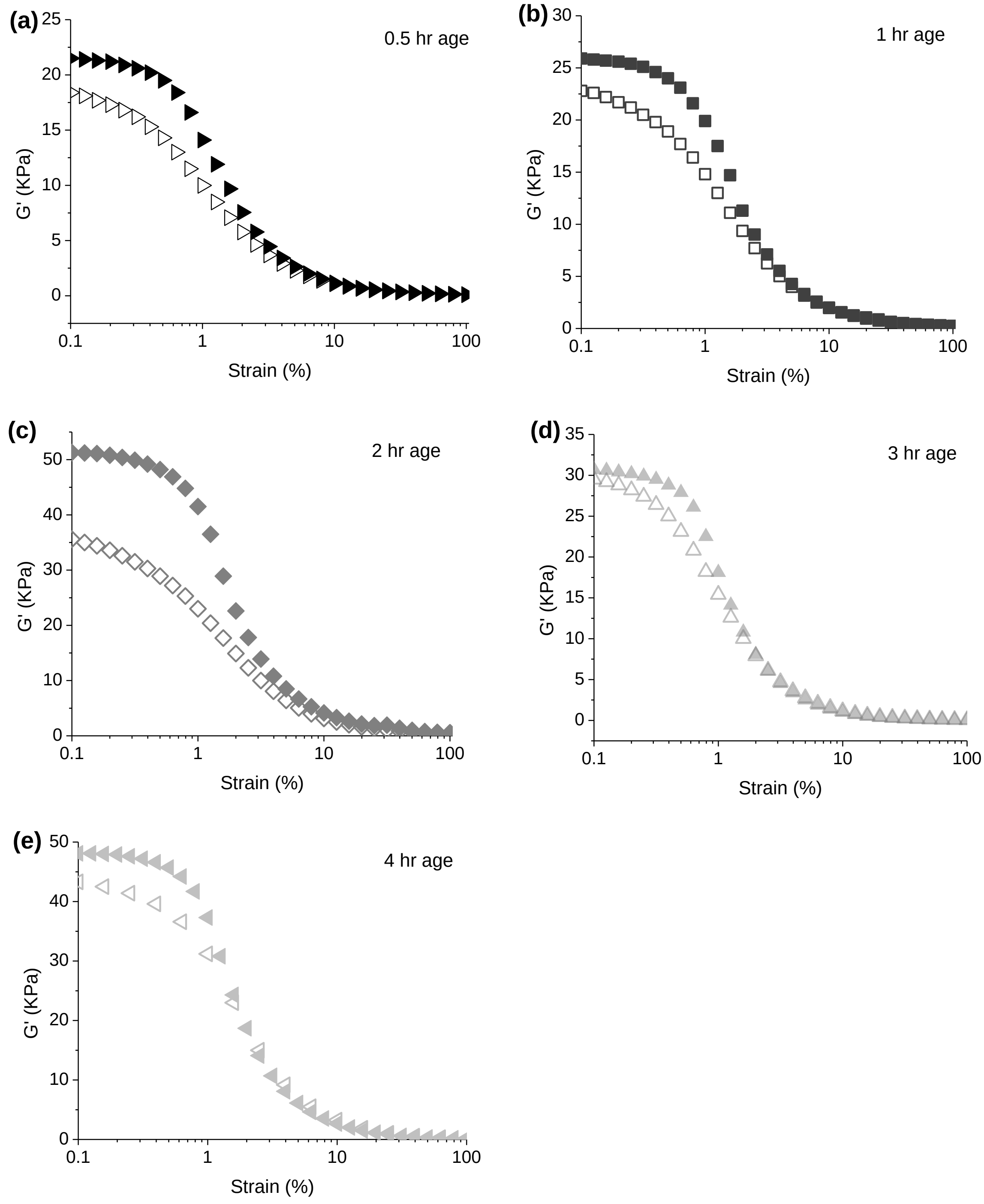


Fig. 10: Storage moduli collected from discretely increasing (closed symbols) and decreasing (open symbols) oscillatory strain amplitude sweeps at constant angular frequency of 10 rad s^{-1} and T = 37°C for alginate rafts formed in Solution A (pH 1.1) at the following aging conditions: (a) 0.5 hr, (b) 1 hr, (c) 2 hr, (d) 3 hr, and (e) 4 hr; symbols and colors correspond with Fig. 4.

Table 4: Composition and pH of aqueous solutions of acetic acid used to model the acidity range of the stomach.

Solution	Acid Concentration (vol.%)	pH
A	57.7	1.1
B	52.8	1.2
C	48.8	1.3
D	39.6	1.4
E	17.4	1.7

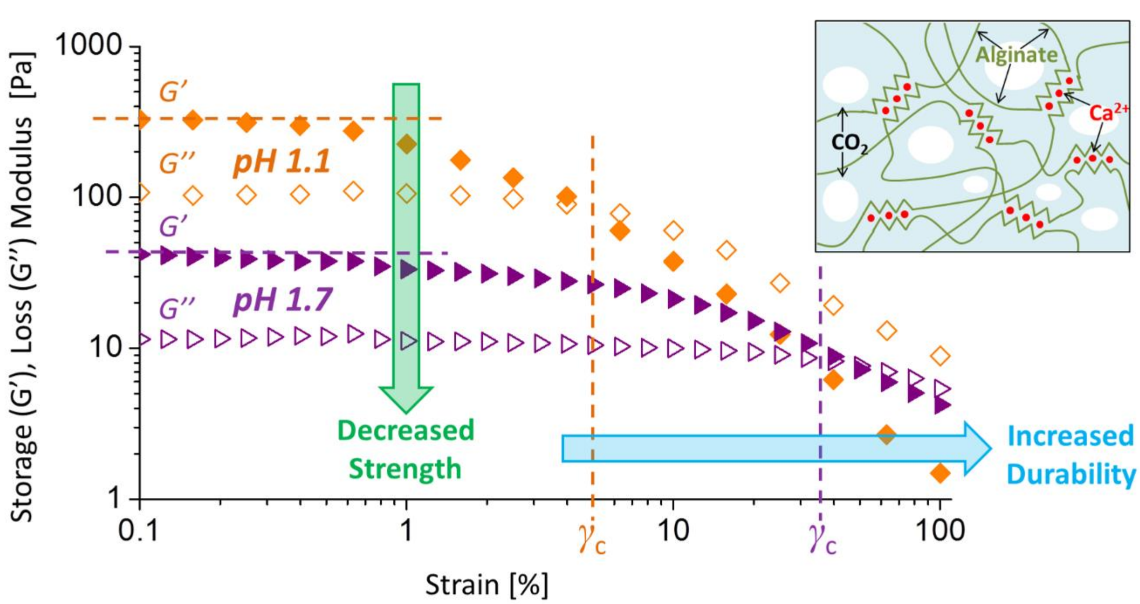
Table 5: The limiting storage modulus, G_0', critical value of strain, γ_c, and measure of hysteresis at $\gamma = 1\%$, $\Delta G'$, for un-aged alginate rafts formed in solutions with varying pH.

Solution	pH	G_0' (Pa)	γ_c (%)	$\Delta G'$ (Pa)
A	1.1	500	2.5	125 (-42%)
B	1.2	330	4.5	106 (-47%)
C	1.3	230	39	159 (-80%)
D	1.4	60	90	40 (-70%)
E	1.7	42	50	20 (-59%)

Table 6: The limiting storage modulus, G_0', critical value of strain, γ_c, and measure of hysteresis at $\gamma = 1\%$, $\Delta G'$, for alginate rafts formed in Solution A (pH 1.1) and aged for 0.5 – 4 hr.

Aging Time (hr)	G_0' (Pa)	γ_c (%)	$\Delta G'$ (Pa)
0 (un-aged)	500	2.5	125 (-42%)
0.5	21,500	2.5	4,110 (-29%)
1	25,900	3.5	5,100 (-26%)
2	51,300	3.0	18,500 (-45%)
3	30,700	1.8	2,700 (-15%)
4	48,100	2.3	6,100 (-16%)

TOC Image


Storage (G'), Loss (G'') Modulus [Pa]
1000
100
10
1
0.1
1
10
100
Strain [%]
G'
G''
pH 1.1
G'
G''
pH 1.7
Decreased Strength
Increased Durability
γ_c
γ_c
Alginate
Ca^{2+}
CO_2