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Influence of Aging on the Physical-Mechanical Properties of Acrylic Resin Films Cast from Aqueous Dispersions and Organic Solutions

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ABSTRACT

The physical-mechanical properties of the enteric copolymers, poly(methacrylic acid, ethyl acrylate) Eudragit® L100-55, and Eudragit® L30D have been investigated. Free films of the copolymer containing varying levels of glyceryl triacetate (triacetin) and citrate ester (Citroflex®) plasticizers were prepared by both aqueous and solvent casting techniques. Conditioned films were stored at different humidities and temperatures for predetermined time periods prior to testing. Free films with plasticizer concentration ranging from 0 to 30% by weight of the polymer demonstrated that physical aging at room temperature resulted in physical-mechanical changes as the stress-strain curves indicated a decrease in the percent elongation with increases in the tensile strength. Films prepared from the aqueous latex approached a constant state of equilibrium at a faster rate than films prepared from isopropyl alcohol, where the mechanical properties approach a relatively constant value. Free films containing varying amounts of the plasticizer, triethyl citrate, were stored under different humidity and temperature conditions. In addition, a headspace-gas chromatography (HSGC) method was developed to correlate solvent residues with mechanical properties. The results indicated that an increase in temperature and humidity accelerated the rate of solvent evaporation as a function of time. High vacuum and low humidity conditions were demonstrated to be ineffective conditions for solvent removal. Solvent residues were found in all films after 48 hours of exposure to temperatures up to 60°C and/or exposure to relatively high humidity conditions. A direct relationship between plasticizer content and rate of solvent evaporation from the film was established. Higher concentrations of the plasticizer were found to augment the evaporation of the solvents. This enhanced evaporation was due to the stronger molecular interaction forces between the polymer and the plasticizer than between the polymer and the solvent.

INTRODUCTION

Acrylic resin copolymers have been used in the pharmaceutical industry for coating purposes for over 30 years.[1] The applications and physical-chemical properties have been well described in the literature.[2] Copolymers of methylmethacrylate and ethyl acrylate as ester components with methacrylic acid have been used extensively because of their properties for enteric protection. These polymers are commercially available as a 30% W/W aqueous dispersion (Eudragit® L 30D) and as a spray-dried powder from the aqueous latex dispersion (Eudragit® L 100-55). Film coating with the Eudragit® polymers can be performed with aqueous dispersions or from organic solvent solutions. Although the present trend in film coating is toward aqueous-based film coating, both aqueous and alcohol-based film-coating processes are still used today in the pharmaceutical industry.

Since many polymeric materials that are used in pharmaceutical formulations are brittle in nature, they usually require the use of plasticizers. Plasticizers will increase the workability, flexibility, and distensibility of the polymeric material.[3] The addition of a plasticizer will modify the physical and mechanical properties of the polymer[4,5] and lower the melt viscosity,[6] elastic modulus, and glass transition temperature.[7,8] These effects are the result of the plasticizer weakening the polymer intermolecular attractions and increasing the polymer's free volume, thus allowing the polymer chains to move more readily and increase its flexibility.

When an amorphous polymer is cooled from the liquid into the glassy state, it is in a metastable condition. The relaxation towards an equilibrium state is commonly referred to as physical aging.[9] Even though this equilibration process is slow at ambient conditions, significant changes in the properties of the polymers may occur during aging.[10,11,12] Several theories have been published to explain the mechanisms involved during the aging process.[13,14,15] Aging of pharmaceutical polymers can occur and may be manifested by changes in the physical and mechanical,[16] dissolution,[17] and permeation properties.[18]

Wicks reported that solvent removal from polymeric films requires heating the film to a temperature significantly above the glass transition temperature of the solvent-free polymer.[19] Since these glass transition temperatures can be well above normal coating conditions, careful attention should be placed on the removal of residual solvents from the film when solvent-based polymer solutions are to be used in film coating. The determination of trace volatile impurities has become a very important issue, particularly if the polymers are to be used in the medical field.[20] Volatile compounds in solid samples may be determined by HSGC. Headspace techniques have been developed that allow volatile compounds to be removed from a non-volatile matrix and injected into the gas chromatograph as a vapor instead of direct injection or such complicated and time consuming procedures as steam and conventional distillation, solvent extraction, adsorption, and purge and trap techniques. Multiple headspace extraction,[21] standard addition,[22] and constant heating[23] are different procedures used to determine volatile compounds in polymers and solid samples. Dynamic headspace gas chromatography has also been shown to be a valuable tool for the determination of these volatile compounds.[24]

The objectives of this investigation were to study the stability and the physical and mechanical changes that occur in acrylic resin copolymers during the aging process and the effects of different types and amounts of plasticizers on the mechanical behavior of aqueous and solvent cast films. In addition, a suitable method to quantitate the residual organic solvents remaining in the films during the equilibration process was developed. Finally, an evaluation of solvent residues was performed as a function of temperature, humidity, storage time, and plasticizer content.

EXPERIMENTAL

MATERIALS

The plasticizers triethyl citrate (TEC), acetyl triethyl citrate (ATEC), tributyl citrate (TBC), and acetyl tributyl citrate (ATBC) were donated by Morflex, Inc., Greensboro, NC. Triacetin was obtained from Aldrich Chemical Co., Milwaukee, WI. The copolymers methacrylic acid and ethyl acrylate (Eudragit® L100/55, L30D) were donated by Röhm Pharma, Weiterstadt, Germany. Isopropyl alcohol, certified A.C.S., was purchased from J.T. Baker, Inc., Phillipsburg, NJ.

METHODS

Film Preparation. The films from aqueous latexes of Eudragit® L 30D were prepared by casting a 10% (W/V) dispersion containing 0-30% plasticizer based on the dry polymer weight. The dispersions were cast onto Teflon® molds (6" x 6") and dried on a leveled plate at 25°C and 50% relative humidity. To facilitate the film sample preparation, the films in the molds were then placed in a 100% relative humidity chamber for 3 hours before being cut to dimensions of 6" x 1/2" with a stainless steel scalpel. For films prepared from isopropyl alcohol, a 20% (W/W) solution was prepared, and the plasticizer content was based on the weight of dry polymer. Solutions were cast with the aid of a Universal Film Casting Knife (Paul N. Gardner Co. Inc., Pompano Beach, FL) onto a Teflon® FEB protective overlay (Cole Palmer Instrument Co. Inc., Chicago, IL), and the films were dried for approximately 12 hours. The dried films were removed from the overlay and cut to dimensions of 6" x 1/2" with a stainless steel scalpel. Films were then allowed to equilibrate in a sealed desiccator chamber under various humidity and temperature conditions for predetermined periods of time.

Stress-Strain Analysis. A minimum of five samples from each formulation were tested using an Instron® 4201 universal testing apparatus. The method used for evaluating the mechanical properties was based on the guidelines of the American Society for Testing Materials method D 882-75b.[25] The initial grip separation was 100 mm. The tensile strength, the elongation at break, and the elongation modulus for each film were calculated from the resulting stress-strain curves.

Solvent Residue Analysis. Films were prepared according to the methodology described above. All films were made with the same initial amount of isopropyl alcohol. Approximately 5 mg samples were taken from aged films and placed in special vials. One milliliter of a 0.5% (W/V) solution of triethanolamine in double distilled water containing n-propanol as the internal standard was added to each sample. Triethanolamine was added to increase the pH of the solution in order to dissolve the polymeric film. Sample vials were tested in a Tekmar® 7000 headspace autosampler connected to a Tracor® 540 gas chromatogram with a Flame Ionization Detector (FID). A 30 meter x 0.53 mm I.D. (J&W Scientific, Folsom, CA) column was used with helium carrier gas at 8 ml/min. The operating conditions were oven temperature, 35°C; inlet temperature, 130°C; and detector temperature, 240°C. The headspace conditions were sample temperature, 80°C; equilibrium time, 10 min.; transfer line temperature, 100°C; vial pressurization (9 psi), 0.5 min.; loop fill, 0.5 min.; injection time, 0.5 min; and sample loop, 2.0 ml.

RESULTS AND DISCUSSION

Exposure of the films prepared from the aqueous dispersion (Eudragit® L 30D) to high humidity conditions after coalescence facilitated the removal of the film from the mold. In addition, film strips with clean, parallel edges were obtained with no visible imperfections, such as scratches or nicks. The casting knife produced uniform films cast from viscous organic polymer solutions. Thin films (150 μm) with less than 5% variation in thickness were obtained from both casting methods. The pure polymeric films were transparent, as were the films that were obtained when triacetin and the water soluble citrate esters were included as plasticizers up to a concentration of 30% by weight of the polymer. The water insoluble plasticizers, tributyl citrate and acetyl tributyl citrate, changed the films from clear to opaque when used in concentrations above 10% by weight of the polymer. This immiscibility was attributed to the differences in polarity and refractive index, as well as the inability of these plasticizers to disrupt the intermolecular hydrogen bonding present in the methacrylic acid copolymer chains.

For all aqueous and organic cast film formulations, physical aging resulted in a stiffening of the acrylic films. This decrease in flexibility was observed as the stress-strain curves of the films changed from a typical ductile behavior to a more brittle behavior at room temperature. Films prepared from the aqueous latex dispersion Eudragit® L 30D reached equilibrium at a faster rate than films prepared from isopropyl alcohol solutions when stored at room temperature. This equilibrium was observed when the mechanical properties of the polymeric films appeared to approach a stable limiting value. Similar results were found by List and Kassis who reported that the permeability of Eudragit® L 30D films reached a final optimal value in a few days when stored at room temperature.[26] These workers related this phenomenon to a marked enthalpy relaxation of the films at room temperature. However, the extent of this relaxation phenomenon has been demonstrated to be affected by the length of drying time and the aging enviroment.[12-14,27] In this study, several types and levels of plasticizers were incorporated in the polymer films, and their effect on the polymer's equilibration process was followed as a function of time. The results in Table 1 show the mechanical properties for films prepared from the aqueous latex dispersion Eudragit® L 30D containing varying amounts of the plasticizer triethyl citrate. At 23°C and 50% relative humidity, a reduction in elasticity was observed with increasing time. After coalescence, films containing 10% triethyl citrate showed no significant changes in the elastic modulus, the percent elongation, or the tensile strength in the first 30 days. Due to an early testing failure of the film, no data on the tensile strength and elongation percent could be obtained for the 90- and 180-day time intervals. However, for films containing 20% and 30% triethyl citrate notable differences in the elongation were detected during the initial days of equilibration. Stress-strain curves exhibited plastic deformation or cold flow during the testing analysis. After this initial equilibration time, the films failed in an apparently brittle manner when tested under the same conditions. This transitional change in mechanical behavior was attributed to residual moisture in the film, since water and the plasticizer will have a synergistic influence on the film's mechanical properties.[28]

Results from the physical-mechanical studies of Eudragit® L100-55 films cast from isopropyl alcohol indicated that film properties change as a function of time during the curing or equilibration period. The results in Figure 1 demonstrate the changes in film

Table 1 Mechanical properties of films prepared from Eudragit® L 30D stored at 23°C and 50% relative humidity containing varying levels of triethyl citrate.

		Tensile Test		
Concentration	**Time** (Days)	**Tensile Strength** (MPa)	**Elongation %**	**Elastic Modulus** (MPa)
10%				
	7	30.341 ± 6.162	0.985 ± 0.334	2485.256 ± 494.558
	30	32.718 ± 9.583	0.825 ± 0.266	3258.145 ± 588.454
	90	-	-	3309.481 ± 400.564
	180	-	-	3179.784 ± 744.470
20%				
	7	18.690 ± 2.105	3.384 ± 0.600	881.142 ± 44.027
	30	24.373 ± 7.377	3.600 ± 1.280	1115.478 ± 304.846
	90	27.095 ± 5.483	2.342 ± 1.250	986.154 ± 187.267
	180	29.847 ± 3.923	1.572 ± 0.157	1117.854 ± 324.453
30%				
	7	5.184 ± 2.252	118.156 ± 49.030	192.475 ± 49.554
	30	6.926 ± 2.281	104.981 ± 42.784	269.350 ± 107.391
	90	10.726 ± 3.301	35.714 ± 27.513	338.906 ± 154.250
	180	15.182 ± 2.253	25.914 ± 14.147	492.451 ± 99.452

[a] Data reported as the mean ± SD of 8 film samples.

properties as a function of time when the films were stored at 23°C and 50% relative humidity. The elongation decreased from 100-150% initially to less than 5% after 60 days, when it contained up to 30% of triethyl citrate. Similar results were found with the other citrate plasticizers studied, as shown in Figure 2, in which the effect of long-term equilibration demonstrated an immediate increase in tensile strength during the first 14 days of storage at 23°C and 50% relative humidity. The effect of long-term equilibration on the elongation of plasticized film samples is presented in Figure 3. In all cases, a decrease in

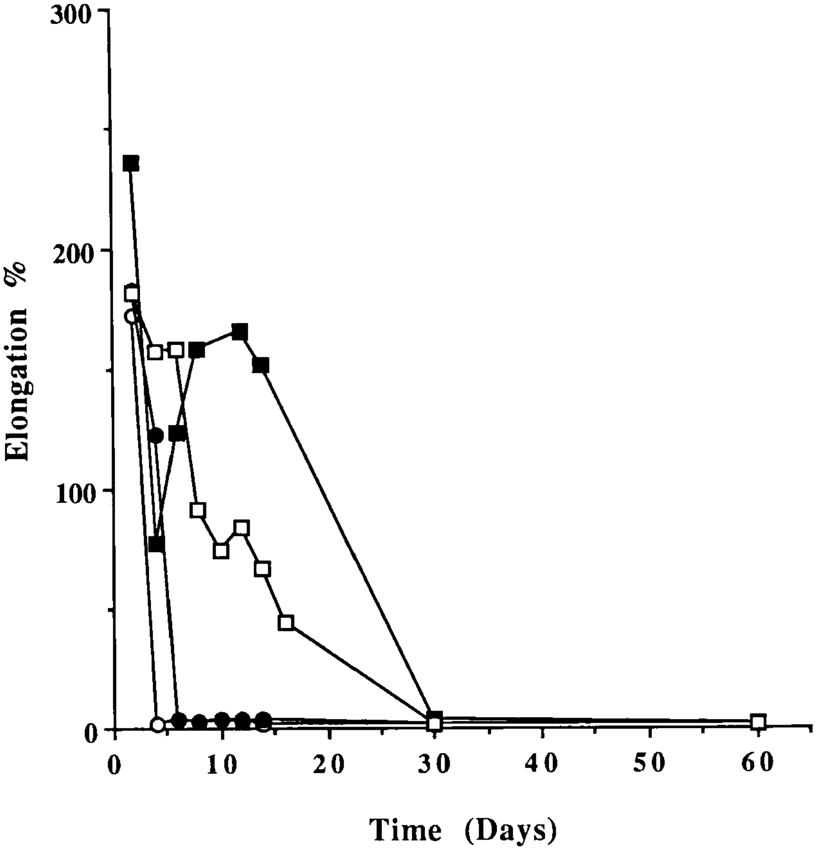

Figure 1: The effect of physical aging on the elongation percent of Eudragit® L100-55 films containing varying levels of triethyl citrate. Key: (○) 0%; (●) 10%; (□) 20%; (■) 30%.

elongation was noted with increasing aging time. The decrease in elongation of the films was attributed to the loss of the plasticizing effect resulting from declining levels of solvent residues, thereby allowing the polymeric chains to proceed towards a more dense equilibrium state. Solvent residues in conjunction with the plasticizers will increase the mobility of the polymeric chains by causing an increase in free volume. This increase in free volume will enable the polymer chains to move and orient themselves parallel to the direction of flow, causing the polymeric film to behave like a tough and ductile material.

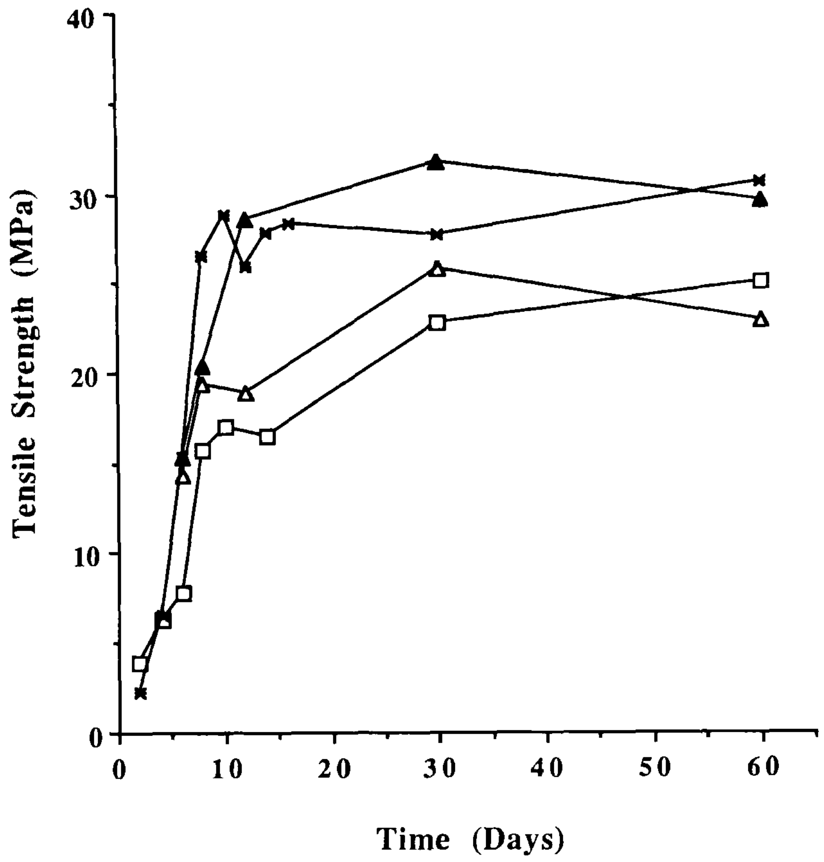

Figure 2: The effect of physical aging on the tensile strength of Eudragit® L 100-55 films containing different types of plasticizer. Key: (O) 20% TEC; (*) 20% TRI; (▲) 20% ATEC; (Δ) 20% ATBC.

In order to quantitate the effect of residual isopropyl alcohol on the physical-mechanical properties of the film, a sensitive assay to determine isopropyl alcohol residues in the film was developed. This assay was performed in a static headspace apparatus connected to a gas chromatogram. The films were completely dissolved prior to analysis to ensure that no solvent was entrapped within the polymer and to promote rapid equilibration. N-propanol was chosen as the internal standard in the assay, due to its high similarity in structure and chemical properties to isopropyl alcohol. The calibration curves obtained for isopropyl alcohol with and without the inclusion of the polymer are illustrated

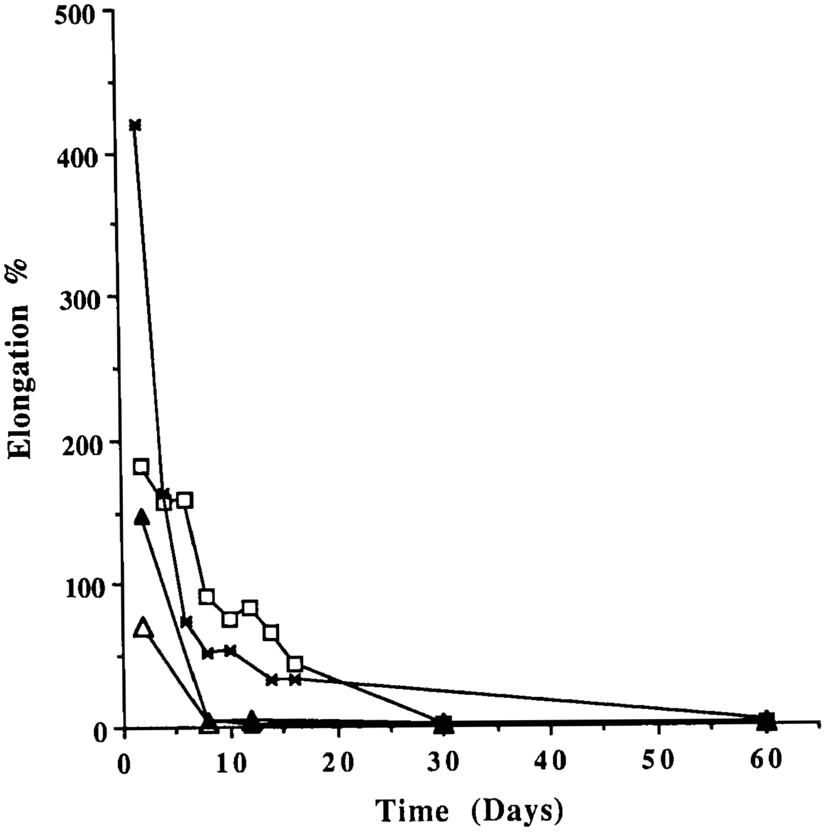

Figure 3: The effect of physical aging on the percent elongation of Eudragit® L 100-55 films containing different types of plasticizer. Key: (□) 20% TEC; (*) 20% TRI; (▲) 20% ATEC; (Δ) 20% ATBC.

in Figure 4. There was a linear relationship between the area ratio of isopropyl alcohol to internal standard and the concentration of the isopropyl alcohol in the polymer solution over the range of 1 to 1000 μg/ml. A typical chromatogram for the quantitation of isopropyl alcohol in 0.5% triethanolamine solution and the chromatogram obtained in the presence of the polymer is shown in Figure 5.

The percent of isopropyl alcohol remaining in the polymeric films stored at 40°C and containing different amounts of plasticizer is presented in Figure 6. As the concentration of the plasticizer increased, the evaporation rate of the isopropyl alcohol also

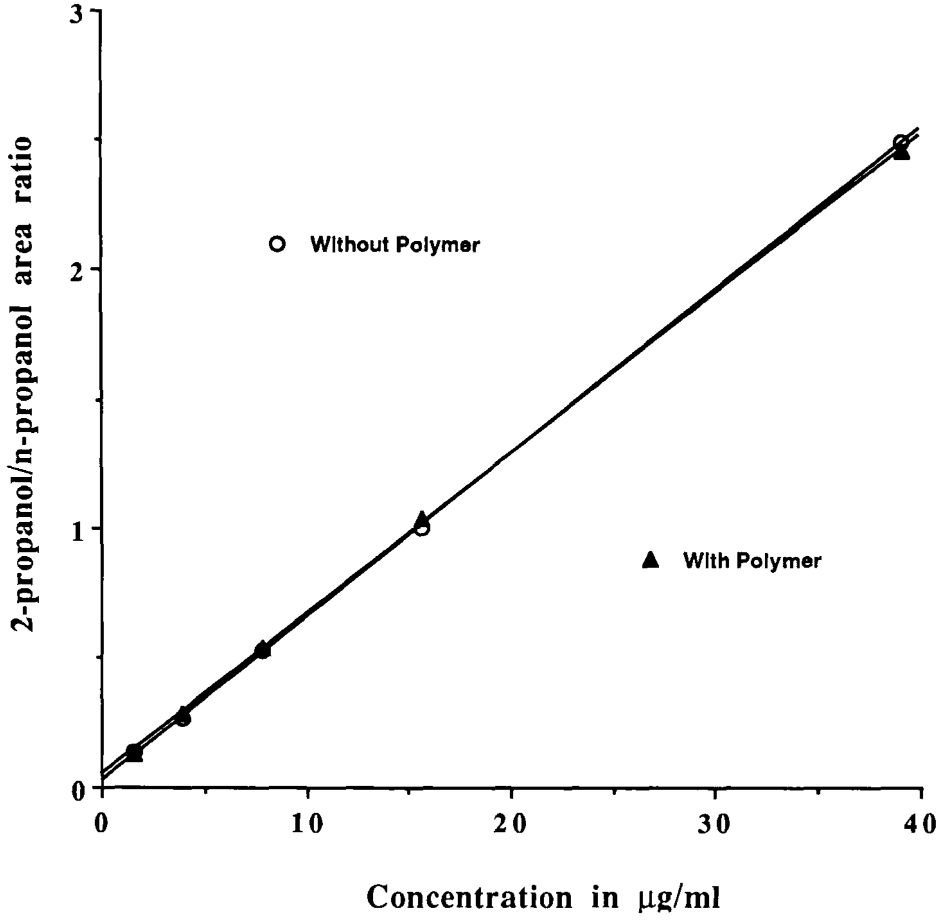

Figure 4: Comparison of plot detector response for standards containing no polymer and standards containing the polymer (peak area ratios of isopropyl alcohol to the internal standard).

increased. This relationship was seen at 23°C, 40°C, and 60°C and for films stored at 23°C and 0%, 50%, and 100% relative humidities. It should be noted that these differences in evaporation rates of the solvent were observed in the first 12 hours of the initial drying process at room temperature before the films were exposed to the different storage conditions. This increase in evaporation rate was due to the stronger molecular interaction forces between the polymer and the plasticizer than with the solvent. Isopropyl alcohol will

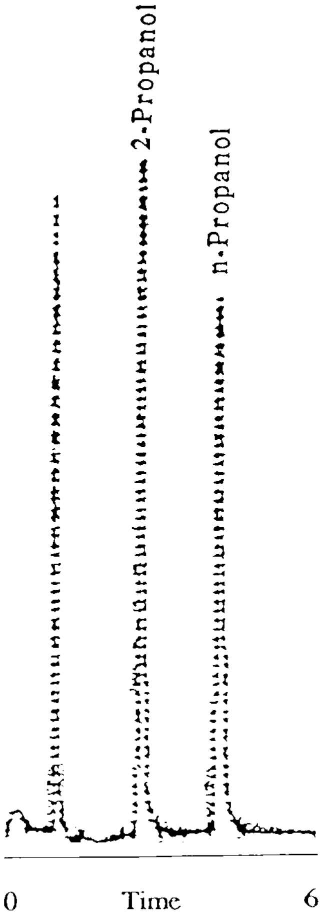

Figure 5: Typical chromatogram of 2-propanol and n-propanol.

interact with the copolymer by electrostatic forces and hydrogen bonding. These are the same forces involved between the plasticizers and the copolymer. The plasticizers will compete with the isopropyl alcohol for the active sites on the copolymers. Since the plasticizers have higher dispersion forces and boiling points than the isopropyl alcohol, removal of the solvent would be favored as the plasticizer concentration is increased. The isopropyl alcohol will then diffuse to the surface of the film under the influence of a concentration gradient. Plasticizers will also increase the mobility of the polymer chains and

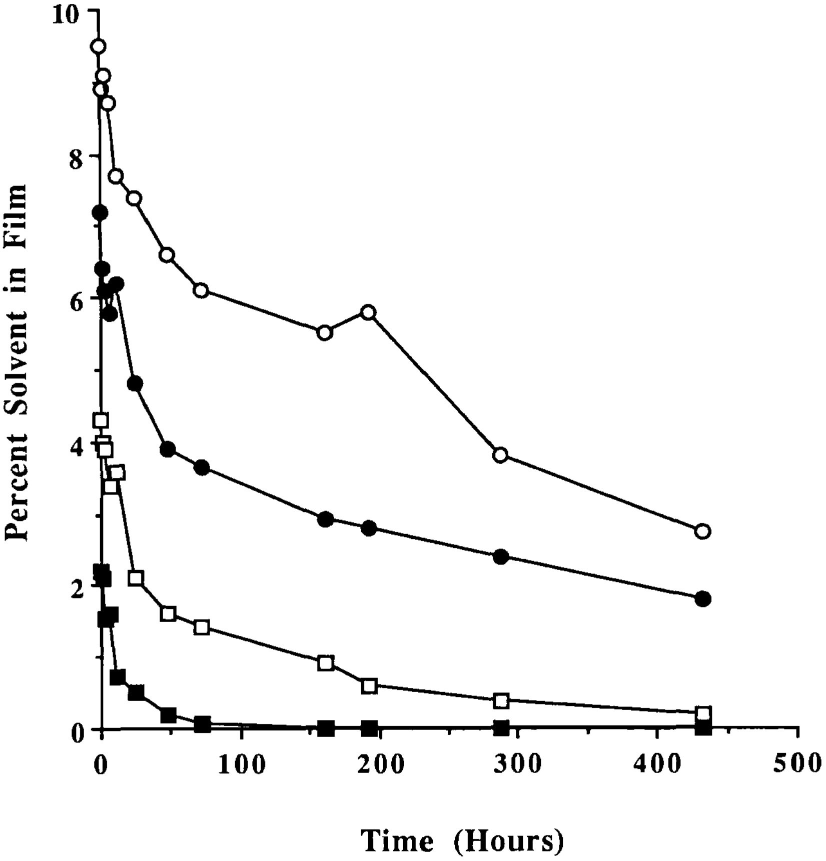

Figure 6: Influence of plasticizer content on the residual levels of isopropyl alcohol remaining in Eudragit® L 100-55 films stored at 40°C. Key: (○) 0%; (●) 10%; (□) 20%; (■) 30%.

cause an increase in the diffusion rate of the solvent to the surface. This proposed mechanism is also supported by the results of an earlier study of Kummins,[29] in which the factors influencing the transport of gases, vapors, and ions through polymeric films were investigated. He proposed that the plasticizer weakened the polymer chain interactions, therefore enhancing the polymer segmental mobility, and this effect caused an increase in the diffusion coefficient of permeating vapors.

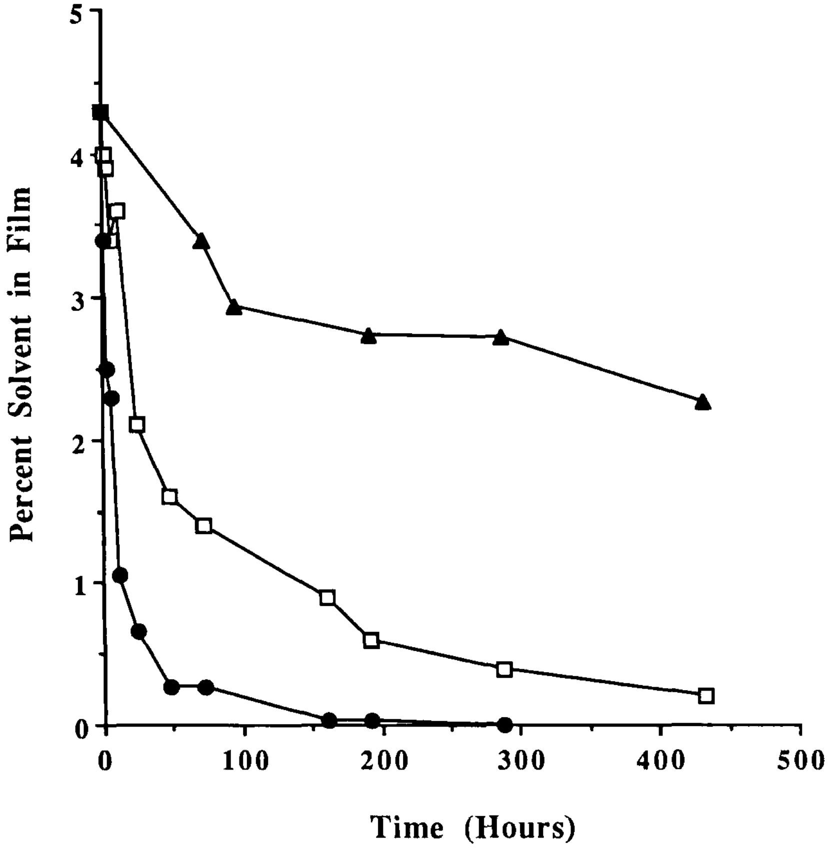

Figure 7: Influence of time and temperature on the residual levels of isopropyl alcohol remaining in Eudragit® L 100-55 films containing 20% triethyl citrate. Key: (▲) 23°C; (☐) 40°C; (●) 60°C.

The effect of temperature on residual isopropyl alcohol levels in films containing 20% triethyl citrate is shown in Figure 7. These films were stored at 23°C, 40°C and 60°C. As the temperature was increased, the rate of isopropyl alcohol evaporation accelerated. However, solvent residues were found in all the films even after 100 hours of exposure at these three temperatures. The magnitude of solvent evaporation was again dependent on the plasticizer concentration. Levels higher than 2% solvent content were found in films containing less than 10% plasticizer concentration after 12 days of storage at 40°C or 60°C.

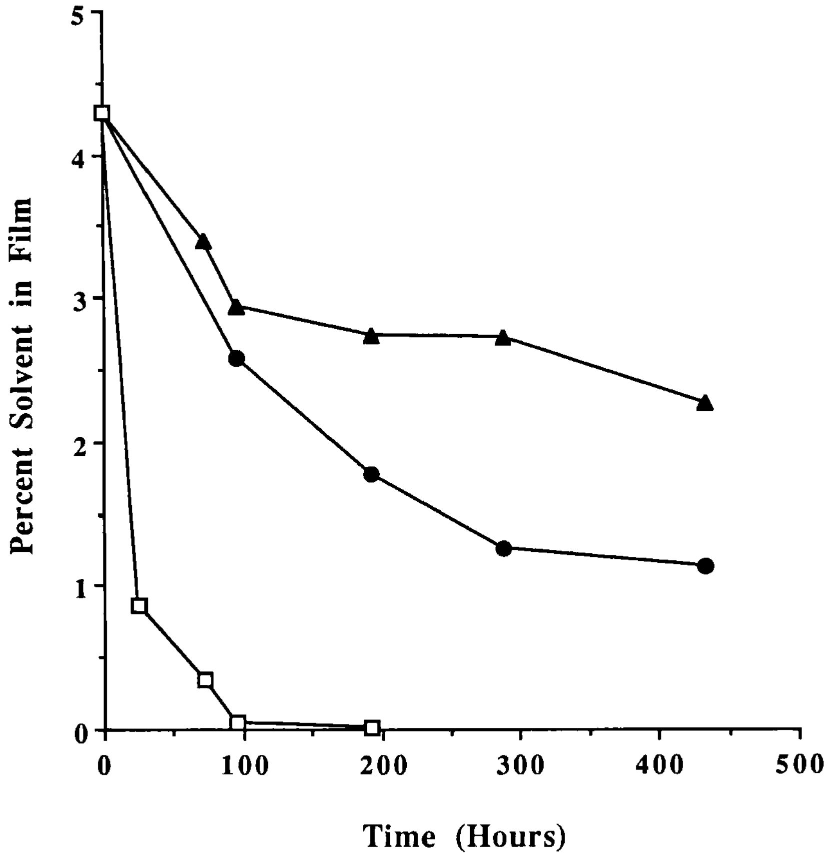

Figure 8: Influence of humidity on the residual levels of isopropyl alcohol remaining in Eudragit® L 100-55 films stored at 23°C and containing 20% triethyl citrate. Key: (▲) 0% R.H.; (●) 50% R.H.; (□) 100% R.H.

Films containing 20% plasticizer concentration or above showed no sign of solvent residues under the same storage conditions.

The results in Figure 8 demonstrate that the process of drying the films under vacuum at very low humidities is not an effective approach to the removal of isopropyl alcohol residuals from cast films. Instead, higher humidity conditions were found to accelerate the removal of solvents. Water can plasticize films, especially those that are hydrophilic. This water plasticization will lead to an increase in the diffusion coefficient as the water concentration increases. This effect will result in a permeability coefficient that will increase with the relative vapor pressure. Water will act as a plasticizer by breaking up the copolymer interchain hydrogen bonding between the carboxylate groups causing an increase in the rate of diffusion of the isopropyl alcohol to the surface.

Conclusions

Tensile tests were used to monitor the changes in physical-mechanical properties caused by the aging of acrylic films. Physical aging of both aqueous and solvent cast films resulted in a decrease in elongation or elasticity, accompanied by an increase in tensile strength. The change in mechanical properties of methacrylic acid copolymers has been related to a relaxation of the copolymer chains toward a state of equilibrium. The extent to which these changes occur was influenced by the amount of plasticizer added, the length of drying time, the solvent residuals, and the temperature and humidity conditions. Headspace-gas chromatography was demonstrated to be a simple and rapid technique to determine low levels of volatile compounds in acrylic polymers. Increases in the concentration of plasticizer in the film were found to augment the evaporation of the solvents. This result is explained in principle by the stronger molecular interaction forces occurring with the polymer and the plasticizer rather than with the solvent.

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