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A rheological study of semisolid preparations of Eudragit®

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Abstract

The present work studies the rheology of semisolid preparations of acrylic polymers of Eudragit®, specifically RS 30 D, RL 30 D and NE 30 D. The parameters of shear deformation were obtained from experimental data and those of compression deformation were determined using previously obtained linear equations relating shear and compression stresses. The results, which were statistically significant, show a linear relationship between the coefficient of regression of these equations and the apparent viscosities of the different semisolid preparations, and between the independent term and the consistency index of each, and corroborate the previously demonstrated linear relationship between shear and compression stresses. The effect of the volume of the spindle used in the viscosimeter was observed in all cases. The equations relating both types of stress, obtained from semisolid preparations of Carbomer® 940, can be used to determine the compression stresses of other semisolid preparations in this case, Eudragit®.

Keywords: Shear deformation; Compression deformation; Eudragit® RS 30 D; Eudragit® RL 30 D; Eudragit NE 30 D

1. Introduction

It is well known that the basic rheological properties of materials can be described by at least three parameters: stress, shear rate and time. A knowledge of these and their interaction is essential for the measurement and interpretation of rheological data (Deem, 1988; Lucero et al., 1991).

When a material is subjected to a force, it is deformed to a greater or lesser degree (Dolz et al., 1988). Thus, the essential factors are the deformation and its rate.

Most suppositions are made on the basis that the material is continuous – i.e., on the assumption that all the properties of the system are uniform at each point. A series of rheological equations derive from this assumption that can be applied to resolving problems of deformation and flow. Thus, the rheological properties of a material can be best understood considering its behaviour in a particular simplified state, called simple shear (Banker and Chalmers, 1981; García et al., 1987).

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Fluid materials can be deformed by both shear and compression. In the former case, a tangential force is applied to the plane of the material (shear stress), while in the latter the force is perpendicular to the direction of fluid movement, with outward tension and compression in the plane (compression stress).

The bibliography consulted includes few works on compression flow from a rheological viewpoint, except those of Campanella and Peleg (1987) and DeMartine and Cussler (1975). In contrast, there are studies on spreadability as a parameter that measures the capacity of bodies to spread on being subjected to a weight (Buenestado and Suñé, 1972a,b; Jiménez-Castellanos et al., 1982; León et al., 1982, 1991; Del Pozo et al., 1987).

Until now spreadability has been considered a parameter indicating stability (Lucero et al., 1994b) in the widest sense, and even, in some works (Shama and Sherman, 1973; Kokini et al., 1977, 1984; Kokini and Cussler, 1983), a sensorial property of semisolid preparations. However, in no case has it been included in the rheological study of fluids, perhaps because the methodology is not universally standardised or because properly rheological concepts such as force, stress, deformation, etc., have not been used.

Following the studies of this research group, correlations have been established between the deformations caused by shear (shear stress) and by compression (compression stress) (Lucero et al., 1994a,c). These equations enable calculation of the shear stress that would have to be applied to a fluid to achieve a tangential deformation coinciding with the perpendicular deformation, obtained by subjecting the sample to a specific compression stress.

Consequently, it can be stated that in order to carry out a complete rheological study it is necessary to monitor both tangential and longitudinal deformations. In this way, the traditional concept of spreadability (of little importance in semisolids) is transformed into a parameter that, together with viscosity, defines the rheology of disperse systems.

One of the problems we encountered was that of determining the ideal compression stress to be applied to any semisolid preparation having a non-Newtonian behaviour.

The present work was aimed at studying the rheology of semisolid preparations of acrylic polymers of Eudragit®, specifically RS 30 D, RL 30 D and NE 30 D. The viscosimetric parameters were obtained from experimental data and the extensimetric ones from equations of correlation obtained previously (Lucero et al., 1994a,c) and here.

2. Materials and methods

2.1. Semisolid preparations

Three semisolid preparations were made with three acrylic polymers of Eudragit®, as indicated in Table 1.

Each semisolid preparation was made by dissolving the respective polymer of Eudragit® (Curtex, Industrias Síntéticas S.A., L'Hospitalet, Spain) in absolute ethanol ACS ISO (Merck, Darmstadt, Germany). Next, this was mixed, by mechanical stirring, into a suspension of hydroxypropylmethylcellulose (Hipromelosa-4000, Acorfarma, Tarrasa, Spain) in distilled water.

All the preparations were left to stand for 24 h before carrying out the deformation tests.

Table 1
Components of the semisolid preparations of Eudragit®

Components	RS 30 D	RL 30 D	NE 30 D
Eudragit® (% w/w)	27	27	27
Hydroxypropylmethylcellulose (% w/w)	1.5	1.5	1.5
Ethanol (ml)	15	15	15
Distilled water (ml)	56.5	56.5	56.5

2.2. Shear deformation

This test was performed using a Searle rotary viscosimeter (Brookfield Model RVT) with spindle nos 5 and 6, depending on the consistency of each preparation.

The Brookfield viscosimeter (Ball et al., 1982; Pugnetti, 1982; Barracó et al., 1985; Deem, 1988; Dolz et al., 1988; Lucero et al., 1991) measures the viscous traction exerted on a spindle rotating in a fluid in a vessel. The rate of slip is very variable throughout the sample. The spindle is driven by a synchronized rotor via a beryllium-copper torsion wire of 7187 dyn cm. The correspondence of the spring to a determinate number of revolutions per min is shown by an indicator on a dial calibrated in units of rotational force (Wood, 1986; Lucero et al., 1991). For this apparatus, the shear rate and stress are determined as follows:

$$\dot{\gamma} = \frac{2\omega R_c^2 R_b^2}{X(R_c^2 - R_b^2)} \quad (1)$$

$$\tau = \frac{T}{2\pi R_b^2 L} \quad (2)$$

where ω is the angular velocity of the spindle, R_c the radius of the container, R_b the radius of the spindle (no. 6, 0.75 cm; no. 5, 1.125 cm), X the radius of the determined point, T the torsion (7187 dyn cm) and L the effective length of the spindle (5.0 cm).

The non-Newtonian behaviour can be determined applying the model of Ostwald-De Waele (Shotton and Ridgway, 1974; Pugnetti, 1982; Sherman, 1983; Schramm, 1984; Wood, 1986; Deem, 1988; Opota et al., 1988; Lucero et al., 1991):

$$M = KD^n \quad (3)$$

$$\tau = K\dot{\gamma}^n \quad (4)$$

where n is the flow index, K the consistency index, M the moment of rotation and D the deformation rate (rpm).

Lastly, the apparent viscosity (η_{ap}) can be defined as:

$$\eta_{ap} = K\dot{\gamma}^{n-1} \quad (5)$$

The methodology was standardised for the test. In all cases, the viscosimeter rotated for 1 min and was still for 30 s. After reaching maximum velocity (100 rpm), each preparation was left to stand (15 min) in order to recover its initial structure. The measurement was then repeated, beginning with the highest deformation rate and ending with the lowest. The temperature was kept at 22 ± 1°C.

The apparent viscosities were determined by calculating the following parameters: Moment of rotation (M) from the dial reading and the torsion of the viscosimeter, indices of flow (n) and consistency (K) (Eq. 3), shear or cutting stresses (τ) (Eq. 2), shear rate ($\dot{\gamma}$) (Eq. 4), and apparent viscosities (η) (Eq. 5).

The selection of deformation rates between 5 and 50 rpm is important, as measurements at higher or lower speeds lead to instrumental errors (Brookfield).

2.3. Compression deformation

The method used for this test was that described by various authors (León et al., 1982; Lucero et al., 1994a,c). The compression stresses applied were 3302, 6191, 12 383 and 20 638 dyn/cm^2. As the lowest of these gave a very high deformation, the compression stresses necessary to cause longitudinal deformation were determined theoretically.

Previous studies (Lucero et al., 1994a,c) showed the existence of a direct correlation between shear and compression stresses. The compression stresses were determined from these equations.

3. Results

3.1. Shear deformation: fluidity curves

Fig. 1 shows the fluidity curves of the preparations assayed.

The indices of flow and consistency were determined applying the model of Ostwald-De Waele (Eq. 3) (Table 2), using the descending legs of the rheograms (Lucero, 1989).

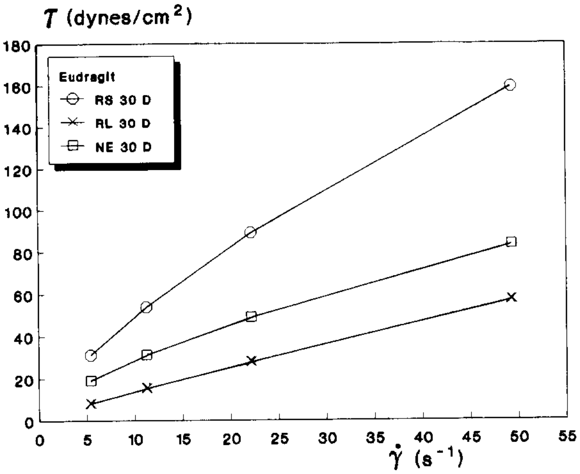

Fig. 1. Fluidity curves of semisolid preparations.

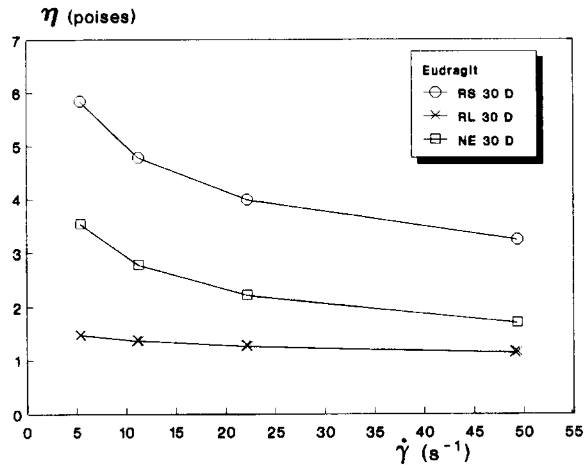

Fig. 2. Viscosity curves of semisolid preparations.

The values of τ_c were obtained from Eq. 2, taking into account the spindle used in each case. $\dot{\gamma}$ was obtained from Eq. 3 and 4, transforming the consistency indices (expressed in units of moment of rotation) into units of τ_c dividing by the volume of each spindle.

3.2. Shear deformation: viscosity curves

The apparent viscosities were obtained either by dividing $\tau_c/\dot{\gamma}$ or from Eq. 5.

Fig. 2 shows the viscosity curves obtained for each semisolid preparation studied.

3.3. Determination of compression stresses

The parameters A, B and τ_p were calculated from the equations of $\tau_c = A\tau_p + B$ obtained previously (Lucero et al., 1994a,c).

3.3.1. Determination of A

Correlations were obtained between the values of A and the apparent viscosities, at deformation rates of 5, 10, 20 and 50 rpm. These correlations are shown in Table 3.

Table 2
Indices of flow (n) and consistency (K) and shear stresses (τ_c) at K of the preparations indicated

Semisolid preparation	Spindle no./volume		n	K (dyn cm)	τ_c (dyn/cm^2)
RS 30 D	6	17.67 cm^3	0.7341	159.63	9.03
RL 30 D	5	39.76 cm^3	0.8884	70.91	1.78
NE 30 D	5	39.76 cm^3	0.6698	246.32	6.20

Table 3
Statistical parameters for the correlations between A and η_{ap}

D (rpm)	r_{xy}	$F_{(1,17)}$	Probability	CV	Equation
5	0.9388	245.64	< 0.0001	10.10	$A = 0.0005518\eta_{ap} + 0.002735$
10	0.9338	225.52	< 0.0001	10.51	$A = 0.0009179\eta_{ap} + 0.002638$
20	0.8895	128.83	< 0.0001	13.57	$A = 0.001513\eta_{ap} + 0.003249$
50	0.8549	94.25	< 0.0001	15.55	$A = 0.002705\eta_{ap} + 0.013960$

Table 4
Statistical parameters for the correlation between B and K

r_{xy}	$F_{(1,17)}$	Probability	CV	Equation
0.9803	794.61	< 0.0001	6.27	$B = 1.5907K + 30.4478$

Table 6
Statistical parameters for the correlation between τ_c and τ_p

r_{xy}	$F_{(1,8)}$	Probability	CV	Equation
0.8521	40.33	< 0.0001	28.27	$\tau_c = 0.01052\tau_p - 6.1590$

3.3.2. Determination of B

Correlations were obtained between the values of B and the consistency indices (K). The resulting equation is shown in Table 4.

Parameter K is expressed in units of moment of rotation (dyn cm). It is necessary to transform it into units of stress, depending on the spindle used for each preparation (no. 5 or 6) according to Eq. 2. The values of B were obtained from semisolid preparations of a consistency in which it was possible to use spindle no. 7 (the smallest of the series of the viscosimeter Model RVT), so that it is necessary to subtract the volume of this spindle from that actually used in each case.

3.4. Correlation between rheological parameters

Table 5 lists all the results obtained for calculating the compression stresses.

Table 6 shows the correlations obtained between the rheological parameters τ_c and τ_p, for the semisolid preparations of acrylic polymers of Eudragit®.

4. Discussion

The fluidity curves (Fig. 1) show a non-Newtonian behaviour of pseudoplastic flow in all the semisolid preparations. At the same time, no thixotropic phenomenon has been detected experimentally. This behaviour is characterized by a decrease in apparent viscosity and an increase in shear deformation. The causes of pseudoplastic flow may be due to the progressive breakdown of the internal structure of the preparation (under increasing shear) and its later reconstruction by means of brownian movement (Vemuri, 1988). Application of the model of Ostwald-De Waele (Table 2) – in particular the flow index ($n < 1$) – corroborates the type of flow shown by the rheograms.

The viscosimetric study demonstrates the very low viscosity of these semisolid preparations, giving an idea of their great capacity of spreading over a flat surface. The test shows that with $\tau_p = 3302$ dyn/cm^2 (Lucero et al., 1994a,c), deformation is such that the surface of spreading does not change with higher stresses. The results have enabled calculation of the compression stresses necessary to deform these semisolids. They coincide with the shear stresses obtained experimentally.

τ_p was calculated using the equations of correlation between it and τ_c (Lucero et al., 1994a,c). These correlations were obtained from gellified semisolids of Carbomer® 940 of high viscosity, in which it was necessary to use spindle no. 7 to

Table 5
Shear rates ($\dot{\gamma}$), apparent viscosities (η_{ap}), A, B and compression stresses (τ_p) obtained for the different semisolid preparations assayed

Semisolid preparation	$\dot{\gamma}$ (s^{-1})	η_{ap} (P)	A	B	τ_p (dyn/cm^2)
RS 30 D	5.34	5.84	0.0060	16.83	2391.7
	11.24	4.79	0.0070	16.83	5291.4
	22.30	3.99	0.0090	16.83	8030.0
RL 30 D	5.47	1.47	0.0035	3.67	1250.0
	11.27	1.36	0.0039	3.67	2980.1
	22.17	1.26	0.0051	3.67	4750.1
NE 30 D	5.40	3.53	0.0047	10.83	1754.9
	11.17	2.78	0.0052	10.83	3888.1
	21.99	2.22	0.0066	10.83	5763.3

achieve the shear deformation. In the equations obtained, ($\tau_c = A\tau_p + B$), there are three unknown parameters: A, B and τ_p.

It was attempted to obtain these parameters from other, known ones, such as indices of flow and consistency, moment of rotation, shear rate and apparent viscosity.

4.1. Parameter A

This is the slope of the straight line mentioned above. Another straight line is obtained on representing τ_c against $\dot{\gamma}$, whose slope is the apparent viscosity. Based on this, the two parameters were correlated and the results are shown in Table 3. Thus, A is a parameter related with the apparent viscosity, and is consequently dependent on the deformation rate (D) applied.

4.2. Parameter B

This shows the independent term of the equation under study, and is thus expressed in units of stress (dyn/cm^2). In all the equations applied, there is another independent term, K (Eq. 3 and 4), but expressed in units of moment of rotation (dyn cm). After carrying out the appropriate correlation and obtaining the results shown in Table 4, it was decided to transform the value of B into values of shear stress, applying Eq. 2, thereby taking into account the volume of the spindle used in each case.

4.3. Parameter τ_p

After calculating the values of $\dot{\gamma}$, A and B and applying the equation relating both stresses (shear and compression), the values of τ_p were calculated (Table 5). The results show that these were generally lower than those applied previously (3302 dyn/cm^2). It is noteworthy that for deformation rates of 50 rpm the values of these stresses are lower than those obtained at 20 rpm. This leads to the idea that for deformations at high rates of deformation, the established relationships do not hold true. On the other hand, since the US Pharmacopeia (1990) indicates that the ideal apparent viscosity for comparison of semisolids is that at 20 rpm, elimination of the data for the higher rate has no effect.

Finally, the correlation between the two stresses maintains the same linear relationship as obtained with the semisolids of the polymer of Carbomer® 940 (Table 6).

5. Conclusions

The linear equations relating the shear and compression stresses, obtained from experimental data – both viscosimetric and extensimetric – of Carbomer® 940 gels, can be used to determine the compression stresses necessary to deform longitudinally semisolid preparations of acrylic polymers of Eudragit®.

The independent term (B) of these equations is a shear stress and is directly related with the consistency index (K). It is demonstrated that this index is expressed in units of stress, so that the volume of the spindle used in calculating the experimental viscosimetric values must be taken into account.

The slope of the straight line (A) under study is intimately related with the apparent viscosities, and is thus dependent on the deformation rates selected. This gives a different equation for each apparent viscosity.

Lastly, the linear equations used in this work do not hold true at a deformation rate of 50 rpm. However, they do so at 2.5 rpm, although are not included in this study as this is within the instrumental error of the viscosimeter.

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