Rheological Properties of Ethylcellulose Latex

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ABSTRACT: Because of their large specific surface area, aqueous-based pseudolatex systems of ethylcellulose can absorb large amounts of drugs. In addition, the stability of polymeric particles in biological fluids delays the release of the drug as in controlled drug delivery systems. The aim of the present study was to characterize the rheological properties of latex particles as a measure of their colloidal stability. Here, we report the effect of three variables: pH, electrolyte concentration, and temperature. The rheograms clearly show that the polymer suspensions displayed Bingham plastic behavior. Internal structuring of the latex was greatest at acid and natural pH values, particularly at the highest ionic strength. In acid solutions, only temperature appeared to play a fundamental role; both the shear stress corresponding to the onset of nonlinear viscoelasticity and the elastic modulus at all frequencies were higher at 37°C than those at room temperature. This is assumed to be a consequence of deformation of the polymer particles upon heating. The effect of ionic strength was noticeable only at the natural pH (pH $\cong$ 6.5). At high concentrations of sodium chloride, the particles aggregated because of the decrease in double layer repulsion, and as a result, the latex became structured and its elastic modulus subsequently increased. Interestingly, when the temperature was increased further, this structure presumably broke, down, at least partially, and the storage modulus was reduced. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 102: 847–851, 2006

Key words: viscoelastic properties; rheology; viscosity

INTRODUCTION

Colloidal particles have attracted increasing attention in the past decade because of their potential of applications.[1–3] Some applications have already been achieved (e.g., surface coatings, rheological control, and stabilizing agents),[4–6] whereas many more are yet to be realized, such as the development of chemical and biomedical applications and controlled drug delivery systems. Many authors have reported important industrial and technological applications of colloid suspensions. Controlled-release systems, for example, are intended to maintain a constant level of drug in the organism and are a subject of permanent interest within the field of industrial pharmaceutics.

Both synthetic and natural polymers have been studied and used as drug delivery systems. Because of their high specific surface area, polymer particles can adsorb large amounts of the active drug, and their stability in biological fluids delays drug release.[7] The advantages of these systems and their applications have been thoroughly studied in recent years,[8–11] and these include protection against inactivation, better acceptance by the patient, increased safety, and fewer toxic metabolites. We therefore developed a polymer-based suspension in which the pseudolatex particles act as a vehicle for drugs for pharmaceutical formulations destined for oral use.[12] The result is a biocompatible suspension with suitable organoleptic characteristics. The role of the pseudolatex is to regulate therapeutic drug release in the organism after oral administration.

Cellulose-based pseudolatexes have traditionally been approved for use in health products. We prepared a latex with ethylcellulose, a derivative of cellulose,[13] suitable for this type of application primarily because of its rheological properties. Here, we report the findings of a rheological study of this preparation to measure its colloidal stability. In addition, we describe changes in rheological behavior at different pH values, monovalent electrolyte concentrations (NaCl), and temperatures.

EXPERIMENTAL SECTION

Materials

All chemicals were analytical quality manufactured by Panreac (Spain). All water used to prepare the solutions and suspensions was of Milli-Q quality (Milli-Q Academic, Millipore, France).

Ethylcellulose pseudolatex preparation and particle analysis

The latex was synthesized according to the procedures developed by Vanderhoff et al.[14] Synthesis was started by dissolving 18.75 g ethylcellulose 9004-57-3 (ICN, USA) in 106.25 g of an 85 : 15 benzene–ethanol (Panreac, Barcelona, Spain) mixture. An emulsion was then prepared of this organic solution in 375.0 mL water containing 2 g sodium dodecylsulfate (Panreac, Spain). Then the organic solvent was evaporated by mechanical stirring at room temperature. The resulting whitish suspension was cleared by dialysis against Milli-Q water (Milli-Q Academic, Millipore, France).

The resultant suspension had a solid content of about 4.5% (w/v); however, a concentration of 10% (w/v) was needed for the rheological study. The mixture was therefore centrifuged at 15,000 rpm for 30 min.

The shape, surface characteristics, size, and size distribution of the final polymer particles were investigated by scanning electron microscopy (SEM DSM 950, Zeiss, Oberkogen, Germany). Two mean particle diameters were found: most particles measured 3–5 μm, but 10% measured ∼20 μm. All particles were spherical and had a porous surface. The polymers had the characteristics of a true latex, in terms of colloidal stability, particle size uniformity, film-forming properties, and other parameters, and their pH was 6.5 ± 0.1.

A 30% ethylcellulose pseudolatex is commercially available to the industry (Aquacoat, FMC, PA). Aquacoat® and our latex differ mainly in solid concentration and particle size (Aquacoat < 1 μm). Our formulation has advantages over other pseudolatexes, the most important of which may be its easy synthesis in laboratory. This facilitates the preparation of formulations with active drugs.[15,16]

Rheological measurements

The rheological properties of ethylcellulose microparticles were measured in a Bohlin CS-10 controlled-stress rheometer with CSS-25 geometry. The bob (28.5 mm high, 25.0 mm diameter) was immersed in the cup (26 mm diameter), followed by preshearing at 5 Pa for 60 s. Then the system was allowed to relax for 180 s. This time was chosen to permit the normal force to reach a stable value, a necessary condition to obtain reproducible results. The geometry setups were equipped with a circulating water bath and Peltier plate to ensure a uniform temperature of 25°C ± 0.1°C in the samples.

Three types of experiment were performed:[17]

- Viscometry, or steady-state measurements. A shear stress ramp was applied to the suspensions under study.

- Oscillatory rheology. Stress sweeps were conducted at 1 Hz to determine the elastic modulus (G') of the suspensions in the linear viscoelastic region.
- Creep-recovery. All samples were subjected to a constant shear for a period of 120 s, and the compliance modulus (J) was measured. Then the stress was removed and recovery was measured for another 120 s.

RESULTS AND DISCUSSION

Viscometry

Flow curves of suspensions were characterized by a low shear rate ($d\gamma/dt \leq 300$ s^{-1}), which limited stress. Note that for the shear rate investigated, shear-thinning behavior was observed for suspensions. Figure 1 shows that colloidal suspensions displayed Bingham plasticity. Plastic materials require a certain shear stress (yield stress) to begin to flow. At rest, cohesive forces produce the characteristics of a solid, but when the fluidity limit is exceeded the bonds break and the product behaves as a fluid.[17,18]

The yield stress was higher at the natural pH of the latex, indicating a higher degree of internal structure, but it was notably affected by temperature (Figs. 2 and 3). In contrast, temperature did not affect the samples at extreme acid or alkaline pH values nor were they affected by the electrolyte concentration under alkaline conditions. This observation can be explained by the deformation the particles undergo,[19,20] since characteristics such as size and shape influence the mechanical properties of systems.

At an acid pH and the lowest electrolyte concentration (10^{-5} M), the systems showed a higher yield stress, in contrast to expectations. This fact suggests that the structure was more consolidated under these conditions, with a greater resistance to flow, as
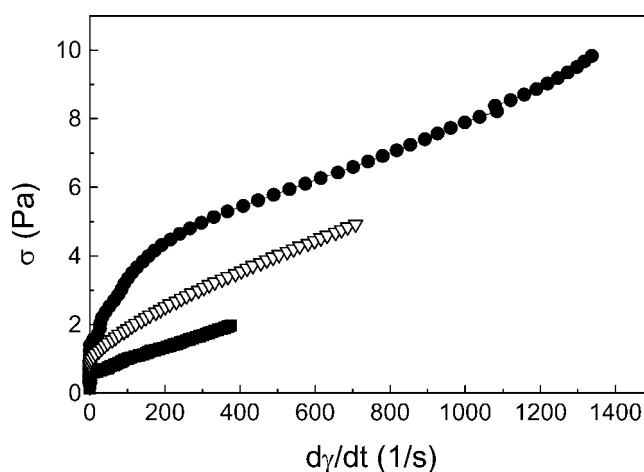
Figure 1 Flow curves for latex at 25°C, $10^{-2}M$ NaCl, and at different pH values: (■) pH 2, (●) pH 6.5, and (▽) pH 8.
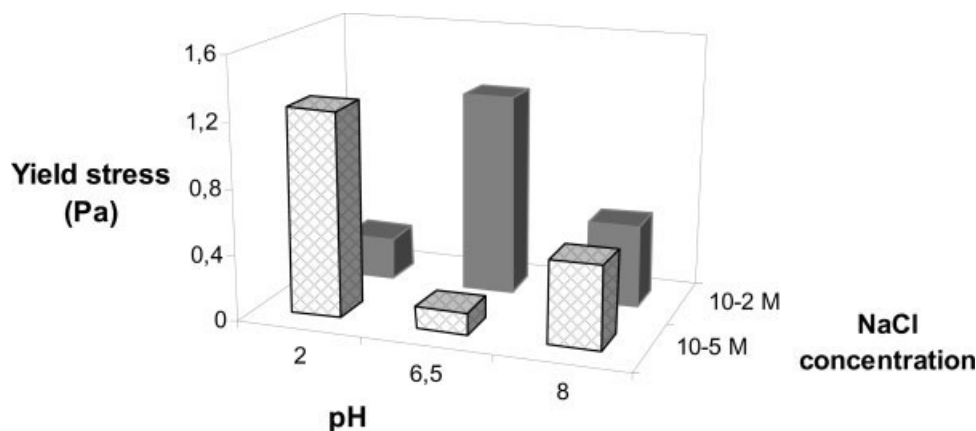
Figure 2 Yield stress of latex at 25°C and at different pH values and concentrations of NaCl.

a result of the ion-induced changes in the electrostatic double-layer.[21–23]

Under alkaline conditions the apparent viscosity was higher than that at the other pH values investigated for all values of shear stress. Temperature had little effect on the results.

Figures 2 and 3 summarize the changes in yield stress as a function of the different variables. The criterion used to determine yield stress was that the sample was assumed to begin to flow when viscosity reached its maximum.

Oscillatory rheology

We determined the range of stress amplitudes (σ_0) for which linear viscoelastic behavior was observed (Figs. 4 and 5). This range is known as the viscoelastic linear region and is found by measuring the elastic modulus G' as a function of stress (σ) at constant frequency (1 Hz). This zone is seen up to a critical stress value and then decreases when this value is exceeded. The data obtained above this value reflect the destruction of the three-dimensional structure of the suspension due to the large amplitude of the oscillatory stress, with the formation of isolated floccules.

At the lowest electrolyte concentration ($10^{-5}M$ NaCl), temperature changes did not affect the elastic modulus (the plateau value) or the critical stress at the natural pH of the latex, or under alkaline conditions. Although the critical stress was around 10 Pa, at an acid pH, these parameters increased with temperature by approximately one order of magnitude. The critical stress shifted from 0.1 Pa (at room temperature) to 1 Pa (at 37°C). This finding may be due to deformation of the particles, as both the size and shape of the particles noticeably influence the mechanical properties of suspensions.

When ionic strength increased up to $10^{-2}M$ NaCl, the behavior at an acid pH was the same. However, the results were completely different at the natural pH of latex for this electrolyte concentration. The elastic modulus was greater although the critical stress was 1 Pa. These values varied with temperature, with G' decreasing and the critical stress nearing 10 Pa. The degree of internal structuring was also greater. In contrast, at an alkaline pH there was
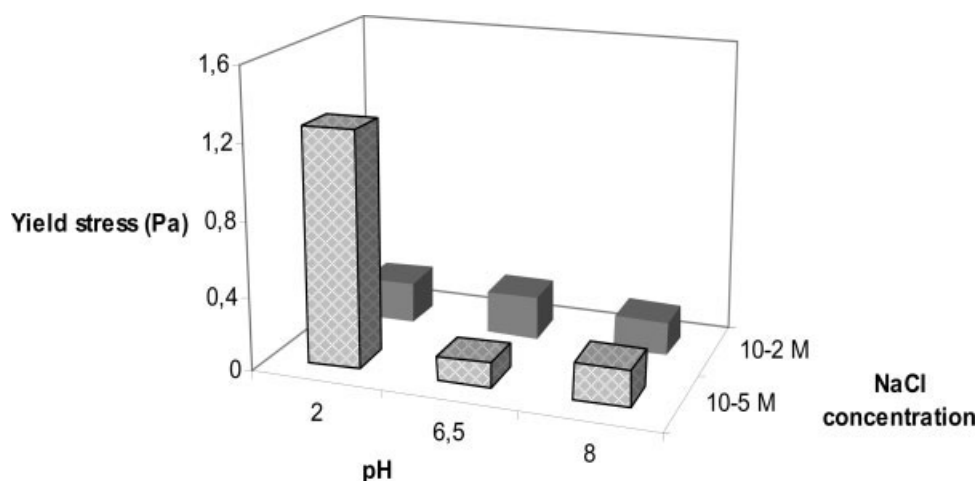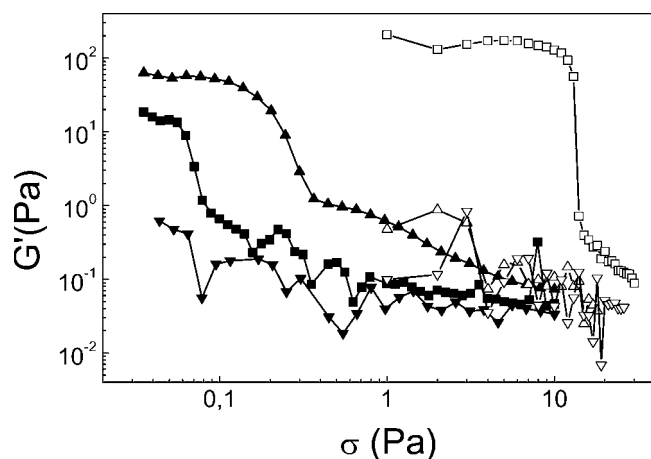

Figure 3 Yield stress of latex at 37°C and at different pH values and concentrations of NaCl.
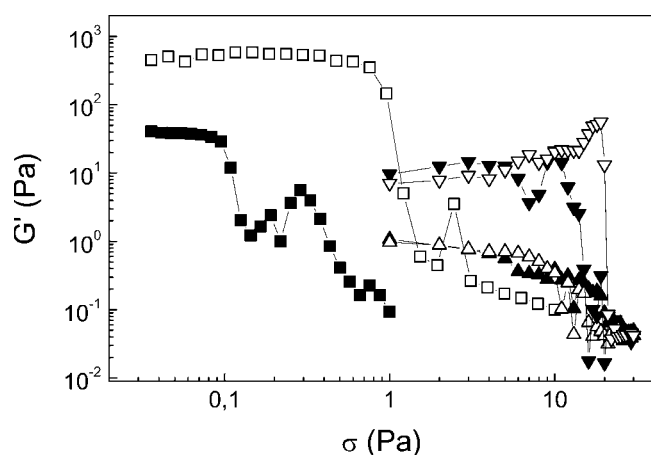
Figure 4 Elastic modulus G′ as a function of shear stress amplitude σ applied in oscillatory tests. The viscoelastic linear region was obtained with $10^{-2}M$ NaCl, for different pH values and temperatures: (■) pH 2 and 25°C, (▲) pH 6.5 and 25°C, (▼) pH 8 and 25°C, (□) pH 2 and 37°C, (△) pH 6.5 and 37°C and (▽) pH 8 and 37°C.

almost no linear viscoelastic zone. The suspensions underwent increasing linear deformation over time that was unrecoverable. Thus, the samples can be considered viscous liquids.

Creep-recovery

These tests demonstrated shear creep compliance J(t), when a constant stress was applied for a given time (120 s) and recovery of the system for an equivalent amount of time after the stress was removed (120 s).[20,24] At a constant stress, strain in an ideal elastic material would be constant due to lack of flow, and the material would return to the original

Figure 5 Elastic modulus G′ as a function of shear stress amplitude σ applied in oscillometric tests. The viscoelastic linear region was obtained with $10^{-5}M$ NaCl, for different pH values and temperatures : (■) pH 2 and 25°C, (▲) pH 6.5 and 25°C, (▼) pH 8 and 25°C, (□) pH 2 and 37°C, (△) pH 6.5 and 37°C and (▽) pH 8 and 37°C.
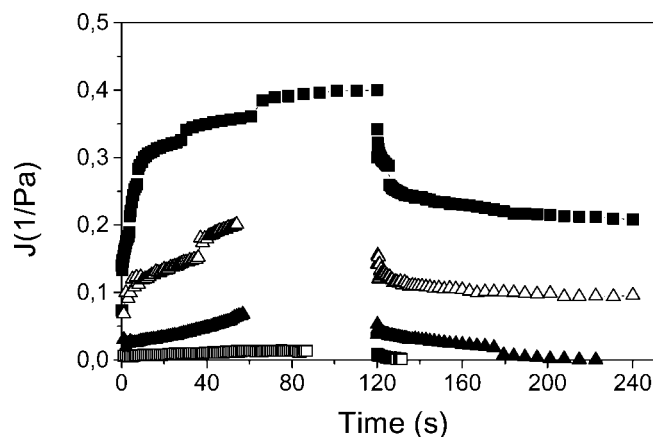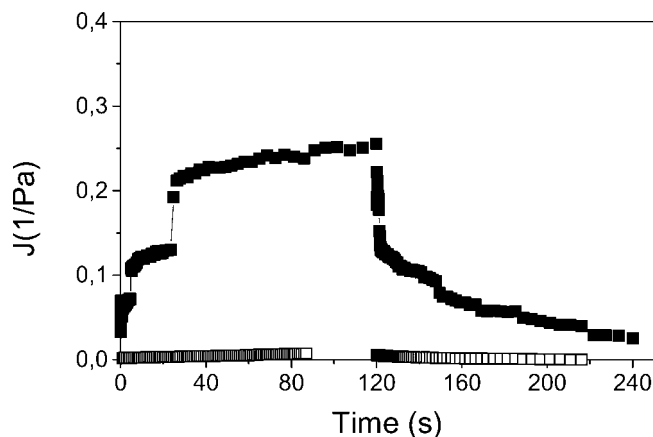

Figure 6 Compliance modulus J as a function of time obtained in creep-recovery experiments with latex and $10^{-2}M$ NaCl, for different pH values and temperatures: (■) pH 2 and 25°C, (▲) pH 6.5 and 25°C, (□) pH 2 and 37°C and (△) pH 6.5 and 37°C.

shape when the stress is removed. Similar to an ideal viscous material, our samples exhibited a non-linear response to strain. Because of their ability to recover structure to some degree by storing energy, permanent deformation in our samples was less than the total deformation applied (Fig. 6).

Nevertheless, this behavior was not seen in every case. Under alkaline conditions, the samples underwent increasing linear deformation over time that was unrecoverable. Thus, they can be considered viscous liquids. This result has also been observed at the natural pH for the lowest electrolyte concentration.[25–27]

Some systems showed instantaneous deformation when subjected to a stress. Recovery was also immediate when the stress was withdrawn; in other words, they behaved like elastic solids. This occurred at an acid pH at 37°C, regardless of the electrolyte concentration, and at natural pH for $10^{-2}M$ at room temperature (Fig. 7).

Figure 7 Compliance modulus J as a function of time obtained in creep-recovery experiments with latex, $10^{-5}M$ NaCl, and acid pH values at different temperatures: (■) 25°C and (□) 37°C.
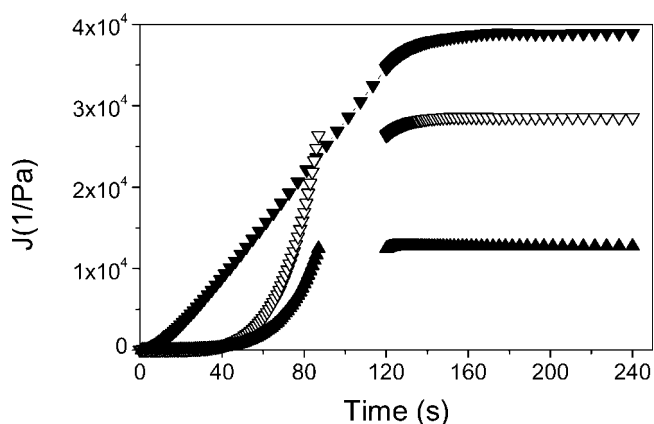
Figure 8 Compliance modulus *J* as a function of time obtained in creep-recovery experiments at 37°C with latex and different pH values and concentrations of NaCl: (▲) pH 6.5 and $10^{-5}M$ NaCl, (▼) pH 8 and $10^{-2}M$ NaCl, and (▽) pH 8 and $10^{-5}M$ NaCl.

Therefore, only the systems at pH 2 and 25°C, as well as the sample at natural pH and $10^{-2}M$ at physiological temperature were viscoelastic fluids *per se* (Fig. 8).

CONCLUSIONS

The results show that our suspensions behaved differently under different conditions. At an alkaline pH, the samples were liquid-like, especially at higher temperatures. This is supported by the fact that the low stress threshold value diminished more markedly at 37°C because of the lack of a linear viscoelastic zone, as shown by the creep-recovery diagram. This tendency did not change with electrolyte concentration.

At its natural pH and at the lowest ionic strength tested here, the latex showed a similar behavior, since the system required less stress for creep to appear, and when the stress was removed there was no recovery. When the concentration of NaCl was increased at this pH, the σ_0, G′, and σ_c were higher. This indicates a greater degree of internal structuring with a greater elastic component. However, the suspension was markedly affected by temperature, and it underwent a certain degree of destructuring as temperature increased because of deformation of the latex particles.

At an acid pH, the samples were not influenced by temperature, although as the electrolyte concentration rose, the stress threshold decreased. This is an unmistakable sign that the structure lost consistency, which was confirmed by the oscillometric results. The increase in critical stress with temperature can also be explained by particle deformation, since the structure did not break down easily.

We therefore found a clearly viscoelastic behavior for the suspensions at an acid pH and at the natural pH of the latex, when the NaCl concentration was $10^{-2}M$. Viscoelastic behavior was affected by temperature, since heating led to changes in particle shape. Changes in particle shape also occurred at an alkaline pH, leading to breakdown of the internal structuring and liquid-like behavior of the suspension.

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