Drug Development and Industrial Pharmacy, 25(5), 597–604 (1999)

RESEARCH PAPER

Influence of Pigment Concentration and Particle Size on Adhesion of an Acrylic Resin Copolymer to Tablet Compacts

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ABSTRACT

The effects of the particle size and the concentration of pigments in aqueous polymeric dispersions on the adhesive properties of an acrylic resin copolymer were investigated. Aqueous polymeric dispersions containing up to 20% (v/v) pigment were coated onto hydrophilic and hydrophobic tablet compacts, and polymer adhesion was assessed using a novel butt adhesion technique. An inverse relationship was found between the particle size of the pigment present in the aqueous polymeric dispersion and film-tablet adhesion. As the particle size of the pigment increased, the adhesive strength of the polymer to the tablet compact decreased. Increased concentrations of the opacifying agent titanium dioxide in the acrylic dispersion resulted in stronger film-tablet adhesion. No clear relationship could be established between the wettability of the tablet compact by the pigmented polymeric dispersion and the strength of film-tablet adhesion. The hydrophobicity of the tablet compact was found to affect the glass transition temperature of the polymeric film to a greater extent than the particle size, morphology, or concentration of the pigment incorporated into the acrylic dispersion.

INTRODUCTION

Pigments are generally included in polymeric film-coating formulations to improve the appearance of the final dosage form, to provide easy product identification for both health care professionals and patients, and to enhance the stability of drugs susceptible to photolytic degradation (1–4). Pigments commonly used in pharmaceutical systems include the aluminum lakes of water-soluble dyes, opacifying agents such as titanium dioxide,

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and other various inorganic materials, including the iron oxides. Reports of color migration and stability issues have curtailed the use of water-soluble dyes in pharmaceutical products (5). Pigments differ significantly in their physical properties, including density, particle size, and morphology, and these differences contribute to the complex relationship with aqueous film coatings (6,7).

The utilization of pigments in film-coating systems has been shown to influence polymer properties. The elasticity of both hydroxypropyl methylcellulose and cellulose acetate phthalate was found to decrease with the addition of pigments to the coating formulation (7,8). More recently, Maul and Schmidt demonstrated that the particle size of the pigment in a polymeric film could influence drug release from film-coated solids. Limited studies, however, have addressed the effects of pigments in coating formulations on adhesion of polymeric films to tablet compacts.

Good adhesion between a polymeric film and the surface of a tablet is desirable for a pharmaceutical product. Loss of adhesion may compromise the mechanical protection the film coating provides to the solid substrate. Accumulation of moisture at the film-tablet interface may occur as a result of a loss in polymer adhesion, presenting significant stability problems for drugs susceptible to degradation by hydrolytic mechanisms. In addition, experiments on adhesion may be useful to the pharmaceutical scientist during preformulation stages of product development as a tool to investigate the relationship between tablet excipients and polymeric film-coating formulations.

While pigments have been incorporated into film-coating formulations, the effects of pigments on the adhesive properties of aqueous-based polymeric films to tablet compacts have not been fully studied. The objective of the current research was to investigate the influence of both the particle size and the concentration of pigments in aqueous polymeric dispersions of an acrylic resin on film-tablet adhesion.

EXPERIMENTAL

Materials

Aqueous dispersions of the acrylic resin copolymer Eudragit® L 30 D-55 were donated by Hüls America, Incorporated (Somerset, NJ). The plasticizer triethyl citrate (TEC) was donated by Morflex, Incorporated (Greensboro, NC). The pigments investigated in the present study included titanium dioxide, yellow and red iron oxide (Crompton and Knowles, Mahwah, NJ), blue aluminum lake (Warner Jenkinson Pharmaceutical Ingredients, S. Plainfield, NJ), and surface-treated mica (Mearl Corp., New York, NY). The physical properties of the pigments used in the present study are shown in Table 1. Anhydrous lactose was purchased from Sheffield Products (Norwich, NY), and Capital City Products (Columbus, OH) supplied the hydrogenated castor oil under the trade name Sterotex® K. The magnesium stearate was purchased from Spectrum Chemical Manufacturing Corporation (Gardena, CA), and the Cab-O-Sil® M-5P was donated by Cabot (Tuscola, IL). Scotch® double-coated tape 665 was supplied by 3M (St. Paul, MN).

Preparation of Tablets

Tablets were prepared using a Stokes B2, 16-station rotary tablet press (Stokes-Merrill Corp., Bristol, PA). The two formulations used in the present study are shown in Table 2. Concentrations of the glidant and lubricant were held constant, while the amount of wax varied from 0% to 30% (w/w). Excipients were passed through a 40-

Table 1

Physical Properties of the Pigments Investigated

Pigment	Density (g/cc)[a]	Morphology[b]	Particle Size (μm)[2]
Titanium dioxide	4.08	Rounded	1
Yellow iron oxide	4.53	Acicular	5
Red iron oxide	5.42	Spherical	15
Aluminum lake (blue no. 1)	1.84	Irregular	30
Mica (surface treated)	3.19	Flake	35

[a] Determined using helium pycnometry.
[b] Determined visually using scanning electron microscopy.

Table 2

Tablet Core Formulations

Excipient	Formulation I (%)	Formulation II (%)
Anhydrous lactose	99.0	69.0
Sterotex K	0.0	30.0
Cab-O-Sil M-5P	0.5	0.5
Magnesium stearate	0.5	0.5

mesh screen prior to compression. Flat-faced punches with a beveled edge were employed to compress the tablets to a hardness of 10 kg. All tablets had a diameter of 10.20 mm and a height of approximately 6.20 mm.

Preparation of Coating Dispersions

Formulations Containing Titanium Dioxide

Titanium dioxide and TEC were added to sufficient water to prepare a dispersion containing 30% (w/w) solids content. A Polytron® (Brinkmann Instruments Inc., Westbury, NY) was used to mix the preparation thoroughly. The mixture was then added to the acrylic polymeric dispersion and agitated using a magnetic stirrer for 30 min prior to the initiation of coating.

Formulations Containing All Other Pigments

A 2% (w/w) solution of sodium carboxymethylcellulose (NaCMC) was prepared by dispersing the suspending agent in sufficient water using a magnetic stirrer until a clear solution was obtained. The pigment and TEC were added to the solution and thoroughly mixed using a Polytron. The pigmented dispersion was then added to the acrylic dispersion and mixed using a magnetic stirrer for 30 min prior to the initiation of coating.

Coating of Tablets

Coating of 300-g batches of tablets took place in a Mini Hi-Coater Model HCT-20 (Vector, Marion, IA). The bed temperature was held constant at 30°C, while the inlet temperature varied from 65°C to 75°C. The spray rate of the polymeric dispersion was 2.0 g/min. The atomizing air pressure was 0.9 kg/cm^2. The rotational speed of the coating pan was set at 20 rpm. Sufficient polymer to achieve a 10% weight gain was applied. After the coating process was completed, the coated tablets were stored at 40°C for 2 hr to promote further coalescence of the polymeric film (10–13).

Determination of Adhesive Properties

Butt adhesion experiments were conducted using a Chatillon digital force gauge DFGS50 attached to a Chatillon TCD-200 motorized test stand (Chatillon Force Measurement, Greensboro, NC). A more detailed description of the apparatus has been published in previous reports (14,15). The film coating at the beveled edge of the tablet was carefully removed using a scalpel. The tablet was affixed to the lower, stationary platen using double-sided adhesive tape. Tape was placed on top of the tablet and the upper platen was lowered to the surface of the tablet, as described in an earlier publication (16). The adhesive tape was selected due to minimal interaction with the polymeric film. Other adhesives, such as cyanoacrylate esters or epoxy resins, required longer contact times with the polymer and had a greater potential for interaction with the film (15). The upper platen was raised at a slow, constant rate of 2.5 mm/min. Force and deflection values were recorded on a computer at 10 to 20-μm intervals. Force-deflection profiles were constructed from the data. The force required to remove the film coating from the surface of the tablet, known as the adhesive force, and the elongation at adhesive failure, equivalent to elongation at break in tensile testing of free films, were determined.

Contact Angle Measurements

A horizontal microscope (Zeiss, Oberkochen, Germany) fitted with a protractor lens retical was used to determine contact angles between the tablet surfaces and the Eudragit L 30 D-55 polymeric dispersion. Uncoated tablets were mounted on glass slides using a cyanoacrylate ester adhesive (Loctite Corp., Rocky Hill, CT). A 2-ml glass pipette was used to deliver the pigmented polymeric dispersions onto the tablet surfaces. The contact angles were measured within 10 sec. At least 15 measurements were made for each coating formulation.

Thermal Analysis

The glass transition temperature T_g of the films of the coated tablets was determined using a modulated differential scanning calorimeter model DSC 2920 (TA Instruments, Houston, TX). The apparatus was calibrated using the melting transition of indium. An earlier study demon-

strated that the hydrophobicity of the tablet core will influence the T_g of the acrylic polymer for films containing water-soluble plasticizers, such as TEC (15). Rather than cast free films, therefore, approximately 15 mg of the film from the coated tablets were removed from the tablet compact and accurately weighed in aluminum pans. Thermal analysis was performed at a scan rate of 10°C per minute from −10°C to 130°C. The modulating signal was set at 0.32°C per min. No previous heating or quenching was performed on the samples. The T_g was calculated as the midpoint of the endothermic curve. Three samples were tested for each formulation.

RESULTS AND DISCUSSION

The force-deflection profiles of the Eudragit L 30 D-55 polymer obtained using the Chatillon butt adhesion technique as a function of titanium dioxide concentration are shown in Fig. 1. As the concentration of titanium dioxide in the polymeric dispersion was increased from 0% to 20%, film-tablet adhesion increased, and greater forces were required to separate the film coating from the surface of the tablet. These findings were attributed to the extent of interfacial interaction between the polymeric dispersion and the surface of the tablet. Okhamafe and York (17) and Lehtola and coworkers (18) reported similar findings when titanium dioxide was added to organic- and aqueous-based hydroxypropyl methylcellulose.

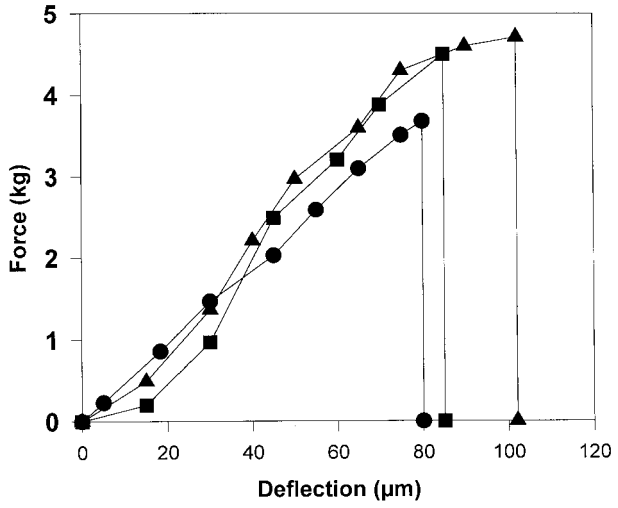

Figure 1. Force-deflection profiles of Eudragit L 30 D-55 as a function of titanium dioxide concentration in the acrylic dispersion (tablet formulation II): ●, 0% titanium dioxide; ■, 10% titanium dioxide; ▲, 20% titanium dioxide.

Increased concentrations of the opacifying agent also caused an increase in the elongation at adhesive failure, as shown in Fig. 1. This was a surprising result that, at first, suggested that titanium dioxide may be plasticizing the polymeric film. Previous studies have demonstrated that increased plasticization of the polymer resulted in an increase in the elongation at adhesive failure (15). Film thickness, however, has also been shown to influence this parameter (16). Table 3 shows the thickness of the polymeric films as a function of titanium dioxide concentration in the acrylic dispersion. The increased elongation at adhesive failure, which occurred with increased concentration of titanium dioxide in the coating formulation, was attributed to the increase in the film thickness rather than the plasticization of the polymer.

Measured adhesion is dependent on both the strength of the interfacial bonds and the internal stresses within the film (19,20). When a polymeric solution or dispersion is applied to a solid substrate, internal stresses within the film inevitably develop . These stresses include stress due to shrinkage of the film as the solvent evaporates, thermal stress due to the differences in the thermal expansion of the film and the substrate, and volumetric stress due to volume changes when the substrate swells during storage (22–24). Increasing the internal stresses within the film generally decreases polymer adhesion (15). Previous research has demonstrated that the addition of pigments to film-coating formulations generally results in increased stresses within the film, as evidenced by an increase in the modulus of elasticity (7).

The glass transition temperature T_g of the polymeric film as a function of titanium dioxide concentration is shown in Table 4. Increased concentration of titanium

Table 3

Influence of Titanium Dioxide Concentration in the Aqueous Acrylic Dispersion on the Thickness of the Polymeric Film (Tablet Formulation II)

Titanium Dioxide[a] (%)	Film Thickness[b] (μm)
0	105
5	115
20	125

[a] v/v, based on dry polymer volume.
[b] Determined using scanning electron microscopy.

Table 4

Influence of Titanium Dioxide Concentration on the Glass Transition Temperature of Eudragit L 30 D-55 Film Coated on Hydrophilic and Hydrophobic Tablet Compacts

Titanium Dioxide[a] (%)	Glass Transition Temperature (SD)	
	I	II
0	36.5°C (1.5)	49.3°C (0.8)
5	40.2°C (1.0)	49.9°C (0.3)
20	49.3°C (0.8)	51.9°C (0.4)

[a] v/v, based on dry polymer volume.

dioxide present in the film coating resulted in significant increases in the T_g of the polymeric film when coated onto the hydrophilic substrate. Only small, incremental increases in the T_g of the polymeric film with increased titanium dioxide concentration were noted when the polymeric dispersion was coated onto hydrophobic tablet compacts. These findings demonstrate that the hydrophobicity of the tablet compact affected the T_g of the polymer to a greater extent than the concentration of titanium dioxide in the film-coating formulation. Previous research has shown that increased hydrophobicity of the tablet compact increased the T_g of unpigmented films of the acrylic polymer when the water-soluble plasticizer TEC was incorporated into the coating formulation (15). While further studies are needed to understand the implications fully, these findings suggest that the mechanisms of bonding between the polymeric film and the tablet compact contribute more to the internal stresses than previously reported.

To investigate further the theory that the titanium dioxide present in the film-coating formulation was improving adhesion due to increased interfacial interaction, the contact angles between the polymeric dispersion and the surface of the tablet were determined; the data are presented in Fig. 2. On the addition of titanium dioxide to the polymeric dispersion, the contact angle decreased, indicating that the polymeric dispersion containing the opacifying agent wetted the tablet compact more readily. Further increases in titanium dioxide concentration in the polymeric dispersion, however, did not produce additional changes in tablet wettability. Previous researchers have demonstrated that increased wettability of a tablet compact by a polymeric solution resulted in improved adhesion due to increased interfacial contact (25). These findings support the theory that the addition of titanium dioxide to an acrylic polymeric dispersion improved

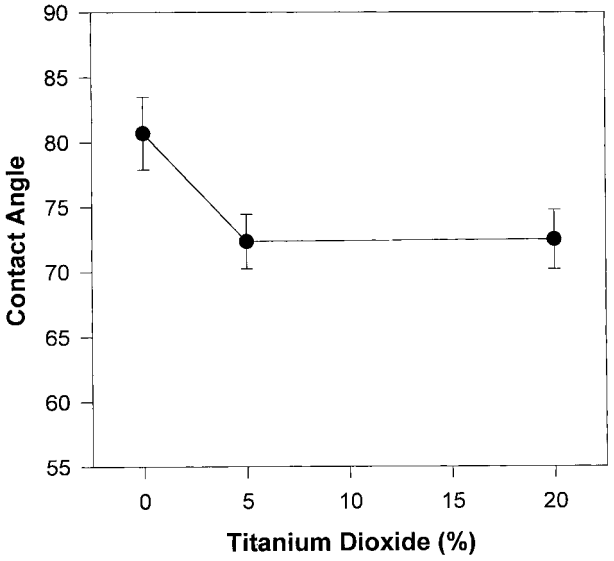

Figure 2. Contact angles between the polymeric dispersion and the surface of the tablet as a function of titanium dioxide concentration in the film coating formulation (tablet formulation II).

polymer adhesion by increasing the interfacial contact between the tablet surface and the polymeric dispersion.

The physical properties of the other pigments investigated in the current study are shown in Table 1. Due to the wide variations in the densities of the colorants, the amount of pigment added to the film-coating formulation (10%) was based on volume fractions rather than weight fractions (7). The force-deflection profiles of the Eudragit L 30 D-55 polymeric film obtained using the Chatillon butt adhesion technique as a function of pigment is shown in Fig. 3. Films containing the yellow iron oxide pigment exhibited the strongest adhesion, while the mica-containing formulation showed the weakest film-tablet adhesion. These findings are in agreement with the scanning electron micrographs of the film-tablet interface (Fig. 4). Large gaps or spaces at the film-tablet interface are indicative of poor polymer adhesion (16). The formulation containing yellow iron oxide exhibited few voids, indicating good interfacial contact between the polymeric film and the tablet surface. All other formulations exhibited more significant gaps at the film-tablet interface. Furthermore, the mica-containing polymeric film showed the largest interfacial void.

To explain the data presented in Fig. 3, the contact angles between the acrylic dispersions and the hydrophobic tablet compacts were determined and are presented

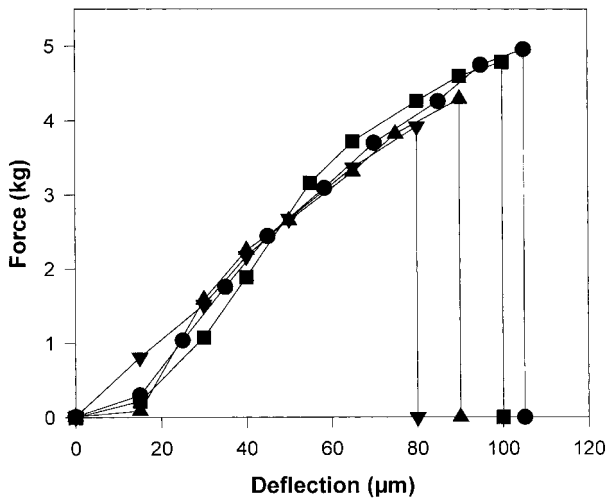

Figure 3. Force-deflection profiles of Eudragit L 30 D-55 as a function of pigment in the acrylic dispersion (tablet formulation II): ●, yellow iron oxide; ■, red iron oxide; ▲, blue aluminum lake; ▼, surface-treated mica.

Table 5

Contact Angles Between the Acrylic Dispersion and the Hydrophobic Tablet Surface (Formulation II) as a Function of the Pigment in the Coating Formulation

Pigment	Contact Angle (SD)
Yellow iron oxide	75.9 (2.9)
Red iron oxide	68.1 (2.4)
Blue aluminum lake	79.6 (2.6)
Mica (surfaced treated)	84.8 (2.4)

in Table 5. The acrylic dispersion containing mica exhibited the greatest contact angle and the poorest polymer adhesion. While mica is a hydrophobic pigment and one could attribute the poor adhesion and tablet wettability to the hydrophobicity of the pigment, the surface of the mica used in the present study was treated with titanium

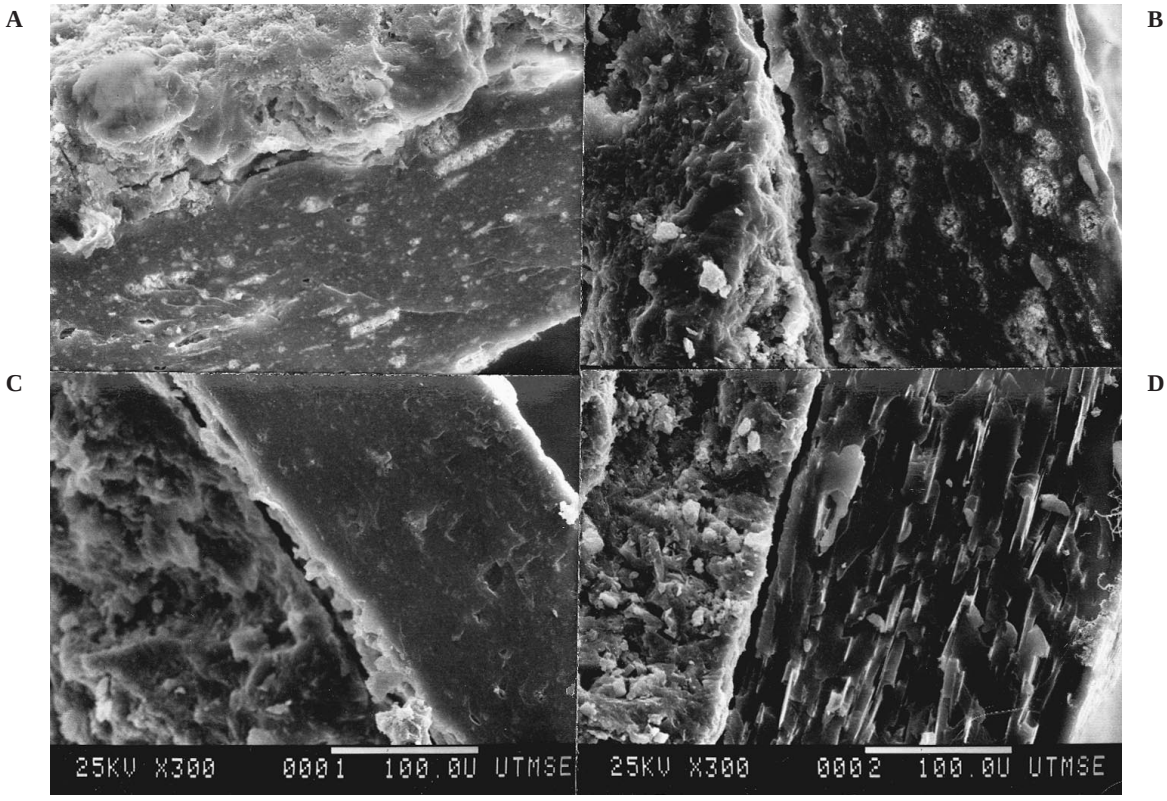

Figure 4. Scanning electron micrographs of the film-tablet interface as a function of pigment in the acrylic dispersion (tablet formulation II): (A) yellow iron oxide; (B) red iron oxide; (C) blue aluminum lake; (D) surface-treated mica.

dioxide, altering the hydrophobicity of the material. No clear relationship, however, between polymer adhesion and tablet wettability by the acrylic dispersion as a function of pigment could be established.

To understand better the influence of the pigment in the coating formulation on polymer adhesion and explain the data presented in Fig. 3, the T_g of the pigmented films was determined, and the data are presented in Table 6. While differences in the T_g as a function of pigment were noted when the polymer was coated onto hydrophilic substrates, no significant differences in the T_g were found for the films coated onto hydrophobic substrates. Any effect of the pigments in the aqueous polymeric dispersions on the internal stress within the film coating was not detectable when the polymer was coated onto the hydrophobic tablet compact. These findings again demonstrate that the hydrophobicity of the tablet compact affected the T_g of the polymer to a greater extent than the addition of the pigments to the film-coating formulation. Furthermore, these results suggest that the interfacial binding between the polymeric film and the tablet compact affect the internal stresses of the film more significantly than the addition of excipients to the coating formulation.

The particle size of the pigment incorporated into the coating formulation was found to influence polymer adhesion. Film-tablet adhesion was found to be strongest when the small yellow iron oxide pigment was incorporated into the film-coating formulation, whereas the presence of the large mica pigment in the acrylic dispersion resulted in poorer polymer adhesion. The pigment particles embed themselves within the polymeric film and at the film-tablet interface (17). The larger pigment particles disrupt the interfacial contact between the film and the tablet surface to a greater extent than smaller particles. In addition, these findings suggest that the particle size of the pigment incorporated into a polymeric dispersion may influence film-tablet adhesion to a greater extent than the wettability of the tablet compact by the aqueous film coating.

Table 6

Influence of Pigments[a] *on the Glass Transition Temperature of Eudragit L 30 D-55 Film Coated on Hydrophilic and Hydrophobic Tablet Compacts*

	Glass Transition Temperature (SD)	
Pigment	I	II
Unpigmented	36.5°C (1.5)	49.3°C (0.8)
Yellow iron oxide	41.8°C (0.2)	50.4°C (0.2)
Red iron oxide	38.5°C (0.8)	50.0°C (0.1)
Blue aluminum lake	46.9°C (1.2)	49.9°C (0.1)
Mica (surface treated)	51.2°C (1.2)	50.3°C (0.2)

[a] 10% v/v, based on dry polymer volume.

CONCLUSIONS

The current study demonstrated the usefulness of the Chatillon apparatus in the investigation of film-tablet adhesion. The pigments in the film-coating formulation were found to influence polymer adhesion to tablet compacts, tablet wettability by the acrylic dispersion, and the glass transition temperature of the polymeric film. The particle size of the pigment present in the aqueous dispersion was found to influence film-tablet adhesion significantly. Increased concentrations of the opacifying agent titanium dioxide in the acrylic dispersion resulted in stronger film-tablet adhesion. Tablet hydrophobicity was found to affect the glass transition temperature of the polymeric film to a greater extent than the particle size, morphology, or concentration of the pigment present in the acrylic dispersions.

ACKNOWLEDGMENTS

Supported (in part) by a Pharmaceutical Research and Manufacturers of America Foundation Research Starter Grant.

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