Drug Development and Industrial Pharmacy, 26(7), 797–801 (2000)

COMMUNICATION

A Study of the Spread Surface of Polymeric Dispersions of Eudragit®

M. J. Lucero,* J. Garcia-Andreu, F. Roman, and M. J. Leon

Departamento de Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, Universidad de Sevilla, Sevilla, Spain

ABSTRACT

The rheology of non-Newtonian fluid systems is complex. Their experimental study is difficult because of the existence of many dependent variables. In the present work, a mathematical equation is proposed to calculate the spread surface from a simple viscosimetric study in a theoretical way. It was determined for multiple parameters. The spread surface has to be marked because of its direct relation to the shear stress; this fact enabled us to connect one variable dependent on the compression deformation with another dependent on the shear deformation. At the same time, the viscoelastic phenomenon can be evidenced by applying this mathematical equation.
Key Words: *Compression deformation; Eudragit®; Shear deformation; Shear stress; Spread surface; Viscoelastic fluids.*

INTRODUCTION

The basic rheological properties of materials can be described by at least three parameters: stress, shear rate, and time (1,2). Most suppositions are made on the basis that the material is continuous—that is, on the assumption that all the properties of the system are uniform at each point. Thus, the rheological properties of a material can be understood best by considering its behavior in a particular simplified state, called *simple shear* (3,4).

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). Until now, spreadability has been considered a parameter that indicates stability (5,6) in the widest sense and, in some works (7–10), a sensorial property of semisolid preparations. But, in few cases has it been included in the rheological study of fluid (11).

* To whom correspondence should be addressed.

 www.dekker.com

Following the studies of this research group, correlations have been established between the deformations caused by shear (shear stress) and by compression (compression stress) (11–13). Consequently, it can be stated that, to make a complete rheological study, it is necessary to monitor both tangential and longitudinal deformations.

The present work aims to study the spread surface of dispersions of acrylic polymers of Eudragit®, specifically RS30D, RL30D, and NE30D, and hydroxypropylmethylcellulose (HPMC) and its correlation with the shear stress.

MATERIALS AND METHODS

Semisolid Preparations

Nine polymeric dispersions were made with three acrylic polymers of Eudragit (Röhm Gmbh Pharma Polymers, Darmstadt, Germany) (27% w/w of RS30D, RL30D, and NE30D) and three different concentrations of HPMC (1.25%, 1.5%, and 1.75% w/w).

Each polymeric dispersion was made by dissolving the respective polymer of Eudragit in 15 ml of absolute ethanol ACS ISO (Merck, Darmstadt, Germany). Next, this was mixed by mechanical stirring into a suspension of HPMC (Hipromelosa-4000, Acofarma, Barcelona, Spain) in 56.5 ml of distilled water.

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

Compression Deformation

The method used for this test was described by various authors (5,6); the compression stress applied was 3302, 6191, 12,383, and 20,638 dyn/cm^2. Previous studies (11–13) showed the existence of a direct correlation between shear and compression stresses. The compression stresses were determined from those equations. As the lowest of these gave a very high deformation, the compression stress necessary to cause longitudinal deformation was determined theoretically (11).

In the present work, relationships between shear stress τ_c and spread surface *SS* were also evaluated.

RESULTS

Spread Surface

The values of τ_c and *SS* are related using the following equation:

$$\tau_c = J[SS] + L \tag{1}$$

Determination of *J*

Correlations were obtained between the values of *J* and η_{ap} at deformation rates *D* of 5, 10, 20, and 50 rpm. The correlations are shown in Table 1.

Determination of *L*

Correlations were obtained between the values of *L* and τ_K depending on the spindle used for each preparation. The resulting equation is shown in Table 1.

Determination of Rheological Parameters

Table 2 shows the results obtained for calculating the spread surface.

Table 3 shows the correlations obtained between the rheological parameters τ_c and *SS* for the semisolid preparations of acrylic polymers of Eudragit.

DISCUSSION

The *SS* was calculated from the mathematical model using the equations of correlation between *SS* and τ_c. These correlations were obtained from experimental data

Table 1

Statistical Parameters for the Correlations Between J *and* η_{ap} *and* L *and* τ_k

D	r_{xy}	$F_{(1,17)}$	Probation	CV	Equation
5 rpm	0.8569	95.85	<.0001	19.89	$J = 3.9084\ \eta_{ap} - 69.0202$
10 rpm	0.8572	96.07	<.0001	19.87	$J = 6.5240\ \eta_{ap} - 71.0771$
20 rpm	0.8433	86.09	<.0001	20.82	$J = 10.6423\ \eta_{ap} - 56.3760$
50 rpm	0.7829	57.70	<.0001	24.51	$J = 19.1919\ \eta_{ap} + 9.8571$
	0.7517	48.43	<.0001	29.89	$L = 0.8236\ \tau_k - 183.1894$

Table 2

Shear Rates γ, *Shear Stress* τ_c, *Apparent Viscosities* (η_{ap}), J, L, *and Spread Surface* SS *Obtained for the Different Polymeric Dispersions Assayed*

Polymeric Dispersions	Shear Rates *D* (rpm)	Shear Rates γ (sec^{-1})	Shear Stress τ_c (dyn/cm^2)	η_{ap} (poises)	|*J*|	*L*	*SS* (cm^2)
HPMC 1.25%	5	1.34	2.53	1.89	53.74	−185.15	3.43
	10	2.85	5.06	1.77	59.53	−185.15	3.14
	20	5.08	8.61	1.69	38.39	−185.15	4.97
	50	12.18	19.24	1.58	40.18	−185.15	5.01
HPMC 1.5%	5	5.15	2.88	0.56	66.83	−181.62	2.76
	10	11.17	5.58	0.50	67.81	−181.62	2.76
	20	20.01	9.18	0.46	51.48	−181.62	3.71
	50	50.24	20.16	0.40	17.53	−181.62	11.51
HPMC 1.75%	5	5.54	6.30	1.14	64.56	−180.80	2.90
	10	11.00	11.70	1.06	64.16	−180.80	3.00
	20	21.68	21.60	1.00	45.73	−180.80	4.43
	50	49.92	45.90	0.92	27.51	−180.80	8.24
RS 30 D/1.25% HPMC	5	5.05	9.45	1.87	61.71	−181.05	3.09
	10	10.63	17.10	1.61	60.57	−181.05	3.27
	20	21.75	30.24	1.39	41.58	−181.05	5.08
	50	50.38	59.05	1.17	32.31	−181.05	7.43
RS 30 D/1.5% HPMC	5	5.41	17.53	5.76	46.51	−175.75	4.45
	10	11.39	53.87	4.73	40.22	−175.75	5.71
	20	22.61	89.11	3.94	14.44	−175.75	18.34
	50	49.84	159.16	3.19	71.16	−175.75	4.71
RS 30 D/1.75% HPMC	5	5.63	13.37	2.37	59.76	−180.87	3.25
	10	11.3	24.70	2.19	56.79	−180.87	3.62
	20	22.09	44.55	2.02	34.88	−180.87	6.46
	50	48.55	89.10	1.83	44.98	−180.87	6.00
RL 30 D/1.25% HPMC	5	4.95	5.85	1.18	64.41	−181.90	2.91
	10	10.74	11.07	1.03	64.36	−181.90	3.00
	20	20.94	19.17	0.92	46.58	−181.90	4.32
	50	50.87	39.77	0.78	24.83	−181.90	9.83
RL 30 D/1.5% HPMC	5	5.50	8.10	1.47	63.27	−181.76	3.00
	10	11.26	15.30	1.36	62.20	−181.76	3.17
	20	22.15	27.90	1.26	42.97	−181.76	4.88
	50	49.73	57.24	1.15	31.93	−181.76	7.48
RL 30 D/1.75% HPMC	5	5.74	15.80	2.75	58.27	−179.71	3.35
	10	13.65	30.88	2.22	56.59	−179.71	3.71
	20	26.27	49.62	1.90	36.15	−179.71	6.34
	50	61.20	94.17	1.54	39.41	−179.71	6.95
NE 30 D/1.25% HPMC	5	5.53	10.35	1.87	61.71	−180.65	3.09
	10	11.41	17.28	1.51	61.23	−180.65	3.23
	20	21.63	27.18	1.26	42.97	−180.65	4.84
	50	49.76	49.05	0.98	28.67	−180.65	8.01
NE 30 D/1.5% HPMC	5	5.05	13.37	2.65	58.66	−179.65	3.29
	10	11.14	23.29	2.09	57.44	−179.65	3.53
	20	21.97	37.47	1.71	38.18	−179.65	5.69
	50	50.38	66.47	1.33	35.38	−179.65	6.97
NE 30 D/1.75% HPMC	5	5.54	22.28	4.02	53.31	−177.51	3.75
	10	11.19	36.05	3.22	50.07	−177.51	4.26
	20	21.92	57.11	2.60	28.71	−177.51	8.17
	50	48.56	98.42	2.03	48.82	−177.51	5.65

Table 3

Statistical Parameters for the Correlation Between τ_c *and* SS

r_{xy}	$F_{(1,47)}$	Probability	CV	Equation
0.8153	202.99	$<.0001$	48.47	$\tau_c = 5.566\,[SS] - 1.7397$

of gellified semisolids of Carbomer® 940 of high viscosity (16). In the equation obtained (Eq. 1), there are three unknown parameters: *J*, *L*, and *SS*.

Parameter *J* is the slope of the straight line mentioned above (Eq. 1). Another straight line is obtained on representing τ_c against γ, which has a slope that is the apparent viscosity. Based on this, the two parameters were correlated; the results are shown in Table 1. Thus, *J* is a parameter related to the apparent viscosity and is consequently dependent on the deformation rate *D* applied.

Parameter *L* shows the independent term of the equation under study (Eq. 1) and is thus expressed in units of shear stress ($\text{dynas}\cdot\text{cm}^{-2}$). In all the equations applied, there is another independent term, *K* (consistency index) (1,2), but it is expressed in units of moment of rotation (dynes·cm). After carrying out the appropriate correlation and obtaining the results shown in Table 1, it was decided to transform the value of *K* into values of shear stress (κ_k), applying an appropriate equation and thereby taking into account the volume of the spindle used in each case (15–17).

After calculating the values of γ, η_{ap}, *J*, and *L* and applying the equation relating shear stresses and spread surface, the values of *SS* were calculated (Table 2).

It must be marked that, to calculate *SS*, it was necessary to use *J* in absolute values. On the other hand, and compared to the τ_p values, the results after applying 50 rpm might be accepted because, in most cases, the *SS* obtained are higher than *SS* obtained at 20 rpm, although correlation was always maintained. Also, these data provide very interesting information related to rheologic behavior in compression deformation. In the polymeric dispersions of RS 30 D/1.5% HPMC, RS 30 D/1.75% HPMC, and NE 30 D/1.75% HPMC, the *SS* corresponding to shear deformations of 20 rpm are higher than those obtained at 50 rpm. These results led us to think about the possible existence of viscoelastic behavior. It does not happen in the same way in the polymeric dispersions made with the RL 30 D polymer and in the different concentrations of HPMC. Other correlated studies made of these dispersions have confirmed that all show viscoelastic behavior (investigation in process) except the one involving the RL 30 D polymer.

Finally, the correlation between the shear stress and spread surface maintains the same linear relationship obtained with the semisolids of the polymer of Carbomer 940 (Table 3). It must be pointed out that τ_c and *SS* results at 50 rpm corresponding to the dispersions listed above were not taken into consideration as viscoelastic behavior was shown by the dispersions.

CONCLUSION

The spread surface of non-Newtonian fluids can be calculated theoretically with the mathematical equation proposed above. At the same time, different but related to viscous behavior, like the viscoelastic one, can be evidenced. In the viscoelastic phenomenon, correlation between shear stress and spread surface was not seen.

REFERENCES

1. D. T. Deem, in *Pharmaceutical Dosage Forms: Dispersal Systems*, Vol. 1, (H. A. Lieberman, M. M. Rieger, and G. S. Banker, Eds.), Marcel Dekker, New York, 1988, pp. 367–425.
2. M. J. Lucero, M. J. León, J. Vigo, and A. M. Rabasco, Ind. Farm., 6, 62–68 (1991).
3. G. S. Banker and R. K. Chalmers, *Physical Pharmaceutics and Pharmacy Practice*, Lippincott, Philadelphia, 1981, p. 81.
4. S. García, M. Barracó, M. A. Adriá, J. M. López, P. Giner, and L. García-Soto, Cienc. Ind. Farm., 6, 264–268 (1987).
5. M. J. Lucero, J. Vigo, and M. J. León, Drug Dev. Ind. Pharm., 20, 2315–2322 (1994).
6. M. J. León, M. J. Lucero, and R. Millán, Drug Dev. Ind. Pharm., 17, 737–746 (1991).
7. F. Shama and P. Sherman, J. Text. Studies, 4, 111–118 (1973).
8. J. L. Kokini, J. B. Kadane, and L. Cussler, J. Text. Studies, 8, 195–218 (1977).
9. J. L. Kokini and L. Cussler, J. Food Sci., 48, 1221–1225 (1983).
10. J. L. Kokini, M. Poole, P. Mason, S. Miller, and E. F. Stier, J. Food Sci., 49, 47–51 (1984).

11. M. J. Lucero, J. García, J. Vigo, and M. J. León, Int. J. Pharm., 116, 31–37 (1995).
12. M. J. Lucero, J. Vigo, and M. J. León, Int. J. Pharm., 106, 125–133 (1994).
13. M. J. Lucero, J. Vigo, and M. J. León, Int. J. Pharm., 111, 241–248 (1994).
14. G. Schramm, *Documentación Científica*, Laboratorios Haake, Alemania.
15. J. M. Wood, in *The Theory and Practice of Industrial Pharmacy*, 3rd ed. (L. Lachman, H. A. Lieberman, and J. L. Kaning, Eds.), Lea and Febiger, Philadelphia, 1986, pp. 123–145.
16. J. Vigo, Doctoral thesis, University of Seville, Spain, 1993.
17. Brookfield Laboratories, *Why Measure Viscosities*? Author, Brookfield, MA, 1990.