Mechanical Properties of Dry and Wet Cellulosic and Acrylic Films Prepared from Aqueous Colloidal Polymer Dispersions Used in the Coating of Solid Dosage Forms

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The mechanical properties of dry and wet polymeric films prepared from various aqueous polymeric dispersions were evaluated by a puncture test. They were studied with respect to type of polymer dispersion [cellulosic: Aquacoat and Surelease; acrylic: Eudragit NE, L, RS, and RL 30 D], plasticizer type (water-soluble or water-insoluble), drying or curing conditions, method of film preparation (pseudolatex- vs solvent casting) and ratio of Eudragit RS/RL 30 D in mixed Eudragit RS/RL films. Dry and wet mechanical strengths of the polymeric films depended primarily on the types of the colloidal polymer dispersion and the plasticizer. Films prepared from ethylcellulose dispersions resulted in very weak and brittle films when compared to the acrylic films. Pseudolatex-cast ethylcellulose films showed lower puncture strength and elongation values when compared to those of the solvent-cast films. Curing of the pseudolatex-cast ethylcellulose films had minimal effects on their mechanical properties. Eudragit L 30D, an enteric polymer dispersion, resulted in brittle films in the dry state, but in very flexible films in the wet state because of the plasticization effect of water. Wet Eudragit RS 30 D polymer films plasticized with water-insoluble plasticizers were significantly more flexible than the corresponding wet films plasticized with water-soluble plasticizers. The water-soluble plasticizers leached from the films during exposure to the aqueous medium, while the water-insoluble plasticizers were almost completely retained within the wet films. The low permeability of a water-soluble drug, chlorpheniramine maleate, and the weak mechanical properties of Aquacoat films could suggest osmotic driven/rupturing effects as the release mechanisms from Aquacoat-coated dosage forms.

KEY WORDS: aqueous colloidal dispersions; polymeric films; mechanical properties; latexes; film coating; wet strength.

INTRODUCTION

Pharmaceutically acceptable polymers used in the film-coating of solid dosage forms are primarily based on acrylic or cellulosic polymers. Many of these polymers have been formulated into aqueous colloidal dispersions (e.g. latexes or pseudolatexes) in order to overcome problems associated with the use of organic polymer solutions (1–3).

The resulting polymer coating is often characterized with respect to permeability and morphological and mechanical properties. The mechanical properties of dry polymer films are mainly affected by the thermomechanical properties of the polymer, such as glass transition or softening temperature, and by film additives such as plasticizers and fillers (4–7). They are rarely measured to predict the performance of the final coated dosage form under applied stress (e.g. compression, shipment) or in an aqueous environment but primarily to study the effect of certain process or formulation factors on properties such as tensile strength, elongation, and various moduli. However, an important question to be answered relates to the performance of the coated dosage forms in dissolution or biological fluids. With oral drug delivery systems, the drug release process is initiated by diffusion of aqueous fluids across the polymeric coating. The polymer film will be hydrated and can contain significant amounts of water. In addition to film hydration, plasticizers or other film additives could leach into the aqueous environment. What are the mechanical properties of these hydrated films and how could they potentially affect the performance of the drug delivery system? In a previous study, the mechanical properties of Eudragit RS 30 D films in the dry and wet state were significantly different as a result of polymer hydration and/or leaching of the plasticizer (8). The coated dosage form could be exposed to significant mechanical stress factors caused internally by the build-up of osmotic pressure due to water-soluble core ingredients or externally through peristaltic movements in the gastrointestinal tract. A rupturing of the film coat would result in a loss in protective or sustained release properties.

The objective of this study was to evaluate and compare the mechanical properties of polymeric films in the dry and wet state. The films were prepared by casting and drying of aqueous acrylic or cellulosic colloidal polymer dispersions widely used in the coating of pharmaceutical solid dosage forms. The mechanical properties (puncture strength and % elongation) were then evaluated using a puncture test.

MATERIALS AND METHODS

The following chemicals were obtained from commercial suppliers and used as received: triethyl citrate (TEC; Citroflex-2), acetyltriethyl citrate (ATEC; Citroflex A-2), tributyl citrate (TBC; Citroflex-4), acetyltributyl citrate (ATBC; Citroflex A-4) (Morflex Chemical Co., Greensboro, NC), dibutyl sebacate (DBS), diethyl phthalate (DEP), dibutyl phthalate (DBP), glyceryl triacetate (triacetin) (Eastman Kodak Co., Rochester, NY), Aquacoat (30 %w/w ethylcellulose dispersion), (FMC Corporation, Newark, DE), Surelease (25 %w/w ethylcellulose dispersion, pre-plasticized with dibutyl sebacate) (Colorcon, Inc., West Point, PA), Eudragit NE 30 D [poly (ethylacrylate-methylmethacrylate)], Eudragit L 30 D [poly (methacrylic acid-ethylacrylate)] with a ratio of 1:1, Eudragit RS 30 D and RL 30 D [poly (ethylacrylate-methylmethacrylate-trimethylammonioethylmethacrylate chloride)] with the ratios of 1:2:0.1 and 1:2:0.2, respectively (Röhm Pharma, Darmstadt, Germany), chlorpheniramine maleate, ibuprofen (Sigma Chemical Co., St. Louis, MO), methyl alcohol (HPLC grade, Mallinckrodt Specialty Chemicals Co., Paris, KY), and double-distilled water.

The polymer dispersions were plasticized for 5 hours prior to casting on a teflon surface (Cole-Parmer Instrument Co., Chicago, IL) mounted on a levelled glass plate (casting

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area = 9.5 × 13.5 cm^2; casting volume = 40 ml; total solids content = 5 g; approximate dry film thickness = 300 μm). The plasticizers were used at the levels suggested by the manufacturer (Eudragit RS and RL 30 D, 20 %w/w; Aquacoat, 20 or 30 %w/w based on polymer solids). Surelease and Eudragit NE 30 D did not require the addition of a plasticizer (9,10) and were cast after appropriate dilution with water. The films were dried in an oven at 40°C and 30 % relative humidity for 48 h, unless otherwise indicated. The drying temperature, which was above the minimum film formation temperature (MFT) of the colloidal polymer dispersions, was kept constant rather than choosing a drying temperature of MFT + x°C and therefore different drying temperatures for the different polymer dispersions. Films from Aquacoat were also prepared at a drying temperature of 55°C. The differences in the mechanical properties when compared to dispersions dried at 40 °C were insignificant. The dried films were peeled from the teflon surface, cut into 4 × 4 cm^2 test sections with a razor blade, and stored at 22 °C and 54 % relative humidity for 48 h prior to puncture tests or exposure to the aqueous medium. The thickness of dry films was determined in five places using a micrometer (Paul N. Gardner Company, Inc., Pompano Beach, FL).

To study the mechanical properties of wet polymeric films, the dry films were confined individually in bags (7 × 7 cm^2, made from a 40-mesh plastic screen with three sides sewn-closed) in order to prevent folding during exposure to the aqueous medium. The bags were then placed horizontally at the bottom of medium-filled vessels (USP XXII rotating paddle method; 500 ml 0.1 M NaCl or 0.1 M HCl, 37 °C, 25 rpm, exposure time = 24 hours, n = 3).

The puncture test was performed on an Instron (Model 4201, Instron Corp., Canton, MA, 1 kN load detecting transducer). The device consisted of a puncture probe and a film holder (8) and was similar to those previously described (9–11). Dry or wet film specimens were positioned in the film holder between the two mounting plates followed by tightening of the holding screws to prevent slippage of the films. The wet films were carefully blotted to remove water from the film surface prior to mounting. The hemispherical puncture probe (length = 50 mm, diameter = 5 mm), which was attached to the driving load cell, was then driven downward through the center of the mounted film (diameter of the opening of the film holder = 22 mm) at a crosshead speed of 10 mm/min to record load vs displacement data at room temperature. The load (kg) and displacement (mm) at break were converted to puncture strength (MPa) and % elongation (puncture strength = F/A_{cs}, where F was the load required for puncture and A_{cs} was the cross-sectional area of the edge of the dry film located in the path of the cylindrical opening of the film holder; % elongation = $[\{(R^2 + D^2)^{1/2} - R\} / R] * 100$, where R was the radius of the film exposed in the cylindrical hole of the film holder and D was the displacement of the probe from point of contact to point of puncture). The conversion of peak load to the puncture strength provided the normalization of the data for differences in film thicknesses (10). Since it was impossible to obtain accurate values for the thicknesses of the wet films because of their irregular swelling characteristics, the thicknesses of the corresponding dry films were used in the calculations. After the mechanical testing, the punctured wet films were then oven-dried at 40 °C for 24 h in order to determine the water and residual plasticizer content.

The following variables were investigated: type of aqueous polymer dispersion (cellulosic: Aquacoat and Surelease; acrylic: Eudragit NE, RS, RL, and L 30 D); type of plasticizer: water-soluble (TEC and triacetin), water-insoluble (ATBC, ATEC, DBP, DBS, DEP, and TBC); drying conditions of the polymeric films (drying time and temperature); method of film preparation (pseudolatex- or solvent casting); and the ratio of Eudragit RS/RL 30 D in the mixed films, 10:0, 7:3, 5:5, 3:7, and 0:10.

A previously developed HPLC assay was used for the analysis of the plasticizers within the films before and after exposure to the aqueous medium (12). The chromatographic system consisted of a solvent delivery module (LC-9A), a UV spectrophotometric detector (SPD-6A), an automatic sample injector (SIL-9A), an integrator (Chromatopac CR601) (Shimadzu, Kyoto, Japan), and an analytical column (Beckman-Ultrasphere, C-18, 5 μm particle size, 25 cm × 4.6 cm ID). The mobile phases consisted of methanol:double distilled water mixtures [50:50 v/v% for triacetin (I); 70:30 v/v% for TEC, ATEC, DBS, DEP (II); 90:10 v/v% for ATBC, DBP, TBC (III)].

The polymeric films (500–700 mg) were accurately weighed and dissolved in methanol [10 ml for (I); 14 ml for (II); 18 ml for (III)], followed by the addition of water [10 ml for (I); 6 ml for (II); 2 ml for (III)] to precipitate the polymer, and ultracentrifugation (45,000 rpm, 30 min; Beckman Ultracentrifuge L5-50). The supernatant was diluted with the respective mobile phase prior to injection. All film samples were stored in an oven at 40 °C for 16 h prior to extraction for plasticizer content in order to evaporate residual moisture in the films. The loss of plasticizers at this drying temperature/time was negligible (generally <0.5 %, DEP 0.9 %, triacetin 2.6 %).

The residual plasticizer content in the wet films was determined after drying of the films. The amount of plasticizer leached into the aqueous medium and the residual plasticizer content in the films matched the original plasticizer content within 2–5 %.

After exposure to the aqueous medium, the wet films were carefully blotted with a tissue paper to remove water on the film surface and then weighed. The wet films were dried to a constant weight at 40 °C, and weighed to obtain the dry film weight after exposure to the aqueous medium. The water content of wet polymeric films was calculated as follows: water uptake = (weight of wet film − weight of dried film after exposure to the medium) / weight of original film before exposure to the medium excluding plasticizer; the water uptake was expressed as g, water/g, polymer.

The permeability of the drugs across the Aquacoat-cast films was determined in a horizontal Side-Bi-Side diffusion cell (Crown Glass Co., Inc., Somerville, NJ). The polymeric films were clamped between the two well-stirred compartments of equal volume (3.4 ml; 0.1 M pH 7.4 phosphate buffer, 37 °C; area of diffusion = 78.5 mm^2). Two milliliters of samples in the receptor cell were taken and replaced with fresh medium at predetermined time intervals. The amount of drug which diffused across the membrane was determined spectrophotometrically after appropriate dilution of the samples with 0.1 M pH 7.4 buffer (ibuprofen, λ = 224 nm; chlor-

Table I. Mechanical properties of dry and wet films and the water content of wet films prepared from different polymer dispersions plasticized with triethyl citrate (20 %w/w) (S.D. in parentheses; n = 3)

Polymer dispersion (film thickness, μm)	Puncture Strength, MPa		Elongation, %		Water content g, water/ g, polymer
	Dry	Wet	Dry	Wet	
Aquacoat (309)	0.34 (0.11)	0.10 (0.02)	1.34 (0.18)	0.13 (0.02)	0.506 (0.032)
Surelease (394)	0.23 (0.04)	0.74 (0.10)	0.62 (0.12)	4.89 (0.90)	0.100 (0.006)
Eudragit NE 30 D (314)	2.16 (0.19)*	1.58 (0.10)*	>365.00	>365.00	0.268 (0.014)
Eudragit RS 30 D (309)	1.99 (0.23)	0.93 (0.04)	142.83 (4.32)	38.41 (4.65)	0.331 (0.008)
Eudragit RL 30 D (316)	1.81 (0.11)	1.60 (0.14)	126.31 (8.04)	13.02 (2.45)	0.807 (0.008)
Eudragit L 30 D (264)	0.83 (0.05)	1.78 (0.09)*	0.46 (0.25)	>365.00	0.722 (0.023)

* films did not rupture

pheniramine maleate, λ = 264 nm). The thickness of dry polymeric films was determined with a micrometer and was in the range of 170–200 μm.

Nonpareil beads containing drug [chlorpheniramine maleate (CPM) or ibuprofen; 12 mg drug in 100 mg beads] were coated with Aquacoat (solids content of dispersion, 15 %w/w; TEC concentration, 20 %w/w of polymer; plasticization time, 2 h) in a fluid-bed coater (Uni-Glatt Laboratory Unit, Wurster insert, Glatt Air Technique, Ramsey, NJ; 400 g charge, inlet temperature = 45–50 °C, outlet temperature = 40–45 °C, spray rate = 2 ml/min for 10 minutes, then 3–5 ml, pre-heating time = 15 minutes, post-drying time = 5 min). The coated beads were oven-cured for 1 hour at 50°C.

The USP XXI rotating paddle method (1.5–2.0 g beads, 37 °C, 50 rpm, 500 ml 0.1 M pH 7.4 phosphate buffer; n = 3, coefficient of variation < 5 %) was used to study the drug release from the coated beads. The samples (2 ml, not replaced) were withdrawn at predetermined intervals and assayed spectrophotometrically (ibuprofen, λ = 224 nm; chlorpheniramine maleate, λ = 264 nm).

RESULTS AND DISCUSSION

A variety of enteric and non-enteric polymers based on either cellulosic or acrylic polymers are available in the form of aqueous dispersions or powders to be redispersed prior to use. The mechanical properties of dry and wet polymeric films were strongly affected by the type of polymer dispersion (Table I). The ethylcellulose pseudolatexes, Aquacoat and Surelease, resulted in very brittle films in the dry state and weak and soft films in the wet state with low values for puncture strength and elongation (<5 %) in both cases. The brittle nature of the ethylcellulose film could possibly be explained with the interchain hydrogen bonding and the bulkiness of the glucose subunits. Surelease, which is an ethylcellulose dispersion already plasticized with dibutyl sebacate, had slightly better mechanical properties in the wet state when compared to those of Aquacoat films. Both ethylcellulose pseudolatexes are stabilized with anionic surfactants, however, in the case of Surelease, ammonium oleate converts to oleic acid, which then acts as a plasticizer, during drying. With Aquacoat films, the presence of sodium lauryl sulfate might have been responsible for the lower wet strength as well as the higher water uptake when compared to Surelease films. Films of Eudragit NE 30 D, a poly (ethylacrylate-methylmethacrylate) dispersion, were very flexible in both the dry and wet state. The elongation was in excess of the elongation limit of 365 % achievable with this puncture test device. The dispersion had a minimum film-forming temperature of around 5°C (13) and did not require the addition of plasticizers in contrast to the other dispersions evaluated. The molecular structure of the polymer, which is based on acrylic esters, indicates the lack of strong interchain inter-

Table II. Effect of drying conditions on the mechanical properties and triethyl citrate content of dry and wet Aquacoat—triethyl citrate films (S.D. in parentheses; n = 3)

Triethyl citrate, %w/w (film thickness, μm)	Puncture strength, MPa	Elongation, %	Triethyl citrate content in films, %
Dry Films			
Drying temperature and time: 40°C–48 h			
20 (385)	0.21 (0.01)	0.25 (0.03)	19.89 (0.86)
30 (356)	0.23 (0.02)	0.97 (0.26)	27.86 (0.23)
Drying temperature and time: 40°C–24 h + 60°C–24 h			
20 (385)	0.35 (0.02)	0.56 (0.08)	16.78 (0.28)
30 (361)	0.34 (0.05)	1.00 (0.16)	25.77 (0.46)
Wet Films			
Drying temperature and time: 40°C–48 h			
20	0.07 (0.00)	0.08 (0.01)	2.61 (0.70)
30	0.08 (0.01)	0.02 (0.00)	0.84 (0.09)
Drying temperature and time: 40°C–24 h + 60°C–24 h			
20	0.13 (0.01)	0.13 (0.02)	3.98 (0.14)
30	0.17 (0.00)	0.14 (0.00)	2.81 (0.51)

Table III. Mechanical properties and triethyl citrate and water contents of solvent- and pseudolatex-cast ethylcellulose—triethyl citrate films (S.D. in parentheses; n = 3)

Polymeric film (film thickness, μm)	Puncture strength, MPa	Elongation, %	Triethyl citrate content in films, % w/w	Water content, g, water/ g, polymer
Dry Films				
Ethylcellulose* (313)	3.04 (0.00)	2.08 (0.00)	20.02 (0.75)	—
Aquacoat (385)	0.21 (0.01)	0.25 (0.03)	19.89 (0.86)	—
Wet Films				
Ethylcellulose*	0.56 (0.10)	0.45 (0.15)	16.29 (0.81)	0.116 (0.017)
Aquacoat	0.07 (0.00)	0.08 (0.01)	2.61 (0.70)	0.426 (0.005)

* solvent-cast

actions (e.g. hydrogen bonds), thus explaining the flexible character of the polymer films. The hydrophobic character of the polymer, when compared to the other acrylic polymers, was reflected in the low water uptake. With Eudragit RS and RL 30 D, which are dispersions based on the cationic polymer poly (ethylacrylate-methylmethacrylate-trimethylammonioethylmethacrylate chloride), flexible films were obtained in the dry state with elongation values in excess of 125 %. The elongation of wet films was significantly lower. The reduction in elongation could be attributed to the leaching of the water-soluble plasticizer, triethyl citrate, and was not seen with non-leachable plasticizers as described in more detail in Table V.

Another interesting finding was observed when comparing the dry and wet properties of films prepared from the enteric acrylic latex, Eudragit L 30 D [poly (methacrylic acid-ethylacrylate) with a ratio of 1:1]. Dry Eudragit L 30 D films were weak and brittle when compared to the other Eudragit polymers. A possible explanation could be strong interchain hydrogen bonding caused by the presence of the carboxyl groups. The elongation of dry films was less than 1 %, however, the elongation of wet films was in excess of 365 %. This significant increase in flexibility could be explained with the hydration of the polymer and the resulting interference of water with the interchain hydrogen bonding. The glass transition temperature of the unplasticized polymer was 110 °C (13), but was probably significantly reduced in the presence of water. The plasticizing effect of water probably outweighed the leaching of the water-soluble plasticizer, triethyl citrate, and explained the high flexibility of wet films. Drying of wet films after the puncture test resulted in brittle films, thus providing support for the plasticizing effect of water.

The curing (additional heat treatment after coating) of coated dosage forms is often recommended after the coating with colloidal polymer dispersions in order to enhance and complete the coalescence of the colloidal polymer particles in a homogeneous film. The curing of beads coated with ethylcellulose dispersions resulted in significant reductions in drug release, as was shown in a previous study (14). It was thought that curing might improve the mechanical properties of the Aquacoat films. However, as shown in Table II, the drying temperature and time had only minimal effects on the mechanical properties of films plasticized at two triethyl citrate concentrations. Although the puncture strength increased with both dry and wet films after curing, the % elongation was still less than 1 %. The plasticizer almost completely leached from the films during exposure to aqueous media. In dry films, the actual triethyl citrate content decreased with increased drying time and temperature, indicating evaporation and/or possible degradation of the plasticizer.

Ethylcellulose films when cast from organic solutions were stronger (higher puncture strength) in both the dry and wet state when compared with Aquacoat films (Table III). However, the elongation values were still low. Interestingly, triethyl citrate leached almost completely from the pseudolatex-cast film, while more than 75 % of the original plasticizer was still present in films cast from organic solutions. The higher leaching of triethylcitrate could have been the result of the anionic surfactant, sodium lauryl sulfate, being present in Aquacoat films. The pseudolatex-cast films took

Table IV. Mechanical properties of dry and wet Aquacoat films plasticized with different plasticizers (30 %w/w) (S.D. in parentheses; n = 3)

Plasticizer (film thickness, μm)	Puncture Strength, MPa		Elongation, %	
	Dry	Wet	Dry	Wet
TEC (309)	0.34 (0.11)	0.10 (0.02)	1.34 (0.18)	0.13 (0.02)
Triacetin (302)	0.12 (0.04)	0.03 (0.01)	0.10 (0.05)	0.03 (0.01)
ATBC (314)	0.16 (0.05)	0.19 (0.02)	0.18 (0.09)	1.69 (0.21)
ATEC (323)	0.18 (0.05)	0.06 (0.00)	0.38 (0.15)	0.31 (0.05)
DBP (327)	0.60 (0.02)	0.22 (0.02)	1.21 (0.07)	2.28 (0.09)
DBS (324)	0.19 (0.04)	0.09 (0.01)	0.25 (0.09)	0.30 (0.06)
DEP (324)	0.18 (0.02)	0.11 (0.02)	0.21 (0.12)	0.28 (0.12)
TBC (319)	0.50 (0.06)	0.16 (0.01)	2.25 (0.45)	1.79 (0.66)

Table V. Mechanical properties of dry and wet Eudragit RS 30 D films plasticized with different plasticizers (20 %w/w) (S.D. in parentheses; n = 3)

Plasticizer (film thickness, μm)	Puncture Strength, MPa		Elongation, %		Plasticizer remaining, % of original
	Dry	Wet	Dry	Wet	
TEC (309)	1.99 (0.22)	0.93 (0.05)	142.8 (4.3)	38.4 (4.6)	56.29 (1.79)
Triacetin (302)	1.82 (0.38)	0.61 (0.07)	120.9 (6.0)	6.8 (0.6)	35.92 (1.06)
ATBC (314)	4.30 (0.09)	1.11 (0.13)	77.8 (7.6)	85.2 (3.6)	101.84 (1.67)
ATEC (323)	4.01 (0.18)	1.01 (0.02)	86.9 (5.5)	64.3 (8.5)	90.38 (0.05)
DBP (327)	3.18 (0.47)	0.88 (0.19)	93.2 (12.6)	106.9 (9.2)	99.95 (1.88)
DBS (324)	2.37 (0.09)	0.79 (0.04)	91.8 (2.0)	59.7 (3.6)	88.34 (0.66)
DEP (324)	2.47 (0.40)	0.91 (0.03)	91.1 (3.2)	51.0 (3.8)	95.27 (1.53)
TBC (319)	2.37 (0.40)	0.86 (0.03)	113.5 (1.8)	86.6 (3.4)	97.79 (2.06)

up almost 43 % water when compared to only 12 % with the solvent cast films.

Various pharmaceutically acceptable plasticizers have been used with acrylic and ethylcellulose dispersions. Plasticizers are added to induce and enhance the coalescence of the colloidal polymer particles into a homogeneous film by reducing the glass transition and minimum film formation temperature and to improve the mechanical properties of the dried films. The effect of the water-soluble plasticizers, triethyl citrate and triacetin, and of the water-insoluble plasticizers, tributyl citrate, acetyltributyl citrate, acetyltriethyl citrate, dibutyl sebacate, dibutyl phthalate and diethyl phthalate, on the mechanical properties of dry and wet Aquacoat and Eudragit RS 30 D films are shown in Tables IV and V. The mechanical properties of Aquacoat films were similar for all plasticizers. Dry films were very brittle and wet films soft and weak as indicated by a low puncture strength and elongation. The elongation was less than 2 % in most cases. On the contrary, the mechanical properties of dry and wet Eudragit RS 30 D films were strongly affected by the type of plasticizer. Dry Eudragit RS 30 D films plasticized with the water-soluble plasticizers, triethyl citrate and triacetin, had higher elongation and lower puncture strength values (corresponding to a lower modulus at puncture), while films prepared with the water-insoluble plasticizers, had lower elongation and higher puncture strength values (higher modulus at puncture). The differences in the mechanical properties of dry films could be explained with the different plasticizing efficiencies of the plasticizers on the polymer. Plasticization results in a decrease in the intermolecular forces between polymer chains, generally causing a decrease in the glass transition temperature and tensile strength (15,16). It is well known that different plasticizers, at the same concentration level, will affect the glass transition temperature and hence the mechanical properties to a different extent (17). The film formation temperature of this polymer was lowered to a larger extent by water-soluble than water-insoluble plasticizers at corresponding plasticizer levels (14). In this study, the water-soluble plasticizers probably reduced the glass transition temperature more than the water-insoluble plasticizers, thus explaining the lower moduli. The solubility of the plasticizer was an important criteria affecting the mechanical properties of wet Eudragit RS 30 D films. The puncture strength of wet films was reduced when compared to that of the dry films, irrespective of the plasticizer selected. This was caused by the hydration of the polymer. However, wet Eudragit RS 30 D films plasticized with water-insoluble plasticizers were significantly more flexible than the corresponding wet Eudragit RS 30 D films plasticized with the water-soluble plasticizers, triethyl citrate or triacetin, as indicated by the higher elongation values. The water-soluble plasticizers leached from the films during exposure to the aqueous medium (last column in Table IV), while the water-insoluble plasticizers were almost completely retained within the wet films. Polymeric Eudragit RS 30 D coatings plasticized with non-leachable plasticizers should therefore be able to yield to increasing osmotic pressures developing within the coated dosage form upon contact with dissolution or biological fluids without rupturing, while coatings plasticized with the water-soluble plasticizers may rupture and lose their protective function.

Eudragit RS 30 D and RL 30 D are based on cationic polymers, with the latter having twice as many quaternary ammonium groups. The quaternary ammonium groups are responsible for the hydration of the polymer. The two polymers are often blended to obtain films or coatings with vary-

Table VI. Effect of Eudragit RS 30 D/RL 30 D ratio on the mechanical properties of dry and wet films and the water and plasticizer contents of wet films (20 %w/w acetyltributyl citrate) (S.D. in parentheses; n = 3)

RS/RL Ratio (film thickness, μm)	Puncture Strength, MPa		Elongation, %		Plasticizer remaining, % of original	Water content, g, water/ g, polymer
	Dry	Wet	Dry	Wet		
10:0 (314)	4.30 (0.09)	1.11 (0.13)	77.8 (7.6)	85.2 (3.6)	101.84 (1.67)	0.462 (0.046)
7:3 (297)	4.32 (0.31)	0.63 (0.08)	63.9 (5.3)	94.2 (6.5)	98.29 (2.98)	0.738 (0.075)
5:5 (316)	4.33 (0.37)	0.40 (0.04)	62.8 (3.5)	107.1 (9.2)	97.59 (2.10)	1.017 (0.020)
3:7 (320)	4.43 (0.35)	0.23 (0.02)	65.7 (1.5)	111.5 (6.4)	101.52 (0.14)	1.596 (0.045)
0:10 (320)	4.35 (0.28)	0.11 (0.01)	65.5 (8.8)	120.9 (9.4)	96.30 (1.95)	2.498 (0.081)

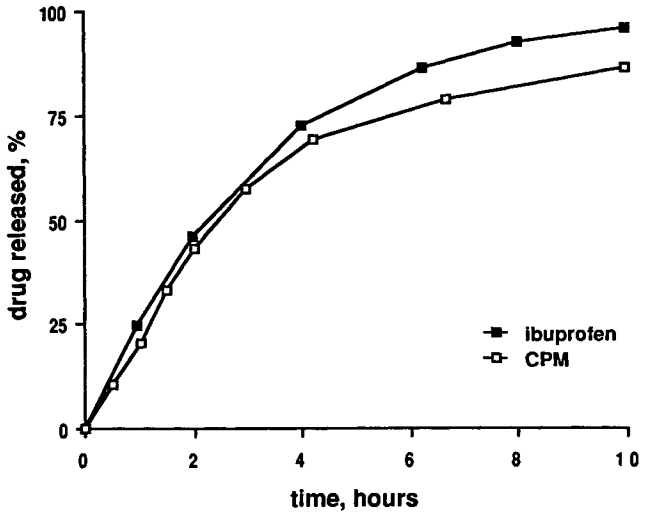

Fig. 1. Chlorpheniramine maleate (CPM) and ibuprofen release from Aquacoat-coated beads (triethyl citrate, 20 %w/w).

ing permeability characteristics. In general, increasing the proportion of the more hydrophilic polymer, Eudragit RL 30 D, results in increased permeabilities (18,19). The puncture strength of dry films was not affected by the proportion of the polymers, while the elongation slightly decreased with an increasing fraction of Eudragit RL 30 D (Table VI). However, with wet films, the puncture strength decreased and the elongation increased (decreasing modulus at rupture) with increasing proportion of Eudragit RL 30 D. This could be explained with the increased hydration or water uptake of the films with increasing fraction of the more hydrophilic Eudragit RL 30 D, resulting in an additional plasticization effect of water.

Several recent articles discussed possible mechanisms by which drug release from multiparticulate dosage forms coated with water-insoluble polymers and in particular ethylcellulose might occur (3,20–23). These mechanisms included solution/diffusion through a continuous polymer phase, solution/diffusion through plasticizer channels, diffusion through aqueous pores, and release driven by osmotic effects. The mechanism of drug release will be determined by the physicochemical properties of the drug, polymer, and the dosage form. In order to elucidate the drug release from Aquacoat-coated dosage forms and to show the importance of the mechanical properties of wet films with respect to drug release, the following studies were undertaken. Chlorpheniramine maleate and ibuprofen were selected as water-soluble and -insoluble model drugs. Ibuprofen had a significantly higher solubility in ethylcellulose films than did chlorpheniramine maleate (24). Drug-containing beads, which were prepared by drug layering onto nonpareils (chlorpheniramine maleate) or extrusion-spheronization (ibuprofen), were coated with the ethylcellulose pseudolatex. Both drugs were released from the coated beads (Figure 1). In order to determine if the drug release was driven by osmosis or occurred primarily by diffusion through the polymer, the drug diffusion across cast films was measured in diffusion cells. Ibuprofen diffused across cast Aquacoat film, while chlorpheniramine maleate did not (Figure 2). Ibuprofen, the water-insoluble drug, was released from the coated beads and diffused across free films, while chlorpheniramine maleate, the water-soluble drug, was released from the beads, but did not diffuse across the polymeric film. The water-insoluble drug, ibuprofen, was therefore released primarily by solution/diffusion through the hydrophobic polymer. The ibuprofen beads consisted of more than 95 % ibuprofen, thus excluding major osmotic effects. On the other hand, chlorpheniramine maleate, the water-soluble drug, was not released by a solution/diffusion mechanism from the beads because of its negligible diffusion across cast films. Chlorpheniramine maleate was layered onto sugar beads, which could exert significant osmotic pressures within coated dosage forms upon dissolution. The osmotic pressures could cause the (micro)rupturing of the polymeric films. As shown above, Aquacoat films were extremely weak in the wet state (% elongation <1 %). Chlorpheniramine maleate was released through aqueous (micro)channels caused by osmotic effects with subsequent rupturing of the weak polymeric membrane.

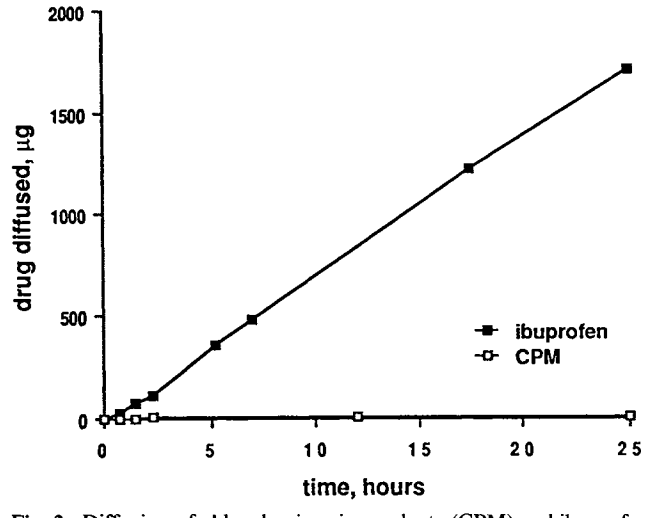

Fig. 2. Diffusion of chlorpheniramine maleate (CPM) and ibuprofen across Aquacoat-cast films (film thickness, 170–200 µm).

In conclusion, it was shown that the mechanical properties of dry and wet films cast from aqueous colloidal polymer dispersions were significantly different and were strongly influenced by the types of polymer dispersion and plasticizer. The mechanical properties of wet polymeric films should also be taken into consideration when formulating sustained release coated dosage forms.

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