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Application of a factorial design to the study of the flow behavior, spreadability and transparency of a Carbopol ETD 2020 gel. Part II

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Abstract

A factorial design (2^3) is applied to study the influence of three of the components of a cosmetic gel (the concentrations of Carbopol ETD 2020, ethanol and glycerine) on flow parameters (Casson's yield value (τ_c), Casson's viscosity (η_c) and apparent viscosity at 125 s^{-1} ($\eta_{ap.}$ 125 s^{-1})), spreadability, and transparency. The first-order polynomial equation allowed by the model suitably accounts for the τ_c and spreadability. Both depend on the concentrations of Carbopol and ethanol, and τ_c also depends on the ethanol–glycerine interaction. The model explains to a certain extent the complex relationships that are established between the components and that influence η_c y $\eta_{ap.}$ 125 s^{-1}. Transparency is independent of the Carbopol concentration and it is also thought to be independent of the ethanol concentration. In addition, a high linear correlation has been found between the τ_c and spreadability and other viscoelastic parameters of the gels that were previously determined (Int. J. Pharm. (2001)). The application of the technique of experimental design has been shown to be a very useful tool for formulating gels. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Carbopol ETD 2020; Factorial design; Flow; Gels; Spreadability; Transparency

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1. Introduction

In the design of a cosmetic gel, it is not easy for the formulator to decide what component or combination of components can be modified since it is difficult to predict the variations of parameters such as the flow behavior, spreadability and transparency. However, these parameters are often decisive in the acceptance or rejection of a cosmetic by the consumer (Lochhead et al., 1987).

In a previous work (Contreras and Sanchez, 2001), a 2^3 factorial design was applied (analysis of only ten samples) to determine the relationships between three components of a gel (the concentrations of Carbopol, ethanol and glycerine) and their viscoelastic properties, which determine the structural properties of a gel at rest (Kleck, 1992). In all cases high linear relations

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were found, revealing the importance of the interactions among the components at a microstructural level.

Using these results, the formulator can modify the ratio of these components according to technological or practical needs, knowing a priori how the microstructure of the gel will be modified. Likewise, the value of a given viscoelastic parameter can be established, thereby deducing the composition of the gel.

The aim of the present study was to determine whether such an experimental design (2^3) could explain equally well the influence of these same components (concentrations of the Carbopol, ethanol and glycerine) on the flow behavior, spreadability and transparency of the samples, which is of great practical use to the formulator.

The components of the cosmetic are the usual ones for an after-shave gel (Pons and Parra, 1995), including allantoin, menthol, Carbopol ETD 2020, glycerine, ethanol, methyl and propylparaben, triethanolamine and water. Carbopol ETD 2020 was chosen due to its interesting toxicologic (Reynier et al., 1998), industrial (Goodrich, 1993) and cosmetic (Brand-Garnys et al., 1994; Contreras and Sanchez, 2001) properties.

2. Materials and methods

2.1. Materials

Menthol, allantoin, ethanol, glycerine and triethanolamine were provided by Henkel–Palera (Barcelona, Spain), Carbopol ETD 2020 by BF Goodrich (Germany), and methyl parahydroxybenzoate and propyl parahydroxybenzoate by Aldabo Julia, S.A. (Barcelona, Spain). All were used as received.

2.2. Experiment

The influence of three factors (the concentrations of the polymer, ethanol and glycerine) were studied with a 2^3 factorial design to which two central points were added to estimate the error. Both the design of the program and the analysis of the results were performed with the statistical program STATGRAPHICS PLUS V. 4.1 (Statgraphics Plus, 2002).

The resolution of the design is V+, which shows the main effects and interactions of two and three factors and allows a first-order polynomial predictive equation to be obtained:

$$y = \text{bo} + \sum \text{bixi} \sum \text{biixixj} + \sum \text{biiixixjxz}$$

Analysis of variance (ANOVA) was used to analyze the significance of the terms of the complete equation, for a level of $\alpha = 0.05$ and $\alpha = 0.05$. The non-significant terms were eliminated from the equation one by one in successive stages and in decreasing order of the P-value (level of significance attained by the test) up until the statistic r^2 adjusted to the degrees of freedom (r^2 adjusted for d.f.) neared unity, the maximum fit allowed. This parameter was chosen as it is more suitable for comparing models with different numbers of independent variables.

For each of the response factors, the definitive predictive equation (in which all of its terms are not always significant, though they may be necessary to describe the effect (Bolton, 1990)), the standard error of the estimate (SEE) and the mean standard error (MSE) are included. Other statistics analyzed are not included here (see Contreras and Sanchez, 2001).

2.3. Formulations

Ten different samples were analyzed (factorial design $2^3 + 2$), with constant concentrations of menthol (0.3% m m^{-1}), allantoin (0.2% m m^{-1}), methylparaben (0.075% m m^{-1}) and propylparaben (0.025% m m^{-1}). We varied the concentrations of Carbopol ETD 2020 (cb) within the recommended limits for a gel (0.5 to 1% m m^{-1}), glycerine (gl) according to the recommendations for this type of preparation (2–5% m m^{-1}), and ethanol (et, 5–30% m m^{-1}), whose upper limit is restricted by its compatibility with the polymer (Contreras and Sanchez, 2001). Triethanolamine was used as a neutralizing agent (all the samples have pH 7, compatible with the skin). De-ionized water was added for a total of 100 g.

Table 1 gives the concentrations of the principal factors for each of the samples.

We prepared 200 g of each formula, dissolving the menthol, allantoin and preservatives in the ethanol. Independently, the polymer was dispersed in the water and the glycerine was added. The two mixtures were then mixed, neutralized and homogenized by hand stirring. The samples were kept at rest at 25 °C in hermetically sealed containers for 48 h before analyzing.

2.4. Response factors

2.4.1. Selection

2.4.1.1. Flow behavior. Casson's model characterizes fluid behavior (variation of the shear stress (τ) against the rate strain (γ) for low γ (Prentice, 1984; Marquard et al., 1997) according to the ratio:

$$\sqrt{\tau} = \sqrt{\tau_c} + \sqrt{\eta_c} \cdot \sqrt{\gamma} \tag{1}$$

Where τ_c, is Casson's yield value and η_c is Casson's viscosity.

The ratio between τ and γ at 145 s^{-1} defines the apparent viscosity of the sample ($\eta_{ap.}$ 145 s^{-1}; Prentice, 1984):

$$\tau = \eta_{ap.} 145\ s^{-1} \cdot \gamma 145\ s^{-1} \tag{2}$$

τ_c and η_c (Eq. (1)) and $\eta_{ap.}$ 145 s^{-1} (Eq. (2)) are used as response factors;

- τ_c represents the initial resistance of the preparation to flow when it is subjected to an external shear force (Prentice, 1984; Kleck, 1992). It is a characteristic parameter of preparations comprising internal three-dimensional (3-D) networks, typical of a gel (Provost et al., 1988). Quantitatively, it reflects the rigidity and cohesion between the molecules forming the internal 3-D structure (Martin et al., 1967);
- η_c *y* $\eta_{ap.}$ 145 s^{-1} represents the ease with which the bonds comprising the structure break during flow (Prentice, 1984). η_c has been determined at low γ, which are representative of the behavior of the systems during dispensing and storage (Warburton, 1996). $\eta_{ap.}$ 145 s^{-1} determines the resistance of the samples to being extended over the skin (Balzer et al. 1995).

2.4.1.2. Spreadability. The spreadability is represented by the thickness of the film that the preparation leaves on the skin, an important feature in a cosmetic (Barry, 1983). Those producing thinner films, that is, higher spreadability, are naturally of greater interest.

2.4.1.3. Transparency. The transparency of a gel, especially in cosmetics, is currently associated with its acceptance by the consumer (Comelles et al., 1992).

Table 1
The concentrations of samples and the response factors

Sample	Carbopol (% m m^{-1})	Ethanol (% m m^{-1})	Glycerine (% m m^{-1})	τ_c (Pa)	η_c (Pa s)	$\eta_{ap.}$ 145 s^{-1} (Pa s)	Spread. (cm^2 g$^{-1/2}$)	*T* (%)
1	0.5	30	5	24.6	2.3	0.157	1.25	81.6
2	0.5	10	2	38.8	3.9	0.118	0.98	4.7
3	1	30	5	43.5	8.5	0.177	0.90	75.4
4	0.5	30	2	25.6	2.0	0.184	1.27	90.8
5	0.75	20	3.5	90.9	1.2	0.291	0.86	0.3
6	0.75	20	3.5	74.4	2.4	0.118	0.83	1.2
7	1	10	2	87.8	2.7	0.173	0.78	23.5
8	1	10	5	107.1	3.3	0.330	0.79	21.6
9	1	30	2	71.8	2.8	0.005	0.94	90.3
10	0.5	10	5	76.5	1.4	0.082	1.19	15.9

τ_c, Casson's yield value; η_c, Casson's viscosity; $\eta_{ap.}$ 145 s^{-1}, apparent viscosity at 145 s^{-1}; Spread., spreadability; *T*, transmitance.

2.4.2. Methods

2.4.2.1. Flow behavior. Continuous flow measurements were performed at 25 °C with a Brookfield DV-II Plus apparatus coupled with an adaptor for small samples (R13) and the elements SC4 25 or 27, at intervals of 0.17 to 22 s^{-1}. The τ variation was analyzed as a function of the γ, maintaining the γ constant for 1 min at each stage of the up and down curves.

Furthermore, apparent viscosities (Eq. (2)) were determined at 145 s^{-1} and 25 °C with a 'Rheotest RV' and the element H1.

2.4.2.2. Spreadability. About 0.4 ± 0.05 g of gel, with an initial surface of 0.78 cm^2 and a cylindrical shape was obtained with a microtome. It was then pressed between the microtome and the surface of a graduated glass plate (6×6 cm, 25 g), on which weights of 50, 100, 200 and 500 g were placed at intervals of 1 min. The diameters during each interval are given as the area (cm^2). The variations of the area as a function of weight were then analyzed as response factors. Each datum is the average of three determinations at 25 °C.

This method is based on the standard method of Pozo et al. (1955) and has the advantage (as compared with Lardy et al., 2000, for example) of starting the assays with an equal surface and weight for the samples. The sample weight was fixed in order to perform the entire assay with all the samples, without surpassing the limits imposed by the glass, avoiding sliding and easily differentiating the behavior of different samples.

2.4.2.3. Transparency. Transmittance measurements at $\lambda = 610$ nm (Lambda 2, Perkin–Elmer) were obtained in cells of 1 cm light path (Vennat et al., 1991).

3. Results and discussion

3.1. Flow behavior

All the preparations gave rheograms characteristic of non-linear plastic flows, which are common in gels of Carbopol 940 and 941 (Barry and Meyer, 1979). In each one, the up curve of the rheograms was fitted by least squares to the usual flow equations (Marquard et al., 1997). The model with the best fit (r^2, residual analysis) was then chosen (Casson's model, Eq. (1)) and its characteristic parameters (τ_c and η_c) were used as response factors.

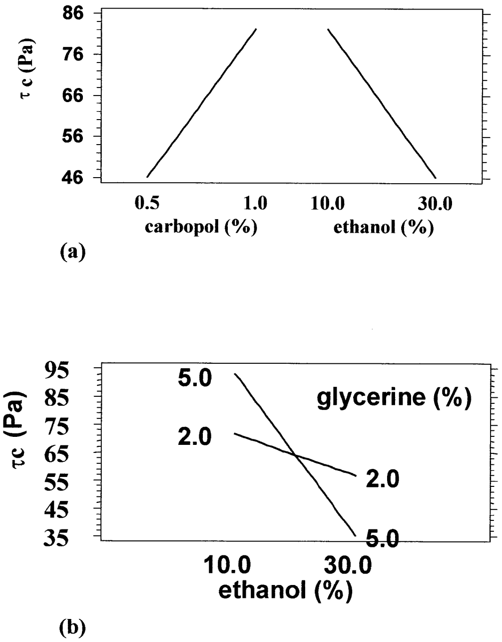

Fig. 1. The effect on Casson's yield value of (a) Carbopol and ethanol and (b) the ethanol–glycerine interaction.

3.1.1. τ_c

Range from 24.6 to 107 Pa (Table 1). The ANOVA design analysis indicates that there is a significant influence of the Carbopol and ethanol concentrations (significance level of $\alpha = 0.05$) and of the ethanol–glycerine interaction ($\alpha = 0.1$). The fitted predictive equation is:

$$\tau_c(\mathrm{Pa}) = -44.433 + 125.783{*}\mathrm{cb} + 0.712{*}\mathrm{et} + 25.843{*}\mathrm{gl} - 15.267{*}\mathrm{cb}{*}\mathrm{gl} - 0.720{*}\mathrm{et}{*}\mathrm{gl}$$

$$r^2(\text{adjusted for d.f.}) = 73.105\%, \quad \mathrm{SEE} = 15.024, \quad \mathrm{MAE} = 9.242$$

Fig. 1(a) shows the influence of the main significant factors, Carbopol and ethanol. Carbopol ETD 2020 is a polyelectrolitic copolymer. The mechanism of gelling by neutralizing (all the samples have a pH of 7) is based on the ionic repulsion of its charges. An increase in the polymer concentration increases the repulsion of the chains and the rigidity (τ_c) of the structure, although the affinity of the polymer for the solvent also affect the structure properties. According to Pena (1990), when the affinity is high, the polymer chains extend and increase their entanglement. At lower affinities, the polymer contracts and entanglement is reduced (a phenomenon observed in previous works; see Contreras and Sanchez, 2001). Since ethanol has a higher affinity for water than Carbopol, it causes the Carbopol to contract and the τ_c to decrease.

The effect of the ethanol–glycerine interaction (Fig. 1(b)) depends on their proportions. Thus, in the preparations low in ethanol (10% m m^{-1}), a rise in the glycerine concentration (5% m m^{-1}) increases the rigidity of the structure (τ_c) and the donor effect of the glycerine hydrogen bonds dominates. Those effect contributes together with the neutralizer, to increase the τ_c. However, when the ethanol concentration increases (30% m m^{-1}), an inverse effect is produced. The preparations low in glycerine (2% m m^{-1}) then produce more rigid structures than those higher in glycerine (5% m m^{-1}). Glycerine thus seems to favor the dehydrating properties of ethanol at the higher concentrations of the latter (see Contreras and Sanchez, 2001).

3.1.2. η_c

This factor represents the ease with which the bonds comprising the structure break during flow. The systems involved forces of van der Walls, ionic and hydrogen bonds of different energy and thereby causing variations in the η_c, which ranges from 8.5 to 1.2 Pa s (Table 1). Notwithstanding, in accordance with the ANOVA results, none of the analyzed factors have a significant influence ($\alpha \leq 0.1$), suggesting that, once the yield value has been exceeded, there is no difference in the behavior of the samples. The design can be expressed by the fitted linear equation:

$$\eta_c(\text{Pa s}) = 14.783 - 12.54{*}\text{cb} - 0.410{*}\text{et} - 3.155{*}\text{gl} + 0.311{*}\text{cb}{*}\text{et} + 2.9\text{cb}{*}\text{gl} + 0.066\text{et}{*}\text{gl}$$

$$r^2(\text{adjusted for d.f.}) = 60.116\%, \quad \text{SEE} = 1.322, \quad \text{MAE} = 0.507$$

Despite the fact that this equation hardly explains the variability observed in η_c (60%), it was used to construct Fig. 2(a), where its variation is represented as a function of the Carbopol and ethanol concentrations. Its slope is important and reflects more complex relationships between the two concentrations, probably including the quadratic effects for each of the variables.

It can be predicted (Fig. 2(b)) that the increase in η_c is related to high Carbopol, ethanol and glycerine concentrations, that is, with systems in which repulsion between the polymer chains dominates (Contreras and Sanchez, 2001). In cosmetics, gels that flow easily are generally preferred, that is, those with a low ηc value. This value is obtained by preparing systems with low proportions of Carbopol and ethanol and high proportions of glycerine, that is, those in which the

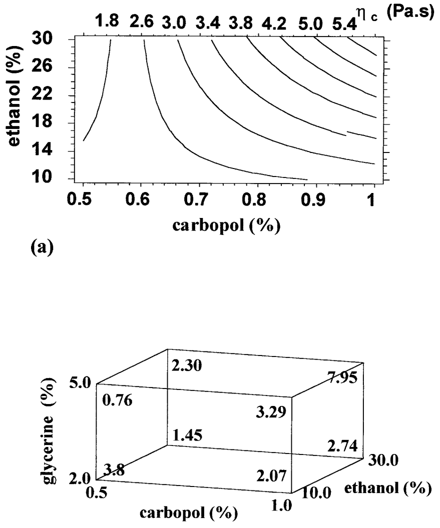

Fig. 2. The relationship between Casson's viscosity and the concentrations of, (a) Carbopol and ethanol and (b) the Carbopol–ethanol–glycerine interaction.

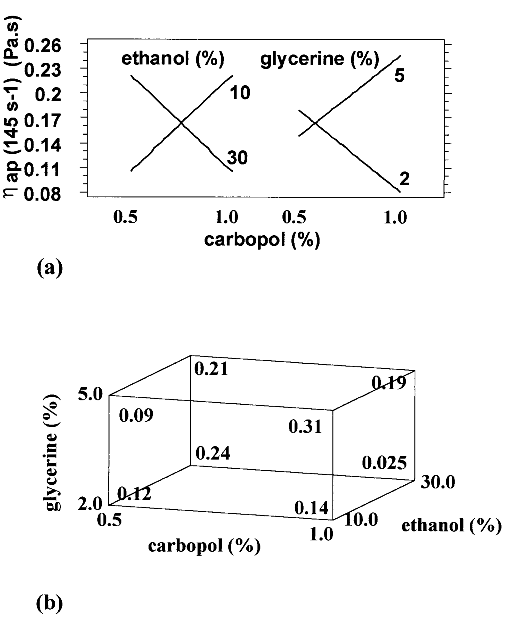

Fig. 3. The variation in the apparent viscosity at 145 s^{-1} vs., (a) the Carbopol–ethanol and Carbopol–glycerine interactions and (b) the Carbopol–ethanol–glycerine interaction.

repulsion forces of the polymer are lower and the number of hydrogen bonds between the Carbopol and the glycerine is high.

3.1.3. $\eta_{ap.}$ 145 s^{-1}

The $\eta_{ap.}$ 145 s^{-1} determines the resistance of the samples to being extended over the skin (Balzer et al., 1995). Easily extended ones are preferred, that is, those with a lower $\eta_{ap.}$ 145 s^{-1}. In our samples this parameter ranges from 0.33 to 0.005 Pa s (Table 1). As expected from the analyses performed, the Carbopol–ethanol interactions significantly affected this response variable for a level of $\alpha = 0.05$ and the Carbopol–glycerine ones for a level of $\alpha = 0.1$. The linear predictive equation (not included) only accounts for 51% of the observed variability. As occurred with η_c, the relationship model between the factors analyzed and $\eta_{ap.}$ 145 s^{-1} is more complex than a linear one. There is no relationship between η_c and $\eta_{ap.}$ 145 s^{-1}.

Fig. 3(a) presents the complex interactions between Carbopol–ethanol and between Carbopol–glycerine. Carbopol–ethanol produce systems with a high and equal $\eta_{ap.}$ 145 s^{-1} in two contradictory situations, (a) systems in which the polymer has a low affinity for the solvent (0.5% Carbopol and 30% ethanol) at the limit of Carbopol–ethanol compatibility and the contraction of the polymer chains dominates; and (b) systems in which the polymer has a greater affinity for the solvent (1% Carbopol and 10% ethanol) and the repulsion of the polymer charges dominates. In the latter systems, however, the addition of ethanol with its subsequent transformation into an adverse solvent means that its dehydrating effect on the polymer diminishes the viscosity.

The Carbopol–glycerine interaction gives rise to intermediate viscosities when the polymer concentration is low (0.5%), regardless of the concentration of glycerine. When the polymer concentration increases (1%), however, the viscosity is dependent on the concentration of glycerine. In the latter case, low glycerine concentrations (2%) produce low-viscosity systems in which the repulsion effect of the polymer chains dominates. A small rise in glycerine (5%) considerably increases the viscosity, which is also affected by the hydrogen bonds originating between the two substances.

Fig. 3(b) shows the influence of the interaction among the three factors. The samples with a high amount of Carbopol, the maximum amount of ethanol and the minimum amount of glycerine have the lowest $\eta_{ap.}$ 145 s^{-1}. They are thus more extendable than the preparations with high concentrations of Carbopol and glycerine and the lowest ethanol. The higher-energy bonds in the internal networks of the latter account for their lower extendability.

3.2. Spreadability

We have determined the ratio between area and weight by the least-squares method. The best fit for each sample is obtained for the ratio of the area the square root of the weight ($r^2 = 99.99$), with the slope being used as the response factor (Table 1), which is directly related to the spreadability. The tests are reproducible, as shown by the results obtained with samples 5 and 6, of identical composition, and the standard deviations (S.D.) obtained for each weight and sample in the three assays performed (data not included).

At the end of the test, the films are homogeneous with no visible fragmentation in any case, with samples 1 and 4 showing the greatest spreadability. The concentrations of Carbopol ($\alpha = 0.05$) and ethanol ($\alpha = 0.1$) have a significant influence. The spreadability can be expressed by the following linear equation:

$$\text{Spread.}(\text{cm}^2\ \text{g}^{-1/2}) = 1.136 - 0.637^{*}\text{cb} + 0.0160\text{et} + 0.0479\text{gl} - 0.00240^{*}\text{et}^{*}\text{gl}$$

$$r^2(\text{adjusted for d.f.}) = 72.056\%, \quad \text{SEE} = 0.0995, \quad \text{MAE} = 0.0696$$

Spreadability is inversely related to the polymer concentration and directly related to the ethanol concentration (Fig. 4(a)). An increase in the polymer concentration increases the repulsion between chains, increase the crosslinking between chains, and reduces the spreadability. The same effect occurs with a reduced ethanol concentration (10%), whereas high ethanol concentrations (30%) increase the spreadability due to the resulting dehydrating effect on the polymer.

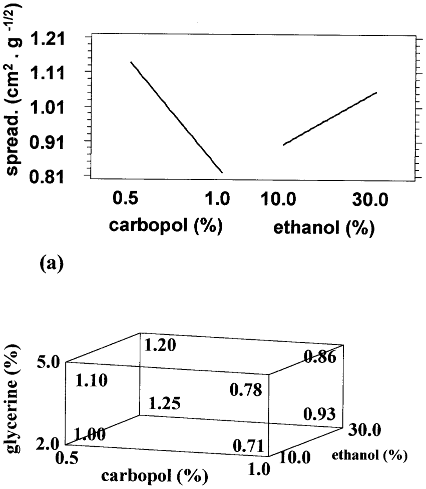

Fig. 4. The influence on the spreadability of, (a) Carbopol and ethanol and (b) the Carbopol–ethanol–glycerine interaction.

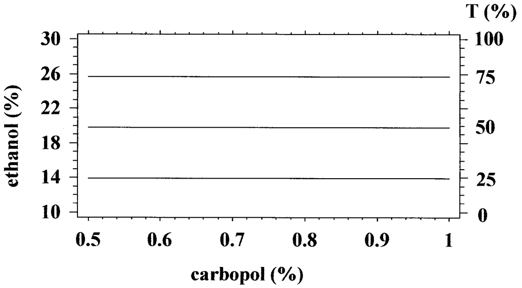

Fig. 5. The influence of Carbopol and ethanol on the transmittance of the samples.

The preparations that produce the thinnest films (Fig. 4(b)), suitable for cosmetics, are, therefore, those with low Carbopol (0.5% m m^{-1}) and glycerine (2% m m^{-1}) and high ethanol (30%). That is, those with the least repulsion between the polymer chains, fewest hydrogen bonds, and least entanglement. A change in any of these parameters (such as higher concentrations of Carbopol and glycerine and lower amounts of ethanol) leads to thicker films. Similar conclusions are obtained when using the individual areas produced with any weight as a response factor.

3.3. Transparency

The percentage of transmittance (T%) in the visible range is used as a response parameter (Table 1), with 100% transmittance equaling maximum transparency. Visually, the samples studied vary from transparent to opaque. The ANOVA analysis of the design reveals that only ethanol, of the factors analyzed, has a significant influence on this parameter ($\alpha = 0.05$), generating the following equation:

$$T(\%) = 27.57 + 3.405^{*}\text{et}$$

$$r^2(\text{adjusted for d.f.}) = 64.163\%, \quad \text{SEE} = 23.280, \quad \text{MAE} = 16.268$$

Despite the fact that the linear model explains only 64% of the variability seen in T%, we deduce that the maximum transparency (greatest T%) is nonetheless directly related to the ethanol concentration (Fig. 5). The increase in ethanol concentration increases the transmittance of the samples, up to 100% transmittance in the systems with the greatest amount of ethanol (30%), regardless of the polymer concentration. This result contrasts starkly with the behavior of other types of Carbopol (Pena, 1990), in which transparency depends on both the polymer and ethanol concentrations. In those cases, for a fixed Carbopol concentration, there is a continuous loss of transparency concomitant with a progressive increase in ethanol up to the limit of its compatibility with the polymer.

In fact, parallel assays have revealed that the substance responsible for the decrease in T% is not the ethanol, but another substance in the formula, menthol. The lipophilic properties of menthol require high ethanol concentrations to dissolve it and thus produce maximum transparency.

It seems that Carbopol ETD 2020, in contrast to other Carbopols, can withstand high amounts of ethanol, up to its compatibility limit with the polymer, with no marked loss of transparency. This quality, briefly remarked on by Goodrich (1993), makes it extremely interesting for use in cosmetics.

3.4. Relationships between different response factors

Any parameter (viscoelasticity, behavior flow, spreadability) depends on the relationships established between the molecules in the systems. The last aim of this work was, therefore, to analyze the possible relationship between the viscoelastic parameters (Contreras and Sanchez, 2001), representing the internal structure of the system, and the rest of the parameters determined. These relationships have been studied by the least-squares method and it can be seen that the linear relationships (with no independent term) provide the highest correlations (Table 2). The lower linear correlations may be due to the lack of good fit for the flow parameters. However, among the high correlations, the following particularly stand out.

(a) The correlation between τ_c and the equilibrium modulus (G_n). The most elastic systems, with the greatest number of chains that contribute elastically to the 3-D network, have the highest resistance to shear flow.

(b) The high correlation among the spreadability and the three viscoelastic parameters studied, especially with the degree of structuring of a gel ($\log G'/\log \nu$) and the ratio of the molecular weight and the critical molecular weight of the Carbopol (M/M_c). The systems with the least degree of structuring as well as those with the greatest entanglement produce thinner films. As this study shows, a remarkable amount of information on the internal structure of Carbopol systems can be obtained by a simple, economic assay with a long tradition in pharmaceutical technology.

4. Conclusions

A 2^3 factorial design (ten samples) only allows first-degree polynomial equations to be deduced. The relationships among the concentrations of Carbopol, ethanol and glycerine, and the τ_c and spreadability of the gels can be explained by these equations. Similar results were obtained with the viscoelastic parameters (Contreras and Sanchez, 2001). Nonetheless, the fit is not as good when it

Table 2
Lineal relationship (r^2) between viscoelastic (a, b, c, d), flow (e) and spreadability (f)

	G_n^a (Pa)	M/M_c^b	Log $G'/\log \nu^c$ (Pa Hz^{-1})	G''^d (Pa)
τ_c (Pa)^e	94.7%	82.33%	77.5%	95.22%
η_c (Pa s)^e	64.98%	65.69%	70.4%	68.21%
$\eta_{ap.}$ 145 s^{-1} (Pa s)^e	81.9%	71.94%	74.9%	82.60%
Spread. (cm^2 g$^{-1/2}$)^f	78.7%	92.6%	96.8%	81.57%

[a], Equilibrium modulus; [b], ratio polymer molecular weight and critical molecular weight; [c], degree of structuring; [d], viscous modulus (see Contreras and Sanchez, 2001); [e], (see Table 1); [f], (see Table 1).

comes to explaining the complex relationships among the components, which determine the values of η_c and $\eta_{ap.}$ 125 s^{-1}.

This lack of fit may be affected by the difficulty in obtaining flow equations (Marquard et al., 1997), which are subsequently used as response variables.

In any case, however, the application of experimental design techniques to gel preformulation studies has been shown to be a useful tool for the formulator, allowing the determination of the relationships among variables, and saving time and money.

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