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Research paper

Rheological characterization and turbidity of riboflavin-photosensitized changes in alginate/GDL systems

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Abstract

Riboflavin (RF) in combination with light, in the wavelength range of 310–800 nm, is used to induce degradation of alginic acid gels. Light irradiation of alginate solutions in the presence of RF under aerobic conditions causes scission of the polymer chains. In the development process of a new drug delivery system, RF photosensitized degradation of alginic acid gels is studied by monitoring changes in the turbidity and rheological parameters of alginate/glucono-δ-lactone (GDL) systems with different concentrations of GDL. Addition of GDL induces gel formation of the samples by gradually lowering the pH-value of the system. The turbidity is measured and the cloud point determined. The turbidity starts to increase after shorter times with enhanced concentration of GDL. Enhanced viscoelasticity is detected with increasing GDL concentration in the post-gel regime, but small differences are detected at the gel point. The incipient gel is 'soft' and has an open structure independent on the GDL concentration. In the post-gel regime solid-like behavior is observed, this is more distinct for the systems with high GDL concentrations. The effect of photosensitized RF on alginate/GDL systems decreases with increasing amount of GDL in the system. The same trend is detected whether the systems are irradiated in the pre-gel or in the post-gel regime.

Keywords: Alginate; Photosensitation; Degradation; Drug delivery; Hydrogel; Viscoelasticity

1. Introduction

Modified release pharmaceutical dosage forms have been studied [1,2] with the intention to improve the pharmacological activity, diminish toxic effects and to obtain better patient compliance by reduction of the number of daily administrations. Most of the modified drug release formulations on the market today focus on sustained release or prolonged action of the drug. Recently a number of studies [3,4] have been carried out on development of new techniques for drug delivery. Among these possible drug delivery systems are pulsed and programmed dosage forms that can be tuned so that drug release coincides with the underlying rhythm of a pathophysiological state. The inherent feature of these systems is to deliver the desired amount of drug at different times over a definite period to correlate with biological needs [2]. These systems can be regulated internally or externally. For internally or self-regulated systems the release is controlled by a feedback mechanism based on physiological parameters independent of external influence. This is in contrast to externally regulated systems where external triggers are required [5–14]. Light activated polymer matrices may constitute an interesting externally regulated system in the administration of drugs in accessible regions of the body, e.g. for dermal, buccal, ocular and vaginal administration, as well as in other tissues.

In this study riboflavin (RF) in combination with light is used to induce degradation of alginate (AL) samples in order to develop a matrix based drug delivery system triggered with light [1,15]. RF or vitamin B_2 is a widely used and approved yellow pigment, which in combination with light is a source of active oxygen species and free radicals and can be reversibly reduced/oxidized by accepting or losing a pair of hydrogen atoms [16–20]. RF is known

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for its ability to act as a photosensitizer in the light-induced degradation of polysaccharides [16,21]. The mechanism seems to be complex, but most likely it proceeds through the triplet state of RF, and the final step is probably free radical induced scission of the glycosidic linkage [22,23]. A small change in molecular weight yields a relatively large difference in physical behavior of the polymer. Therefore these systems have good potentials in light activated drug delivery without changing the initial properties of the polymer used and since there is no formation of oligomers the immunological response of the system is not likely to be affected [24].

Alginate is a negatively charged biocompatible copolymer consisting of mannuronic acid and guluronic acid [22,23]. The polymer is negatively charged at physiological pH, which is of importance for its bioadhesive properties [25]. The European Pharmacopoeia and the Food and Drug Administration (FDA) approve alginate as pharmaceutical excipient and its common use in the food industry diminishes the risk of toxicological incidents [26,27].

The photosensitized RF induced alginate degradation in aqueous solutions have already been investigated [22,23,28] with the aid of both rheology and dynamic light scattering, while alginate gels have not yet been studied in this coherence. There are several ways to form alginate gels. The most used method is alginate binding of alkaline earth metals forming the lateral junction zones in the gel network. In this study the gels are formed from intermolecular associations of alginate under acidic conditions. Alginate acid gels are formed by lowering pH below the pK_a-value of the uronic acid residues. It is argued that they are stabilized by intermolecular hydrogen bonds and are accordingly weaker than the ionotropic gels [24,29–31]. Forming of a homogeneous alginic acid gel is most often carried out by direct addition of D-glucono-δ-lactone (GDL) to a sodium-alginate solution. GDL is hydrolyzed in aqueous solutions, and it lowers the pH by slowly releasing H^+, making an acidic gel.

In this work the rheological behavior and the turbidity of irradiated (wavelength range 310–800 nm) alginate/GDL systems with different concentrations of cross-linking agent, with and without RF, is scrutinized. Information on rheological behavior is important in the development process of polymer based drug delivery systems due to its relations to permeability and therefore also the diffusion of drug from the system and to the site of action. As far as we know, this is the first study where the effect of photo-induced scission of the polymer chains on gelling alginate samples is examined.

2. Experimental section

2.1. Materials and solution preparation

An alginate sample, designated LF 10/60 LS (# 912912), was supplied by FMC Biopolymers, Drammen, Norway. According to the specifications from the manufacturer, the weight-average molecular weight of the sample is 152,000 and the guluronic acid to mannuronic acid (G/M) ratio is 0.75. RF and glucono-δ-lactone (GDL) were supplied by Sigma and Calbiochem, respectively. Both chemicals were of analytical grade and used without any further purification.

The polymer (2.0 wt.%) was dissolved in phosphate buffered saline (pH 7.4) in the absence or presence of the RF (0.1 mM) photosensitizer. These solutions, with different GDL concentrations, were irradiated and the time development of the samples were measured starting immediately after preparation. Great care was exercised to ensure that the samples were homogeneous and freshly prepared. All experiments were conducted at 25 °C.

2.2. Irradiation source

The samples were irradiated in a Suntest CPS (Heraeus GmbH, Hanau) apparatus with water-cooling in the ground plate of the chamber. The Suntest is equipped with a 1.8 kW xenon lamp and a glass filter transmitting irradiation corresponding to exposure behind window glass (wavelength range 310–800 nm). The light intensity was measured to 1.4×10^5 lux and 15 W/m^2 in the visible and UV range, respectively, using a lux meter (Hagner EC1-X Digital luxmeter) in combination with a UV-filter radiometer (Hagner EC1-X UV-A). The irradiation time of 15 min used is sufficient for a substantial photochemical degradation of the polymer [22].

2.3. Turbidity and cloud point measurements

The transmittance of the samples was probed at a wavelength of 500 nm during the gelation process with a Thermo Spectronic Helios Gamma spectrophotometer with temperature control (25.0±0.1 °C). The turbidity, τ, of the samples can be directly related to the transmittance by the equation:

$$\tau = (-1/L)\ln(I_t/I_0) \quad (1)$$

where L is the light path length in the cell (1.0 cm), I_t is the transmitted light intensity and I_0 is the incident light intensity.

The cloud point (CP) of the samples can be determined from the turbidity curves, and is taken as the time of the initial steep increase in the turbidity.

2.4. Rheological experiments

Oscillatory shear experiments were conducted in a Paar-Physica MCR 300 rheometer using a cone-and-plate geometry, with a cone angle of 1° and a diameter of 75 mm. The sample is applied on the plate, and the free surface of the sample was always covered with a thin layer of low-viscosity silicone oil to prevent dehydration from the solution (the viscoelastic response of the sample was not affected by this layer). The measuring device is equipped with an very accurate temperature control unit (Peltier plate).

The samples irradiated in the post-gel regime were measured in a Bohlin VOR rheometer system using a cone-and-plate geometry (CP25), cone angle of 2.5° and diameter of 30 mm. A Teflon ring was installed around the plate to keep the sample in place. Two ml of alginate solution in the presence or absence of RF was placed on the plate of the rheometer, which was in turn kept in a closed water bath glass chamber during gelation (18 h at 20 °C) and irradiation, to diminish evaporation and temperature change. Non-irradiated alginate/GDL-RF samples were used as blanks.

The values of the strain amplitude were checked to ensure that all oscillatory shear experiments were performed within the linear viscoelastic regime, where the dynamic storage modulus (G') and loss modulus (G'') are independent of the strain amplitude.

The gelation process is followed by oscillatory shear measurements, where the storage modulus (G'), the loss modulus (G'') and the complex viscosity (η^*) are measured at different frequencies over time. The complex viscosity is related to the storage and loss modulus by:

$$\eta^*(\omega) = \frac{\sqrt{G'(\omega)^2 + G''(\omega)^2}}{\omega} \tag{2}$$

where ω is the angular frequency.

The viscoelastic properties of an incipient gel are often described by the model of Winter and Chambon [32–36]:

$$G' = G''/\tan\delta = S\omega^n \Gamma(1-n)\cos\delta \tag{3}$$

where $\tan\delta$ is the viscoelastic loss tangent ($\tan\delta = G''/G'$), S is the gel strength parameter, $\Gamma(1-n)$ is the Legendre gamma function, and n is the relaxation exponent ($0<n<1$). The relaxation exponent is related to the fractal dimension, d_f ($1 \le d_f \le 3$) by the theoretical model of Muthukumar [37] where it is assumed that the excluded volume effect is fully screened:

$$n = \frac{d(d+2-2d_f)}{2(d+2-d_f)} \tag{4}$$

where d is the space dimension ($d=3$). According to the model of Winter and Chambon, the gel point is characterized by a frequency independency of $\tan\delta$, and accordingly the dynamic moduli at the gel point are related as $G'(\omega) \sim G''(\omega) \sim \omega^n$.

3. Results and discussions

As can be seen from Fig. 1, the addition of GDL to the alginate solutions, gradually reduces the pH of the system as the GDL is hydrolyzed to gluconic acid, and a constant pH value is reached after a couple of hours. In the absence of alginate the same trend is observed, but the end pH is somewhat lower. A reduction of the pH which crosses the threshold of the pK_a value of the polymer, induces a transition from a polyelectrolyte system to a system containing a more neutral polymer. As the polymer becomes neutralized, the effect of the repulsive forces between the ionic groups is diminished, and the attractive forces between the alginate chains become dominant.

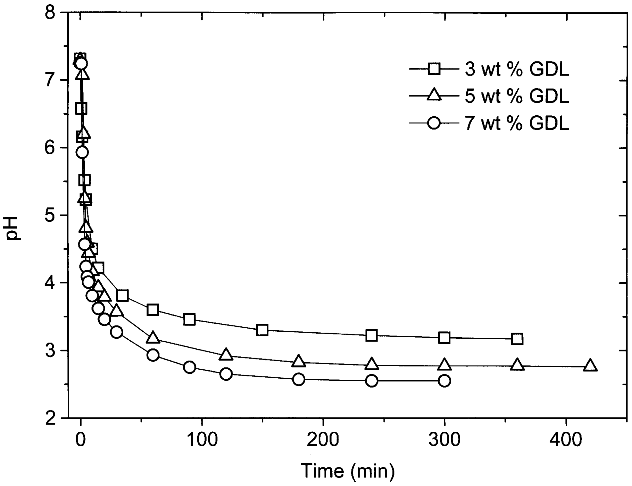

Fig. 1. Variation of pH of the alginate solutions as a function of time and GDL concentration. The GDL concentrations 3, 5 and 7 wt.% have an end pH of 3.2, 2.8, and 2.6, respectively.

The concentration regime (3–7 wt.%) of the gelling agent GDL is used, as all the solutions become gels and the difference in the end pH is low, i.e. 3.2–2.6 (Fig. 1), which is under the pK_a value of the polymer. The pK_a values of the guluronic and manuronic units have been previously measured as 3.7 and 3.4, respectively [25].

Neither GDL in combination with irradiation nor the small amount of RF added were observed to affect the rheological properties of the systems. Therefore the comparison of irradiated alginate/GDL systems in the presence and absence of RF are used throughout most of this study. This will give the same results as comparing non-irradiated and irradiated alginate/RF samples, which is done in the section where the systems are irradiated in the post-gel regime.

To the unaided eye the pre-gel solution and the incipient gel looks completely clear and transparent (except for the yellow RF color in the samples containing RF), but as the reaction proceeds into the post-gel regime the samples becomes successively more turbid. In order to quantify this transformation, the turbidity changes during the gelation process were probed using a spectrophotometer. The turbidity change of the samples containing 3 and 7 wt.% GDL irradiated in the presence and absence of RF is depicted in Fig. 2. The turbidity is low but slowly increasing at short times, and then there is a break point in the curve after which the turbidity rises steeply until it eventually reaches a constant high value. We have determined the cloud point of

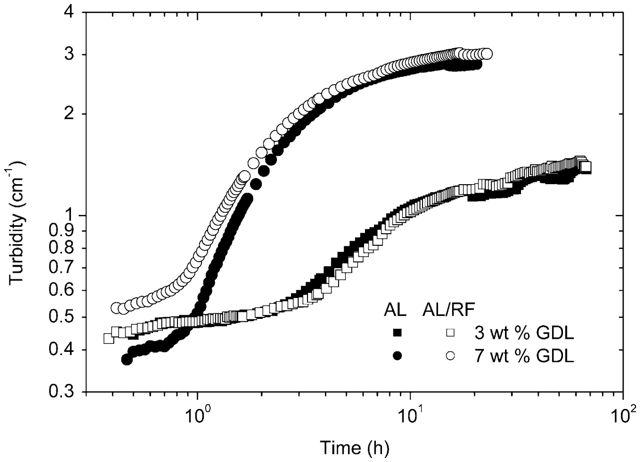

Fig. 2. The turbidity change of the irradiated alginate samples with and without RF in the presence of 3 wt.% (a) and 7 wt.% (b) GDL as a function of time. The cloud points can be determined as the time of the initial steep increase in the turbidity.

the samples as the break point where the curve changes from the initial slow increase to the steeper slope. This CP is in agreement with the point where the samples start to become visibly turbid. An increase in the turbidity is an indication of poorer thermodynamic conditions, leading to large-scale heterogeneities in the sample and the formation of 'lumps' of associated polymer. Although the pH of the samples reaches a constant value after a couple of hours (Fig. 1), the turbidity continues to change. The change in the turbidity after the end-pH is reached shows that it takes a long time before an equilibrium state is reached in the system. This is probably due to the time it takes the polymer to re-arrange its structure. The samples containing a high GDL concentration exhibit a more abrupt change in their turbidity, and the turbidity starts to increase at shorter times than the samples with a lower GDL concentration. Even a small reduction in the end-pH of the samples (3.2–2.6) will have a tremendous effect on the thermodynamic conditions in the samples. A higher pH gives better thermodynamic conditions and the polymer chains rearrange slower than it does at lower pH where the extremely poor thermodynamic conditions causes a much faster association process. The poorer thermodynamic conditions at low pH values is also illustrated by the increase in the final turbidity achieved as the GDL concentration is raised. The successive worsening of the thermodynamic conditions as the pH of the samples decreases can be explained in the following way: as the pH of the samples is reduced, the ionic groups on the polymer are neutralized. This weakens the repulsive forces between the alginate chains and the attractive forces become increasingly dominant. This causes an association between the polymer chains, and associated polymer 'lumps' will grow in the sample leading to an increase in the turbidity. The yellow RF color seems to give rise to a somewhat higher turbidity at short times, at long times this effect is diminished by the much larger turbidity of the post-gel samples. Close scrutiny of the curves reveal that the steep slope starts at longer times for the samples containing RF, indicating that the photo-induced scission of the polymer chains slows down the formation of large clusters in the sample.

The gel points (GP) can be determined rheologically with two methods, one is to find the frequency independence of the loss tangent ($\tan\delta = G''/G'$) in a multifrequency plot of $\tan\delta$ versus time (Fig. 3). In the other approach the 'apparent' viscoelastic exponents n' and n'' ($G' \sim \omega^{n'}$, $G'' \sim \omega^{n''}$) are plotted versus time. The power law exponents n' and n'' are obtained from the approximate scaling laws of the frequency dependence of storage (G') and loss modules (G'') at different times during the gelation process. The cross-over of n' and n'' occurs at gel point where $n' = n'' = n$ (inset plots in Fig. 3). Both methods yield the same gelation time for all the considered gelling systems.

The gel points and cloud points of the alginate/GDL systems is depicted in Fig. 4. The gelation process is faster with enhanced concentration of GDL and the differences in gelation times are probably caused by the pH changes in the samples. As the GDL concentration is increased, the pH of the samples decreases more rapidly and reaches values lower than the pK_a of the polymer faster, and in addition the end-pH is lower for the higher GDL concentrations (see Fig. 1). As was shown by the turbidity measurements (Fig. 2), lower pH values give poorer thermodynamic conditions, causing a faster association between the polymer chains. This process will also give rise to shorter gelation times. As can be perceived from Fig. 4, irradiation in the presence of RF slows down the network evolvement. This is due to the photo-induced scission of the polymer chains. At low GDL concentrations the scission of the alginate chains

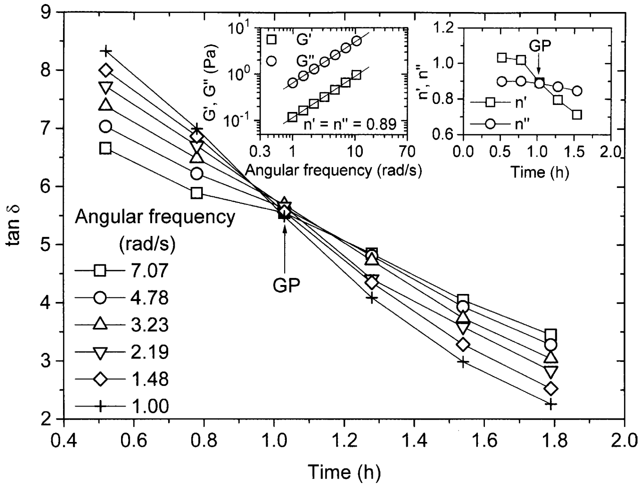

Fig. 3. Illustration of the determination of the gel point for irradiated alginate samples containing 4 wt.% GDL in the absence of RF. Viscoelastic loss tangent as a function of the time after GDL addition at the frequencies indicated. At the gel point, $\tan\delta$ is independent of the frequency. The left inset plot shows the power law behavior of the dynamic moduli at the gel point ($G' \sim G'' \sim \omega^n$). The right inset plot shows the changes in the 'apparent' viscoelastic exponents n' and n'' during the gelation process. A cross-over where $n' = n''$ indicates the gel point.

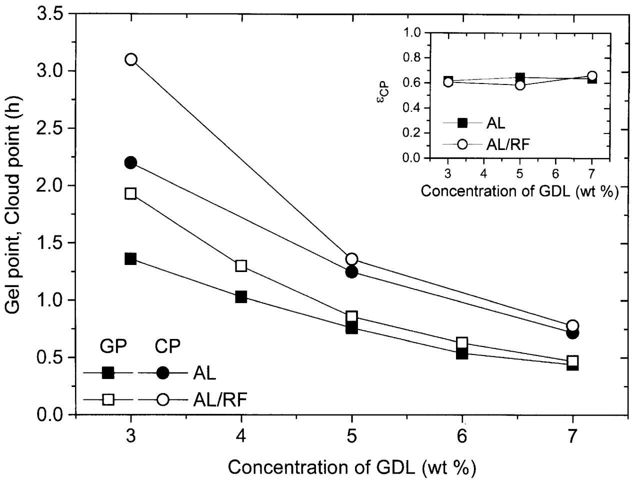

Fig. 4. Effects of the GDL concentration on the gel and cloud points for irradiated alginate samples both in the presence and absence of RF. The inset plot illustrates the distance to the gel point ($\varepsilon_{CP} = (t_{CP} - t_{GP})/t_{GP}$, where t_{CP} is the time of the CP and t_{GP} is the time where the system forms a gel) where the cloud point occurs.

has greater effect on the gel time than at higher concentrations, where the effect is diminished by enhanced associations between the polymer chains.

Previous theoretical studies [38–40] have shown a connection between gelation and macroscopic phase separation. There are also several experimental works that illustrate the interplay between the gel point and the cloud point [41–44]. We have therefore plotted the gel points and the cloud points together in Fig. 4. As can be seen from Fig. 4, the cloud points exhibit the same trends as the gel points, but the cloud points occur at longer times. In order to scrutinize the relation between the cloud points and the gel points, the distance to the gel points at which the CP occurs ($\varepsilon_{CP} = (t_{CP} - t_{GP})/t_{GP}$, where t_{CP} is the CP time and t_{GP} is the time where the system forms a gel) is shown as a function of the GDL concentration in the inset in Fig. 4. From this we find that the CP sets in at a certain distance from the GP, indicating that the same process govern the gel formation and the clouding of the samples. The poor thermodynamic conditions cause the formation of small associated 'lumps' of polymer chain-segments. When there are enough of these lumps to form a connected network, the system forms a gel. In the post-gel regime, the 'lumps' continue to grow, and at a certain distance after the GP, the 'lumps' become so large that the sample becomes visibly clouded.

At the gel point, the relaxation exponent, n, and the fractal dimension, d_f, are constant for all the considered gelling systems, and they assume values of 0.90 ± 0.02 and 1.4, respectively. The high values of the relaxation exponent indicate that the incipient gel has a dominant viscous response [36]. Usually the relaxation exponent assumes lower values than observed here, but values around 0.9 have been observed for other systems earlier [35,36,45]. The low values of d_f indicate that the incipient gel network has a relatively open structure. It is interesting to note that the structure of the system at the gel point is independent of both the concentration of GDL and the scission of the polymer chains. This suggests that the incipient gel is formed at a constant cross-linking density for all the considered systems, indicating that at the gel point a certain amount of associated cross-linking 'lumps' is present in the sample, independent on both the GDL concentration and the photo-induced scission of the polymer chains.

Fig. 5a and b show the time evolution after the addition of GDL of the complex viscosity for the alginate/GDL

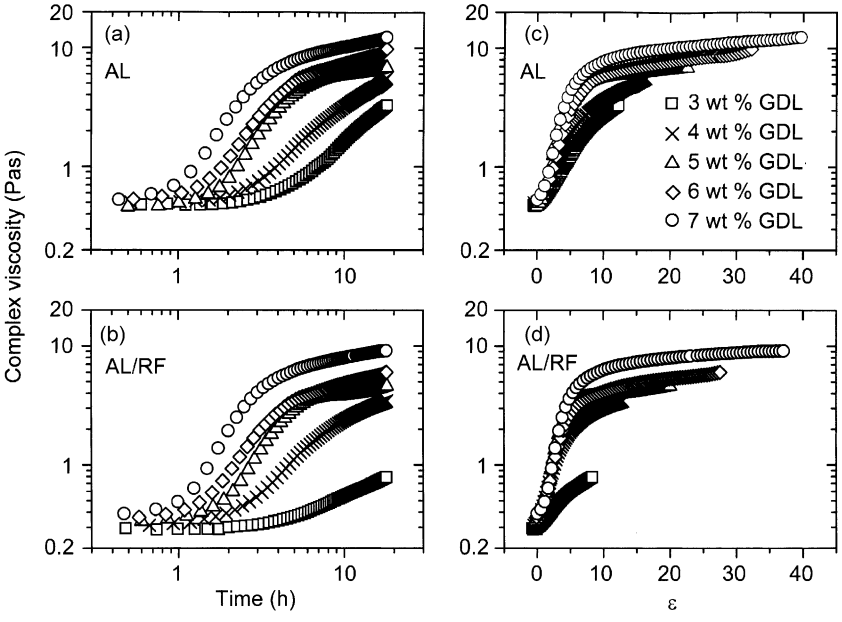

Fig. 5. Complex viscosity of irradiated alginate samples (at a frequency of 10.5 rad/s) as a function of time after the addition of GDL, in the absence (a) and presence (b) of RF, and as a function of the distance from the gel point in the absence (c) and presence (d) of RF.

systems, in the presence and absence of RF, for all the GDL concentrations measured. The figure illustrates that η^* increases with the time after addition of GDL. As for the turbidity, the complex viscosity continues to change even after the pH has reached a constant value (see Fig. 1). This indicates that after the end-pH is attained the poor thermodynamics of the system will cause a gradual association between the polymer chains causing an increase in the viscosity. The rise in the complex viscosity gets stronger as more GDL is added. This increase of the complex viscosity is due to the poorer thermodynamic conditions at low pH leading to an enhanced amount of associations in the polymer network. Fig. 5c and d present the complex viscosity as a function of the distance from the gel point, $\varepsilon = (t - t_{GP})/t_{GP}$, where t is the time from the addition of GDL and t_{GP} is the time where the system forms a gel. The complex viscosity at the gel point ($\varepsilon = 0$) does not vary very much with the GDL concentration, while there is a marked increase in η^* as the concentration of GDL is raised when the system is well into the post-gel regime. This again indicates that the amount of associations in the incipient gel is independent of the amount of added GDL, while the differences in end-pH causes enhanced cross-linking in the post-gel regime. The differences between the various GDL concentrations again indicate that the small difference in the end pH in the system has an important effect on the gelling process, changing the charge density of the polymer chains and thereby the amount of intermolecular associations between the alginate chains.

The complex viscosity of the systems in the presence and absence of RF at two different concentrations of GDL versus time after addition of GDL is depicted in Fig. 6a and b. Fig. 6c and d describe the difference in η^* as a function of the distance from the gel point. The complex viscosity shows a lower value during the whole gelation process for the systems irradiated in the presence of RF, illustrating the effect of the photo-induced degradation in the system. The profile of the time dependence of the complex viscosity is reminiscent of what is observed for the turbidity in Fig. 2. Since the amount of cross-links in the system seems to be independent of the scission of the polymer chains, the lower viscosity is probably caused by a lower connectivity and higher chain flexibility caused by the photo-induced scission of the polymer chains. In the post-gel regime, the difference caused by the scission of the polymer chains is much larger at the low GDL concentration than at the high GDL concentration. This is probably due to the enhanced amount of associations that build up over time at low pH-values. The large quantity of associations will diminish the effect of each scission induced by photosensitized RF on the network, and therefore the effect of photosensitized RF is smaller at high GDL concentrations.

The effect of time on the dynamic moduli (G' and G'') at a relatively low angular frequency of 10.5 rad/s for the alginate/GDL systems, with and without RF and of two concentrations of GDL (same as in Fig. 6) is depicted in Fig. 7. The systems with RF show lower values of both G' and G'', and the difference is greater for the low GDL concentration. This again indicates that in the presence of large amounts of GDL, each scission in the alginate chain has less effect on the whole network. In the beginning, for both GDL concentrations, the loss modulus is higher than the storage modulus. This indicates a dominating viscous behavior in the system. The storage modulus changes more

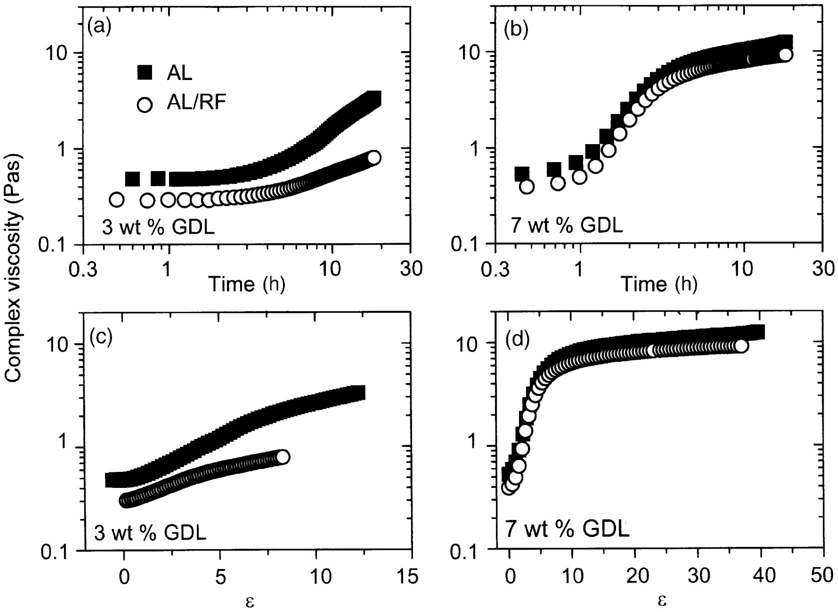

Fig. 6. Complex viscosity of irradiated alginate samples (at a frequency of 10.5 rad/s) with and without RF in the presence of 3 wt.% GDL as a function of time (a) and as a function of the distance to the gel point (c) and in the presence of 7 wt.% GDL as a function of time (b) and as a function of the distance to the gel point (d).

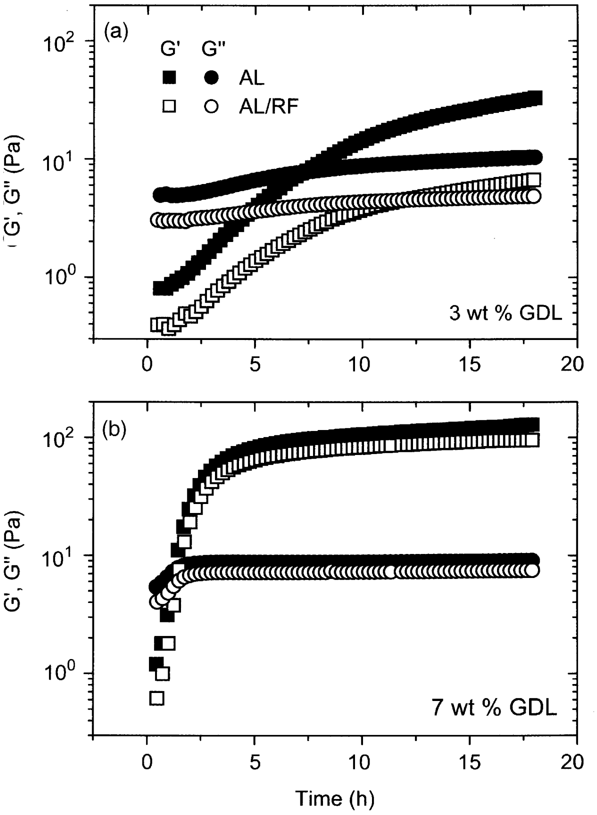

Fig. 7. The change in the dynamic moduli (at a frequency of 10.5 rad/s) during gelation of the irradiated alginate/GDL systems for the two different concentration of GDL indicated, compared to the corresponding systems with RF.

rapidly than the loss modulus during the gelation process, and after the post-gel regime is entered there is a cross-over from a viscous behavior ($G'' > G'$) to an elastic response ($G' > G''$). When the concentration of GDL is raised, the cross-over from viscous to elastic behavior occurs at an earlier time. This can also be perceived from Fig. 8a, where the cross-over time where $G' = G''$ is plotted as a function of GDL concentration. The exact time of the cross-over is dependent on the frequency considered, but the overall trend is the same for all the measured frequencies. The time it takes for the system to go from a dominant viscous behavior to a dominant elastic behavior seems, except for the lowest GDL concentration, to be independent of the addition of RF. This indicates that even though the scission of the polymer chains significantly changes the gelation time, it does not change the time it takes the system to go from a dominant viscous behavior to a dominant elastic behavior. This implies that the cross-over is dependent on the amount of associations present in the system, and is not affected by the scission of the polymer chains. This also gives rise to the apparent counter-intuitive feature in Fig. 8b, where the cross-over occurs longer into the post-gel regime for the systems that do not contain RF. In Fig. 8b the distance from the gel point for the cross-over from $G'' > G'$ to $G' > G''$ is shown. Except for the lowest GDL concentration the intercept seems to be independent on the amount of GDL added, indicating that the transition occurs at a certain distance from the gel point. This again points to a cross-over occurring at a certain cross-linking density. At the lowest concentration of GDL, the cross-over is shifted further into the post-gel regime. The deviations at the lowest GDL concentration are probably due to the very low amount of GDL present, which is just above the GDL concentration needed for the system to form a gel.

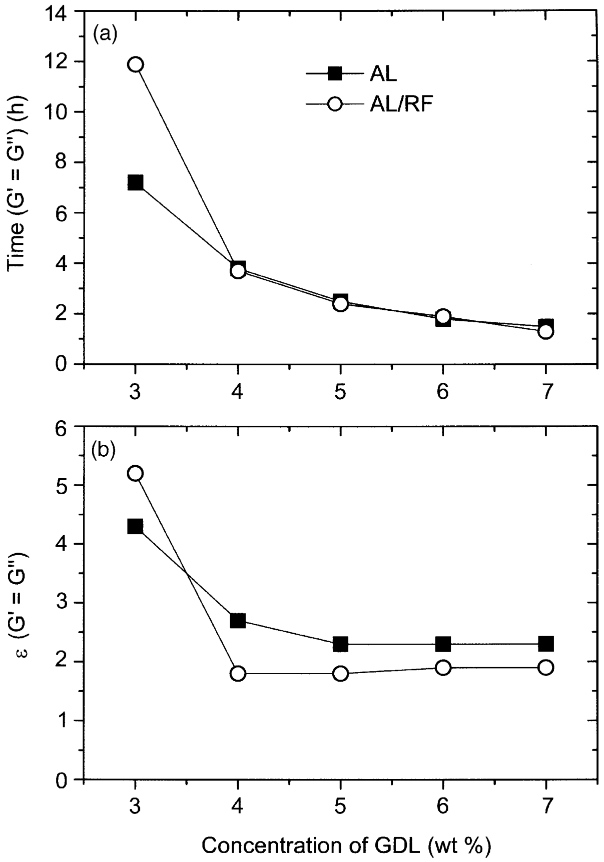

Fig. 8. (a) The time at which the cross-over $G' = G''$ occurs at a frequency of 10.5 rad/s, (b) the distance from the gel point where the cross-over $G' = G''$ occurs at a frequency of 10.5 rad/s. The cross-over times will change somewhat with frequency, but the overall trend is the same.

Fig. 9 shows the frequency dependency of the complex viscosity of alginate/GDL systems of two GDL concentrations (3 and 7 wt.%), with and without RF, at the gel point ($\varepsilon = 0$) and at $\varepsilon = 8$ in the post-gel regime. This shows that the trends discussed in connection with Fig. 5 is valid for the whole frequency range studied. At the gel point the value of η^* is similar for all GDL concentrations but lower for the systems irradiated in the presence of RF. As the post-gel regime is entered much larger values of η^* are obtained as the concentration of GDL is increased. In the post-gel regime, the presence of RF has much less effect on the system containing 7 wt.% GDL compared to the system with 3 wt.% GDL. The frequency dependence of the complex viscosity can be quantified by $\eta^* \sim \omega^{-\nu}$ $(0 \le \nu \le 1)$.

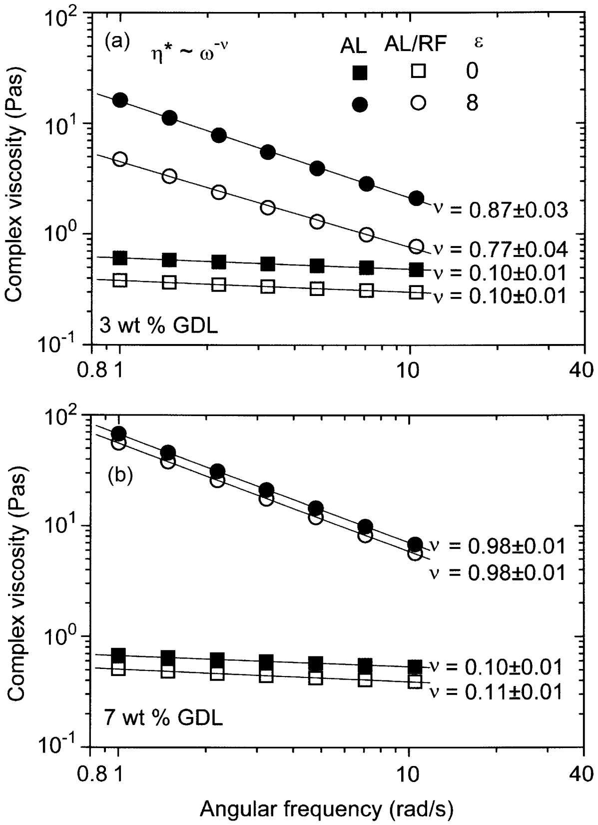

Fig. 9. Frequency dependency of the complex viscosity of irradiated alginate samples in the presence of (a) 3 wt.% and (b) 7 wt.% GDL, with and without RF, at the gel point and in the post-gel regime.

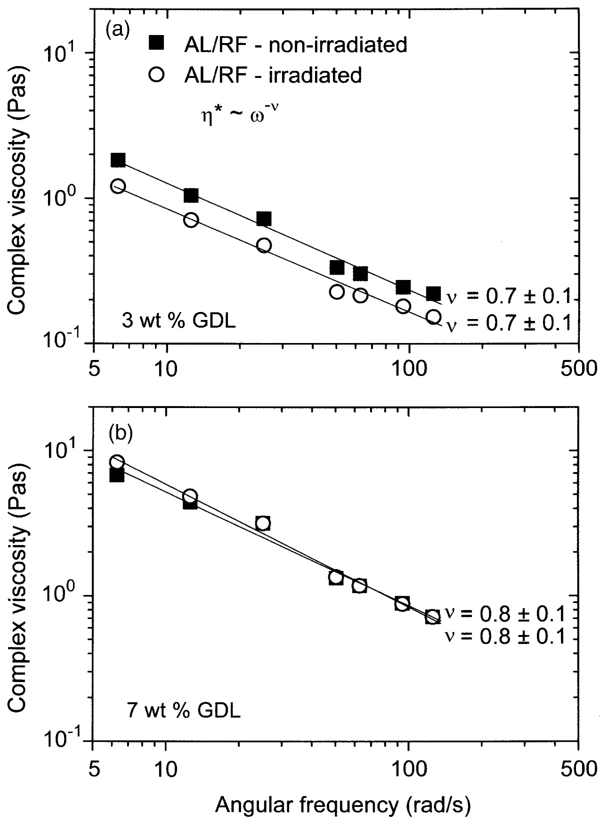

Fig. 10. Frequency dependency of the complex viscosity of alginate samples in the presence of (a) 3 wt.% and (b) 7 wt.% GDL. The measurements are made in the post-gel regime for non-illuminated samples and for the same samples illuminated in the post-gel regime.

Low values of ν indicate viscous-like behavior, while higher values indicate a more elastic response. At the gel point all systems have a ν value of 0.10 ± 0.02 ($\nu = 1 - n$ at the gel point), but in the post-gel regime the value of ν increases and assumes values that are approaching 1, which indicates a solid-like behavior. This illustrates that in the incipient gel there are relatively few cross-links in the system, while at longer times in the post-gel regime the amount of associations have increased with time, and the system characteristics goes towards what is expected of a solid.

For pharmaceutical applications it may be interesting to do the irradiation in the post-gel regime, to break down the network in order to release a drug. In order to see if this effect is similar to that of samples irradiated in the pre-gel region, some gels were prepared from non-irradiated samples containing RF, and the viscoelastic properties of the systems well into the post-gel region were compared before and after the irradiation of the gels. Fig. 10 displays the angular frequency dependency of the complex viscosity of the non-irradiated and irradiated samples in the post-gel regime. Both methods show the same trend (comparing Figs. 9 and 10), lower η^* values for the systems with lower GDL concentration and even more so for the irradiated systems. Enhanced effect of irradiation is observed as GDL concentration decreases, which insinuates that a cut in the alginate chains has less effect on the whole network system with more GDL present, the large amount of associations diminish the effect of the scission of the alginate chains.

4. Conclusions

The rheological parameters of alginate/GDL systems with constant amount of alginate (2 wt.%) but different concentration of GDL have been studied in this work as well as changes of such systems induced by photosensitized RF. As expected, higher values of the complex viscosity are detected with increasing GDL concentration in the post-gel regime. However, the differences in the rheological parameters are much smaller at the gel point. The values of the relaxation exponent, n, is quite high (0.9), which shows that the incipient gel has an open structure and that the system has a dominant viscous response at the gel point. When the system is well into the post-gel regime the turbidity of the samples are quite high and solid-like behavior is observed. This is more distinct for the systems with high GDL concentrations. The irradiation of alginate solutions in the presence of RF under aerobic conditions causes scission in the polymer chain changing the rheological quantities. In the post-gel regime the effect of photosensitized RF decreases with increasing amount of GDL in the system demonstrating that there the effect of chain scission is much smaller for high levels of added GDL. The time that it takes to reach gel point gets shorter with enhanced concentration of GDL but irradiation in the presence of RF slows down the network evolvement. The same trend is detected whether the systems are irradiated in the pre-gel or in the post-gel regime. This study shows that a low concentration of GDL is desired in applications for controlling drug delivery, since these systems will exhibit the greatest change upon light irradiation. However, for some applications it might be preferable to use an intermediate GDL concentration resulting in stronger gels but still an efficient RF photosensitized degradation.

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