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The Effect of Phenol on the Electrolyte Flocculation of Certain Polymeric Dispersions to Thixotropic Gels

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Aqueous dispersions of an acrylate-methacrylate, a water-insoluble copolymer, were prepared by a coacervation technique. Addition of sodium chloride (0.2 *M*) to the dispersion (10%, w/v) converted the system to a thixotropic gel which turns fluid on shaking and reverts to gel on standing. Phenol (0.03 *M*) inhibited the gelling effect of the electrolyte. Among the various phenolic compounds tested, phenol displayed the strongest and chlorocresol the weakest antigelling property. Sodium chloride reduced the electropotentials (index of particle–particle repulsiveness) of the polymer dispersions, while phenol increased the potentials. It is thought that the phenol solution acted as a dielectric which increased the interparticle repulsive potential, hence its antiflocculant effect.

KEY WORDS: acrylate-methacrylate; coacervation; polymer flocculation; repulsive potentials; phenol effect.

INTRODUCTION

The acrylate-methacrylates are water-insoluble copolymers but their aqueous dispersions can be formed readily by the addition of excess water to an ethanol solution of the copolymer (1). Concentrated dispersions can be converted to gels by the addition of an electrolyte (e.g., 0.2 *M* NaCl). These gels display thioxotropic flow behavior (2), becoming fluid on shaking and reverting to a gel on standing. Their viscosity increases rapidly within a few seconds after the addition of an electrolyte to the dispersion. This flow property may be exploited in the development of mucoadhesive gels for sustained-release delivery of biologically active substances to obtain local effects. The compatibility of phenols with these gel systems was studied because they have antiseptic properties used against mucosal inflammations, and they may serve in the gel formulation as preservatives.

MATERIALS AND METHODS

An acrylate-methacrylate copolymer containing a small proportion of quaternary ammonium (cationic) groups, 33 mol mol^{-1} polymer chain (3), was received from Bhom Pharma Darmstadt under the trade name Eudragit RS100. Ethanol (i.e., 96% alcohol BP) was used as solvent for the polymer in the coacervation procedure. Phenol, resorcinol, chlorocresol, methylparaben, and sodium chloride were all analar grade, BDH.

Preparation of the Aqueous Gels and Their Evaluation

The polymer (10 g) was dissolved in ethanol (15 ml) after allowing 24 hr of solvation. Water (85 ml) was added to the ethanolic solution and shaken vigorously to form a gel. This gel was strongly cohesive and could not be dispersed to a fluid by shaking. It was converted to a fluid by stirring with a Silverson mixer (Model VS104) at 1500 rpm for 15 min. The resulting colloidal dispersion was stable and did not revert to a gel on standing (i.e., the system was nonthixotropic). To impart a thixotropic property an electrolyte (5 mL of 4 *M* NaCl) was added to the polymer dispersion (100 mL), giving an electrolyte concentration of 0.2 *M* in the dispersion. The dispersion reverted to a gel on standing. Less concentrated dispersions did not form a gel on standing. Also, the lowest concentration of the electrolyte that readily converted the 10% dispersion to a gel was 0.2 *M* (2). In other experiments a phenolic compound was incorporated in the dispersion either 1 min before or 1 min after addition of the electrolyte. Test concentrations of the phenolic compound in the polymer dispersion varied from 0.01 to 0.05 *M*, while those of sodium chloride varied from 0.1 to 0.4 *M*.

Change in the consistency of the dispersion from fluid to gel (i.e., a thixotropic behavior) was determined by measuring the depth of penetration of a plunger into the sample at time intervals (2). Each determination was carried out in triplicate; results were reproducible to ±8.3% (SD) of the mean.

Electropotentials of the polymer dispersions alone, containing the phenolic compound, and/or sodium chloride were determined using the PHYWE pH meter/potentiometer. Readings were taken immediately after the addition of sodium chloride, before gellation would occur. The pH levels of solutions of the various phenolic compounds were also measured with the same equipment.

RESULTS AND DISCUSSION

A decrease in the extent of penetration of the plunger into the dispersion indicates a change from a fluid to a gel consistency. After the addition of sodium chloride (0.2 *M*), penetrability decreased linearly with time to an equilibrium depth, 2.8 cm (Fig. 1), which is an index of the final gel consistency.

In a previous study (2) it was noted that at the consistency corresponding to a penetration depth of 4 cm, the dispersion could not be poured readily from the container. This consistency was considered the gel point, and the time taken to attain it as the apparent time lag; after the addition of sodium chloride (0.2 *M*) it was 20 min (Fig. 1). When the gel was redispersed to a fluid by manual shaking for 1 min, the redispersed system reverted to a gel at a similar rate. The addition of phenol (0.03 *M*) 1 min before sodium chloride inhibited gel reformation. For instance, the equilibrium depth was then 13.6 cm, and the gel point was not attained during the 1-hr test period. The addition of phenol (0.03 *M*) 1 min after sodium chloride produced a similar result (Fig. 1). A higher phenol concentration (0.05 *M*) completely abolished gel reformation. Phenol thus antagonized the flocculating effect of sodium chloride.

Phenol is a weak acid with a low degree of dissociation to produce phenolate anions (the pH of the 0.03 *M* solution was 6.7); hence, alone it was unable to flocculate the poly-

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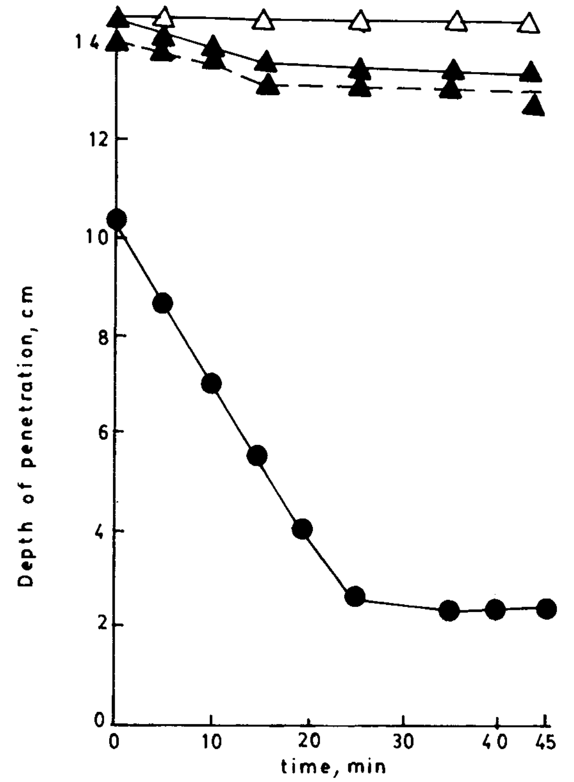

Fig. 1. Changes in the sol-to-gel consistency of the polymer dispersion (10%, w/v) containing phenol at 0.0 *M* (●), 0.03 *M* (▲), and 0.05 *M* (▲) and challenged by sodium chloride at 0.2 *M* (△). Phenol was added 1 min before NaCl (——) and 1 min after NaCl (- - -).

mer dispersion to a gel at the test concentrations 0.01 to 0.05 *M*. Sodium chloride, being a strong electrolyte, flocculated the aqueous polymer dispersions to a gel consistency. The mechanism is based on the absorption of Cl^- anions by the polymer cationic groups to cause charge neutralization and hence a lower particle–particle repulsive potential (2,4). On the other hand, the mechanism for the antigelling effect of phenol is not immediately obvious. However, it is known that the extent of attraction/repulsion between two charged particles depends on the dielectric constant of the intervening medium. The force of interaction (*F*) between two charged particles relates inversely to the dielectric constant of the medium (ϵ) as given by Coulomb's law (5):

$$F = \frac{Z_1 Z_2}{\epsilon r^2} \tag{1}$$

where Z_1 and Z_2 are the charges on the particles separated by a distance, *r*. When the particle charges are similar, as was the case in this study (i.e., the polymer cationic charges), the nature of the interaction is mutual repulsion. The function of a dielectric is to keep charges apart with lesser interaction, thus a high particle–particle repulsion is associated with a low dielectric constant of the medium. It was not possible to measure the actual values of dielectric constants for phenol and water in the present study because of technical constraints. However, values reported in the literature (6) were 9.78 (liquified phenol) and 78.54 (water) at 25°C. These values suggest that the presence of phenol in the polymer dispersion may have reduced the dielectric constant of the medium, leading to higher mutual repulsiveness of the disperse polymer particles. The electropotential of the polymer dispersion may be taken as an index of the particle–particle repulsiveness. Indeed sodium chloride reduced the potentials as a result of Cl^- anion adsorption, while phenol increased the potentials by its dielectric effect (Fig. 2). In the presence of phenol (0.05 *M*), sodium chloride was less effective in decreasing the potentials to a critical level that would result in rapid flocculation of the polymer particles to a gel.

To test the dielectric model the antigelling effects of phenol analogues which were less effective in increasing the electropotentials of the dispersion were measured. The results (Table I) showed that these analogues were also less effective in antagonizing the flocculating power of sodium chloride, compared with the parent compound, phenol. The equilibrium depths of penetration into the dispersions decreased with decreasing values of the electropotentials (Table I), thus supporting the suggestion that the potential was a measure of the particle–particle repulsiveness.

A further increase in electrolyte concentration from 0.2 to 0.4 *M* in the absence of phenol shortened the apparent time lag for attaining the gel point (Table II). With phenol (0.05 *M*) the electrolyte was unable to revert the dispersions to gels even at this high concentration level.

A further decrease in the electropotentials of the dispersions at this electrolyte concentration level (0.2 to 0.4 *M*) was slight (Fig. 2). The increase in electrolyte concentration was not matched by a corresponding decrease in the electropotentials, hence the high electrolyte concentration was unable to reverse the phenol effect. Nevertheless, the high electrolyte concentrations flocculated the dispersions to sus-

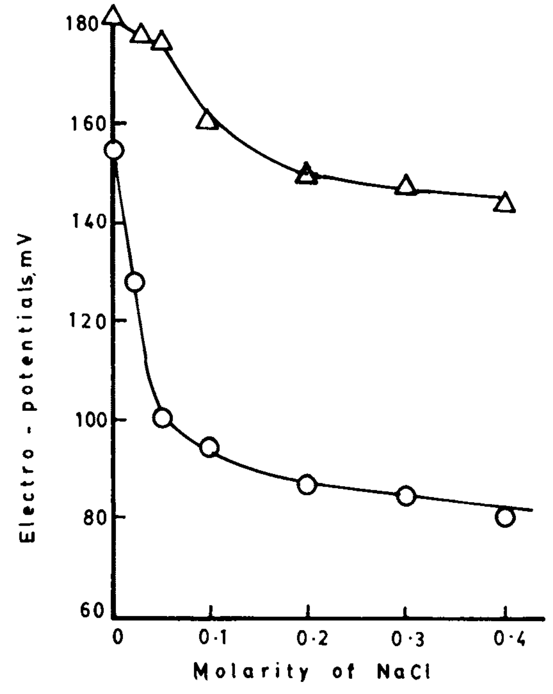

Fig. 2. Effect of electrolyte concentration on the electropotentials of the polymer dispersion only (○) and the dispersion plus 0.05 *M* phenol (△).

Table I. Effect of Phenols on the Penetration of the Plunger to an Equilibrium Depth into the Electrolyte-Challenged Dispersions and Their Electropotentials[a]

Phenol compound	Equilibrium depth of penetration (cm)	Electropotential (mV)	
		With NaCl (0.2 *M*)	Without NaCl
Control 1	14	—	155
Phenol	13.6	150	185
Resorcinol	9	135	165
Methylparaben	5	128	160
Chlorocresol	3.5	125	156
Control 2	2.5	88	—

[a] Control 1 is the polymer dispersion only, and control 2 is the polymer dispersion with sodium chloride (0.2 *M*). The phenolic concentration in the dispersion was 0.05 *M*, and phenol was added 1 min before NaCl.

Table II. Effect of Electrolyte Concentration on the Flocculation Characteristics of the Polymer Dispersions

Electrolyte concentration (*M*)	Equilibrium depth of penetration (cm)		Apparent time lag (min)	
	Without phenol	With phenol (0.05 *M*)	Without phenol	With phenol (0.05 *M*)
0.0	14	14	—[a]	—
0.1	4	14	25	—
0.2	2.8	14	20	—
0.3	2.5	13.5	8	—
0.4	2.5	13	6	—

[a] No reversion to a gel consistency; rather, dispersions containing NaCl (0.2 to 0.4 *M*) changed to coarse suspensions of polymer floccules.

pensions of coarse polymer particles, with eventual separation of a clear aqueous layer from the floccules. The onset of this phase separation depended on the electrolyte concentration, being 30 min (0.4 *M* NaCl), 50 min (0.3 *M* NaCl), and 5 hr (0.2 *M* NaCl). It is believed that in the presence of phenol, the flocculating power of the electrolyte was weak and hence particle aggregation occurred at a slow rate to form discrete particles. Rapid and extensive flocculation, on the other hand, leads to three-dimensional cohesion of particles to form a gel network.

These results show that high concentrations of phenolic preservatives are incompatible with the gel systems studied, as the electrolyte-gelled systems became liquefied in the presence of phenols at concentrations >0.03 *M*. To produce this effect, phenol increased the interparticle mutual repulsiveness; thus in certain situations it may be used to stabilize this type of polymeric dispersion against the flocculating effect of electrolytes.

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