

Effect of Surface Roughness and Coating Solvent on Film Adhesion to Tablets

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Abstract □ The adhesion of a polymer film to selected tablet substrates was studied. The effect of tablet surface roughness and film-coating solvent on the adhesion of the film to the tablet was determined. A film-coating solvent having a solubility parameter close to that of the polymer was found to produce a stronger adhesion bond than a solvent having a lower surface tension. An increase in tablet surface roughness also increased film adhesion to the tablet. The adhesion was measured as the force required to peel a section of film from the tablet with a stress-strain analyzer.

Keyphrases □ Films—adhesion to tablets, effect of surface roughness and coating solvent □ Tablets—effect of surface roughness and coating solvent on film adhesion □ Adhesion—polymer films to tablet substrates, peel strength, effect of surface roughness and coating solvent □ Solvents, coating—effect on polymer film adhesion to tablet substrates

Adhesion to their substrates is a major prerequisite of pharmaceutical film coatings. Assessment of coating adhesion in fundamental terms is very difficult and is undoubtedly a factor that has limited the research in this field. The method of choice for studying coat bonding to substrates appears to be the measurement of the force required to peel the film from the substrate.

In a recent adhesion study involving pharmaceutical systems (1), the adhesion of film coating to tablets was quantified by measuring the force required to pull films from tablet surfaces. A correlation was found between peeling force and the critical surface tension of the tablet surface but not between surface tension of the coating solution and peeling force. As pointed out by Wood and Harder (1), this latter finding was contrary to theory.

The solvent from which a polymer film is cast can significantly affect the film's adhesion to the substrate (2). Engel and Fitzwater (3) found that the nature of the solvent used in film formation significantly affected the peel strength of methyl methacrylate films. They also observed a good correlation between the peel strength and the cohesive energy density of the solvents employed using a tin substrate. Peel strengths of film prepared from polymer solutions containing 25% solvent showed an increase in numerical value with an increase in solvent cohesive energy density. The solvent showing the maximum peel strength was considered the most efficient for a particular polymeric system.

While studying the effect of fillers on peel strength, Brantley (4) noticed that the addition of higher concentrations of talc decreased the peel

strength. He attributed this effect to embedded filler particles between the polymer film and the substrate, which interfered with the polar groups of the film or shielded them from the substrate.

The effect of polymer molecular weight on adhesion has been studied (5, 6), and the peel strength was observed to be independent of molecular weight in one case (5). Vakula *et al.* (6), studying the adhesion of copolymers of acrylonitrile and butadiene, found an initial increase in adhesion with an increase in molecular weight up to 350,000. Beyond this point, the adhesion was independent of molecular weight. The work was carried out on a polyamide substrate.

The effect of the percentage of polar groups of cellulose on adhesion to nonferrous metals was studied, and an increase in adhesion with increased nitration in cellulose and increased ethoxy content in ethylcellulose was found (7). McLaren (8) demonstrated the increase in adhesion of poly(alkyl methacrylate) as the alkyl group was changed from ethyl through *n*-butyl. This increase in peel strength was thought to be due to a change in crystallinity of the film material resulting in an increase in adhesion.

The objective of this research was to investigate the effect of the coating solvent on film adhesion to tablet substrates; in addition, the effect of surface roughness on film adhesion is also reported.

EXPERIMENTAL

Preparation of Substrates—Three tablet substrates (Table I) were prepared by compressing the powder mixtures into disks with a laboratory press¹. Each 2.54-cm (1-in.) diameter, flat-face disk weighed approximately 2 g and was prepared at a compressional load of 9091 kg (20,000 lb), held for 15 sec. For surface roughness studies, disks were also compressed at 4545 kg (10,000 lb) and 6818 kg (15,000 lb). The compressed disks were stored in a desiccator prior to use.

Preparation of Polymeric Coating Solutions—The polymer used was poly(methyl vinyl ether/maleic anhydride), molecular weight 250,000². Eight percent (w/v) solutions of the polymer were prepared in acetone, methyl acetate, methyl ethyl ketone, and tetrahydrofuran. Each solution also contained 6% glyceryl triacetate³. All solvents were reagent grade.

Coating of Compressed Substrate Disks—To facilitate film coating, maintain individual tablet identity, control coating thickness, and facilitate subsequent quantitative testing, compressed substrate disks were coated using an immersion coating method.

¹ Carver model B, Fred S. Carver, Inc., Summit, N.J.

² Courtesy of General Aniline and Film Corp., New York, N.Y.

³ Eastman Organic Chemicals, Rochester, N.Y.

Table I—Tablets Employed in Film Adhesion Studies

Formula for 50 Tablets	Tablet Substrate I ^a , g	Tablet Substrate II ^a , g	Tablet Substrate III ^b , g
Microcrystalline cellulose ^c	100	—	—
Acacia	—	100	—
Magnesium oxide granulation	—	—	100
Talc	0.5	1.0	0.25
Magnesium stearate	1.0	2.0	0.25

^aSubstrates I and II were prepared by hand sieving all ingredients through a 40-mesh sieve, mixing for 20 min in a planetary mixer, and compressing. ^bSubstrate III was prepared by wet massing the magnesium oxide with 7.5% starch paste followed by hand granulating through a 30-mesh sieve. The resulting granules were dried overnight at 48.8° (120° F), sized through a 16-mesh sieve, and compressed. ^cAvicel.

Each compressed substrate disk was brushed with a camel-hair brush to remove dust and was measured for thickness with a micrometer gauge⁴. A penciled rectangle of 0.5 × 0.75 cm was marked on the substrate disks to provide a reference for subsequent film peeling in evaluating adhesion properties of polymeric films.

The tablets were coated individually by maintaining the disk at the end of a small glass tube with suction applied by a vacuum pump. One side of the flat tablet was coated by immersing it into the coating solution 12 times. The resulting film thickness varied from 0.12 to 0.16 mm as measured by a micrometer⁴. Each coat was allowed to air dry for 3–5 min before the next coat was applied. Coated disks were stored at 40° and 52% relative humidity for 12 hr before testing in the peeling studies.

Contact Angle Measurements of Polymeric Solutions on Compressed Substrate Disks—The environmental chamber of a goniometer⁵ was saturated for 24 hr with vapors of the solvent used in the coating solution prior to the contact angle measurements. This operation was carried out to minimize the recession of the contact angle during the measurement. The substrate disks were individually placed on the platform of the goniometer chamber. One small drop of the polymeric coating solution was then placed on the disks with a capillary pipet and the chamber was covered immediately. Measurement of the wetting angles was taken within 60 sec.

Surface Tension Measurement—The surface tension of the polymer solutions and of the pure solvents was determined⁶ at 25°. Correction factors were calculated according to the procedure in the manufacturer's instruction manual. Density determinations necessary for the correction factor calculation were determined using a 25.00-ml pycnometer.

Surface Roughness Measurements of Compressed Substrate Disks—To evaluate the effect of substrate surface morphology upon polymeric film peeling strength, surface roughness characteristics of the substrates were determined. The surface profile measurements were made using a surface analyzer⁷. This instrument is used in the measurement of the surface profiles of thin films and roughness characteristics of solid substrates. The specifications used in the experimental studies were as follows: sensitivity, 500,000 and 100,000 Å full scale; minimum detectable step, 5000 and 1000 Å; scan speed, 0.1–10 cm/min; stylus diameter, 0.0005 cm; and stylus tracking force (preset), 15 mg.

Surface roughness measurements were carried out by the method described by Schwartz and Brown (9). The surface peak-to-valley distance was used to characterize surface roughness, and an average of six such readings was reported as the average peak-to-valley distance.

Peel Strength Determination—The peel adhesion of applied polymeric films was evaluated using a stress analyzer⁸. The tension

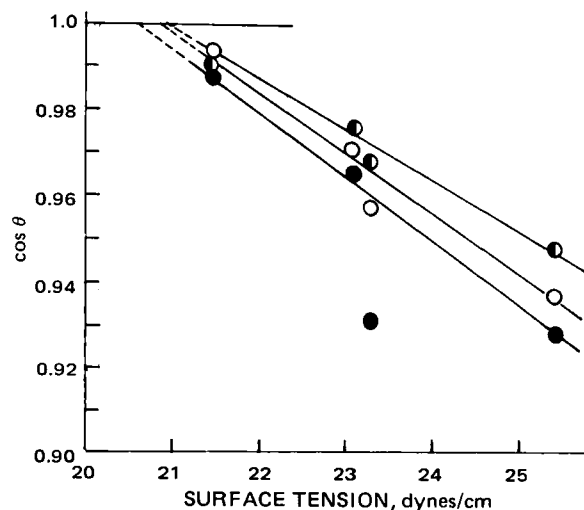


Figure 1—Zisman plot of $\cos \theta$ versus surface tension. The intercept at $\cos \theta = 1$ represents the critical surface tension of the solid. Key: ●, Tablet I; ○, Tablet II; and ●, Tablet III.

load cell was calibrated at the lowest range of 10 g for full-chart deflection. This calibration enabled the use of all ranges of amplification (1–50). The cross-head speed of 1.27 cm/min (0.5 in./min) was chosen to take into account a gradual and slow peeling of the film and reduce elastic deformation of the film. A preset chart speed of 50.8 cm/min (20 in./min) gave a total amplification of deflection by 40X. The gauge and return dials were set to reproduce a predetermined distance of 2.54 cm (1 in.) of peeling of the film from the substrate.

The samples of coated substrate disks previously marked (rectangle of 0.5 × 0.75 cm) were tightly clamped to the platform. One end of the rectangular outline of the film, representing 25% or less of the total gauge length, was cut with a small razor knife and pulled free for insertion into the jaws of the grip. The dimensions of the peeled film was such that when the sample was clamped and inserted into the jaws of the grip, a small initial distance was allowed for weakening of the film contact to the substrate surface. This distance was taken into account prior to recording the actual peeling by zero adjustment. All measurements were carried out using 20X amplifier sensitivity to enable the load cell to record to a maximum of 200 g of force.

The angle of peel was almost constant (90°) during the peeling of films. Due to the very small distance over which the peel adhesion was studied, no attempt was made to slide the platform to maintain a constant angle of peel. Measurements were carried out at 25° and 52% relative humidity.

RESULTS AND DISCUSSION

Relationship between Contact Angles and Film Adhesion—Contact angle measurements of film-coating solutions on the three tablet formulations were made, and the adhesion of the corresponding polymer film to the three tablets was measured as the peel strength of the films from the tablets (Table II). As expected, the film adhesion, as reflected by the force required to peel the film from the tablet, increased with a decrease in the contact angle. Thus, the better the wetting of the tablet by the film solution, the better was the film adhesion.

However, an unusual phenomenon, previously reported (1), was observed with respect to the relationship between film adhesion and the surface tension of the film solution. Instead of an increase in adhesional force with a decrease in solution surface tension, an increase in adhesional force was observed with an increase in solution surface tension. In other words, the contact angle of the solution on the tablet increased as the surface tension of the film solution decreased.

To try to discover the reasons for the observed deviations from theory, the contact angles of the pure solvents used to make the film solutions were determined on the three tablet formulations. The data are given in Table III and are shown in Fig. 1 as a Zisman plot, with the extrapolation intercept at $\cos \theta = 1$ ($\theta = 0$) pro-

⁴ Ames Co., Waltham, Mass.

⁵ Rame-Hart, Inc., Mountain Lakes, N.Y.

⁶ Model 20 Fisher surface tensiometer, Fisher Scientific, Pittsburgh, Pa.

⁷ Dekat, Sloan Technology Corp., Santa Barbara, CA 93103

⁸ Instron universal testing instrument, floor model (TT), Instron Co., Canton, Mass.

Table II—Contact Angle and Peel Strength Data for Films Applied to the Tablets as Affected by Film-Coating Solvent

Tablet	Solvent ^a	Contact Angle ± 1°	Surface Tension of Polymer Solution, dynes/cm	Peel Strength, g/cm	Solubility Parameter of Solvent
I	Acetone	21	22.7	12.7	9.9
	Methyl acetate	18	23.1	19.4	9.6
	Methyl ethyl ketone	18	23.3	24.1	9.3
	Tetrahydrofuran	15	26.1	32.5	9.1
II	Acetone	28	22.7	11.4	9.9
	Methyl acetate	25	23.1	17.0	9.6
	Methyl ethyl ketone	22	23.3	22.0	9.3
	Tetrahydrofuran	19	26.1	29.5	9.1
III	Acetone	32	22.7	8.1	9.9
	Methyl acetate	28	23.1	15.4	9.6
	Methyl ethyl ketone	28	23.3	22.0	9.3
	Tetrahydrofuran	25	26.1	24.5	9.1

^a Each solution contained 8% poly(methyl vinyl ether/maleic anhydride), molecular weight 250,000, and 6% glyceryl triacetate.

viding the apparent critical surface tension of the solid. The contact angle–surface tension relationship for the pure solvent–tablet system is as the Zisman theory would predict. Thus, the theory does hold when considering the pure solvent, which was used to prepare each of the four coating solutions, in contact with the tablet.

To better understand the observed adhesional phenomenon, the polymer solution must be considered further. Since it is the polymer that is adhering to the tablet and not the solvent, it is the wetting of the tablet by the polymer that is important. The adhesional bond that forms between polymer and tablet depends on both the duration of the polymer solution–tablet contact and the intimacy of the contact between the polymer, while in solution, and the tablet. The length of polymer solution contact with the tablet is usually very short because the solvent evaporates very rapidly, producing an immobilized polymer in a viscoelastic film. Yet the wetting of the tablet by the polymer must occur in that short time period while the polymer is in solution and prior to the formation of the viscoelastic film. Therefore, it is important that the polymer solution provide for maximum polymer tablet interaction immediately on contact. It would be expected that for a given polymer the greater the extent of polymer solvation by the solvent, the greater the polymer tablet interaction as the solvent initially contacts and penetrates the tablet surface.

One way of approaching the problem is to use the solubility parameter of the solvent as a qualitative measure of the extent of polymer solvation and to analyze its relationship to the observed contact angles. Table II shows the relationship between the solubility parameters of the four solvents and the observed contact angles. Tetrahydrofuran ($\delta = 9.1$) would be expected to be the most efficient solvent for the polymer ($\delta = 8.7$) since its solubility parameter is closest to that of the polymer. The tetrahydrofuran solvent did produce the lowest contact angle and highest adhesional strength, although it had the highest surface tension. It is certainly apparent that the choice of a film-coating solvent having a solubility parameter close to that of the polymer is important in achieving good film adhesion, and it is even more important than selecting a solvent solely on the basis of surface tension considerations.

Table III—Contact Angles of Pure Solvents on Tablet Substrates

Tablet	Solvent	Surface Tension, dynes/cm	Contact Angle ± 1°	cos θ
I	Acetone	21.5	8.0	0.9903
	Methyl acetate	23.1	12.5	0.9763
	Methyl ethyl ketone	23.3	15.0	0.9659
	Tetrahydrofuran	25.4	17.5	0.9537
II	Acetone	21.5	7.0	0.9925
	Methyl acetate	23.1	14.0	0.9700
	Methyl ethyl ketone	23.3	17.0	0.9563
	Tetrahydrofuran	25.4	20.5	0.9367
III	Acetone	21.5	9.0	0.9877
	Methyl acetate	23.1	15.0	0.9659
	Methyl ethyl ketone	23.3	21.5	0.9304
	Tetrahydrofuran	25.4	22.0	0.9272

The nature of the polymer itself may influence the adhesional bond formed between the film and the tablet substrate. Additional studies are in progress to determine the effect of alkyl ether substitution on the film–tablet adhesional bond.

Wetting and Adhesion as Related to Tablet Surface Roughness—Two of the tablet formulations were compressed at various compressional loads to obtain different surface roughness characteristics. The tablets were compressed at 4545, 6818, and 9091 kg, and the surface roughness characteristics of these tablets were measured (Table IV). For both formulations, the average peak-to-valley height was the greatest for the tablets compressed at 4545 kg and decreased with increasing compressional load; the tablets were becoming smoother with increasing compressional load.

The adhesion of a polymer film to the tablets with differing surface roughness characteristics was determined as the peel strength of the film from the tablet (Table IV). Only one solvent, acetone, was used to deposit the polymer on the tablet formulations, so the surface tension of the coating solution remained constant. From Table IV it is apparent that the peel strength correlates with the roughness data; the rougher the tablet, the higher the peel strength. The differences in peel strength are quite significant and must result from the increased surface area of the rougher tablet which provides for greater interfacial contact between polymer solution and tablet.

A relationship between the contact angle and surface roughness was proposed by Wenzel (10):

$$r = \frac{\cos \theta'}{\cos \theta} \quad (\text{Eq. 1})$$

where θ' is the apparent contact angle on a rough surface, θ is the contact angle on an ideal smooth surface, and r is the roughness factor and is defined as:

$$r = \frac{\text{true surface area}}{\text{apparent plane area}} \quad (\text{Eq. 2})$$

Since r is always greater than unity, the apparent contact angle, θ' , is less than the true contact angle θ when θ is less than 90°. Thus, the effect of roughening the tablet surface is to make the apparent contact angle between the coating solution and the tablet less than the true contact angle. In other words, the polymer solu-

Table IV—Wetting Angle and Adhesion Peel Strength of Films Applied to Substrates as Related to Substrate Surface Roughness

Tablet	Compressional Load, kg	Roughness, Average Peak-to-Valley Distance, A	Wetting Angle	Peel Strength, g/cm
I	4545	17,330	14°	29.1
	6818	16,000	19°	17.7
	9091	7,666	22°	12.7
II	4545	12,400	17°	24.1
	6818	12,000	21°	16.5
	9091	6,833	28°	11.4

tion appears to spread more when the the tablet surface is rough, making the exact determination of the critical surface tension, γ_c , of a compressed tablet very difficult.

In most cases ($\theta \leq 90^\circ$), the true critical surface tension is greater than that determined experimentally. However, from a film-coating standpoint, the influence of surface effects on film adhesion may well be minimal, with the correlation of solvent-polymer solubility parameters being the major factor in determining film adhesion. Regardless of the tablet surface characteristics, the adhesional bond between tablet and polymer must form at a faster rate than the cohesive forces in the polymer film. When this occurs, a strong adhesional bond is established between the tablet and the film.

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Laboratory Automation of High-Pressure Liquid Chromatography

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Abstract □ An automated system for high-pressure liquid chromatography was developed. The system is built around commercial modules wherever possible, modified to varying degrees. An automatic sampler, a sample pump, a high-pressure sampling valve, a recorder with an integrator, and a high-pressure liquid chromatograph comprise the commercial instruments. Relays, solenoid valves, and timers control chromatographic events, *i.e.*, duration of sampling and rinse, mobile phase pump refill, sample injection, and chromatographic time. The automated system is dependable over long periods of unattended operation. With the 40-sample capacity of the sample tray and the last sample stop capability, the automated system produces, for example, 40 20-min chromatograms in approximately 13 hr of unattended operation. Data demonstrate the reliability and utility of the system.

Keyphrases □ High-pressure liquid chromatography—automated equipment developed and discussed □ Automated analysis—high-pressure liquid chromatographic equipment developed and discussed

High-pressure liquid chromatography (HPLC), with its widespread use over the last 5 years, has undergone dramatic growth from the standpoint of methodology and instrumentation. Michaelis *et al.* (1) made it apparent that HPLC is of major importance in quantitative analysis and identification of various pharmaceutical agents. An HPLC equipment review (2) covers a large number of domestic and foreign manufacturers.

The application of HPLC for stability-indicating assays because of specificity, sensitivity, and relative ease of sample preparation is clearly indicated, particularly for labile compounds. Specific applications

of HPLC were reported for various pharmaceutical products containing various active compounds (3) and for steroid formulations (4–7). The increased use of HPLC for stability-indicating assays of steroid formulations, for example, has produced the need for an automated HPLC system. Specific applications of the automation of particular aspects of HPLC have been reported. Among these are the use of short columns and low pressures (8) and the determination of the antibiotic tetracycline (9). More recent work (10) covers the use of a dedicated small computer to study the precision in HPLC.

Although automated HPLC systems are obtainable from commercial manufacturers^{1,2}, they are not readily available. A symposium presentation (11) covered an automated HPLC system developed at Lederle Laboratories. To increase the output of HPLC assays, an automated HPLC system (patent applied for) was developed from commercially available instruments, relays, solenoid valves, and timers and is the subject of this report.

EXPERIMENTAL

The commercial instruments comprising a portion of the automated HPLC system, modified to varying degrees, follow.

Instruments and Modifications—A liquid chromatograph³

¹ DuPont, Wilmington, Del.

² Altex, Berkley, Calif.

³ Model 820, DuPont.