ELSEVIER

www.elsevier.nl/locate/farmac

Il Farmaco 56 (2001) 443–445

IL FARMACO

# Viscosity and temperature relationship in ethanol/water mixtures gelified with Carbopol® Ultrez™ 10[☆]

M.J. Fresno Contreras *, A. Ramírez Diéguez, M.M. Jiménez Soriano

*Department of Pharmacy and Pharmaceutical Technology, Faculty of Pharmacy, Alcalá University, Alcalá de Henares, Madrid E-28871, Spain*

Received 31 October 2000; accepted 10 January 2001

## Abstract

The rheological characterization of Carbopol® Ultrez™ 10 ethanolic (15%) gels is complemented by studying flow behavior as a function of temperature (20–50°C) at different pH (4.0–7.0) and polymer concentrations (0.1–0.5%). Flow curves were adjusted to the Ostwald model, showing a fall in viscosity, together with an enhancement in flow index with increasing temperature. Calculated flow activation energies at constant shear rate ($E\gamma$) were found to be related to the final pH of hydroalcoholic gels. Nevertheless, at the polymer concentration range evaluated, no significant correlations were obtained between activation energy and concentration. In general, the Carbopol® Ultrez™ 10 gels exhibit little viscosity change under the temperature variations of normal use and storage, which minimizes possible unacceptable changes in the product's characteristics. © 2001 Éditions scientifiques et médicales Elsevier SAS

*Keywords:* Carbopol® Ultrez™ 10; Hydroalcoholic gels (15:85, ethanol:water, % v/v); Viscosity/temperature; Flow activation energy; Empirical models

## 1. Introduction

The viscosity of real 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 [1].

During production and storage of pharmaceuticals it is important to know how flow properties are affected by changes in temperature. In this sense, the technological interest is limited to the interval 0–50°C [2–4]. Specially, the study of the temperature dependence of the viscosity is most important to the understanding of the mechanism of their flow process and the elucidation of 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 more often than not the quality of these systems. Also of great interest is the experimental determination of the activation energy of flow, and its relationship with the structure and composition.

From the above mentioned it is evident that the study of the temperature dependence of flow behavior of Carbopol® Ultrez™ 10 hydroalcoholic gels, is another important aspect of an exhaustive characteriza-

Table 1
Composition of hydroalcoholic Ultrez™ 10 gels studied (EtOH 15% v/v)

| pH | Carbopol® Ultrez™ 10 concentration (%, w/w) | | | | |
|---|---|---|---|---|---|
| | 0.1 | 0.2 | 0.3 | 0.4 | 0.5 |
| 4.0 | F-1 | F-2 | F-3 | F-4 | F-5 |
| 4.5 | F-6 | F-7 | F-8 | F-9 | F-10 |
| 5.0 | F-11 | F-12 | F-13 | F-14 | F-15 |
| 5.5 | F-16 | F-17 | F-18 | F-19 | F-20 |
| 6.0 | F-21 | F-22 | F-23 | F-24 | F-25 |
| 6.5 | F-26 | F-27 | F-28 | F-29 | F-30 |
| 7.0 | F-31 | F-32 | F-33 | F-34 | F-35 |

---

[☆] XXIV International Congress of the Latin-Mediterranean Pharmaceutical Society, Assisi, Italy, 20–23 September 2000.

* Corresponding author.

*E-mail address:* mjose.fresno@uah.es (M.J. Fresno Contreras).

0014-827X/01/$ - see front matter © 2001 Éditions scientifiques et médicales Elsevier SAS
PII: S0014-827X(01)01058-8

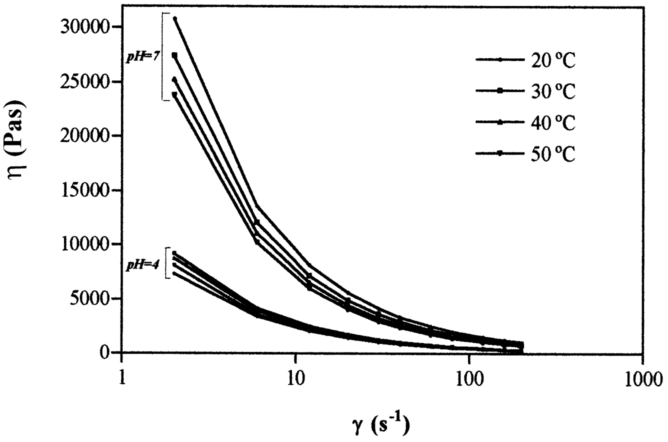

Fig. 1. Flow curves of (15:85% v/v ethanol:water) hydroalcoholic gels at 0.4% w/w of Carbopol® Ultrez™ 10 (pH 4 and 7) in the 20–50°C temperature range.

tion which may provide rheological parameters with potential application in topical bioavailability studies. 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 (4.0–7.0) and polymer concentrations (0.1–0.5% w/w).

## 2. Materials and methods

### 2.1. Materials

Carbopol® Ultrez™ 10 was purchased from BF Goodrich Chemical Co (Cleveland, OH); all other reagents were of analytical grade.

To elaborate the gelification medium, double distilled-deionized Milli-Q® water and ethanol 96% PA (Panreac Quimica S.A., Barcelona, Spain) were utilized. The triethanolamine (TEA) 50% solution was obtained by dissolution of TEA PA (E. Merck, Darmstadt) in Milli-Q® water.

### 2.2. Hydroalcoholic gel elaboration

Appropriate quantities of Carbopol® Ultrez™ 10 were added to 15:85 v/v ethanol/deionized water mixtures, to obtain the following polymer concentrations: 0.1, 0.2, 0.3, 0.4 and 0.5% w/w (Table 1). These mixtures were agitated at 2000 rpm 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 50% triethanolamine 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. All the samples were allowed to equilibrate for 72 h at room temperature prior to the evaluation of their rheological properties.

### 2.3. 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 sample-container temperature. The data obtained was analyzed and adjusted to Ostwald's model with Rheocalc for Windows 1.01 software. The viscosity determinations were done in 0.5 ml of sample, for 21 sequentially increasing and decreasing values of shear rate in the range 2–200 $s^{-1}$. All samples were equilibrated at each run temperature (20, 30, 40 and 50°C) on the plate for 5 min prior viscosity measurements [5,6].

## 3. Results and discussion

The influence of temperature on flow properties of Carbopol® Ultrez™ 10 hydroalcoholic gels was evaluated by recording rheograms at varying temperatures from 20 to 50°C at different pH and polymer concentrations. As 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 $n$, since polymer chains are more mobile and the lifetimes of the chain entanglements shorter, giving more Newtonian flows.

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 apparent viscosity may be treated assuming the condition $\tau = \text{constant}$ or $\gamma = \text{constant}$. Hence, with the aim of comparatively studying the hydroalcoholic gels, apparent viscosity values obtained for constant $\gamma$ were correlated with temperature for each concentration and pH value according to the Arrhenius–Frenkel–Eyring equation:

$$\eta = B\,e^{(E_\gamma/RT)} \qquad (1)$$

where $E$ is the activation energy of flow process at constant shear rate ($E_\gamma$), $T$ the absolute temperature in K and $R$ the gas constant. Activation energy values, calculated as the slope of straight lines in representing $\ln \eta$ versus $T^{-1}$ (K), are given in Table 2 for each pH and polymer concentration. Experimentally $E_\tau$ has been

Table 2
Flow activation energies ($E_\gamma \pm S_{x,y}$ (kJ/mol)) of Carbopol® Ultrez™ 10 gels ($S_{x,y}$: typical error)

| pH | $E_\gamma$ (kJ/mol) | | | | |
|---|---|---|---|---|---|
| | 0.1 | 0.2 | 0.3 | 0.4 | 0.5 |
| 4.0 | | 0.67 ± 0.016 | 1.38 ± 0.042 | 1.45 ± 0.043 | 1.49 ± 0.019 |
| 4.5 | 0.61 ± 0.007 | 1.14 ± 0.002 | 1.75 ± 0.017 | 1.96 ± 0.026 | 1.98 ± 0.024 |
| 5.0 | 1.11 ± 0.014 | 1.79 ± 0.024 | 2.33 ± 0.025 | 2.28 ± 0.014 | 2.31 ± 0.022 |
| 5.5 | 1.51 ± 0.016 | 1.96 ± 0.016 | 2.56 ± 0.034 | 2.55 ± 0.021 | 2.53 ± 0.020 |
| 6.0 | 2.06 ± 0.035 | 2.72 ± 0.036 | 2.77 ± 0.047 | 2.88 ± 0.020 | 2.84 ± 0.044 |
| 6.5 | 2.23 ± 0.009 | 2.69 ± 0.040 | 2.84 ± 0.038 | 2.91 ± 0.018 | 2.91 ± 0.027 |
| 7.0 | 2.47 ± 0.030 | 2.67 ± 0.030 | 2.81 ± 0.022 | 3.00 ± 0.042 | 3.02 ± 0.038 |

found to be nearly constant and independent of shear stress, while $E_\gamma$ depends on shear rate, but the latter becomes an important parameter in some technological processes that are accomplished at constant rates of shear.

In general the results given in Table 2 show relatively low values of $E_\gamma$ (0.6–3.1 kJ/mol), in conjunction with an increase of both parameter with pH for a constant polymer concentration. Considering that 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, the low activation energies obtained are determined by the low polymer concentration range studied.

Furthermore, the increase of $E_\tau$ and $E_\gamma$ 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 generates negative charges along polymer chain. The increase of pH seems to induce a disorder → order transition, that allows the polymeric chains to form stronger intermolecular interactions [7].

According to experimental results there is no clear relationship between polymer concentration and activation energies at constant pH (Table 2). This result can be due to the low accuracy of experimental measurements in the narrow range of concentrations studied. Consequently the effect of concentration on $E_\gamma$ is difficult to quantify. In general the Carbopol® Ultrez™ 10 hydroalcoholic gels (15:85%, ethanol:water v/v) exhibit little viscosity change under the temperature variations of normal use and storage, which minimizes possible unacceptable changes in the product's characteristics [6,8].

## Acknowledgements

The authors acknowledge financial support received from the research project (E043/2000) forwarded by the University of Alcalá, Madrid, Spain.

## References

[1] V.P. Kapoor, *Cassia spectabilis* DC seed galactomannan: structural, crystallographical and rheological studies, Carbohydr. Res. 306 (1998) 231–241.

[2] I. Capron, G. Brigand, G. Muller, Thermal denaturation and renaturation of a fermentation broth of xanthan:rheological consequences, Int. J. Biol. Macromol. 23 (1998) 215–225.

[3] F.B. Ahmad, P.A. Williams, Effect of sugars on the thermal and rheological properties of sago starch, Biopolymers 50 (1999) 401–412.

[4] M. Paulsson, S.K. Singh, Colloidal and thermal characteristics of concentrated dispersions of polymethacrylate-based lattices for aqueous enteric coating, J. Pharm. Sci. 88 (1999) 406–411.

[5] I.T. Norton, D.A Jarvis, T.J. Foster, A molecular model for the formation and properties of fluid gels, Int. J. Biol. Macromol. 26 (1999) 255–261.

[6] A. Ramírez, M.J. Fresno, M.M. Jiménez, E. Sellés, Rheological study of Carbopol® Ultrez™ 10 hydroalcoholic gels. I: Thermal and mechanical properties as a function of pH and polymer concentration, Die Pharm. 54 (1999) 531–533.

[7] M.F. Lai, C. Lii, Rheological and thermal characteristics of gel structures from various agar fractions, Int. J. Biol. Macromol. 21 (1997) 123–130.

[8] C. Michon, G. Cuvelier, P. Relkin, B. Launay, Influence of thermal history on the stability of gelatin gels, Int. J. Biol. Macromol. 20 (1997) 259–264.