



Pharmaceutical Nanotechnology

Evaluation of dissolution kinetics of hydrophilic polymers by use of acoustic spectroscopy

Giulia Bonacucina, Marco Cespi, Giovanni F. Palmieri*

University of Camerino, Department of Chemical Sciences, via S. Agostino 1, 62032 Camerino, Italy

ARTICLE INFO

Article history:

Received 8 January 2009

Received in revised form 17 March 2009

Accepted 29 April 2009

Available online 6 May 2009

Keywords:

Ultrasound

Acoustic spectroscopy

Rheology

Hydrocolloids

Dissolution kinetics

ABSTRACT

This paper seeks to demonstrate the feasibility of using a novel analytical technique, acoustic spectroscopy, to characterize the dissolution kinetics of hydrophilic polymers, in particular, three different model polysaccharides: lambda carrageenan, gellan gum, and xanthan gum.

The influence of particle size and of analysis temperature (25 or 45 °C) was evaluated through the evolution over time of the microrheological acoustic parameters G' and G'' . This new method was then compared with classical rheological analysis. To better compare acoustic spectroscopy and rheological analysis, the initial dissolution rate from the slope of the first part of the G' or viscosity versus time curves was calculated.

Both analytical techniques gave the same rank order of kinetics for the powder types and fractions examined; differences in absolute values were due to the fact that the two methods measured different parameters and had different stirring efficiencies.

The rheological data obtained with both methods of analysis and their modelling confirmed that acoustic spectroscopy is an effective tool for monitoring and quantifying dissolution kinetics and hence affords a powerful technique for following over time a great number of physical changes occurring in a specific system.

© 2009 Elsevier B.V. All rights reserved.

1. Introduction

Hydrocolloids are hydrophilic macromolecules and much used because of their atoxicity, biocompatibility, availability, and abundance. Furthermore, their chemical structure can be easily modified by introducing different functional groups along their backbone. Their ability to interact with water medium is essential, making them suitable for manifold applications in the biomedical, food, and pharmaceutical fields. For instance, gels for biomedical analyses, jams, desserts and a great number of dosage forms such as hydrophilic monolithic matrices or hydrogels for *in situ* drug administration can be formulated using polysaccharides, their derivatives, and other types of hydrocolloids.

A fundamental step in the use of a water-soluble hydrocolloid is its dissolution in the aqueous medium. For this reason, it is essential to understand the mechanisms governing hydrocolloid/water interactions, which are basic to polymer dissolution kinetics. Solvent penetration and swelling of the particle surface are two phenomena preceding polymer dissolution. In solvent penetration, the hydrocolloid changes from a glassy to a rubbery state; as it swells, the polymeric chains disentangle and move away from the surface of

the swollen layer of the hydrocolloid through the boundary layer of the solution. (Kravtchenko et al., 1999; Parker et al., 2000).

Measurements of the dissolution rates can be affected by the random formation of lumps, the occurrence of which may be due to several parameters, such as small particle size or any factors that increase the dissolution rate (for example, temperature) (Parker et al., 2000).

Lumps are sacks of dry grains encapsulated in a homogeneous skin of gel that form when the dry grain bed comes into contact with the solvent; they form more quickly than the characteristic time of dissolution of individual grains (Parker et al., 2000). Lump formation may be prevented by working in so-called dispersing conditions, that is, by mixing the polymer powder with a rapidly dissolving non-polymeric diluent (such as sucrose). Another method consists in slowly adding the powder to the stirred solvent so that the grains remain separated before the hydration process starts (Parker et al., 2000).

Different methods described in the literature to track polymer dissolution kinetics include the determination of intrinsic and dynamic viscosity (Kravtchenko et al., 1999; Parvathy et al., 2007) and the use of solution calorimetry (Conti et al., 2006).

These methods do not directly measure the concentration of the dissolved molecule; rather, they identify the variation of some parameters of the system in bulk (such as viscosity), caused by the dissolution of the polymer molecules themselves.

* Corresponding author. Tel.: +39 0737 402289; fax: +39 0737 637345.

E-mail address: gianfilippo.palmieri@unicam.it (G.F. Palmieri).

At the same time, a fair number of theories and mathematical models have been developed to analyse the hydration process of macromolecules. Specific theoretical models take into account the process involved in dissolution, such as polymer chains reptation (Brochards and De Gennes, 1983; Herman and Edwards, 1990). Other semi-empirical models such as the first order kinetics model (To et al., 1994), the logarithmic model (Wang et al., 2002) and the Weibull function (Weibull, 1951) have been proposed, including one that takes into account the effects of various physicochemical parameters and the effect of dissolution conditions on solvation kinetics (Kravtchenko et al., 1999). Other works have pointed out limitations in the practical use of some models (Abdou, 1989; Devotta et al., 1994; Ranade and Maschelkar, 1995).

The aim of this paper was to investigate the feasibility of using acoustic spectroscopy as a method for studying the dissolution kinetics of hydrophilic polymers.

Acoustic spectroscopy offers a unique possibility for characterizing concentrated colloidal dispersions, since it avoids sample dilution and can be used to analyse non-transparent and even highly structured systems (Dukhin and Goetz, 2002). At the same time, it is a non-destructive technique that can act as a microrheometer, providing information on the microstructure of the dispersed systems (Dukhin and Goetz, 2002). Recently, acoustic spectroscopy has been applied in the pharmaceutical field for the characterization of colloidal systems (Saluja et al., 2007; Bonacucina et al., 2008), but the real potential of this analytical technique has yet to be adequately exploited. Some models of acoustic spectrometers can work in a continuous on-line mode and therefore could be used for monitoring industrial processes in real time. All these characteristics make acoustic spectroscopy a potentially powerful technique for following over time a great number of physical changes occurring in a specific system.

In the present work, the variation of the microrheological parameters G' and G'' with time was used for the step-by-step monitoring of hydrophilic polymer dissolution.

In order to compare acoustic spectroscopy results, classic shear viscosity measurements were also performed to follow the variation of viscosity over time, as this physical parameter is directly proportional to the concentration of dissolved polymer.

Well-known polysaccharides, lambda carrageenan, xanthan gum and gellan gum, were chosen as model polymers simply because they are among the most widely used of their kind, not only in the pharmaceutical field but also in foods and cosmetics.

2. Materials and methods

Lambda carrageenan (Viscarin GP-109) was obtained from FMC Corporation, while gellan gum (Kelcogel F) and xanthan gum (Xantural 75) were acquired from CP Kelco. Deionised water was prepared from an MF3 ion-exchange system (San Salvatore di Cogorno, Genova, Italy).

2.1. Preliminary sieving operation

In order to investigate the influence of grain size on dissolution kinetics, the polysaccharide powders were fractionated using 0.300, 0.180, 0.106, and 0.053 mm sieves. The mean diameters of the fractions thus obtained are summarized in Table 1. Both the unsieved powders and the different fractions were then tested.

2.2. Acoustic spectroscopy measurements

The operating principle of acoustic spectroscopy is based on the generation of sound pulses that pass through a sample and are measured by a receiver. During the passage through the sample, sound

Table 1
Mean diameters of polysaccharide fractions obtained after sieving.

Polysaccharides	Fractions (mm)	Weight %
Gellan gum	0.143	41.39
	0.0795	40.15
	<0.053	17.65
Lambda carrageenan	0.143	23.76
	0.0795	34.36
	<0.053	40.91
Xanthan gum	0.0795	45.6
	<0.053	52.5

is attenuated by the presence of the liquid medium and any particles in dispersion, and the energy changes in intensity and phase are measured. Fig. 1 reports the block diagram of an acoustic spectrometer. It is important to note that the power density used by the spectrometer is very low and does not influence colloid characteristics, as demonstrated in previous works (Dukhin and Goetz, 2002).

There are six mechanisms of sound interaction with a dispersed system: *viscous* (related to the shear waves generated by the particles oscillating in the acoustic pressure field due to the difference in the densities between particle and medium), *thermal* (related to the temperature gradients generated near the surface of the particles), *scattering* (the same principle as light scattering), *intrinsic* (this mechanism causes losses of acoustic energy due to the interaction of the sound wave with the particles and the medium as a homogeneous phase), *structural* (caused by the oscillation of a network of particles, this mechanism is specific for structured systems), and *electrokinetic* (interactions between the ultrasounds and the double layer). Electrokinetic losses are negligible in terms of the total attenuation, a fact that makes it possible to separate electroacoustic spectroscopy from acoustic spectroscopy (Dukhin and Goetz, 2002).

Through complex treatment and modelling of such energetic contributions to total acoustic attenuation, it is possible to calculate the particle size and the zeta potential of the dispersed particles (Dukhin and Goetz, 2002).

The acoustic spectrometer can also act as a microrheometer: in this case, “longitudinal” viscoelastic properties are measured because the stress is not tangential, as for an oscillation experiment in a rotational rheometer, but normal.

It can be demonstrated (further explanations can be found in more specialized texts) that ultrasonic absorption and velocity are related to the real and imaginary parts of a complex modulus (Litovitz and Davis, 1964), and that G' and G'' moduli are related to sound speed (V), sound attenuation (α), sound frequency (ω) and density (ρ) of the system by the following equations (Litovitz and Davis, 1964):

$$G' = \rho V^2 \quad (1)$$

$$G'' = 2V^3 \frac{\alpha}{\omega} \quad (2)$$

In our study, the cell of the DT-1200 acoustic and electroacoustic spectrometer (Dispersion Technology, USA) was filled with 15 ml of water. At the same time, a polysaccharide powder was wetted in a

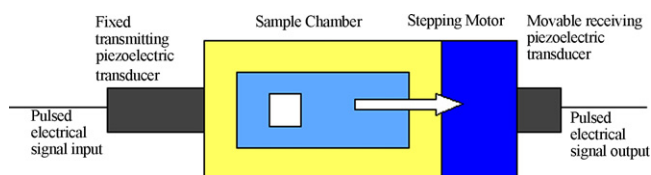


Fig. 1. Block diagram of an acoustic spectrometer.

mortar with a small amount of glycerine in order to reduce lump formation (dispersing conditions), and then added to the spectrometer cell until a final concentration of 1% (w/w) was reached, with sound attenuation and speed being monitored over time. The magnetic stirring system of the spectrometer and the internal circulating loop were started immediately after the cell was filled with water.

Analyses were performed in the gap interval of 0.325–20 mm between transmitter and receiver and in the frequency range of 3–100 MHz at the temperatures of 25 and 45 °C. The evolution of G' and G'' moduli was considered to follow the kinetics of polymer solvation and dissolution with time (180 min).

Calculation of the slopes obtained from the linear fitting of the first part of the viscosity versus time curves served to quantify the initial swelling rates (Conti et al., 2006).

Finally, it should be noted that the first data point used in the fitting was not time zero, but the first real value acquired by the acoustic spectrometer (the first reading), which occurs after more or less 5 min.

2.3. Rheological characterization

These analyses made it possible to follow the variation of viscosity over time and consequently to obtain the dissolution kinetics of samples, as this physical parameter is directly proportional to the concentration of the dissolved polymer.

Rheological analyses were performed in triplicate using a stress control rheometer (Stress-Tech, Reologica) equipped with a concentric cylinder measuring geometry (Mooney-type cell, 25 mm diameter). A shear stress of 10 Pa was maintained for the duration of the test (180 min.). The polysaccharide powder was gently tipped into the geometry, where a certain amount of deionised water was present, in order to obtain a final concentration of 1% (w/w). As already mentioned in the acoustic spectroscopy section, the polysaccharide powders had been previously wetted with a small amount of glycerine in order to reduce lump formation. As done in the acoustic spectroscopy tests, the influence of grain size on the dissolution kinetics was investigated, with rheometer analyses carried out at 25 and 45 °C to study how temperature influences dissolution. The calculation of the slopes obtained from the linear fitting of the first part of the viscosity versus time curves was used to quantify the initial swelling rates (Conti et al., 2006).

3. Results

3.1. Acoustic spectroscopy analysis

Fig. 2 reports as an example the G' and G'' moduli versus time plots related to the unsieved gellan gum powder. The values considered were those related to the frequency of 50 MHz. This frequency was chosen arbitrarily as the mean value of the frequency range used (3–100 MHz). In fact, the frequency spectra showed a nearly linear increase in attenuation with frequency. Thus the same evolution of G' and G'' with time could be obtained at any other frequency. As already mentioned, the dynamic moduli obtained from acoustic spectroscopy measurements are not comparable with those derived from rotational rheometers working in the oscillation mode, since the applied stress is not tangential, as in an oscillatory experiment, but “normal,” and the tested frequencies are much higher.

As can be noted, complete dissolution occurs after 100 min. The microrheological parameters showed a mirror trend: the G' increased with time while the G'' decreased. This trend denoted progressive polymer solvation, which corresponded to an increase in the structural contribution (G') and a decrease in the viscous one (G''). Calculation of the slope from the first part of the G' curve yielded a solvation rate of $2.55 \times 10^5 \text{ min}^{-1}$. Table 2 summarizes

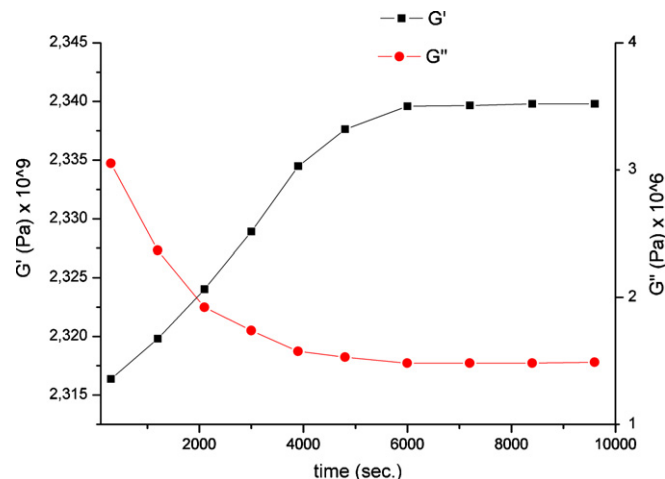


Fig. 2. Evolution of the G' and G'' moduli for the unsieved gellan gum powder at 1% (w/w) concentration calculated at the frequency of 50 MHz and at the temperature of 25 °C.

all fitting parameters for gellan gum dissolution kinetics. Standard deviations have been voluntarily omitted because in some cases their absolute value was very low. In most cases, the standard deviation value was below 10% of the presented mean.

The increase in the G' modulus values with progressive polymer dissolution may be explained by a corresponding increase, during this process, of the polysaccharide/water interaction, which leads to a smaller amount of “free” water in the system. Thus, solvation gives rise to an increase in “sound speed,” since sound speed in free water is lower than in water engaged in the interaction with the polysaccharide. Thus, at a microrheological level, the interaction with water at the water/macromolecules interface is definitely higher as the polymer dissolution goes on, giving rise to a more structured system.

Analysis of the G'' curves (Fig. 2B) showed that this parameter is strictly related to the variation of sound attenuation, as already mentioned. In this case, the decrease in the G'' values can be explained by the microrheological modification in the system, due to a higher polysaccharide/water interaction. It causes sample structuring and a corresponding decrease in “free” water. Thus, the progressive solvation can be identified with an increase in the G' modulus, in agreement with the reduction of the G'' modulus previously described.

When the temperature of the analysis increased to 45 °C, samples showed faster dissolution kinetics. The value of the slope corresponding to the initial dissolution rate increased to $7.14 \times 10^5 \text{ min}^{-1}$.

Similar considerations can be made for the sieved powders.

For example, the G' spectra related to the different fractions of gellan gum indicated dissolution kinetics dependent on particle size (Fig. 3). The smaller fraction (<0.053 mm) reached the plateau value for both moduli, showing complete polymer dissolution after

Table 2
Slope parameters for gellan gum dissolution kinetics.

°C	Fractions	Acoustics $10^5 \text{ (min}^{-1}\text{)}$	Rheology $10^{-6} \text{ (s}^{-1}\text{)}$
25	Unsieved	2.55	1.36
	0.143	3.24	2.07
	0.0795	5.51	2.23
	<0.053	13.0	4.29
45	Unsieved	7.14	7.17
	0.143	6.37	8.82
	0.0795	7.56	8.83
	<0.053	7.60	12.9

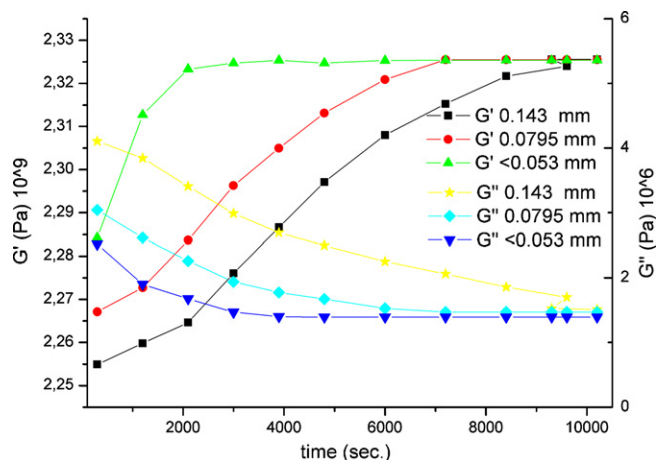


Fig. 3. Evolution of the G' and G'' moduli for the different fractions of gellan gum at 1% (w/w) concentration calculated at the frequency of 50 MHz and at the temperature of 25 °C.

50 min. This effect of the particle size on particle dissolution rate is not unusual, as smaller particles have a greater specific surface. The other fractions showed complete but slower rates of dissolution with values of G' modulus that reached a plateau value practically at the end of the analysis. Once the plateau value was reached, the rheological parameters remained constant over time, proving the attainment of the equilibrium state.

The calculation of the slopes from the first part of the G' curve indicated a definitely higher solvation rate for the <0.053 mm fraction. The calculated values ranged from $1.3 \times 10^6 \text{ min}^{-1}$ for the smaller fraction to $3.24 \times 10^5 \text{ min}^{-1}$ for the 0.143 mm mean diameter fraction (a value comparable to that obtained for the unsieved powder).

The calculation of the slope values of the G'' curves was quite difficult, as these plots are less linear. In any case, it is possible to observe from Fig. 3B that the G'' curve related to the 0.143 mm fraction showed a slower decrease in this rheological parameter, corresponding to the slower increase already observed for the G' modulus.

The analysis performed at 45 °C (Fig. 4) gave a higher dissolution rate, as expected. For example, the bigger fraction (0.143 mm) showed an initial solvation rate of $6.37 \times 10^5 \text{ min}^{-1}$. However, at this temperature the slope values were quite similar for all fractions,

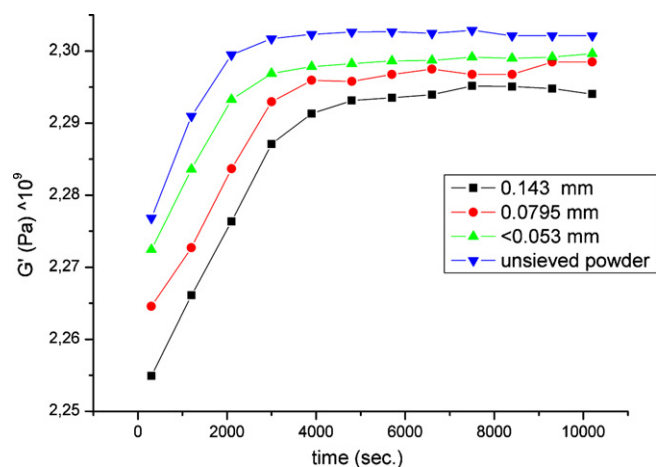


Fig. 4. Evolution of the G' modulus for the different fractions of gellan gum at 1% (w/w) concentration calculated at the frequency of 50 MHz and at the temperature of 45 °C.

proving that a temperature increase tends to reduce the differences in the dissolution rate.

The lambda carrageenan and the xanthan gum (data not shown) showed similar behaviour, characterized by higher dissolution ability for the <0.053 mm fraction, even though the dissolution kinetics were slightly slower. Calculation of slopes of the curves related to the lambda carrageenan indicated an initial dissolution rate of $5.8 \times 10^5 \text{ min}^{-1}$ for the 0.143 mm fraction, while the <0.053 mm mean diameter fraction had the greater dissolution rate ($6.3 \times 10^5 \text{ min}^{-1}$) in this case as well. The temperature increase to 45 °C did not noticeably increase the dissolution rate. In fact, the calculated slope values still ranged within 5.8×10^5 and $6.38 \times 10^5 \text{ min}^{-1}$ for the 0.143 mm and <0.053 mm mean diameter fractions respectively.

Regarding the xanthan gum, only two fractions were obtained for this polymer after the sieving operations, but in any case they showed different solvation characteristics. The solvation rate obtained from the fitting of the 0.0795 mm fraction was definitely slower than that obtained for the smaller one (7.8×10^5 and $1.16 \times 10^6 \text{ min}^{-1}$ respectively).

At 45 °C, the dissolution rate increased slightly, narrowing the differences between the two fractions: slope values ranged from 1.24×10^6 to $1.49 \times 10^6 \text{ min}^{-1}$ and demonstrated that temperature influences this parameter to some degree.

3.2. Rheological analysis

As already mentioned, rheological analyses, in particular, shear viscosity measurements, were performed in order to compare the acoustic spectroscopy results with those obtained from another technique.

Analysis of the gellan gum dissolution kinetics showed, as already observed in the acoustic spectroscopy measurements, that both the unsieved polysaccharide (Fig. 5) and the different fractions had complete solvation at 25 and 45 °C within the experimental time of the test, demonstrated by the presence of a plateau in the viscosity values. To examine the differences among the systems, the slopes of the first part of the viscosity/time curve were calculated to quantify the initial dissolution rate. The slope values at 25 °C lying between 4.29×10^{-6} and $1.36 \times 10^{-6} \text{ s}^{-1}$ confirmed quite fast dissolution kinetics, even though a higher solvation rate for the <0.053 mm fraction was evident, in agreement with the results obtained with the acoustic spectroscopy analysis. As expected, the temperature increase to 45 °C (Fig. 6) lead to a higher solvation rate,

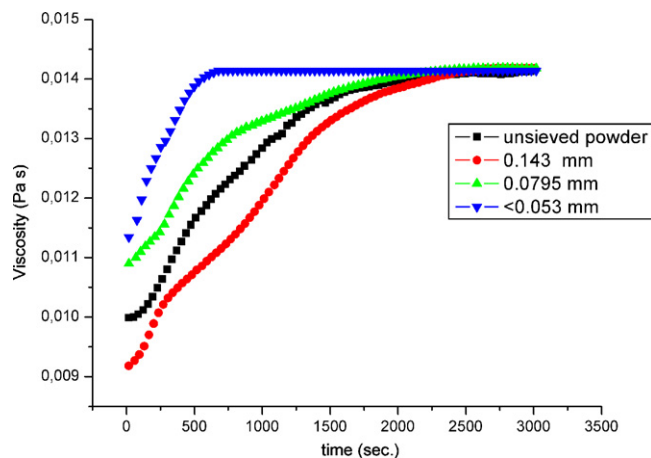


Fig. 5. Evolution of the viscosity for the unsieved powder and for the different fractions of gellan gum at 1% (w/w) concentration calculated at the temperature of 25 °C.

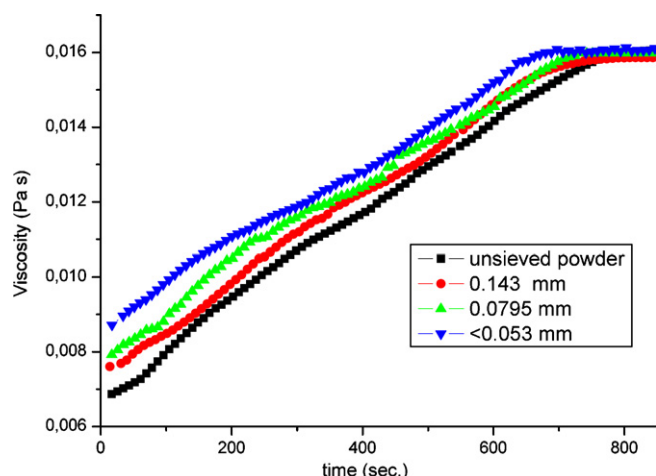


Fig. 6. Evolution of the viscosity for the different fractions of gellan gum and for the unsieved powder at 1% (w/w) concentration calculated at the temperature of 45 °C.

as can be observed from the change of the slope of the smaller fraction, whose value was $12.9 \times 10^{-6} \text{ s}^{-1}$.

The lambda carrageenan showed slightly slower dissolution kinetics compared to the gellan gum at both the temperatures tested, even though complete polymer dissolution was reached during the analysis (data not shown), as already observed for the acoustic spectroscopy analysis. Calculation of the slope values of the curves obtained at 25 °C confirmed a progressive decrease in system rates of solvation going from the <0.053 mm fraction to the 0.143 (slope values are 3.085×10^{-5} and $4.734 \times 10^{-6} \text{ s}^{-1}$ respectively). The increase in temperature did not substantially affect sample dissolution kinetics, as the slope values obtained were very similar to those calculated for the analysis carried out at 25 °C. Regarding the unsieved powder, its dissolution behaviour was comparable to that of the two smaller fractions.

The xanthan gum was the polysaccharide that showed the slowest dissolution kinetics, even if in this case as well, complete polymer dissolution was reached during the analysis (data not shown). The samples tested at 25 °C had slope values ranging between $2.24 \times 10^{-5} \text{ min}^{-1}$ for the fraction with particle size <0.053 and $1.5 \times 10^{-6} \text{ s}^{-1}$ for the fraction with a particle size of 0.0795. Thus a decrease in the particle size meant an increase in the rate of solvation. At 45 °C, the difference among the various samples is smaller, demonstrating that the analysis temperature influences to some degree the hydration properties of the studied systems.

3.3. Comparison between the two techniques

Some factors should be taken into consideration in this comparison of acoustic spectroscopy and classical rheology.

First of all, it is well to point out that in both techniques, polymer dissolution kinetics were defined indirectly by monitoring parameters such as viscosity or longitudinal elastic moduli.

It is also fundamental to take into consideration the fact that dissolution kinetics were monitored directly inside the cell measure of the rheometer and the acoustic spectrometer. In this way, the two techniques could be better compared, as measurement variability due to the withdrawal from a viscous system was avoided. Since the measure cells of the two instruments have different stirring systems, the time scale of the corresponding kinetics obtained will inevitably differ.

The most important finding is that kinetics obtained from the three-polysaccharide powders and those obtained from the different size fractions of a specific polysaccharide are in the same rank order. Of course, the absolute value of the fitting param-

eters changes, but it should be taken into account that acoustic analysis measures viscoelastic longitudinal parameters, and at very high frequencies. On the other hand, rheological analysis measures dynamic viscosity in a classic manner.

Certainly, the stirring system of the acoustic spectrometer cell is less effective than the coaxial cylinders of the rheometer; this is the reason for the more rapid kinetics obtained with the latter technique.

In effect, these two techniques can be considered complementary. Classical rheological analyses essentially describe the “in bulk” properties of a system, even if some observations on the microstructure can be made from the modelling of the frequency sweep tests. Because acoustic longitudinal elastic moduli depend strictly on the energy and phase variation of the ultrasound wave, they reflect the microstructural changes of the system, such as those concerning the colloid/medium interface and the amount of water bound to the colloid itself. As already mentioned in Section 1, molecular acoustics can provide information on many characteristics of the solvated polymer, offering myriad possibilities for studies on colloids, which, however are not within the purview of the present work.

4. Conclusion

Acoustic analysis has been used to explore the mechanisms underlying the dissolution process, a progressive polymer/solvent interaction that necessarily leads to a change in system structure. Acoustic spectroscopy has proven effective in tracking water displacement, making it possible to investigate particle/water interactions and to identify the microstructural modifications that happen to system structure. Dissolution was found to correspond with an increase in the G' modulus and a reduction of the G'' modulus, which can be identified with a gradual decrease in the “free” water in the systems.

The efficacy of using acoustic spectroscopy to monitor the dissolution kinetics of hydrophilic polymers has been confirmed by the results obtained with classical rheological analysis. In fact, acoustic spectroscopy effectively identified the differences among the tested polysaccharides and fractions, in some cases with greater accuracy than rheology, probably because of the different stirring mechanisms.

Given the efficacy of this technique and considering that the market offers some models of acoustic spectrometers designed to work on-line, it can be concluded that this technique might prove very useful, particularly for industrial applications, because processes can be monitored constantly over time, avoiding periodical probing.

References

- Abdou, H.M., 1989. Theory of Dissolution, Bioavailability and Bioequivalence. Mack Publishers, Easton.
- Bonacucina, G., Misici Falzi, M., Cespi, M., Palmieri, G.F., 2008. Characterization of micellar systems by the use of acoustic spectroscopy. *J. Pharm. Sci.* 97, 2217–2227.
- Brochards, F., De Gennes, P.G., 1983. Kinetics of polymer dissolution. *Physicochem. Hydrodyn.* 4, 313–322.
- Conti, S., Gaisford, S., Buckton, G., Conte, U., 2006. Solution calorimetry to monitor swelling and dissolution of polymers and polymer blends. *Thermochim. Acta* 450, 56–60.
- Devotta, I., Ambeskar, V.D., Mandhare, A.B., Maschelkar, R.A., 1994. Life time of a dissolving polymer particle. *Chem. Eng. Sci.* 49, 645–654.
- Dukhin, A.S., Goetz, P.J., 2002. Ultrasound for Characterizing Colloids. Particle Sizing, Zeta Potential, Rheology. Elsevier.
- Herman, M.F., Edwards, S.F., 1990. A reptation model for polymer dissolution. *Macromolecules* 23, 3662–3671.
- Kravtchenko, T.P., Renoir, J., Parker, A., Brigand, G., 1999. A novel method for determining the dissolution kinetics of hydrocolloids powders. *Food Hydrocolloids* 13, 219–225.
- Litovitz, T.A., Davis, C.M., 1964. Structural and shear relaxation in liquids. In: Mason, W.P. (Ed.), *Physical Acoustics*. Academic Press, NY, pp. 285–290.
- Parker, A., Vigouroux, F., Reed, W.F., 2000. Dissolution kinetics of polymer powder. *Fluid Mech. Transport Phenomena* 46, 1290–1299.

- Parvathy, K.S., Susheelamma, N.S., Tharanathan, R.N., 2007. Hydration characteristics of guar gum samples and their fractions. *Food Hydrocolloids* 21, 630–637.
- Ranade, V.R., Maschelkar, R.A., 1995. Convective diffusion from a dissolving polymeric particle. *Am. Inst. Chem. Eng.* 41, 666–676.
- Saluja, A., Badkar, A.V., Zeng, D.L., Kalonia, D.S., 2007. Ultrasonic rheology of a monoclonal antibody (IgG₂) solution: implication for physical stability of proteins in high concentration formulations. *J. Pharm. Sci.* 96, 3181–3195.
- To, K.M., Mitchell, J.R., Hill, S.E., Bardon, L.A., Matthews, P., 1994. Measurements of hydration of polysaccharides. *Food Hydrocolloids* 8, 243–249.
- Wang, Q., Ellis, P.R., Ross-Murphy, S.B., 2002. Dissolution kinetics of guar gum powders. I Methods for commercial polydisperse samples. *Carbohydr. Polym.* 49, 131–137.
- Weibull, W., 1951. A statistical distribution function of wide applicability. *J. Appl. Mech.* 18, 293–297.