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ORIGINAL CONTRIBUTION

Peculiar behavior of polysaccharide/borax hydrogel tablets: a dynamomechanical characterization

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Abstract The peculiar unidirectional elongation observed during swelling of tablets prepared with scleroglucan (Sclg) and borax was compared with that of other synthetic and natural polymers capable of physical/chemical interactions with borate ions. A dynamomechanical characterization of "squared" Sclg/borax tablets was carried out to study the differences detectable on the two sides of the matrix corresponding to the two directions, respectively, the parallel and perpendicular one with respect to the applied compression force. Different compression forces were used and, in some cases, a second compression was applied on the tablets along a direction perpendicular to the first one. Birefringence experiments were carried out on the swelled tablets along the two directions. Obtained results allow correlating the anisotropic swelling behavior with the detected dynamomechanical and optical properties of the Sclg/borax system. Among the various tested polymers, only guar gum and, to a lesser extent, locust bean gum, showed an anisotropic elongation during swelling.

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Introduction

Polymers appear to be very attractive for their peculiar physicochemical characteristics that often allow improving the efficacy of drug therapy in biomedical applications [1, 2]. A precise description of these systems is quite complex [3–9] and the practical use of hydrogels for biomedical applications is often not supported by a well-defined knowledge of the polymeric network structure. This study deals with the characterization of a matrix obtained with scleroglucan (Sclg) when cross-linked with borax. Owing to the structural features of the triple helix of Sclg, we proposed a parallel arrangement of the helices which are held together partially by covalent linkages and partially by physical interactions with borate ions [10–12]. Thus, the hydrogel can be identified as a "mixed" gel whose network is built up by means of both physical and chemical interactions between the polymer and the cross-linker.

We have also reported that, when this hydrogel is used to prepare tablets, it shows a very peculiar unidirectional elongation during water uptake experiments. A molecular insight of this peculiar behavior has been recently proposed: in particular, we showed, by means of molecular dynamics simulations (MD) and atomic force microscopy (AFM) data, that the presence of borax confers to Sclg triplexes the ability to form *soft* nanochannels that are able to affect the diffusion of drug molecules depending on their steric hindrance [13]. In this paper, the possibility that other polymers, synthetic (polyvinyl alcohol [PVA]) or naturals (guar gum (GG), locust bean gum (LBG), dextran, pullulan, and starch), may give the same macroscopic effect is investigated. The possible relation of macromolecules' structural parameters with the water uptake data is discussed. Furthermore, the influence of the compression force applied during the preparation of the Sclg/borax tablets, in terms of different application directions and different intensities, is evaluated. A novel kind of Sclg/borax tablets with a squared geometry was prepared and the dynamomechanical properties as a function of tablet geometry are reported. Parameters like hardness, cohesiveness, and adhesiveness are evaluated at different imbibition times and for different tablet sides. Relaxation experiments are carried out on the same system and the mechanical spectra are elaborated by applying the generalized Maxwell model. Birefringence experiments were also carried out to confirm the anisotropic behavior of the swelled matrix.

Experimental

Materials

Sclg (Carbomer, USA; degree of polymerization [DP]=800), GG (Carbomer, USA), and LBG (Carbomer, USA) were used after dialysis and freeze-drying processes. PVA (average molecular weight 30,000–70,000) and starch from wheat were Sigma-Aldrich products, while dextran (average molecular weight 40,000) and pullulan (average molecular weight 400,000) were provided by Fluka. Borax was a Carlo Erba (Italy) product. The hydrogels were prepared as previously reported [10], using an amount of cross-linker equimolar to the repeating unit mass of the polysaccharides, $r=1=$(borax moles)/(molar mass of the polymer repeating unit). In the case of PVA, the same amount of borax used for Sclg was added leading to an r value equal to 0.070; smaller quantities were also tested, $r=0.030$ and $r=0.015$. Distilled water was always used.

Hydrogel and tablet preparation

For the preparation of the tablets, an appropriate amount of polymer (about 200 mg) was magnetically stirred in water for 24 h. Then, the calculated amount (i.e., moles of borax= moles of repeating units of polymer) of 0.1 M borax solution was added and the system was left under magnetic stirring for 5 min. It must be pointed out that the pH value remained constant at 9.0 during salt addition because of the self-buffer effect of borax. The obtained sample ($c_p=0.7\%$ [w/v]) was kept overnight at 7 °C for gel-setting and then freeze-dried. Tablets were prepared from the freeze-dried sample with an IR die (Perkin Elmer hydraulic press) using a force of 5.0 kN for 30 s. The weight of the Sclg/borax tablets was 230±10 mg, the diameter was 13.0±0.1 mm, and the thickness was 1.4±0.2 mm. In some cases, a force of 1.0 and 10 kN for 30 s was applied, obtaining tablets with a thickness of 2.5±0.2 and 1.3±0.2 mm, respectively.

Some Sclg/borax tablets, once prepared (using a force of 5.0 kN for 30 s), were pressed again (using always a force of 5.0 kN for 30 s) along a direction perpendicular to the previously applied pressure direction; hereafter, such tablets will be called double compressed (dc).

Sclg/borax tablets were also prepared with a different die, ad hoc built by Valid Plastic (Strangolagalli, FR, Italy), in order to obtain tablets with a squared geometry (see Fig. 1a). The side of the squared tablets was 14.0±0.1 mm and the thickness was 1.5±0.2 mm (5 kN, 30 s).

Methods

Water uptake and dimensional increase studies

The swelling of tablets prepared with all systems (Sclg/borax, GG/borax, LBG/borax, PVA/borax, dextran/borax, starch/borax, and pullulan/borax) and the swelling of "dc" tablets

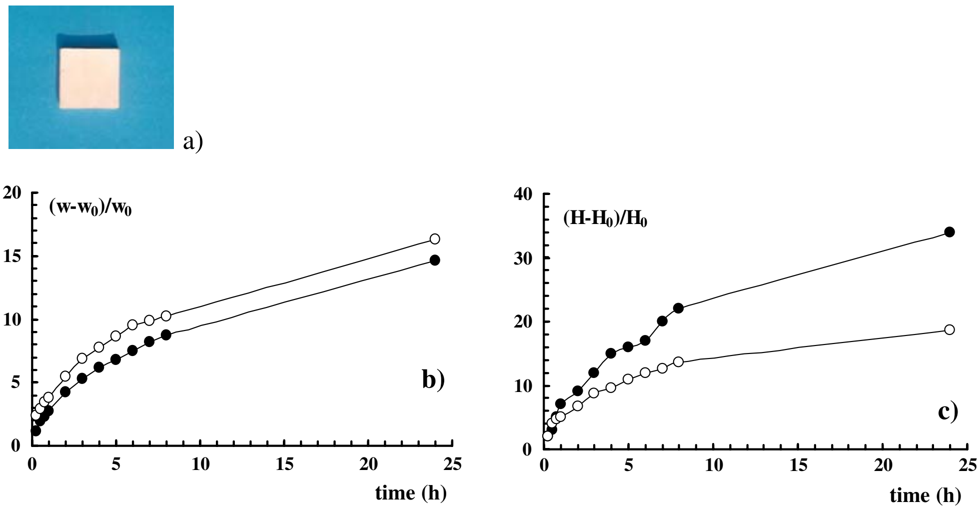

Fig. 1 **a** Picture of a squared tablet of Sclg/borax. Relative increase of the weight (**b**) and height (**c**) for tablets of Sclg/borax (*filled circles*) and for tablets of Sclg/borax "dc" (*open circles*) in water at 37 °C, as a function of time. The *solid lines* are only a guide to the eye

(of Sclg/borax) was carried out by soaking the tablets in distilled water at 37 °C. At fixed time intervals, the tablets were withdrawn, the excess of water was removed with soft filter paper for 5 s, and then the corresponding dimensional variations along the longitudinal axis were determined by means of a screw gauge with an accuracy of ±0.1 mm. No remarkable variations of cross-section dimensions were detected during the swelling process.

Texture analyzer

A software-controlled dynamometer, TA-XT2*i* Texture Analyzer (Stable Micro Systems, UK), with a 5-kg load cell, a force measurements accuracy of 0.0025%, and a distance resolution of 0.0025 mm (according to the instrument specifications), was used for the mechanical characterization of the gel samples [14, 15].

Two types of experiments were performed: compression and relaxation tests. In the first approach, the sample resistance to the compression applied by the probe was measured. The trigger force was set equal to 0.002 N, the pretest speed was set up at 2.0 mm/s, the test speed at 1.0 mm/s, the post-test speed at 2.0 mm/s, and the compression depth was variable, being imposed a fixed deformation of 8% with an acquisition rate of 200 points per second. The probe used was an aluminum cylinder with a diameter of 35 mm (P35).

For the relaxation experiments, the pretest speed was set up at 2.0 mm/s, the test speed at 4.0 mm/s, and the post-test speed at 1.0 mm/s. A 15% deformation was imposed to the samples and then the relaxation of the system was recorded until the baseline was reached.

Before performing the compression and the relaxation tests, the range of linear viscoelasticity was monitored for all samples for both kinds of experiments and the imposed deformations (8% and 15%) were chosen within these intervals.

The study was carried out at room temperature (25 °C). The systems were allowed to reach the proper temperature in approximately 20 min and then left at that temperature for other 20 min before the test. All analyses were performed on three replicate samples.

The squared tablets were first imbibed in water at 37 °C for different periods of time and then the compression and the relaxation experiments were carried out on the parallel and on the perpendicular direction to the compression force. Thus, the obtained parameters will be indexed with the subscript “paral” and “perp,” respectively. For the measurements carried out after 24 h, the tablets, due to their high height increase, were cut in three parts and the compression and relaxation experiments were performed on all three samples. In all cases, no remarkable differences were recorded (less than 5%) and then the average values were reported.

Polarized optical microscopy

Hydrogel texture was observed using a polarized light optical microscope Olympus model BX60 with a coupled camera PiXeLink. Images were taken by means of I.A.S Ver. 006 001 by DELTA SISTEMI (1994) at room temperature (~25 °C) at two different rotation angles (0° and 45°). The tablets, swelled for 24 h in distilled water at 37 °C, were cut along the perpendicular and parallel directions in order to obtain thin sections suitable for optical measurements. The slices were placed on microscope glass slides and dried at room temperature for several days. The samples were then observed between crossed polarizers for the detection of optical anisotropy.

Results and discussion

Water uptake of tablets

The relative increase of weight of tablets (in distilled water, 37 °C) prepared with the freeze-dried hydrogel of Sclg/borax was monitored together with the relative increase of height along the direction of the elongation, this aspect being the peculiarity of the system. Furthermore, the same experiment was performed on tablets that, after the first compression along one direction, were compressed a second time along a direction perpendicular to the previous one. The results reported in Fig. 1b, c clearly show that, while there are no significant differences in water uptake for the two samples, an appreciable different behavior is detected for the anisotropic elongation. When the tablets are compressed two times, the relative increase in height is reduced, confirming the hypothesis that the force, applied anisotropically to the freeze-dried samples, plays an important role in determining the peculiar subsequent elongation of the matrix, being present, at the molecular level, a tendency to assume ordered structures [13, 16].

Other experiments of water uptake and elongation were carried out on tablets of Sclg/borax prepared applying, for 30 s, a stress equivalent to 1, 5, and 10 kN, i.e., applying stresses lower (1 kN) or higher (10 kN) in comparison to the standard procedure followed in previous works (5 kN for 30 s) [10]. In Fig. 2, the obtained results are reported together with the picture of a tablet prepared applying 5 kN after 24 h of swelling. It is interesting to observe that, while the uptake of water is similar in all cases, a noticeable difference is found when the anisotropic elongation is considered. When a compression force of only 1 kN was applied, the tablets still follow a height increase essentially along one preferential direction at an extent much lower than that observed when 5 or 10 kN was used. Thus, the applied compression force, equivalent to 5 kN, represents

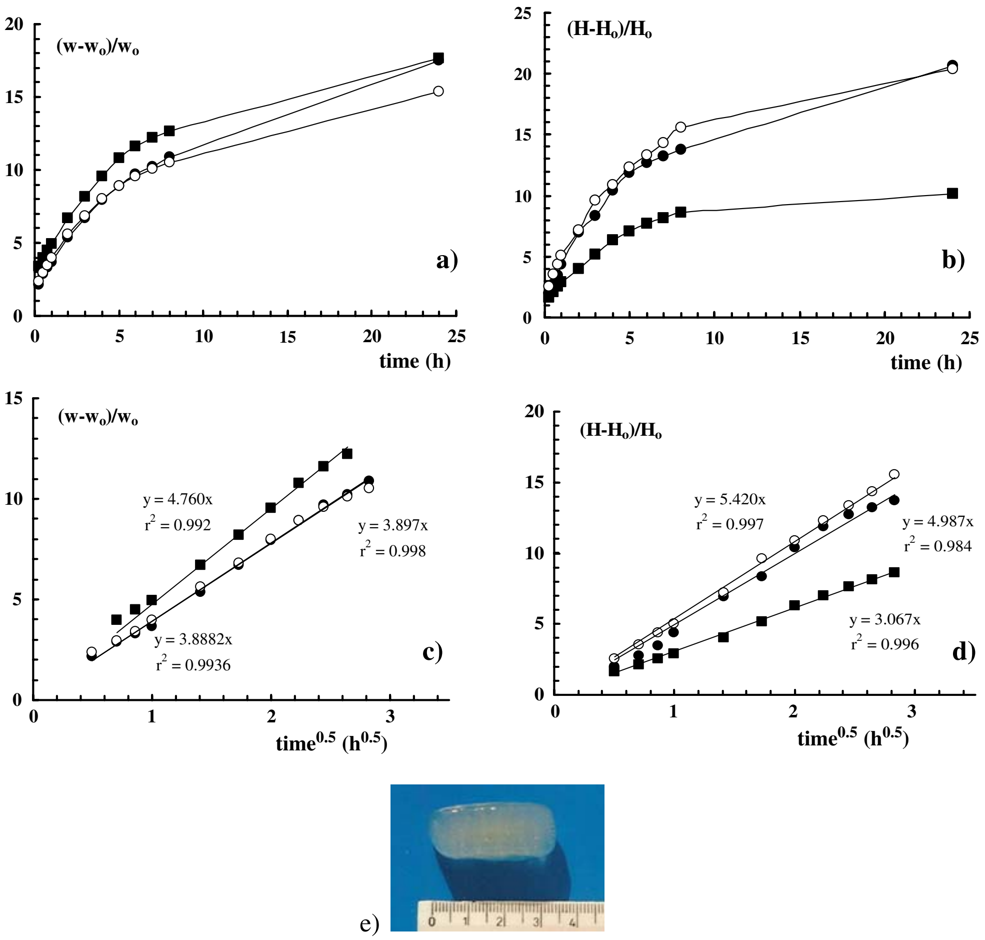

Fig. 2 Relative increase of the weight (**a**) and height (**b**) for Sclg/borax tablets (swelled in water at 37 °C), prepared applying a force of 1 kN (*open circles*), 5 kN (*filled circles*), and 10 kN (*filled squares*), as a function of time. The *solid lines* are only a guide to the eye. **c** and **d** The same data shown in **a** and **b** as a function of the square root of time. The *solid lines* represent the data best fitting. **e** Picture of the Sclg/borax tablet, prepared applying a force of 5 kN, after swelling in water for 24 h

the lowest tested value capable to induce the maximum possible elongation. In fact, doubling the force (10 kN), no increase in the elongation was detected. These evidence confirm that the anisotropic elongation observed in the tablets is related to the applied force and to the value of this force, being necessary an application of at least 5 kN to obtain the maximum relative height increase. Both the relative weight and height increases, regardless of the amount of solvent taken up, always follow a Fickian process (Fig. 2c, d).

In order to understand more deeply the mechanism related to the anisotropic and peculiar elongation of Sclg/borax, the same experiments were carried out on tablets prepared with GG/borax, LBG/borax, dextran/borax, pullulan/borax, starch/borax, and PVA/borax.

PVA is chosen according to the well-known capability of this synthetic polymer to interact and form gels in the presence of borate ions. Due to the nature of the linkages present in its chemical repeating unit, PVA is one of the most flexible polymers. GG and LBG are galactomannans, i.e., polysaccharides with a backbone of mannose units (M), both bearing galactose (G) side chains, but at different extent. In fact, the ratio mannose/galactose (M/G) is about 2 for GG and about 4 for LBG. Dextran, synthesized from sucrose by lactic acid bacteria consists of a straight chain of (1→6)-linked α-D-glc*p* units, while branches begin from α-(1→4) linkages (and in some cases, α-(1→2) and α-(1→3) linkages as well).

Pullulan is a neutral glucan whose basic structure consists of three α-(1→4) glc*p* units which are linked α-(1→6).

Starch generally contains amylose (20–25%) and amylopectin (75–80%). Amylose consists of (1→4)-linked α-D-glc*p* units, while amylopectin consists of (1→4)-linked α-D-glc*p* units and (1→6)-linked α-D-glc*p* units.

Besides Sclg, which is one of the most stiff systems present in nature (with a backbone build up by (1→3)-linked β-D-glc*p* units with single glc*p* side chains linked β-(1→6) to every third residue in the main chain), that exhibits, in aqueous solutions, a rigid rod behavior, all other polymers are very flexible and assume, in aqueous media, expanded random coil conformations. The obtained results for Sclg/borax, GG/borax, LBG/borax, and PVA/borax are shown in Fig. 3a, b. The data relative to the other polymer/borax systems cannot be reported because their tablets, after a few minutes, disaggregate in the water medium. On the other side, tablets of Sclg/borax and GG/borax, surprisingly, exhibit a similar behavior. They roughly assume the same amount of water and they roughly

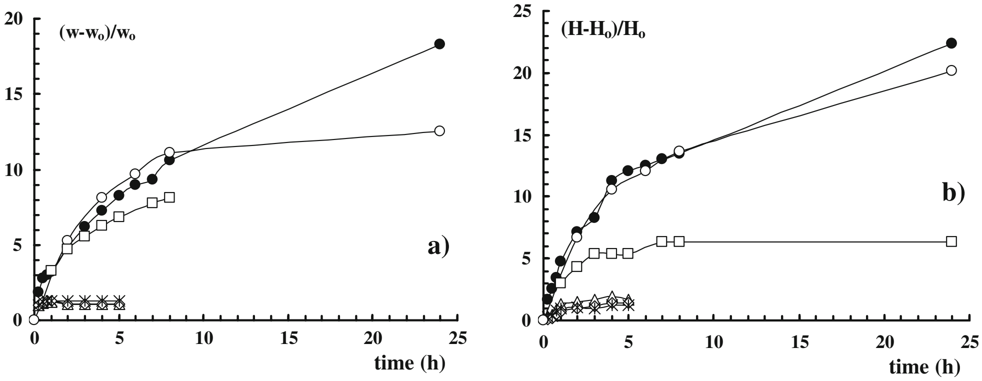

Fig. 3 Relative increase of the weight (**a**) and height (**b**) for tablets of PVA/borax at different cross-linker molar ratios (r= 0.07 *open triangles*, 0.030 *open diamonds*, 0.015 *asterisks*), for tablets of Sclg/borax (r=1, *filled circles*), GG/borax (r=1, *open circles*), and LBG/borax (r=1, *open squares*). The tablets were swelled in water at 37 °C. The *solid lines* are only a guide to the eye

elongate at the same extent along the direction where the compression pressure was applied.

On the other hand, LBG, though its water uptake is not much different from that of the Sclg/borax and GG/borax tablets, shows an anisotropic elongation much smaller in comparison to the previous two systems.

A completely different situation is depicted when PVA/borax tablets are tested. The water uptake is very small for all three kinds of tablets prepared at different r values. At the same time, it is not possible to define a specific anisotropic elongation, and after 7 h, the tablets, regardless of the borate content, start to break in smaller pieces, thus leading to the end of the experiments.

It has to be added that tablets of Sclg, GG, and LBG without borax were also previously tested and no anomalous swelling was detected [10, 17].

These data clearly indicate that the anisotropic elongation does not always occur and it cannot be considered as general evidence. Tanaka's theory asserts that a gel system, regardless of its starting geometry, swells isotropically in all directions [18]; nevertheless, according to the data reported in this paper, some branched polysaccharides behave quite differently showing an anomalous elongation that is not evidenced with the polymer bearing the –OH groups along alkyl chains. Thus, the anomalous behavior observed with the tablets obtained from the freeze-dried Sclg/borax and GG/borax hydrogels should be ascribed to the existence of domains with an intrinsic ordered structure that, in the presence of a spatial mechanical perturbation (e.g., compression), are being enhanced leading to an asymmetrical disposition of the chains along a preferentially oriented pre-established direction [13].

It appears interesting to point out the difference detected between the Sclg/borax and GG/borax data on one side and the LBG/borax data on the other side: Sclg is a stiff polymer while GG is a flexible one: thus, it seems that, in order to observe an atypical elongation, the intrinsic degree of freedom of the starting chains cannot be considered as a key parameter. On the other side, the nature of the chain might play a crucial role, being the polysaccharides with side chains suitable to elongate while the aliphatic chains do not possess such property. Among the different polysaccharides investigated, another important difference is detected in the case of LBG. This polymer has the same backbone as GG but bears a lower number of galactose units as side chains. As reported in Fig. 3b, the anisotropic elongation of LBG/borax tablets is still evident but at an appreciably lower extent in comparison to GG/borax tablets. Thus, it can be concluded that, most probably to detect an anomalous swelling, the –OH groups that link to borate ions should be present on the side chains of polysaccharides, regardless of the intrinsic flexibility of the backbone, while the degree of branching appears crucial. In fact, with a higher number of side chains, the relative height increases observed in the tablets also increase.

Mechanical characterization

Texture analysis is a technique that was extensively employed in the mechanical characterization of food materials and, in the last few years, it has also emerged as a useful technique in the field of pharmaceutical gel studies [12, 19–22].

Tablets of Sclg/borax were prepared using a squared die obtaining the so-called squared tablets in order to evaluate the different behaviors on the parallel and perpendicular directions with respect to compression. Experiments of water uptake were carried out in distilled water at 37 °C. At fixed intervals of time, 2, 4, 6, 8, and 24 h, the samples were tested by means of compression experiments (at room temperature) and the following parameters were acquired: (1) the system hardness, i.e., the maximum positive force required to attain a given imposed deformation, $F_{\max}$; (2) the work of cohesion (cohesiveness), proportional to the positive area under the force–time curve from zero to the maximum deformation imposed, it represents the work needed to overcome the internal bonds of the material; (3) the work of adhesion (adhesiveness), proportional to the negative area under the force–time curve, it represents the work needed to pull the probe away from the sample; (4) the viscoelastic loss, the positive area under the decompression force–time curve, located to the right of the maximum force.

In Fig. 4, the profiles obtained from a compression experiment carried out on tablet samples at different intervals of time on both directions, parallel and perpendicular, are reported. The force data are reported as a function of time (Fig. 4a, c) or as a function of the distance traveled by the probe (Fig. 4b, d) according to the imposed deformation. In Table 1, all the data acquired from the various hydrogels are summarized.

It is worth noting that the ability of the sample to stick to the probe decreases as the hardness increases, i.e., when the solid character of the matrix becomes more remarkable.

The values reported in Table 1 allow to obtain information on the mechanical properties of the tested systems in terms of the effect of imbibition time. Increasing this time from 2 to 24 h, the work of cohesion decreases almost 14 times in the perpendicular direction and almost four times in the parallel direction. It is interesting to note that, after 2 h, the cohesiveness in the perpendicular direction is 3.5 times higher than the cohesiveness detected in the parallel direction, while after 24 h, this difference becomes almost negligible.

In more details, in Fig. 5, the data of the compression experiments carried out in both directions are directly compared. A different behavior between perpendicular and parallel directions is observed: in the perpendicular direction, the system always shows higher values of F_{max} and cohesiveness, the difference being highest after 2 h and becoming smaller and smaller as the time proceeds (see Table 1). After 2 h, the adhesiveness is very low while it becomes more and more important as the swelling time increases. The initial slope of the curve force–distance, which represents Young's modulus, is well-defined and always higher for the perpendicular direction, while it is much smaller for the parallel direction. Furthermore, from Table 1, the adhesiveness is roughly of the same order of magnitude along the first 8 h, while after 24 h the adhesiveness shows an abrupt increase especially for the perpendicular direction. Concerning the viscoelastic loss, from 2 to 24 h, a decrease is observed for both directions and, after 24 h, the obtained values per unit volume become comparable. The overall set of compression data indicate that the water uptake of squared tablets leads to a systems with different properties depending on the side that is tested. Remarkable differences are detected in the first hours, while a roughly homogeneous system is revealed after imbibition of 24 h. This is in agreement with the hypothesis that the anisotropic force, applied to the freeze-dried gel to prepare the tablets, induce into the system an anisotropy that can be subsequently detected macroscopically also by means of mechanical tests. The highest hardness and the highest work of cohesion are related to the perpendicular side of the squared tablets while appreciable lower values are obtained for the parallel side, especially during the first hours, i.e., when the system still keeps "memory," at molecular level, of the exerted compression. Furthermore, the mechanical anisotropy

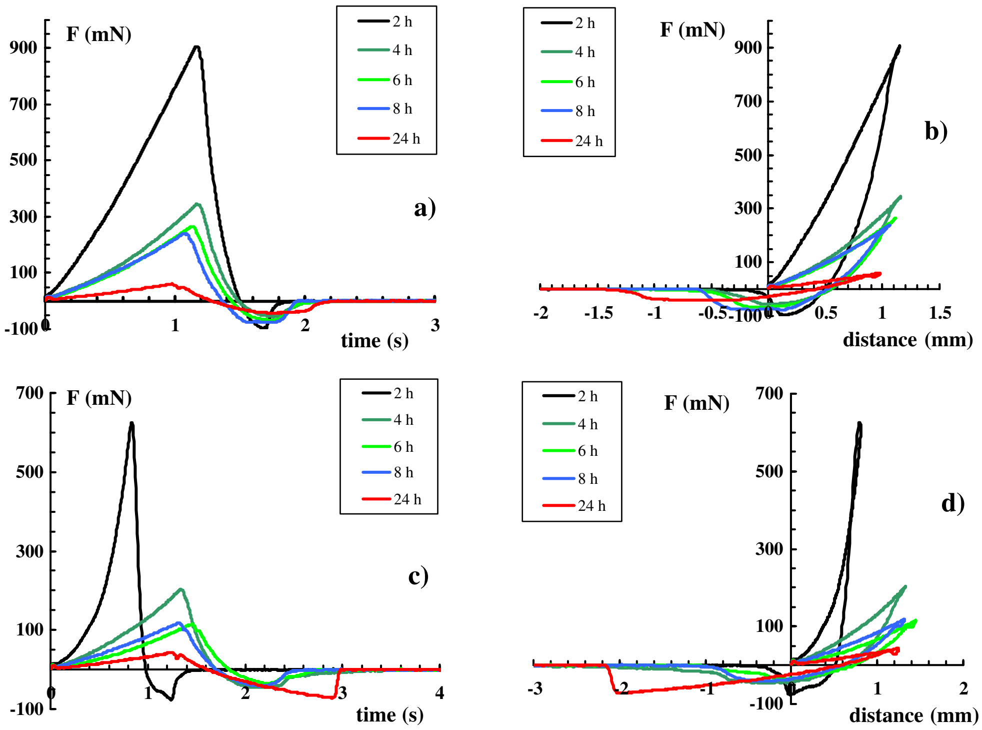

Fig. 4 Compression profiles obtained on the perpendicular (**a**) and parallel (**c**) directions to the applied force of squared Sclg/borax tablets after swelling in distilled water at 37 °C for different periods of time. The positive area under the curve until the maximum value is proportional to the work of cohesion, while the negative area is proportional to the work of adhesion of the sample to the probe. The hardness of the sample is given by the maximum F value recorded, F_{max}. **b** and **d** The same data of **a** and **c** reported as a function of the distance traveled by the probe along the samples The initial slopes of the curves represent Young's modulus

Table 1 Ratio of the work of cohesion, the work of adhesion, and the viscoelastic loss determined with the texture analyzer between the two tested sides of the Sclg/borax squared tablets after imbibition in distilled water for different periods of time at 37 °C (the actual detected values are reported in parentheses)

Time (h)	Cohesion perp/paral	Adhesion perp/paral	Viscoelastic loss perp/paral
2	3.5 (172.4/49.6)	1.0 (6.6/6.6)	2.4 (52.2/21.5)
4	1.5 (44.4/29.5)	0.5 (4.7/9.4)	1.5 (13.6/8.9)
6	1.8 (36.8/20.1)	1.4 (7.1/5.1)	1.9 (11.3/6.0)
8	1.6 (37.6/23.3)	1.5 (10.2/6.7)	1.7 (11.8/7.0)
24	1.1 (12.6/11.3)	4.5 (113.0/25.2)	1.1 (3.9/3.5)

decreases and almost vanishes after 24 h when a nondirectional diffusion of water occurs inside the system that also starts to undergo an erosion process.

In order to acquire further information about hydrogel mechanical properties and, consequently, on network characteristics, hydrogel relaxation behaviors can be matched resorting to the generalized Maxwell model [23].

In this model, the viscoelastic properties of the gel matrix are represented by a mechanical device made up by a series combination of a Hookean spring of rigidity E_i and a Newtonian dashpot of viscosity η_i. For uniaxial stress relaxation, this model yields to:

$$\sigma(t) = \int_0^t \phi(t - t') \frac{\partial \varepsilon}{\partial t} \partial t' \tag{1}$$

where σ is the tension, $\boldsymbol{\varepsilon}$ is the deformation, t is the time, and ϕ is the relaxation modulus whose expression is:

$$\phi(t) = E_0 + \sum_{i=1}^{n} E_i \exp\left(-\frac{E_i}{\eta_i} t\right). \tag{2}$$

As the relaxation test is preceded by a compression phase lasting t_1, Eq. 1 needs to be integrated with the following conditions:

$$\frac{\partial \varepsilon}{\partial \tau} = \frac{\varepsilon_0}{t_1}; \quad 0 < t < t_1 \quad \text{compression,} \tag{3}$$

$$\frac{\partial \varepsilon}{\partial \tau} = 0; \quad t > t_1 \quad \text{relaxation} \tag{4}$$

where $\boldsymbol{\varepsilon}_0$ is the final constant deformation applied.

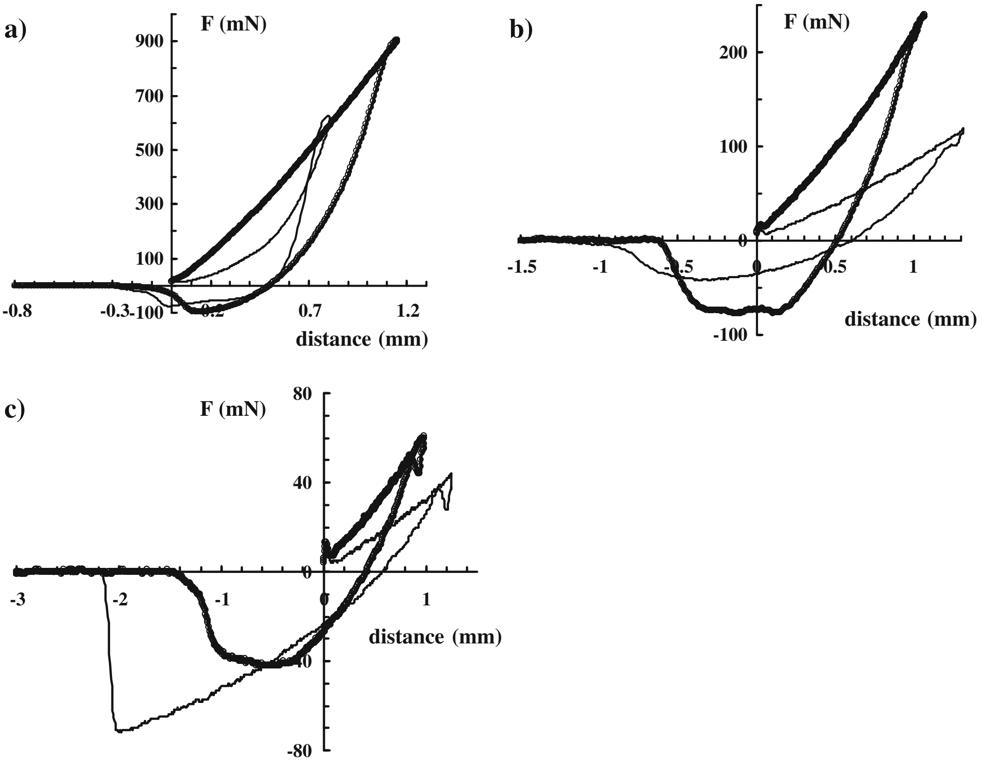

Fig. 5 Compression profiles obtained on the directions parallel (*thick line*) and perpendicular (*thin line*) to the applied force for squared Sclg/borax tablets after swelling in distilled water at 37 °C for 2 h (**a**), 8 h (**b**), and 24 h (**c**)

Accordingly, we get:

$$\sigma(t)=\frac{\varepsilon_0}{t_1}\left[E_0t_1+\sum_{i=1}^{n}\eta_i\exp\left(-\frac{E_i}{\eta_i}t\right)\left(\exp\left(\frac{E_i}{\eta_i}t_1-1\right)\right)\right]. \tag{5}$$

Figure 6a, b shows the relaxation spectra recorded at different swelling times on the parallel and perpendicular sides of the squared tablets. Figure 6c, d shows the good agreement between the relaxation experimental data (symbols) and Eq. 5 best fitting (solid lines) relative to different swelling times and to the different side of the tablets.

Interestingly, four to five Maxwell elements, plus a pure elastic element characterized by E_0 (whose value is almost negligible in the perpendicular direction; see Fig. 7a), are sufficient to represent the swelling tablet relaxation behaviors.

Figure 7b, c, showing the mechanical spectra of the swelling tablets at different times (E_i vs. $\tau_i=\eta_i/E_i$) evidence how, apart from the first pure elastic element, the behavior of the remaining viscoelastic part, for both sides of the tablets, is typical of liquid-like materials, since the elements characterized by low relaxation times τ_i are associated with higher values of the spring constants E_i; accordingly, they prevail in determining the time-dependent response.

Polarized optical microscopy

Further evidence of the anisotropy of the system was acquired by means of polarized optical microscopy. It can be observed (Fig. 8) that the textures obtained for the perpendicular cut are typical of isotropic systems, whose optical anisotropy is null. On the other side, the parallel cut showed a significant birefringence with the presence of elongated structures. It can thus be concluded that the swelled tablets show the typical behavior of an anisotropic system.

Conclusions

Results showed in the present work indicate that the peculiar height relative increase of tablets during swelling experiments carried out in distilled water is a characteristic that is shared only by few polysaccharides (e.g., Sclg and GG) when they are cross-linked with borax. On the other side, no evidence of anisotropic elongation is observed for tablets prepared with PVA, dextran, pullulan, and wheat starch when cross-linked with borax.

In this sense, an important parameter appears to be the degree of branching: Sclg and GG, with a quite similar number of side chains along the backbone, show almost superimposable elongation data. On the other side, LBG, with a degree of branching about one half with respect to GG, still shows the anisotropic swelling but at a much lower extent. These data suggest that a prerequisite for unidirectional swelling is the occurrence of the reaction between the borate ions and the hydroxyl groups carried by the side chain sugars of the polymers. Surprisingly, the

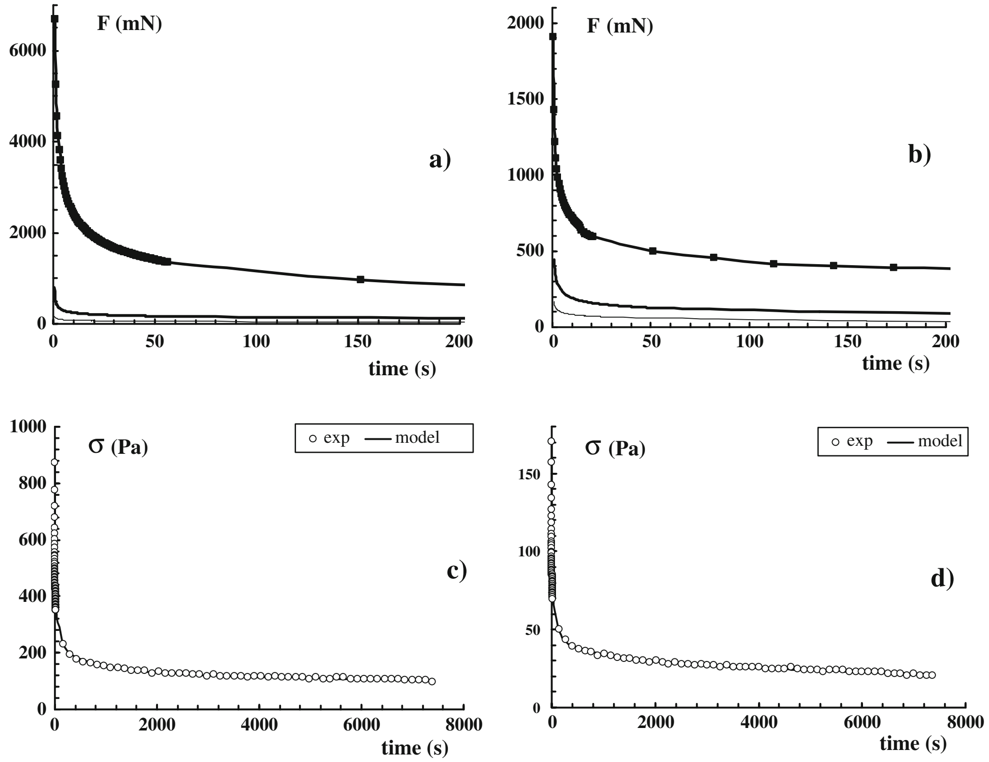

Fig. 6 Relaxation spectra recorded on Sclg/borax tablets on the perpendicular (**a**) and parallel (**b**) directions with respect to the compression for different periods of swelling in water at 37 °C (2 h, *filled squares*; 8 h, *thick lines*; 24 h, *thin lines*). Relaxation spectra recorded on Sclg/borax tablets on the perpendicular (**c**) and parallel (**d**) directions with respect to the compression, after 2 h of swelling in water and 37 °C. *Solid lines* are the best fittings obtained applying the generalized Maxwell model

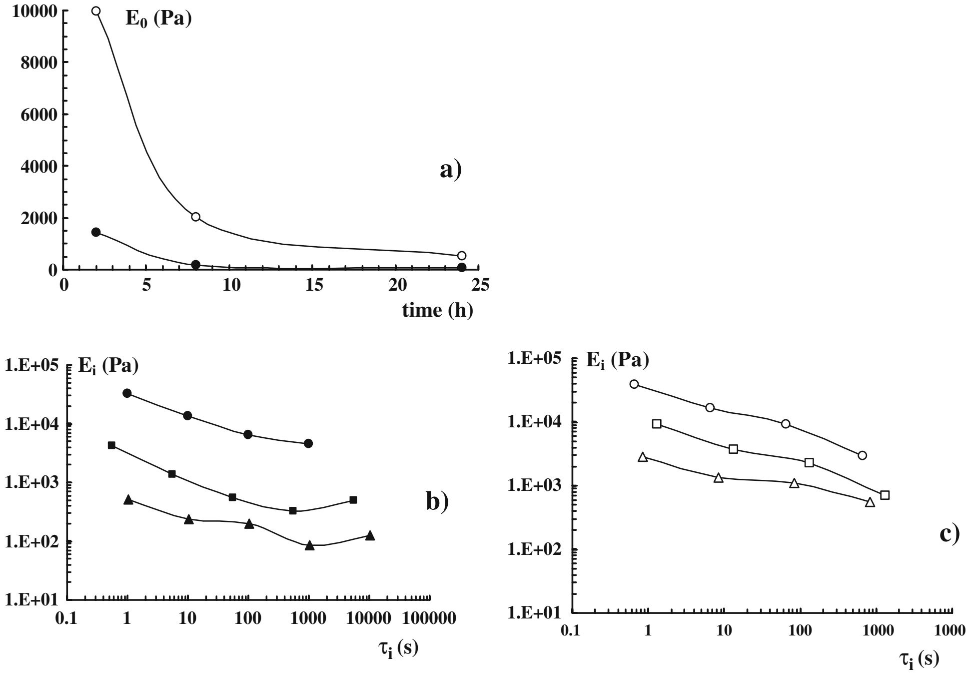

Fig. 7 **a** Dependence of E_0 on the swelling time for the parallel (*open circles*) and perpendicular (*filled circles*) sides of the Sclg/borax tablets. Dependence of E_i on τ_i for the perpendicular (**b**) (2 h, *filled circles*; 8 h, *filled squares*; 24 h, *filled triangles*) and parallel (**c**) (2 h, *open circles*; 8 h, *open squares*; 24 h, *open triangles*) sides of the Sclg/borax tablets. The *solid lines* are only a guide to the eye

intrinsic flexibility of the backbone, as well as the nature of the monomers, seems to have no influence in that sense: in fact, both polymers, the flexible one, GG, and the rigid one, Sclg, show a similar behavior.

Another crucial parameter for anisotropic elongation is the compression step. Tablets of Sclg/borax, pressed two times applying the force along perpendicular directions, show an elongation much smaller than that evidenced when the force is applied only once and along one direction. Thus, the unidirectional application of the force induces to retain the ordered configuration of parallel aligned chains that, as supported by MD and AFM, exists at molecular

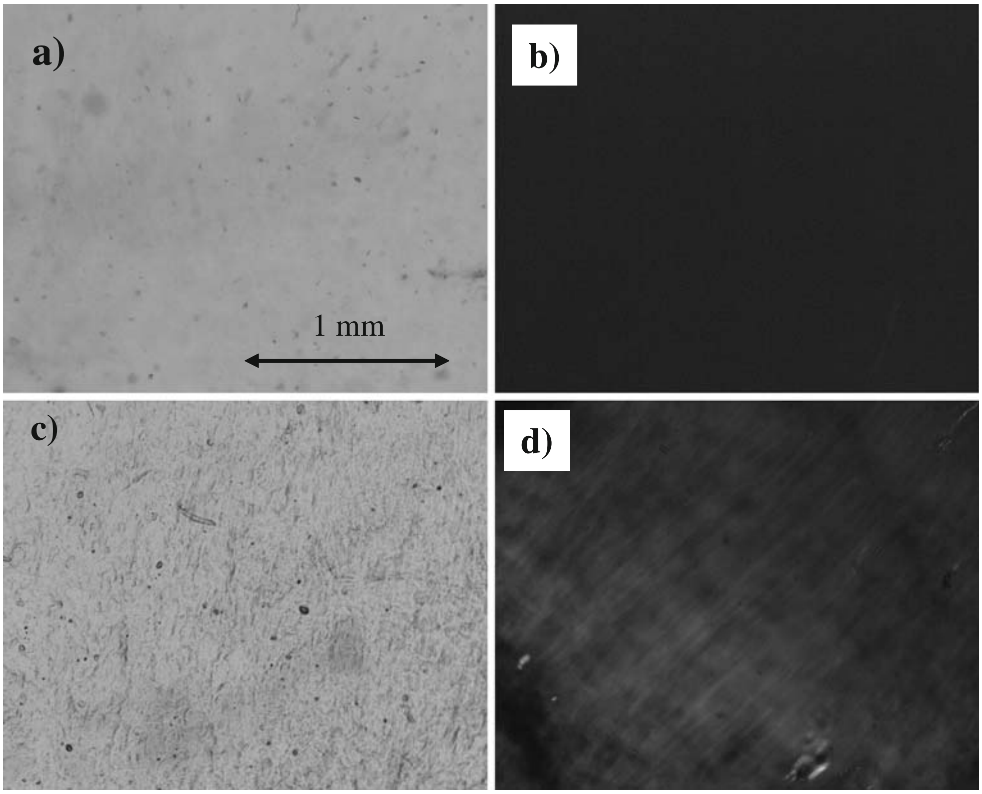

Fig. 8 Optical micrographs (magnification ×40) of a Sclg/borax swelled tablet taken along the perpendicular (**a** and **b**) and parallel (**c** and **d**) directions; **a** and **c** observed using polarized light, **b** and **d** observed between crossed polarizers

level [13, 16] and that disappears completely in the absence of borax.

Also, the force actually applied during the compression step is a parameter influencing the extent of the elongation. When forces of 5 or 10 kN are applied to the freeze-dried samples, the maximum tablet elongation is observed; while if a force of 1 kN is used, a remarkable smaller elongation effect is detected. This evidence further confirms that the compression force plays a fundamental role, exerting a positive synergic effect in the assembling of the chain at microscopic scale. This effect increases from 1 to 5 kN and then remains constant, indicating that 5 kN represents the lower tested value of the applied force to obtain the biggest effect on height increase.

Furthermore, when the Sclg/borax system is used to prepare squared tablets, it is possible to detect a different mechanical behavior during the swelling process along the two tested directions of the tablets. The strength and the cohesion reach a maximum value after 2 h of swelling together with the maximum difference in the two directions, while, after 24 h, the difference becomes almost negligible. As the system uptakes water, the mechanical strength tends to assume, as time goes on, the same value, indicating a homogeneous texture, at least at a superficial level. It has to be kept in mind that the dynamometer can give an insight only on the first layers of the matrix, being the deformation imposed very small in order to carry out the experiments within the linear viscoelastic range. The data values relative to the direction parallel to compression are always smaller than those obtained on the perpendicular one. This can be explained considering that water uptake occurs essentially along the parallel direction and, therefore, the internal cohesion along this direction decreases appreciably more than along the perpendicular one. As expected, the cohesion is very high at the beginning of the experiment and decreases with time while the adhesion follows, as expected, an opposite trend.

A different approach has to be considered for the relaxation experiments. In this case, a high and almost instantaneous deformation is imposed (differently from the compression test procedure) and the relaxation of the system is then recorded. Again, a different behavior is found for the two directions. The mechanical spectra indicate a clear viscoelastic character for both directions with a predominance of the liquid character. Interestingly, the residual elastic component E_0 results to be higher in the parallel direction than in the perpendicular one. Thus, the internal relaxation of the chains is somehow detected and the “answer” of the ordered structure to an abrupt compression is different along the two directions (aligned and not aligned chains). This should not be surprising if we consider that the relaxation experiment, differently from the compression test, records the behavior of the sample within a long interval of time. Also, the polarized optical microscopy, carried out on both sides of the swelled tablets, confirms the anisotropy of the matrix.

The overall results reported in this paper indicate how our approach allows correlating the imbibition properties along different directions with dynamomechanical parameters detected specifically on the same directions and with the optical birefringence behavior.

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