

A study of shear and compression deformations on hydrophilic gels of α -tocopherol

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Abstract

A rheological study of hydrophilic gels of Carbomer® 940 with α -tocopherol as drug, and ascorbic acid as antioxidant, has been carried out. At the same time, the effect of storage time has been determined. Both shear and compression deformations were applied. From the results obtained, correlations between both types of deformation have been established. The results were statistically significant between shear and compression stresses, and between shear stress and area of spreading.

Keywords: Shear deformation; Compression deformation; pH; α -Tocopherol; Ascorbic acid; Carbomer® 940

1. Introduction

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 deforms to a greater or lesser degree (Dolz et al., 1988) as a function of the deformation and its rate.

It is interesting that 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. The result

is that the rheological properties of a material can be best understood considering their behaviour in a particular simplified state, called simple shear (Banker and Chalmers, 1981; García et al., 1987).

Fluid material can be deformed by both shear and compression. In the former case, a tangential force is applied to the material, while in the latter the force is perpendicular to the direction of fluid movement.

In the bibliography consulted, there are works on spreadability (Buenestado and Suñé, 1972a,b; Shama and Sherman, 1973; Kokini et al., 1977, 1983, 1984; Jiménez-Castellanos et al., 1982; León et al., 1982, 1991; Del Pozo et al., 1987; Lucero et al., 1994a) as a sensorial parameter, and on the determination of yield value, applying flow by compression (Campanella and Peleg, 1987; De-

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Table 1
Components of the hydrophilic gels assayed

	Gel G	Gel AA	Gel E	Gel EAA
Carbomer® 940	1%	1%	1%	1%
Ethanol 96%	15 ml	15 ml	15 ml	15 ml
Triethanolamine	3 ml	3 ml	3 ml	3 ml
α-Tocopherol	–	–	2.5 %	2.5 %
Ascorbic acid	–	0.1 %	–	0.1 %
Distilled water	85 ml	85 ml	85 ml	85 ml

Martine and Cussler, 1975). In contrast, no works have been found on both types of deformation, except that of Lucero et al. (1994b).

The present work aims to study the rheology of semisolid preparations of α-tocopherol, and/or ascorbic acid, made with the polymer Carbomer® 940, in particular the determination of pH and shear and compression deformations. At the same time, it will corroborate the correlation between rheological parameters previously found by this research group (Lucero et al., 1994b).

2. Experimental

2.1. Semisolid preparations

Hydrophilic gels, prepared with the components shown in Table 1, were used as base (Vigo, 1993).

Gel G was prepared with Carbomer® 940 (Acofarma, Tarrasa, Spain) by the traditional process.

Gels AA, E and EAA were obtained by solution of ascorbic acid (AA) (Merck, Darmstadt, Germany), α-tocopherol (E) (dl-α-tocopherol, Merck, Darmstadt, Germany) or both substances at the same time, in ethanol, followed by incorporation into the rest of the formula.

Before preparation of gel G, the amount of TEA necessary to neutralize the gels (BF Goodrich, 1981) and yield a pH around 5.4 units – ideal for the stability of AA (Deritter, 1982) – was determined.

The different formulations prepared were kept at ambient temperature for 24 h before assays.

2.2. Study of pH

These preparations are intended for application to the skin, so that this parameter should be between 4 and 6.5 units to avoid the risk of irritations or alterations of the cutaneous tegmen-tum (Clearly, 1984).

The study was carried out exhaustively on gel G, as AA has a narrow pH range of maximum stability. Otherwise, there would occur early oxidation of AA favouring oxidation of E.

The assay was performed using a pH meter (MicropH 2001, Crison). Measurement was by direct contact of the electrode with the different formulations.

To detect possible pH variations with time, samples were assayed at 1, 30 and 60 days after preparation.

2.3. Shear deformation

This assay was carried out using a Searle rotary viscosimeter (Brookfield Model RVT) with spindle no. 7. The deformation rates (*D*) used were 0.5, 1, 2.5, 5, 10, 20, 50 and 100 rpm.

The Brookfield viscosimeter measures the viscous traction exerted on a spindle rotating in a fluid in a vessel. The spindle is rotated by a synchronized rotor via a beryllium-copper torsion wire of 7187 dyn cm (Ball et al., 1982; Pugnetti, 1982; Barraco et al., 1985; Wood, 1986; Deem, 1988; Dolz et al., 1988; Lucero et al., 1991, 1994a,b). For this apparatus, shear rate and stress are determined as:

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

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

where ω is the angular velocity of the spindle, R_c the radius of the container, R_b the radius of the spindle (0.15 cm), X the radius of the determined point, T the torsion (7187 dyn cm) and L the effective length of the spindle (5.5 cm).

The rheological model of Ostwald-De Waele can be applied to the resolution of problems of

deformation and flow (Shotton and Ridgway, 1974; Pugnetti, 1982; Sherman, 1983; Schramm, 1984; Wood, 1986; Deem, 1988; Opota et al., 1988; Lucero et al., 1991, 1994a,b):

$$\tau = K\dot{\gamma}^n \quad (3)$$

$$M = KD^n \quad (4)$$

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

Finally, apparent viscosity can be defined as:

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

The methodology for the assay was standardized. In each case, the viscosimeter rotated for 1 min and was still for 30 s. After reaching maximum speed (100 rpm), each preparation was left to settle (15 min) 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 $22 \pm 1^\circ\text{C}$.

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. 4), shear stresses (τ) (Eq. 2), shear rate ($\dot{\gamma}$) (Eq. 3), 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).

Times of 1, 30 and 60 days from preparation of the semisolid preparations were established to determine the rheological changes provoked by storage time.

2.3. Compression deformation

The method chosen was that described previously by some authors (Jiménez-Castellanos et al., 1982; Del Pozo et al., 1987) and modified subsequently by us (Lucero et al., 1994b). A manual microtome (Ranvier type) was used with the following characteristics: perfectly flat plate of 5 cm diameter, screw bore of 1.2 cm diameter and thread of 0.68 mm.

A sequence of masses of 80, 150, 300 and 500 g, equivalent to compression stresses of 3302, 6191, 12383 and 20638 dyn cm^{-2} , respectively, was placed on the cylinder of sample of 77 mm^3 , under normal conditions of temperature ($22 \pm 1^\circ\text{C}$). The duration of each force was 1 min of compression with intervals of 30 s of rest between each.

To evaluate the deformation caused in the different formulations by each of these stresses, photographic plates (Kodak Tmax 400) were printed with the areas of spreading produced (Nikon 501, close-up lens +5), using a lamp of constant situation and intensity. Lastly, these areas were determined by direct reading of the perimeters using a planimeter (Staedtler Mars 927).

The same times as in the assay of shear deformation – 1, 30 and 60 days – were used to determine rheological changes provoked by storage time.

3. Results

3.1. Study of pH

Table 2 lists the results obtained for pH in all the formulations. The data demonstrate the diminution of pH as a function of time, except in

Table 2
pH values of the hydrophilic gels indicated

Gel	Time (days)	pH		
		<i>x</i>	SD	CV
G	1	5.82	0.045	0.77
	30	5.82	0.058	0.99
	60	5.81	0.051	0.87
AA	1	5.46	0.086	1.58
	30	4.64	0.102	2.19
	60	4.46	0.016	0.37
E	1	5.00	0.047	0.94
	30	4.65	0.066	1.42
	60	4.74	0.052	1.10
EAA	1	4.97	0.154	3.10
	30	4.66	0.128	2.76
	60	4.46	0.143	3.22

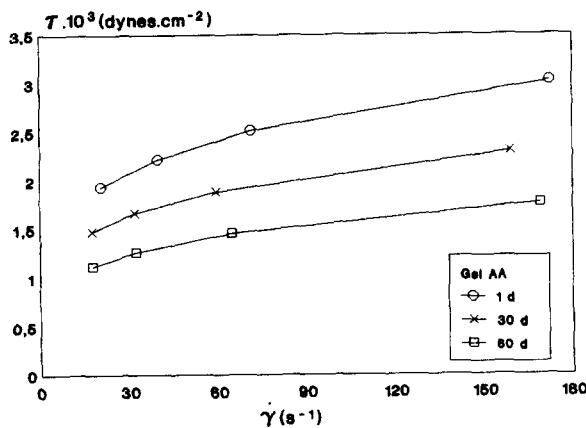
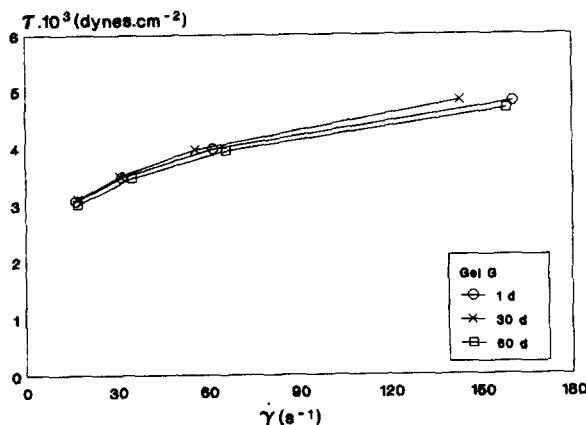


Fig. 1. Fluidity curves of the gels G and AA for the indicated times.

gel G (in which no variations were found) and gel E (which showed a slight increase at 60 days with respect to 30 days).

3.2. Shear deformation: fluidity curves

Fig. 1 and 2 show the fluidity curves of the gels assayed for the indicated times.

The flow and consistency indices were determined applying the model of Ostwald-De Waele (Eq. 4) (Table 3), using the descending legs of the rheograms (Lucero, 1989). The results obtained reflect the fact that all the gels show a non-Newtonian behaviour of the pseudoplastic flow as the values of n were under 1.

3.3. Shear deformation: viscosity curves

Fig. 3 and 4 show the viscosity curves obtained for each gel studied. The shear rate ($\dot{\gamma}$) was taken as that at 20 rpm (USP, 1990) for the rheological study.

3.4. Compression deformation

Table 4 lists the areas of spreading obtained subjecting the gels to compression. The relationship between the applied compression stress and the measured area of spreading can be observed.

Irregular behaviour was found in all gels. This reflects the influence of other factors, such as

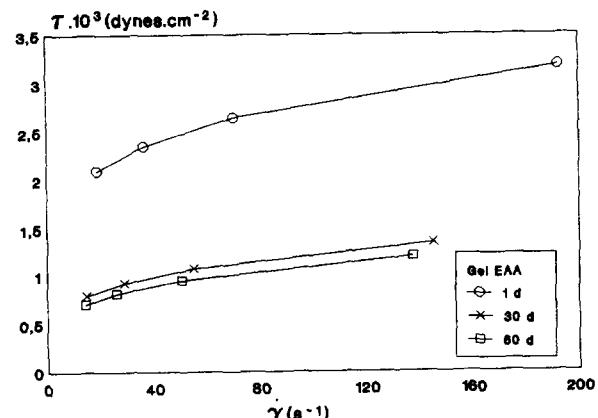
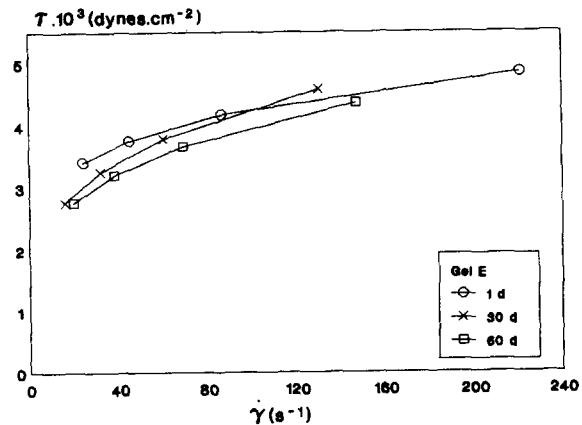


Fig. 2. Viscosity curves of the gels E and EAA for the indicated times.

Table 3
Indices of flow (n) and consistency (K) of the hydrophilic gels indicated

Gel	Time (days)	n	K
G	1	0.20	1737.8
	30	0.21	1698.2
	60	0.20	1698.2
AA	1	0.21	1023.3
	30	0.20	831.8
	60	0.20	631.0
E	1	0.16	2041.7
	30	0.24	1412.5
	60	0.23	1380.4
EAA	1	0.18	1230.3
	30	0.23	426.6
	60	0.24	371.5

chemical interactions between the components of the formulas.

3.5. Correlation between rheological parameters

All possible correlations between the data obtained by shearing and those by compression have been established. Of these, those that relate shear stresses with compression stresses (Table 5) and shear stresses with areas of spread (Table 6) are those showing the best statistical parameters. These results are consistent with those obtained in hydrophilic gels of tretinoin (Lucero et al., 1994b).

4. Discussion

From the fluidity curves (Fig. 1 and 2), non-Newtonian behaviour of pseudoplastic flow is observed in all the gels. At the same time, no thixotropic phenomenon was detected experimentally. The causes of pseudoplastic flow may be due to progressive rupture of the internal structure of the preparation (by increasing shear) and its later reconstruction by means of Brownian movement (Vemuri, 1988). Applying the model of Ostwald-De Waele (Table 3) – in particular the flow index (n) – corroborates the type of flow found from the rheograms.

Various factors participate in the formation of gel G. On the one hand, the concentration of the polymer (1% w/w), and on the other, the amount of TEA added to decrease the initial acidity of this formulation ($\text{pH} \approx 3$). Consequently, to be able to explain the rheological behaviour of these semisolid preparations, it is necessary to follow the pH. According to the scientific documentation (BF Goodrich, 1981), Carbomer® 940 in water has a pH range of maximum rheological stability between 6 and 8 units. Independently of this factor, gel G was given a final pH close to 5.4, to achieve maximum chemical stability of one of the components present in the formulations – AA (Deritter, 1982).

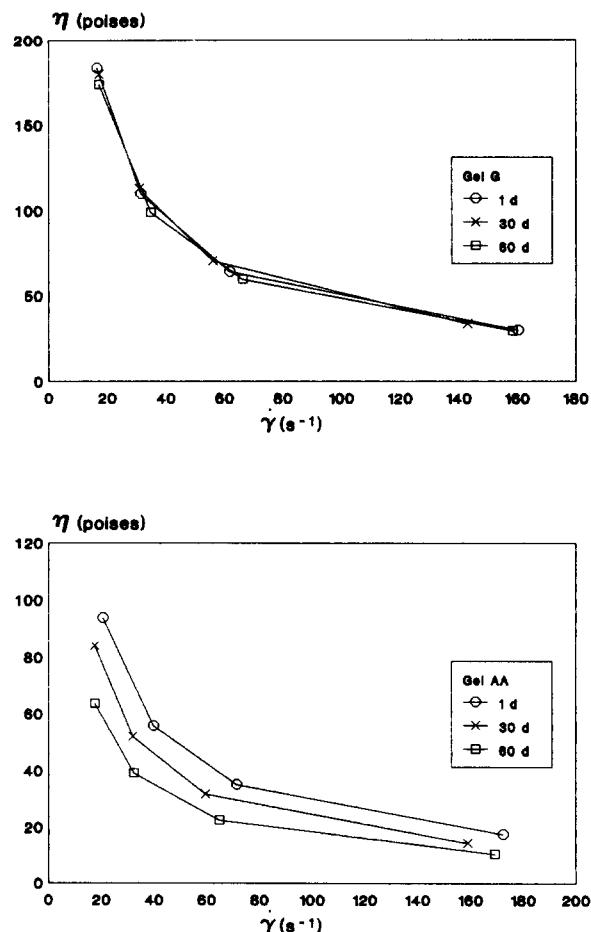


Fig. 3. Viscosity curves of the gels G and AA for the indicated times.

Table 4

Areas of spreading obtained from compression deformation of the hydrophilic gels indicated

Gel	Time (days)	Area of spreading (cm ²)			
		[compression stress (dyn cm ⁻²)]			
		3302	6191	12383	20638
G	1	3.30	3.80	4.90	6.20
	30	2.80	3.70	4.70	5.40
	60	2.70	3.50	4.30	5.10
AA	1	2.82	3.67	4.69	5.63
	30	3.28	4.61	5.52	6.04
	60	3.73	4.76	6.17	6.67
E	1	2.39	3.34	4.25	4.88
	30	1.87	2.85	3.85	4.36
	60	2.20	2.96	3.91	4.79
EAA	1	2.81	3.69	5.03	5.76
	30	5.80	6.66	8.17	8.36
	60	4.40	5.42	6.33	7.32

Therefore, gel G with a pH of 5.82 units (Table 2) is very close to the pH range mentioned above. No variations were found in this parameter with storage time or the slight changes in apparent viscosity (Fig. 3) and area of spreading (Table 4). From the results obtained in the rheological study, it may be deduced that the modifications provoked by deformations are more evident applying an increasing perpendicular force than an increasing tangential one.

With storage time, the pH of gel AA decreased (Table 2). This was due to oxidation of AA to form the ascorbyl radical which, although not reacting normally, can do so with itself, giving rise to dehydroascorbic acid (Burton et al., 1983; Willson, 1983). Apparent viscosity diminished with decreasing pH (Fig. 3). This can be explained by the fact that the pH zone is not one of maximum rheological stability, so that a slight decrease in pH causes coiling of the polymer

Table 5

Parameters of correlation between shear stress (τ_s) and compression stress (τ_c) of the hydrophilic gels indicated

Gel	Time (days)	r_{xy}	$F_{(1,22)}$	Probability	Equation
G	1	0.9923	2817.6	< 0.0001	$\tau_s = 0.0945\tau_c + 2758.5$
	30	0.9798	1066.4	< 0.0001	$\tau_s = 0.0901\tau_c + 2801.2$
	60	0.9712	742.2	< 0.0001	$\tau_s = 0.0949\tau_c + 2714.4$
AA	1	0.8594	134.5	< 0.0001	$\tau_s = 0.0602\tau_c + 1776.7$
	30	0.8729	151.1	< 0.0001	$\tau_s = 0.0455\tau_c + 1343.3$
	60	0.8890	176.2	< 0.0001	$\tau_s = 0.0358\tau_c + 1017.1$
E	1	0.9271	279.6	< 0.0001	$\tau_s = 0.0800\tau_c + 3188.2$
	30	0.9732	797.7	< 0.0001	$\tau_s = 0.0997\tau_c + 2516.6$
	60	0.9609	540.3	< 0.0001	$\tau_s = 0.0883\tau_c + 2544.4$
EAA	1	0.8806	162.2	< 0.0001	$\tau_s = 0.0598\tau_c + 1925.4$
	30	0.9042	207.6	< 0.0001	$\tau_s = 0.0302\tau_c + 712.6$
	60	0.9405	348.0	< 0.0001	$\tau_s = 0.0282\tau_c + 621.3$

molecule (BF Goodrich, 1981), diminishing the viscosity. The areas of spreading increased with time (Table 4) at the same time as the pH increased.

Obviously, the addition of AA modified both the rheological parameter and the pH of gel G.

α -Tocopherol (E) is an acid substance ($pK_a = 6.0$) (Burton et al., 1983). This acidity is shown by the initial pH of the formulation, which is lower than that of gel G (Table 2). It decreases with storage time. The apparent viscosities (Fig. 4) show a slight decrease, which did not correspond with those of pH.

Apparently, the areas of spreading (Table 4) have a direct relationship with the data of pH obtained as a function of time, although the statistical correlation could not be established.

The association of AA and E in gel G to make gel EAA gives rise to a semisolid preparation with pH similar to that of gel E (Table 2); however, these values of pH as a function of time seem closer to those of gel AA.

The explanation could be the oxidation of AA (Burton et al., 1983; Wilson, 1983) which increases the chemical stability of E.

In the rheological study, the results (Fig. 4 and Table 4) demonstrate similarity to gel AA when comparing the initial and final periods. In contrast, the apparent viscosities were lower and the areas of spreading were greater than those of gel

E. This could be explained by oxidation of either AA or E. These reactions occur at high speed and consecutively, and give rise to chemically unstable structures, which subsequently generate chemically stable and definitive structures (Tappel, 1972; Nobile and Woodhill, 1981). These new chemical structures can modify the rheological parameters. Concretely, the reactive groups of E, AA and even Carbomer® 940 could react through weak links that could break with the shear and compression deformations.

Two types of stress were applied: normal and shear. The former is a force that acts on the component perpendicular to the plane (tension outward and compression on the plane), while a stress on the component tangential to the plane is the shear stress.

It seems obvious that there must be some type of relationship between shear and compression (Lucero et al., 1994b). Correlations have been established between the different parameters of shear deformation (shear stress, shear rate and apparent viscosity) and compression deformation (compression stress, area of spread and masses). Of these, the best statistical results have been obtained comparing the two types of stress and from the semilogarithmic relationship between shear stress and area of spread.

Table 5 shows the results obtained in the correlation between the shear and compression

Table 6
Parameters of correlation between shear stress ($\log \tau_s$) and area of spreading (S) of the hydrophilic gels indicated

Gel	Time (days)	r_{xy}	$F_{(1,22)}$	Probability	Equation
G	1	0.9913	1244.7	< 0.0001	$\log \tau_s = 0.0634S + 3.2813$
	30	0.9715	369.1	< 0.0001	$\log \tau_s = 0.0689S + 3.2822$
	60	0.9916	1296.0	< 0.0001	$\log \tau_s = 0.0818S + 3.2459$
AA	1	0.8827	77.6	< 0.0001	$\log \tau_s = 0.0603S + 3.1235$
	30	0.6884	19.8	< 0.0001	$\log \tau_s = 0.0422S + 3.0510$
	60	0.8026	39.8	< 0.0001	$\log \tau_s = 0.0502S + 2.8713$
E	1	0.8352	50.8	< 0.0001	$\log \tau_s = 0.0472S + 3.4259$
	30	0.9231	126.7	< 0.0001	$\log \tau_s = 0.0735S + 3.3082$
	60	0.9331	148.1	< 0.0001	$\log \tau_s = 0.0645S + 3.3124$
EAA	1	0.8343	50.4	< 0.0001	$\log \tau_s = 0.0480S + 3.1963$
	30	0.9023	96.3	< 0.0001	$\log \tau_s = 0.0683S + 2.5085$
	60	0.8375	51.7	< 0.0001	$\log \tau_s = 0.0594S + 2.6067$

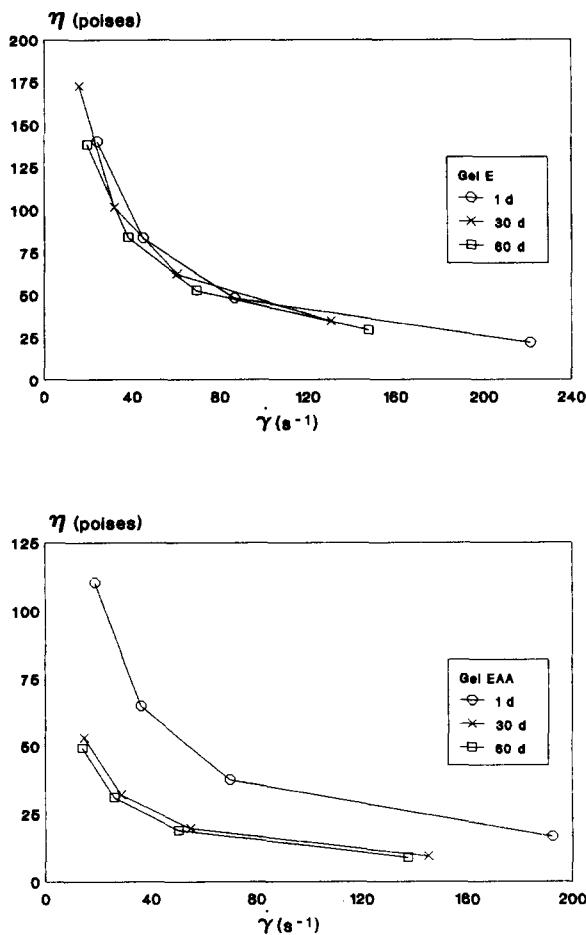


Fig. 4. Viscosity curves of the gels E and EAA for the indicated times.

stresses. There is a significant statistical difference in all the gels assayed, independently of the composition of the formulation. Thus the shear stress can be calculated that would have to be applied to a fluid to achieve a tangential deformation equal to a perpendicular deformation obtained by subjecting the sample to a concrete compression stress. This explains the decision to use the compression stress of 12 383 dyn/cm² to relate with the shear stresses resulting from application of a deformation rate of 20 rpm (USP, 1990).

At the same time, the shear stresses have been related with the areas of spread obtained from compression. The results obtained (Table 6) also

indicate significant statistical correlation, permitting calculation of the shear stress corresponding to a determinate area of spreading.

5. Conclusions

The pH and the presence of AA in the final formula determine the stability of the tridimensional structure of hydrophilic gels, and their rheological behaviour with storage time.

We have corroborated the correlations established between shear and compression stresses, and between shear stress and the area of spreading. These relationships are independent of the components of the gellified disperse systems assayed.

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