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Rheological Behavior of Some Aqueous Gels of Carbopol with Pharmaceutical Applications

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The concentration and temperature dependence of the viscosity is observed for some aqueous dispersions of Carbopol. The experimental data are analyzed with the power model, and reveal non-Newtonian behavior (shear thinning) of the samples.

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A large category of pharmaceutical products with dermatological applications use the polymeric matrix as support for the active medical substance. The advantage is the long-time contact between the product and the biological tissues, good adhesion of the product to the skin, the flexibility under the motions of the body, and the possibility to control the delivery rate of the active substance.[1−5] The Carbopol is one of the polymeric systems widely used for this purpose, due to its capacity to form gels in aqueous solution, compatibility with many active ingredients, and good patient acceptance.[6−9] It can be used without supplementary stabilization, or after neutralization with TEA (tri ethanolamine). TEA neutralizes the carboxylic groups of the polymer and facilitates the formation of cross-links between the polymeric chains. Many works were reported on these systems.[10−12] However, for better understanding of the microscopic behavior of the polymeric matrix, the study of the Carbopol system without supplementary stabilizers is suitable.

The compatibility with the motions of the human body, the drug release, and the mechanical stability of the pharmaceutical products, are sensitive to the rheological behavior of the polymeric matrix. Usually the rheological investigations are based on the measure of the viscosity as functions of temperature and polymeric concentration.[13,14] In this work, we observe these dependences for some aqueous dispersions of Carbopol 940 not stabilized with TEA. The experimental data are analyzed using the power models. Some works have been reported in literature on similar systems, but the composition of the samples, the domain of concentration and the methods of investigation are different.[15]

The samples were obtained by mixing the polymer with distilled water during 3–4 h. The gel network structures can be classified into two large categories, i.e., honeycomb and irregular fibrous network structure. These structures appear either by increasing the polymer concentration, or by neutralizing agent content. The irregular fibrous network appears at low polymeric concentration, whereas the honeycomb structure appears above 2% polymeric concentration.[15] In addition, above 2% concentration, the viscosity of the matrix is high, without interest for medical applications. Taking into account the viscosity domain of interest for clinical applications and the change of the microstructure of the polymeric matrix with the concentration, we limit our study only to low polymeric concentrations, 0.5%, 1% and 1.5%. The viscosity was measured at different rotation speeds between 0 and 200 rot/min with a Brookfield DV Ⅱ Pro viscometer, using cylindrical spindle. The determinations were made in the temperature range 26–55°C.

A particularl characteristic of the polymeric samples is the existence of a temporary or permanent junction between the polymeric chains. In a molten state or in the solutions these connections are extended only to limited domains of the sample, allowing a high mobility of the macromolecules. A special situation appears in polymeric systems containing important proportions of solvents, when the connections are extended to large areas of the sample, allowing a continuous passing between every two points of the sample. A spatial disordered and elastic structure appears in this case, containing both the solid and liquid phases, known as the gel state. Compared to the solution, the gel is characterized by high viscosity.[16,17] The polymeric concentration and the thermal agitation are two important factors that affect the viscosity. The thermal agitation increases the local mobility of the chains and enhances the elastic behavior of the temporary network. The effect on macroscopic scale is the variation of the viscosity with the temperature. The increase of the polymeric concentration facilitates the formation of the connections between the chains and leads to the increase of the viscosity.[18,19] Another characteristic effect of the polymeric gels is the dependence of the viscosity on the shear rate. The dependences of viscosity on temperature, concentration and shear rate, were observed in our work. The study

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was conducted following the increase of the viscosity.

The smallest value of the viscosity was measured at 0.5% polymeric concentration and a temperature of 26°C. For this sample we observed the decrease of the viscosity with the increase of the shear rate, and the increase of the viscosity with the increase of the temperature. This anomalous behavior of the viscosity as a function of temperature was observed previously for some Carbopol systems and was reported in literature by Noah *et al.*[20,21] This behavior of the viscosity as functions of the shear rate and temperature was observed for all the samples, but the dependence on the temperature is less pronounced when the polymeric concentration increases, i.e., sample 1.5%. Under external mechanical solicitations the gel behaves like a viscoelstic domain characterized by a specific relaxation time. At a low shear rate, the time of solicitation is long enough to allow smooth disengagement from the entanglement of the polymeric chains located in different neighboring layers of flow. It results in an elastic deformation of the local polymeric network, without fracture. The mechanical solicitations propagate at a long distance, perturbing many neighboring polymeric layers, and the viscosity is high.[22] When the shear rate increases, the time of solicitation is short as compared to the relaxation time of the chains from the entanglements. The chains located in neighboring layers have not enough time to disengage smoothly from the entanglements, and a brutal separation of gel domains is produced. The mechanical solicitation propagates at a short distance between the layers of flow, and the viscosity decreases. On a microscopic scale these processes are strongly influenced by thermal agitation. At low temperatures the local dynamics of the chains is reduced and the elasticity of the temporary polymeric network is low. The sample behaves like a brittle structure. Under external mechanical solicitations the connections between different layers of flow are broken, the solicitations propagate only at a short distance, and the viscosity decreases. High thermal agitation enhances the elasticity of the temporary network, the sample is more elastic, the external solicitations propagate at a long distance, and the viscosity increases.

Table 1. Values of parameters a and n in our calculation.

Concentration	t (°C)	a (Pa·s^n)	n	x	x_{av}	a^* (Pa·s^n)
0.5%	32	0.16	0.34	−0.66	−0.67	0.16
	42	0.23	0.34	−0.66		0.23
	55	0.58	0.29	−0.71		0.57
1%	32	0.84	0.16	−0.83	−0.82	0.84
	42	1.07	0.19	−0.81		1.08
1.5%	26	4.06	0.19	−0.84	−0.83	4.23
	32	4.38	0.18	−0.83		4.53
	42	4.87	0.18	−0.82		5.06

For the simplest molecular liquids the behavior of the viscosity is described by the Newtonian model, which predicts a linear dependence of the shear stress σ on the shear rate,[14,22]

$$\sigma = \eta \cdot \dot{\gamma}, \tag{1}$$

where $\dot{\gamma} = \partial\gamma/\partial t$ represents the shear rate, and η is the viscosity. Usually this model is applied when the viscosity is constant. When the viscosity depends on the shear rate, many other models, such as Ostwald, Bingham, Casson, Herschel-Bulkley, derived from the Newtonian law, are applied.[15,22] One of the simplest model used for the first approximation is the power law,[22,23]

$$\sigma = a \cdot \dot{\gamma}^n. \tag{2}$$

In this equation the variables have the same meaning as Eq. (1). The parameter a represents a proportionality factor and n represents the power law index. The exponent n contains the correction added to the Newtonian model and it expresses the character of the fluid flow, shear-thinning ($n < 1$), or shear-thickening ($n > 1$).[23–25] If we denote $n = 1 + x$ we can separate the Newtonian contribution from Eq. (2). In this expression x represents the correction factor added to Newton's law,

$$\sigma = a \cdot \dot{\gamma}^{1+x} = a \cdot \dot{\gamma}^x \cdot \dot{\gamma}. \tag{3}$$

In Eq. (3), the first two factors play the role of viscosity. Following this observation, we can express the dependence of the viscosity on the shear rate by the equation

$$\eta = a \cdot \dot{\gamma}^x. \tag{4}$$

We use this dependence to analyze the variation of the viscosity observed in our study. With Eq. (2) we calculate the values of parameters a and n. These values are listed in Table 1 and the best fit lines of data $\sigma(\dot{\gamma})$ for the sample 0.5% are presented in Fig. 1. Our values of n are very closes to those of Islam *et al.*, and Kim *et al.*, obtained for systems of Carbopol slightly different from ours.[10,15] For each temperature we calculate the exponent x of the viscosity from the relation $x = n - 1$.

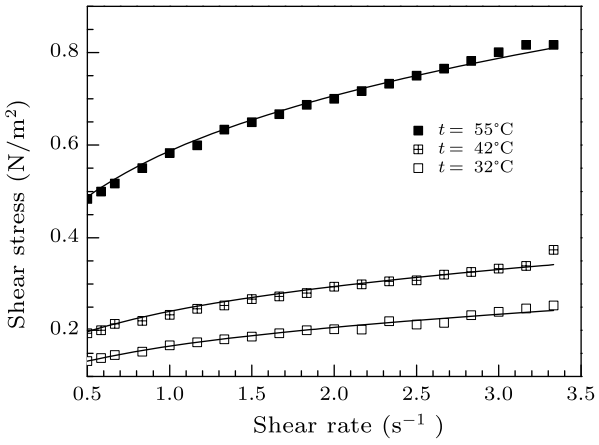


Fig. 1. Shear stress vs. shear rate curves, at different temperatures, for the sample with polymeric concentration 0.5%.

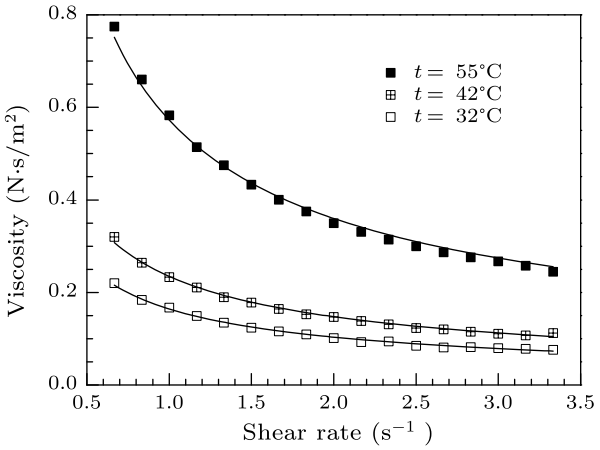


Fig. 2. Viscosity vs. shear rate curves, at different temperatures, for the sample with polymeric concentration 0.5%.

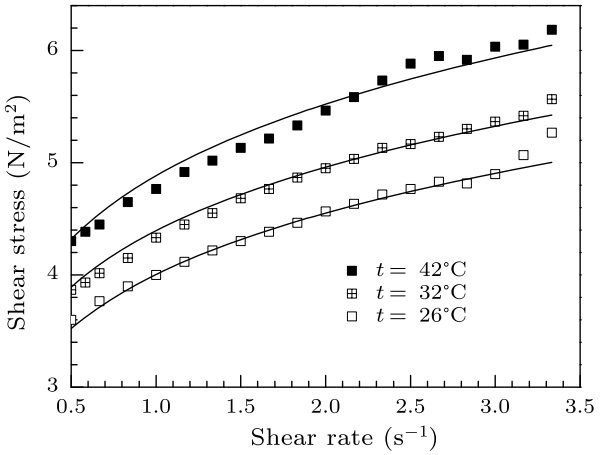


Fig. 3. Shear stress vs. shear rate curves, at different temperatures, for the sample with polymeric concentration 1.5%.

At constant concentration the variation of parameter x with the temperature is very small. Similar observations were reported in the literature.[10] This fact allows us, in the first order of approximation, for a given concentration, to neglect the variation of x with the temperature. For each concentration we calculate the average value of x, i.e. $x_{av} = -0.67$ for concentration 0.5%, $x_{av} = -0.82$ for concentration 1% and $x_{av} = -0.83$ for concentration 1.5%. Using these values of parameters a and x_{av} we approximate the experimental data $\eta(\dot{\gamma})$ with the equation

$$\eta = a^* \cdot \dot{\gamma}^{x_{av}}. \tag{5}$$

The adjustment of experimental data with this equation, for concentration 0.5%, is presented in Fig. 2. The values of parameter a resulting from this fit (denoted by a^*) are compared with the values resulting from the fit with Eq. (2). The good agreement between these values confirms the validity of the power model and of the algorithm of analysis proposed for our experimental data, (Eqs. (2) and (4)). Similar results were obtained for the samples with the polymeric concentrations 1% and 1.5%. The parameters of the fit are listed in Table 1, and the best fit lines of the data, for the sample 1.5%, are presented in Figs. 3 and 4. Knowing the power law index n we can characterize the rheological behavior of the samples. For our experimental data the power law index n decreases with the increase of the polymeric concentration from $n = 0.34$ at 0.5% to $n = 0.18$ at 1.5%. The samples are characterized by non-Newtonian behavior (shear-thinning), $n < 1$.[24,25]

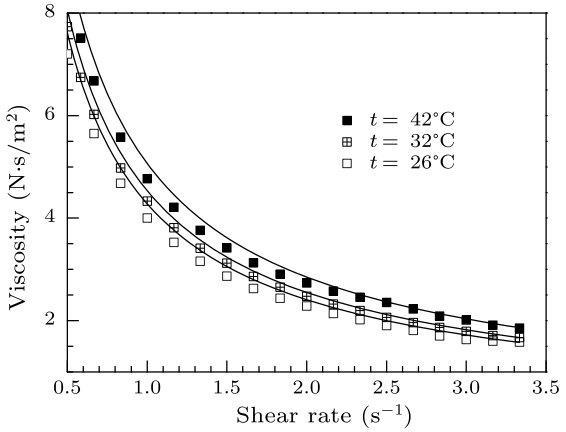


Fig. 4. Viscosity vs. shear rate curves, at different temperatures, for the sample with polymeric concentration 1.5%.

Both the temperature and polymeric concentration affect the viscosity of the gels, however, the influence of the concentration is dominant. High polymeric concentration facilitates the extension of the gel state to large areas of the sample with respect to the increase of the viscosity. The thermal agitation reduces the stability of the temporary connections between the chains but enhances the elasticity of the sample. The two mechanisms are responsible for the specific dependence of the viscosity on the temperature. The dependence of the viscosity on the shear rate is determined by the mechanism of relaxation of the polymeric chains from the entanglements. For our samples this dependence reveals the non-Newtonian flow, shear-thinning ($n < 1$), and the variation of the shear stress versus the shear rate is described by the power model. The algorithm of analysis proposed in our study, based on this model, allows a good approximation of the experimental data with Eqs. (2) and (4). Similar analyses were reported in literature for other categories of polymeric gels.[26]

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