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# A comparison of capillary and rotational viscometry of aqueous solutions of hypromellose

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A comparison of capillary and rotational viscometry of gentle pseudoplastic solutions of hypromellose (HPMC 4000) by using only single-point value of viscosity is difficult. Single-point comparison becomes topical in consequence to the pharmacopoeial requirement that the apparent viscosity of 2% hypromellose solution should be read at the shear rate of approximately 10 $s^{-1}$. This communication is focused on the estimation of the suitable shear rate, $D_\eta$, at which the apparent viscosity read using the rotational viscometer is numerically equal to the dynamic viscosity read using a capillary viscometer. For the solutions of HPMC in concentrations up to 2% w/v, the non-linear regression equations generated showed the influencing of the $D_\eta$ value by the dynamic viscosity and/or by the originally derived linear velocity of the solution flowing through the capillary viscometer tube. To compare the apparent viscosity read using the rotational viscometer with the dynamic viscosity read using capillary viscometer, the exact estimation of the shear rate $D_\eta$ at which both viscosities are numerically equal is essential since it is markedly affected by the concentration of HPMC solution.

## 1. Introduction

One way to optimize ocular drug delivery is to prolong precorneal drug residence time by the addition of soluble polymers. A number of substituted cellulose ethers have been introduced as viscosity-enhancing ophthalmic vehicles (Ludwig 2005) and for artificial tear solutions (Kulkarni et al. 1997). To prepare viscous eye drops of the required level of viscosity, the rational technological way is to dilute more concentrated stock polymer solutions extemporaneously. For this reason, a good specification of the stock solution viscosity properties becomes the most important requirement of their quality and successful use in practice.

Many viscosity types of cellulose derivatives are obviously used in ophthalmic preparations. To specify their viscosity properties, generally, the viscosity of 2% (w/v and/or w/w) aqueous solution at 20 ± 0.1 °C is measured according to Pharmacopoeias. In the USP (2005), the capillary (Ubbelohde) viscometer is directed for cellulose derivatives. The dynamic viscosity of solution, $\eta$ (in mPa · s), could then be obtained as the product of the kinematic viscosity (in $mm^2 \cdot s^{-1}$) and the density of the solution (in $g \cdot cm^{-3}$). If the density of the solution approaches one, the dynamic viscosity is said to be equal to the kinematic one. Contrary to the USP, Ph. Eur. (2004) directs the use of the rotational viscometer. In respect to the pseudoplastic properties of the hypromellose solutions, the standard shear rate at which the measurement of the apparent viscosity, $\eta'$ (in mPa · s), is made should be specified. In Ph. Eur., a shear rate of approximately 10 $s^{-1}$ is recommended.

## 2. Investigations, results and discussion

In this work, the viscosity data obtained for 0.25–2.00% aqueous solutions of hypromellose (hydroxypropyl methylcellulose, HPMC 4000) with the Ubbelohde capillary viscometer as well as with the rotational viscometer were used to compare the dynamic ($\eta$) and the apparent ($\eta'$) viscosity of the hypromellose solutions. In focus on the pharmacopoeial recommendations, the appropriate shear rate at which the dynamic viscosity is equal to the apparent viscosity is discussed.

The relationship between the dynamic viscosity readings obtained for the Ubbelohde viscometer (listed in Table 1) and the apparent viscosity readings obtained for the rotational viscometer at the commonly used shear rate D = 100 $s^{-1}$ ($\eta'_{100}$, listed in Table 2) could be characterized by the regression Eq. (1) with the coefficient of determination $r^2 = 0.999$ and the mean difference between the apparent viscosity and the dynamic viscosity equal to 4.4%.

$$\eta'_{100} = 3.048 \cdot \eta^{0.717} \quad (1)$$

Although the regression Eq. (1) showed the close relationship between both types of viscosity, on the other hand, their geometrical means (104.7 mPa · s for the dynamic viscosity and 85.6 mPa · s for the apparent viscosity, respectively) strongly differed. In addition, the most important differences were observed comparing values of the both viscosity types measured for the same concentrations of the HPMC solutions. For example, while the dynamic viscosity was equal to approximately one half of the ap-

**Table 1: Parameters and results of the capillary viscometer method**

| Concentration of HPMC (% w/v) | K ($mm^2 \cdot s^{-2}$) | R (mm) | t (s) | η (mPa · s) | φ ($mm^2$) | v ($mm \cdot s^{-1}$) |
|---|---|---|---|---|---|---|
| 0.25 | 0.01 | 0.64 | 568 | 5.68 | 0.322 | 30.6 |
| 0.50 | 0.1 | 1.15 | 265 | 26.5 | 1.039 | 20.3 |
| 1.00 | 1 | 2.06 | 201 | 201 | 3.333 | 8.36 |
| 2.00 | 10 | 3.70 | 397 | 3970 | 10.75 | 1.31 |

**Table 2: Parameters and results of the rotating viscometer method**

| Concentration of HPMC (% w/v) | Parameters of rheogram | | $r^2$ | $\eta'_{100}$ | $D_\eta$* |
|---|---|---|---|---|---|
| | k (mPa · $s^n$) | n | | (mPa · s) | ($s^{-1}$) |
| 0.25 | 36.37 | 0.735 | 0.999 | 10.7 | 1104 |
| 0.50 | 106.7 | 0.725 | 0.998 | 30.1 | 158 |
| 1.00 | 621.4 | 0.689 | 0.996 | 148 | 37.7 |
| 2.00 | 14140 | 0.451 | 0.995 | 1128 | 10.1 |

* shear rate for $\eta = \eta'$

parent viscosity $\eta'_{100}$ for the lowest (0.25%) concentration of the HPMC, in contrast, the dynamic viscosity was three times greater than the latter in case of the highest concentration (2.00%) of the HPMC solution. We concluded, therefore, that the conventional requirement to read the apparent viscosity at only one value of the shear rate D regardless of the solution concentration did not make possible the both pharmacopoeial methods and the viscosity types to be easily compared.

In order to use the recommended pharmacopoeial methods, the appropriate value of shear rate, at which the comparison of the dynamic and the apparent viscosity for the solutions of HPMC 4000 is possible, needs to be searched. To solve this, first, the viscosity curve can be expressed in consequence to the power equation of the pseudoplastic rheogram:

$$\eta' = k \cdot D^{n-1} \tag{2}$$

Due to the mathematical manipulation, the direct estimation of the shear rate, $D_\eta$, at which the dynamic viscosity is equal to the apparent one ($\eta = \eta'$) could be possible using Eq. (3). The values of $D_\eta$ obtained in our work are listed in the last column of Table 2.

$$D_\eta = \left(\frac{k}{\eta}\right)^{\frac{1}{1-n}} \tag{3}$$

For the solution with a dynamic viscosity known from the capillary viscometry measurement, the value of $D_\eta$ could be estimated using the exponential Eq. (4) that is characterized with $r^2 = 0.995$ and the mean difference between the estimated value of $D_\eta$ and the experimentally obtained one equal to 13.6%.

$$D_\eta = \exp\left(9.034 \cdot \eta^{-0.167}\right) \tag{4}$$

According to the Pharmacopoeia, the basic condition of the standard capillary viscometer method is that the flow times of the examined liquid should be comparable and the minimum flow time should be respected (Ph Eur 2004). Although generally assumed, the liquid flowing down the capillary viscometer tubes of the different diameter with the comparable flow times does not pass with the comparable linear velocity. Here, the linear velocities of the liquid were used to solve the estimation of the $D_\eta$ value.

The linear velocity v could be estimated using the pharmacopoeial Table 2.2.9.-1 (Ph Eur 2004). The cross section of the capillary viscometer tube φ can be calculated using Eq. (5) where R (in mm) is the internal diameter of the tube:

$$\varphi = \pi \cdot \left(\frac{R}{2}\right)^2 \tag{5}$$

Then, the linear velocity of the liquid through the capillary viscometer tube could be estimated as:

$$v = \frac{C}{\varphi \cdot t} \tag{6}$$

where C is the volume of capillary viscometer bulb equal to 5600 $mm^3$ (Ph Eur 2004) and t is the flow time in seconds. The calculated values of the capillary cross section φ (in $mm^2$) and those of linear velocities v (in $mm \cdot s^{-1}$) are presented in two last columns of Table 1.

Using the values of v, the generated power Eq. (7) made possible the estimation of the shear rate $D_\eta$ with $r^2 = 0.992$:

$$D_\eta = \exp\left((0.1547 \cdot v) + 2.160\right) \tag{7}$$

Although the precision of the $D_\eta$ estimation (16.4%) by Eq. (7) was comparable with that of Eq. (4) at first sight, Eq. (7) was more useful in solving of $D_\eta$ value since it disposed the linear velocity of liquid passing through the capillary viscometer tube which is more suitable to be compared with the angular velocity of the shear rate of the rotational viscometer. The direct comparison of the linear velocity with the circumference velocity of the rotational viscometer, of course, is not possible.

From our findings here, we concluded that the pharmacopoeial requirement of the single-point measurement of the apparent viscosity of the 2% stock hypromellose solution at a shear rate of $10\ s^{-1}$ (Ph Eur 2004) might be enlarged with the similar standard conditions of measurement for diluted HPMC solutions. This conclusion was proposed in context to viscous eye drops when the diluted polymer solutions are used. Regardless of the solution concentration, the comparison of the single-point apparent viscosity obtained with the rotational viscometry method and the dynamic viscosity read by using the capillary viscometer method was not possible. To solve this, the systematic study of the relationship between the rotational viscometry method and the capillary viscometer method is required, the methodology of which is presented in this paper.

## 3. Experimental

The 0.25, 0.50, 1.00 and 2.00% w/v solution of hypromellose (hydroxypropyl methylcellulose, HPMC 4000, Methocel® F4M Premium, Dow Chemical Company, USA) were obtained using the stationary method of preparation in which polymer powder was layered on the surface of preheated water (90–95 °C) filled in the infusion bottle and wetted without mixing. After that, slow dissolution by mixing followed for 60 min. The bottles were then tightly closed and stored in the refrigerator at 4 ± 1 °C for three months. Distilled water was used throughout the study.

The dynamic viscosity of the HPMC solution samples was measured using an Ubbelohde capillary viscometer (Jenaer Glaswerk Schott & Gen., Jena, Germany) according to the Pharmacopoeial standard conditions of capillary viscometry (Ph. Eur. 2004, part 2.9.9.) at $20 \pm 0.1$ °C. All solutions were kept in the water bath at the temperature of measurement for 30 min to reach the temperature equilibrium. As the kinematic viscosity is the product of the viscometer constant K and the actual flow time t, and since the densities of water and those of hypromellose viscous solutions do not significantly differ (Mutalik et al. 2006), the dynamic viscosity $\eta$ could be estimated as:

$$\eta = K \cdot t \cdot \rho \approx K \cdot t \quad (8)$$

where $\rho$ is the density of the solution. The viscometer constants K ($mm^2 \cdot s^{-2}$) and diameters of their tubes R (mm) are presented in Table 1. Table 1 is completed with the mean flow times t (s) of the five measurements with the variability coefficients lower than 1% as well as the dynamic viscosities $\eta$ (in $mPa \cdot s$) obtained.

The apparent viscosity of the HPMC solution samples was measured using rotational viscometer Rheotest 2 (Mechanik Prüfgeräte, Medingen, Germany) according to the Pharmacopoeial standard conditions of rotational viscometry (Ph. Eur. 2004, part 2.9.10.) at $20 \pm 0.1$ °C. Before the viscosity measurement, the sample of solution was placed into measuring set N of two coaxial cylinders for 30 min to reach the temperature equilibrium. The shear stress values $\tau$ (mPa) were measured at shear rates D up to 1312 $s^{-1}$. The results are summarized in Table 2 where the pseudoplastic rheograms of hypromellose are characterized by two parameters of the power Eq. (9), i.e. the power law consistency factor k ($Pa \cdot s^n$) and the flow behaviour index n (dimensionless) (Bailey & Weir 1998), and the coefficients of determination in range of $0.995 \leq r^2 \leq 0.999$ (Draper and Smith 1981):

$$\tau = k \cdot D^n \quad (9)$$

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