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Rheological study of Carbopol® Ultrez™ 10 hydroalcoholic gels, II: Thermal and mechanical properties as a function of pH and polymer concentration

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The rheological characterization of Carbopol® Ultrez™ 10 alcoholic (30%) gels is complemented by studying flow behavior as a function of temperature (20–50 °C) at different pH values (4.0–7.0) and different polymer concentrations (0.1–0.5%). Flow curves were adjusted to the Ostwald model, showing a fall in viscosity, together with an enhance in flow index with increasing temperature. Calculated flow activation energies at constant shear stress (E_τ) and at a constant shear rate (E_γ) were found to be related to the final pH of the hydroalcoholic gels. A further study was done to evaluate hardness (H) and compressibility (A) of gels as a function of pH and polymer concentration, obtaining similar correlation patterns for mechanical properties and consistency indexes. A significant linear dependence was also found between consistency indexes and the mechanical properties of the gels.

1. Introduction

The viscosity of materials can be significantly affected by some variables such as shear rate, time of shearing, pressure and temperature. Consequently an exhaustive rheological characterization of pharmaceutical disperse systems may assess the dependence of viscosity on such variables. It is in particular important to study the temperature dependence of the viscosity, to understand of the mechanism of their flow process and to elucidate the relation between the structure of macromolecules and their behavior on deformation. Furthermore, the temperature dependence of the viscosity of gelled systems has a substantial effect on their processibility, since the sensitivity toward changes in temperature governs not only the choice of the processing conditions, but often the quality of this systems.

The experimental determination of the activation energy of flow and its relationship to the structure and composition is of great interest, as well. [1, 2].

As in the case of the rheological behavior, the mechanical properties of Carbopol® Ultrez™ 10 dispersions are also strongly dependent on neutralization and polymer concentration, since hardness (H) and compressibility (A) are components of shearing stress, too. Texture profile analysis has been proven as an adequate method for the determination of the most important mechanical properties of polymeric systems [3, 4]. By this method it is possible to describe the mechanical properties of hydroalcoholic gels in terms of hardness and compressibility, factors also closely related to the ease of removal of the product from the container and its spreadability.

The study of mechanical properties and temperature dependence of the flow behavior of Carbopol® Ultrez™ 10 hydroalcoholic gels is another important aspect of an exhaustive characterization which may provide rheological parameters with potential application in topical bioavailability studies [5–7]. Consequently the aim of the present work was to complete the rheological characterization of Carbopol® Ultrez™ 10 hydroalcoholic gels by studying its flow behavior as a function of temperature (20–50 °C) for different pH values (4.0–7.0) and polymer concentrations (0.1–0.5% w/w) and to evaluate the mechanical properties of these systems as a function of these variables.

2. Investigations, results and discussion

2.1. Flow behavior as function of temperature

During manufacture and storage of pharmaceuticals it is of great importance to know how the flow properties of dispersed systems are affected by changes in temperature. Interest is confined to the range of 0–50 °C. Therefore, the influence of temperature on flow properties of Carbopol® Ultrez™ 10 hydroalcoholic gels was evaluated by recording rheograms at varying temperatures from 20 °C to 50 °C at different pH and polymer concentrations [8, 9]. As an example, Fig. 1 shows viscosity-shear rate curves for 0.4% w/w Carbopol® Ultrez™ 10 hydroalcoholic gels at pH 4.0 and 7.0. At all temperatures, the gels were shear thinning, with increasing flow index values as temperature increased. The effect of increasing temperature is to increase chain mobility, causing a fall in viscosity together with an increase in the value of n. The polymer chains ar becoming more mobile and the lifetimes of the chain entanglements shorter, giving more Newtonian flows [10–12].

In non-newtonian systems the apparent viscosity is a function not only of the temperature but also of shear stress and shear rate. Because many rheometers are unable to make measurements under Newtonian conditions, it is often necessary to evaluate the activation energy of flow in the power law region. The temperature dependence of the apparent viscosity may be treated assuming the condition τ = constant or γ = constant. Hence, with the aim to study the hydroalcoholic gels comparatively, apparent viscosity values obtained for constant τ and constant γ were correlated for each concentration with temperature and pH according to the Arrhenius-Frenkel-Eyring formula:

$$h = B \cdot \exp\left(E/RT\right), \qquad (1)$$

where E is the activation energy of the flow process at constant shear stress (E_τ) or at constant shear rate (E_γ), T is the absolute temperature in K and R is the constant of gases. Both activation energy values, calculated as the slope of straight lines in representing $\ln \eta$ versus T^{-1} (°K), are given in Table 1 for each pH and polymer concentration. Experimentally E_τ has been found to be nearly constant and independent of shear stress, while E_γ depends on shear rate, which is an important parameter in some technological processes that are accomplished at constant rates of shear [2].
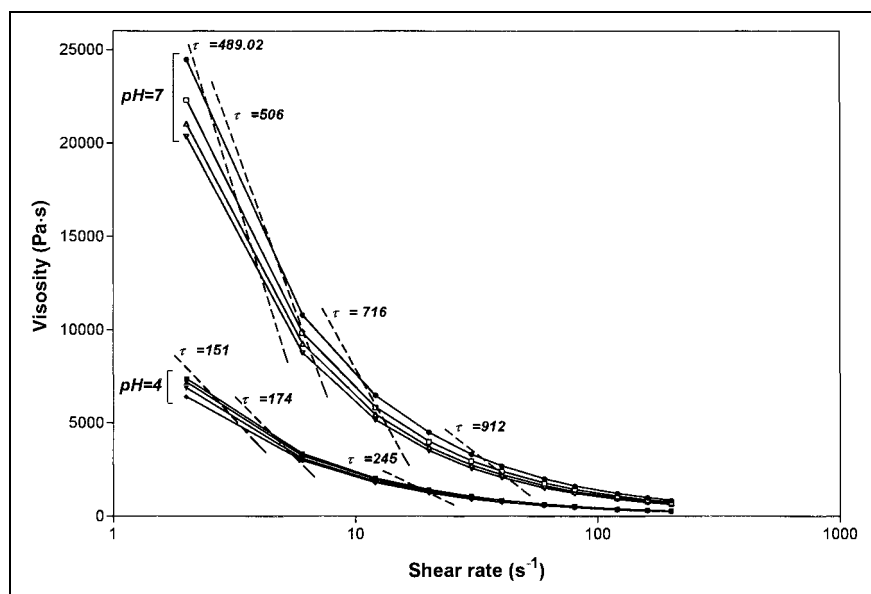
Fig. 1:
Flow curves of 0.4% Carbopol® Ultrez™ 10 hydroalcoholic gels (pH 4 and 7) in the temperature range 20–50 °C. Dashed lines represent constant shear stress

In general the results given in Table 1 show relatively low values of E_τ and E_γ (0.7–4.5 kJ/mol), in conjunction with an increase of both parameters with pH for a constant polymer concentration. The activation energy of flow has been found to be primarily related to molecular parameters like molecular weight, chain branches, chain rigidity and intermolecular forces of attraction. Consequently, low activation energies obtained are determined by the low polymer concentration range studied. Furthermore, the increase in E_τ and E_γ with neutralization demonstrates the structure forming effect of pH, which can be related to an increase in chain rigidity and intermolecular forces of attraction due to the ionization of carboxyl groups in polymeric chains, which generate negative charges along the polymer chain. The increase in pH seems to induce a disorder → order transition, that allows the polymeric chains to form stronger intermolecular interactions [10].

According to experimental results there is not a clear relationship between polymer concentration and activation energies at constant pH (Table 1). This result can be due to the low accuracy of experimental measurements in the narrow range of the concentrations studied. Consequently the effect of concentration on E_γ and E_τ is difficult to quantify. In general the Carbopol® Ultrez™ 10 hydroalcoholic gels exhibit little viscosity change under the temperature variations of normal use and storage, which minimizes the possibility unacceptable changes in the product characteristics.

2.2. Mechanical properties

Formulations designed for topical application may exhibit acceptable mechanical characteristics such as easy removal of product from container, easy application, and low hardness. Texture profile analysis has been proven as an adequate method for the determination of the most important mechanical properties of polymeric systems, such as hardness and compressibility [6, 7].

This two parameters, hardness (the force required to attain a given deformation) and compressibility (the work required to deform the product during a first compression cycle), were evaluated as a function of pH and polymer concentration of hydroalcoholic gels, and were found to be dependent on both variables. The evolution of both mechanical properties (MP) as a function of pH for the different polymer concentrations studied shows a marked similarity with the previously obtained pH profile of the consistency index, i.e. an initially pronounced increase with increasing pH (in the range 4.0–5.5) and a further stabilization or reduced increment for pH values between 5.5 and 7.0. Similarities observed with the k-pH profile are also confirmed by the good correlations obtained between hardness, compressibility and pH with equations of the type:

$$MP = \frac{MP_{max}}{1 + 10^{(pH_{struc} - pH)}} \qquad (2)$$

whose correlation parameters are shown in Table 2. According to eq. (2) both mechanical properties of hydroalcoholic gels increases with pH and tend to a maximum value (k_{max}) at neutral pH, which is in agreement with the evolution of the consistency index of acrylic acid poly-

Table 1: Activation energies of flow (E_γ and E_τ; kJ/mol) of Carbopol® Ultrez™ 10 hydroalcoholic gels

Conc. (%, w/w)		pH						
		4.0	4.5	5.0	5.5	6.0	6.5	7.0
0.1%	E_τ	n.a.	n.a.	1.44	2.56	3.21	4.23	3.56
	E_γ	n.a.	n.a.	0.39	1.23	1.47	2.01	1.75
0.2%	E_τ	n.a.	1.53	2.54	3.77	4.11	3.95	4.29
	E_γ	n.a.	0.79	1.35	1.69	1.94	1.82	2.03
0.3%	E_τ	1.72	2.28	2.79	3.93	3.74	4.08	3.91
	E_γ	0.95	1.14	1.42	2.03	1.86	2.21	2.19
0.4%	E_τ	1.56	2.93	3.21	3.79	4.21	4.47	4.38
	E_γ	0.85	1.32	1.68	1.71	2.19	2.31	2.27
0.5%	E_τ	1.75	2.86	3.52	3.93	4.19	4.12	4.25
	E_γ	0.98	1.47	1.73	1.89	2.22	2.15	2.34

Table 2: Values of the variables H_{max} (N), A_{max} (N · mm) and pH_{struc} obtained with eq. (2) as a function of polymer concentration

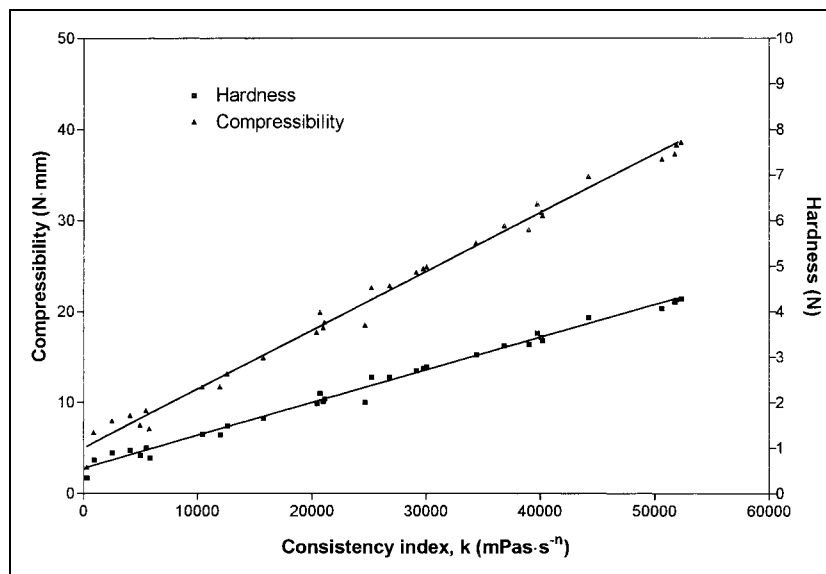|		Polymer concentration (%, w/w)				
		0.1	0.2	0.3	0.4	0.5
Hardness	H_{max}	0.99	2.05	2.77	3.47	4.27
	pH_{struc}	5.04	4.75	4.41	4.15	4.03
Compressibility	A_{max}	8.99	18.52	24.86	31.24	38.28
	pH_{struc}	5.00	4.86	4.44	4.16	4.07

Fig. 2:
Linear dependence of hydroalcoholic gels hardness and compressibility with consistency indexes for the same pH and polymer concentration

mers upon neutralization. From analogy with the consistency index − pH profile the variable pH_{struc} (Table 2) determines the rate at which the system reaches the maximum value for mechanical properties (MP_{max}), and can be interpreted as inflection points on the pH dependence of structural development of the polymer network. Also as in the case of the equation obtained for the pH dependence of the consistency index, eq. (2) predict an erroneous nearly constant maximum of the mechanical properties for pH > 7.0. Obviously, it is unable to account for any change that may occur in the physical state and flow mechanism of gels at pH > 8.0.

The effect of changing polymer concentration on the mechanical properties of hydroalcoholic gels was also analyzed. An increase in the Carbopol® Ultrez™ 10 concentration, while keeping pH constant, results in a linear increase in H_{max} and A_{max} (Table 2). Both parameters were correlated with the polymer concentration obtaining linear models with correlation coefficients in excess of 0.990.

In general it is observed that increasing consistency of hydroalcoholic gels by increasing pH and polymer concentration produces an enhancement in hardness and compressibility. A graphical representation of hardness and compressibility plotted vs. the consistency index is shown in Fig. 2. The influence of viscosity on compression characteristics of the studied gels is demonstrated by the statistically significant linear correlation obtained between hardness, compressibility and consistency index (k) for the same polymer concentration and pH:

$$H = (0.072 \pm 1.2 \cdot 10^{-3}) \cdot k + (0.55 \pm 0.04),$$

$$r^2 = 0.9908, \qquad (3)$$

$$A = (0.647 \pm 1.1 \cdot 10^{-2}) \cdot k + (4.91 \pm 0.32),$$

$$r^2 = 0.9917. \qquad (4)$$

This finding agrees with previously reported studies on the compression characteristics of other polymers [6, 7, 13]. Recently, Jones et al. reported significant correlations between product hardness and compressibility and the viscosity enhancement effect of a series of polymers including hydroxyethylcellulose, polyvinylpyrrolidone and polycarbophil. Linear models obtained with our polymer confirm that results, since express the hardness and com-

pression properties of hydroalcoholic gels as a function of the viscosity enhancement effect of Carbopol® Ultrez™ 10 [6].

3. Experimental

3.1. Hydroalcoholic gels elaboration

Appropriate quantities of Carbopol® Ultrez™ 10 (B. F. Goodrich Chemical Co.) were added to 30 : 70 ethanol/deionized water mixtures to obtain the following polymer concentrations: 0.1, 0.2, 0.3, 0.4 and 0.5% w/w. The mixture was agitated at 2000 r.p.m. for 10 min with a Silverson L4R agitator equipped with an axial flow head in conjunction with a disintegrating head. Polymer dispersions were immediately neutralized with Triethanolamine 50% until the desired pH value (4.0, 4.5, 5.0, 5.5, 6.0, 6.5, 7.0), measured "in situ" with a digital Crison 2000 pH-meter. The samples were allowed to equilibrate for 72 h at room temperature prior to the evaluation of their rheological properties [14, 15].

3.2. Viscosity measurements

Rheograms were determined with a cone and plate Brookfield Digital Viscometer DV III, equipped with a recirculating water-bath Brookfield TC 200 for control of the sample-container temperature. The viscosity determinations were done in 0.5 ml of sample, for twenty-one sequentially increasing and decreasing values of shear rate in the range 2–200 s⁻¹ at a constant temperature (T ± 0.1 °C). All samples were equilibrated at each run temperature (20, 30, 40 and 50 °C) on the plate for 5 min prior to the viscosity measurements. The data was analyzed with Rheocalc for Windows 1.01 software.

3.3. Compression study

The compression study was performed using a Load and Tensile Penetrometer Model PNR 20 fitted with a 20 N sensor and a cylindrical aluminium holed disk 18-0254 (plate diameter 55 mm, diameter of holes 4–5 mm/ 30°) under the following conditions: speed of travel 1.0 mm/s and compression depth 40 mm. The gels were analyzed in their original containers (500 ml) without stirring or shaking.

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