Characterization of Tablet Surfaces by Their Critical Surface-Tension Values

S. W. HARDER, D. A. ZUCK, and J. A. WOOD

Abstract □ Experiments were conducted to determine the critical surface-tension (γ_c) values of a range of acetylsalicylic acid tablets in combination with various adjuvants. A telemicroscope was used to measure the contact angle (θ) as test liquids with known surface tensions (γ_L) advanced across the tablet surface. The cosine of the contact angles ($\cos\theta$) were plotted as a function of the γ_L of the test liquids. Straight-line extrapolation to $\cos\theta = 1$ resulted in γ_c values for each particular type of tablet. These values were determined for each group of tablets, using different sets of test liquids. The γ_c values obtained by this method indicated that pure acetylsalicylic acid tablets presented a surface with intermediate activity, having a γ_c value of about 31 dynes/cm. The addition of a lubricant like magnesium stearate presented a surface richer in $-CH_3$ and $-CH_2-$ groups, resulting in a lower value, whereas the addition of adjuvants such as starch, cellulose, and talc resulted in surfaces richer in =O and —OH, causing an increase in the γ_c values. Increased γ_c values result in increased wetting by the coating solution and in an increased bonding force between the tablet surface and the polymer film coating after the solvent has evaporated. Characterization of the tablet surface should eliminate some of the guesswork involved in developing an adequate film coating for a particular type of medicinal tablet.

Keyphrases □ Tablet surfaces—characterization □ Critical surface-tension values—tablet surface characterization □ Telemicroscopy—liquid, tablet surface contact-angle measurement □ Adjuvant effect—liquid, tablet surface contact angle

The strength of the adhesive bond between a film coating and a solid surface, as well as the uniformity of the coating, is influenced by surface energy forces acting at and across an interface (1–4). It is, therefore, important to understand the energy forces present at the surface of a tablet and to be able to characterize a tablet according to the cohesional energy density (CED) of its surface. Knowledge of the forces operative at the tablet surface will assist in prediction of the degree of bonding and permit the design of coating solutions, resulting in optimum utilization of these forces to obtain adequately bonded and uniform film coatings. Preliminary tests indicated that there is a certain amount of correlation between the critical surface-tension values and film-coating characteristics such as degree of adhesion and film texture (5).

Although no direct method of measuring solid surface energy has yet been found, critical surface-tension (γ_c) values do represent an indirect approach to the characterization of solid surfaces according to their CED.

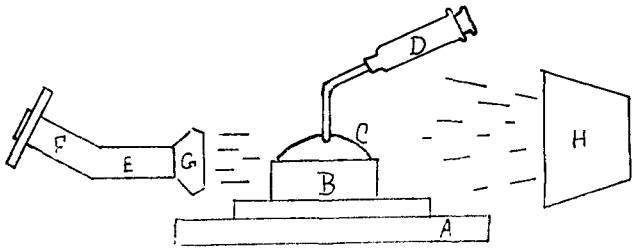

Figure 1—*Schematic arrangement of apparatus. Key: A, moveable microscope stage; B, tablet resting on glass microscope slide; C, test liquid being applied to tablet surface; D, glass syringe with bent needle used to deliver test liquid to tablet surface; E, telemicroscope; G, ring light; F, erecting eye prism and protractor eyepiece; and H, diffuse light source for backlighting the drop of liquid on the tablet surface.*

In the articles cited in the previous paper (5), γ_c values were determined using a selection of pure liquids with surface tensions in the range necessary for the determination of these values. Some investigators did use liquids of a homologous series in an effort to overcome variations in contact angles due to specific interactions. Since it is not always possible to find a homologous series with surface tensions in the required range, a decision was made to use series of high and low surface-tension liquid mixtures. These could be prepared as series of solutions with similar physical-chemical properties and with a gradual gradation of surface-tension values. Other investigators (6–11) have also used such mixtures of high and low surface-tension liquids to determine the γ_c of a variety of surfaces.

In the present study, two series of mixtures of solvents with high and low surface tensions were used to characterize the surfaces of various tablets. The methanol–water series and the 1-butanol–formamide series represent two such systems, with both polar and dispersion forces operative and a range of surface-tension values suitable for determining the γ_c values of the solid surfaces under investigation. This study consists of observations on the validity of such characterizations

Table I—Percent w/w Composition of the Tablets for which Critical Surface-Tension Values Were Determined

Tablet Number	Acetylsalicylic Acid[a]	Magnesium Stearate[b]	Talc[c]	Cornstarch[d]	Starch USP[e]	Microcrystalline Cellulose[f]
1	100	—	—	—	—	—
2	99	1	—	—	—	—
3	99	—	1	—	—	—
4	90	—	—	10	—	—
5	90	—	—	—	10	—
6	95	—	—	—	—	5

[a] Asagran, Monsanto Can. Ltd., Ville La Salle, P.Q., Canada. [b] Magnesium stearate USP, Chemical Manufacturing Division, Fisher Scientific Co., Fair Lawn, N. J. [c] Talc USP, Anachemia Chemicals Ltd., Montreal, Canada. [d] Starch, cornstarch, Canada Corn Starch, Best Foods Division, Canada Corn Starch Co. Ltd., Montreal, Canada. [e] Starch USP, Sta-Rx Starch 1500, A. E. Staley Mfg. Co., Decatur, Ill. [f] Microcrystalline cellulose, Avicel, FMC Corp., American Viscose Division, Newark, Del.

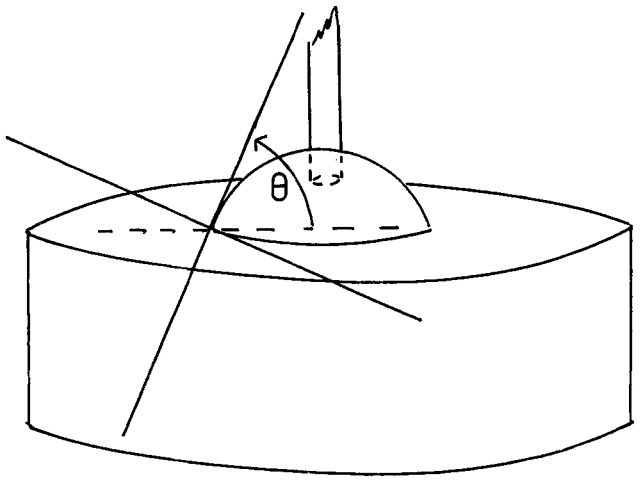

Figure 2—*View through telemicroscope showing cross hairs aligned with the advancing edge of the liquid to determine θ, the contact angle a particular test solution makes with a particular tablet surface.*

and on possible reasons for differences in γ_c values when different series of test liquids are used.

Modifications have been made in the procedure previously used in an effort to get more reproducible results. In the previous work, the contact angles reported were measurements made as soon as possible after a single drop was placed on the tablet surface. Because of the porous nature of the tablet, considerable difficulty was experienced in obtaining true initial contact-angle readings that actually reflected the surface energy of a particular tablet surface. In this paper, the contact-angle data reported are the results of successive contact-angle readings as the test liquid was being continuously applied and advanced across the surface of the tablet. This method ensured that the angles of contact measured were advancing contact angles. Also, the mean contact-angle value for a tablet surface obtained from successive measurements as the liquid advances across the tablet surface is a more accurate measure of the surface energy of that tablet. It is not as prone to distortion due to heterogeneity and tablet imperfections, as is a single measurement on one discreet drop made some time after the drop is placed on the tablet surface.

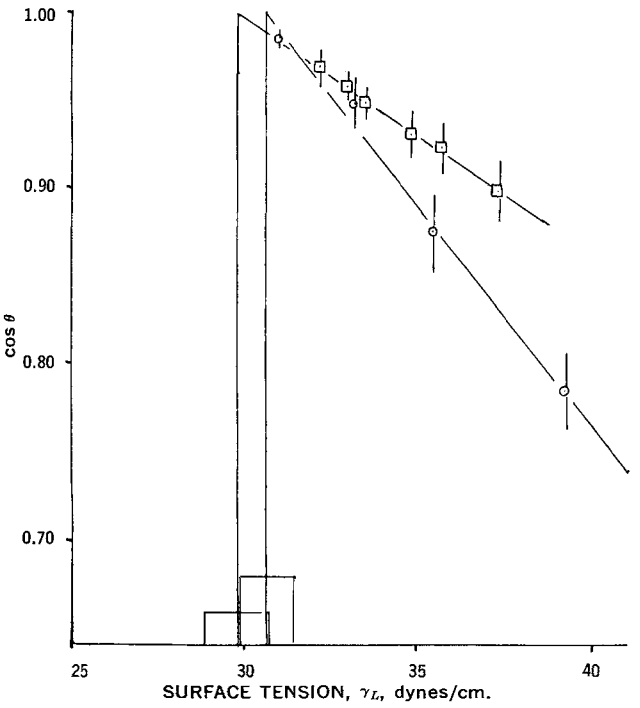

Figure 3—*Tablets of pure acetylsalicylic acid; cos θ* versus γ_L *plots of two liquid series. Key: ⊡, 1-butanol–formamide; and ⊙, methanol–water.*

Table II—Composition and Surface Tension of Test Liquids

Methanol–Water		1-Butanol–Formamide	
Concentration, %w/w	Surface Tension, dynes/cm.	Concentration, %w/w	Surface Tension, dynes/cm.
26	43.5	4	43.7
30.7	41.6	5	41.8
34	39.2	6	40.3
37.5	37.9	6.5	39.6
40	37.4	7	39.1
46	35.2	8.5	37.3
54.2	33.2	10	35.6
63.8	31.0	11.5	34.8
72.9	29.1	13.75	33.5
80.6	27.4	15	33.0
87.7	25.8	17	32.2
94.2	24.3	30	29.2
100	23.1	35	28.6
		50	27.6
		60	27.1
		75	26.2
		90	25.4
		100	24.9

EXPERIMENTAL

Materials—Tablets were prepared using a pure granular amorphous acetylsalicylic acid (ASA) with adjuvants as indicated (Table I). The tablets were prepared on a single-punch tablet machine using 1.27-cm. (0.5-in.) flat faced punches.

The two series of test liquids were mixtures of absolute methanol[1]–water[2] and 1-butanol[3]–formamide.[3] Table II indicates the surface tensions and compositions of the test liquids.

Su face-Tension Measurements—The surface tensions of the test liquids were determined with a Fisher Tensiomat.[4] Each recorded measurement is the mean of at least 10 trials, corrected for ring dimension and density of the liquid.

Contact-Angle Measurements—The apparatus used to measure the contact angles consisted of a horizontal telemicroscope[5] fitted with an erecting adapter, a protractor eyepiece (eyepiece 10X), and an objective lens (objective 2.8X) with a ring light. A further diffuse light source in the form of a microscope light was mounted behind the sample.

The sample holder consisted of a glass microscope slide mounted horizontally on a mechanical microscope stage fitted with a micrometer.

The test liquids were delivered onto the tablet surface by means of a 1-ml. glass syringe mounted in a horizontal position, fitted with a 21-gauge stainless steel needle bent in a 90° curve and containing a polyethylene tubing[6] insert protruding from the end. The syringe piston was driven by a syringe pump[7] set to deliver between 0.0355

[1] Analar, Analytical reagent, British Drug Houses (Can.) Ltd., Toronto, Canada.
[2] Doubly distilled water.
[3] Reagent grade, Chemical Manufacturing Division, Fisher Scientific Co., Fair Lawn, N. J.
[4] Fisher Surface Tensiomat, Fisher Scientific Co., Fair Lawn, N. J.
[5] Telemicroscope model M101T, Gaertner Scientific Corp., Chicago, Ill.
[6] Intramedic polyethylene tubing, i.d. 0.028 cm. (0.011 in.) × o.d. 0.061 cm. (0.024 in.), Clay-Adams, Inc., New York. N. Y.
[7] Sage Syringe Pump, model 255-1, Sage Instruments, Inc., Subsidiary of Orion Research Inc., White Plains, N. Y.

Table III—Contact Angles for the Methanol–Water Solution Series

Surface Tension of Liquid, dynes/cm.	Mean Contact Angle $\theta \pm SD$					
	Pure Acetylsalicylic Acid	Acetylsalicylic Acid–Magnesium Stearate	Acetylsalicylic Acid–Talc	Acetylsalicylic Acid–Cellulose	Acetylsalicylic Acid–Starch	Acetylsalicylic Acid–Starch USP
43.5					35.2 ± 2.6	41.2 ± 2.3
41.6			45.0 ± 1.6		33.5 ± 4.3	37.6 ± 2.1
39.2	38.1 ± 2.1			38.5 ± 1.9		34.9 ± 1.6
37.9				34.2 ± 2.1		27.9 ± 2.1
37.4			35.7 ± 1.9	33.7 ± 2.2	24.6 ± 3.1	28.1 ± 2.0
35.2	28.8 ± 2.7		29.4 ± 1.2	24.6 ± 2.9	13.2 ± 2.2	17.1 ± 1.4
33.2	18.5 ± 2.7		21.9 ± 1.9	14.3 ± 2.3	7.0 ± 1.5	8.6 ± 1.4
31.0	9.4 ± 2.0		10.4 ± 2.5			
29.1		57.1 ± 2.5				
27.4		48.8 ± 2.1				
25.8		41.7 ± 2.5				
24.3		32.7 ± 1.6				
23.1		25.3 ± 1.7				

and 0.0450 ml./min. Figure 1 shows a schematic arrangement of the apparatus.

The contact angles were measured at approximately 10-sec. intervals as the test liquid advanced across the tablet surface. Prior to testing, the tablet surface was wiped on a clean paper towel and brushed with a camel hair brush to remove any materials or loose powder which might have contaminated the surface and could affect the contact angle.

Figure 2 shows a view of the contact angle through the telemicroscope.

All experimental work was carried out in a controlled environment at 20° and 45% relative humidity.

RESULTS

Mean contact angles were determined for the six sets of tablets indicated in Table I, using the relevant members of the series of test liquids indicated in Table II. Each contact angle reported is the mean of approximately 100 readings. Ten readings were made on each of 10 tablets. The mean contact angle and standard deviation ($\theta \pm SD$) of each set were calculated. Tables III and IV are a tabulation of the contact-angle data obtained.

Figures 3–8 show graphically the results when $\cos \theta \pm SD$ is plotted against the surface tension of the test liquid applied to the surface. A linear regression analysis was used to determine the best line through the points, the slope of the line, the degree of correlation, an estimate of critical surface tension (extrapolate to $\cos \theta = 1$), and the error of the estimate. Table V shows a summary of these results.

DISCUSSION

The degree of correlation between surface tension of the test liquids and contact angle is especially good for the tests carried out with the methanol–water solutions. Between 95 and 99% of the variation in contact angle can be attributed to the variation in surface tension of the test liquid.

Although the γ_c values obtained by the use of one test liquid fall within the error of the estimate of the γ_c value obtained by using the

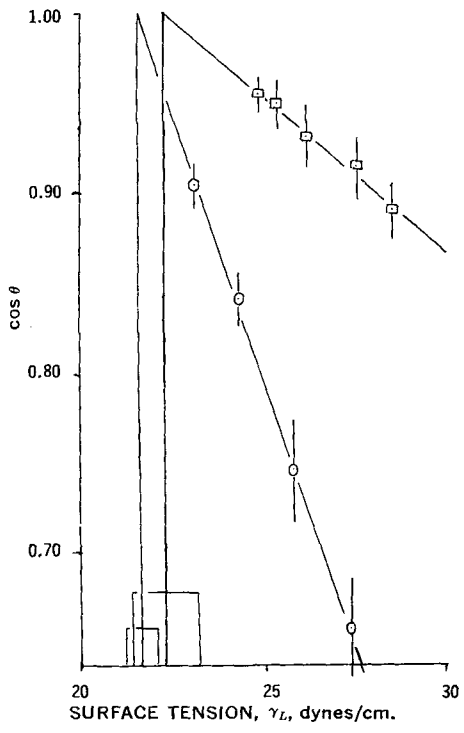

Figure 4—*Tablets of acetylsalicylic acid with 1% magnesium stearate; cos θ versus γ_L plots of two liquid series. Key: ⊡, 1-butanol–formamide; and ⊙, methanol–water.*

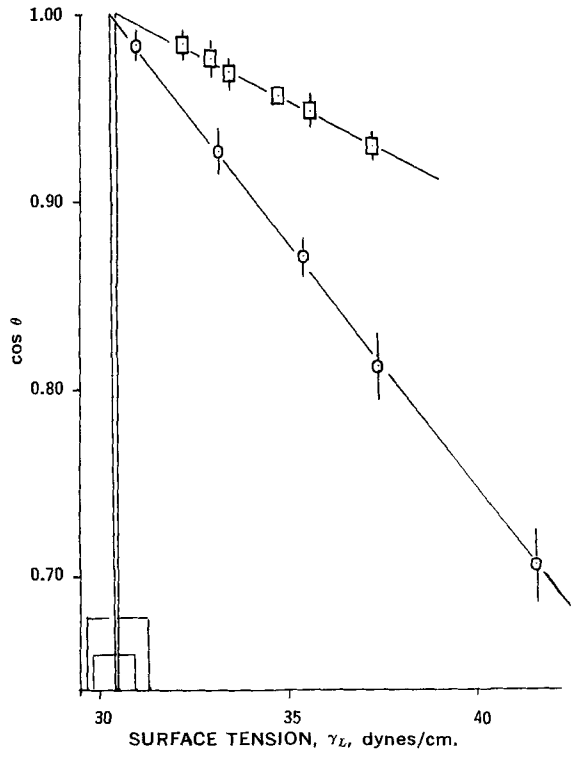

Figure 5—*Tablets of acetylsalicylic acid with 1% talc; cos θ versus γ_L plots of two liquid series. Key: ⊡, 1-butanol–formamide; and ⊙, methanol–water.*

Table IV—Contact Angles for the 1-Butanol–Formamide Solution Series

Surface Tension of Liquid, dynes/cm.	Mean Contact Angle $\theta \pm SD$					
	Pure Acetylsalicylic Acid	Acetylsalicylic Acid–Magnesium Stearate	Acetylsalicylic Acid–Talc	Acetylsalicylic Acid–Cellulose	Acetylsalicylic Acid–Starch	Acetylsalicylic Acid–Starch USP
43.7					19.4 ± 1.3	
41.8					18.3 ± 1.5	
40.3					17.2 ± 1.0	20.1 ± 2.4
39.6				21.8 ± 1.3	15.7 ± 1.4	19.2 ± 1.4
39.1				20.7 ± 1.4	15.2 ± 1.3	18.7 ± 2.5
37.3	25.8 ± 2.3		21.6 ± 1.2	18.2 ± 2.1	14.2 ± 1.2	16.0 ± 1.5
35.6	25.5 ± 2.1		18.5 ± 1.7	15.9 ± 1.9	11.0 ± 1.6	13.4 ± 1.3
34.8	21.3 ± 2.2		17.1 ± 1.8	15.0 ± 1.8	9.4 ± 1.9	11.3 ± 1.2
33.5	18.5 ± 1.7		14.4 ± 1.9	10.5 ± 2.1		
33.0	16.5 ± 1.7		12.6 ± 2.5			
32.2	14.2 ± 2.5		10.5 ± 3.0			
29.2						
28.6		27.1 ± 2.1				
27.6		23.9 ± 2.6				
27.1						
26.2		21.3 ± 2.8				
25.4		18.4 ± 2.6				
24.9		17.4 ± 1.8				

other test liquid, there is an indication that for the tablets with a higher surface energy, a higher γ_c value is obtained when methanol–water contact-angle data are used. It would appear that the γ_c value obtained for a particular tablet is dependent on the type of test solution employed.

The slopes of the curves for methanol–water in all cases are greater than the slopes of the curves for the 1-butanol–formamide solutions. This indicates that changing the concentration of the methanol–water solution so as to increase its surface tension by a fixed amount would cause a greater deterioration in the wetting properties than would be caused by a similar increase in the surface tension of the 1-butanol–formamide solution.

A straight-line relationship between cos θ and the surface tension of the liquid as cos $\theta \rightarrow 1$ has been assumed. One is aware that the overall relationship is not linear, but the part of the curve cos θ between 0.7 and 1.0 so closely approximates a straight line that it is felt that this approach is valid. The high degree of correlation, despite the considerable variation in cos θ values across a tablet surface and between tablets with the same composition, seems to justify this approximation. The results published by Dann (12) for ethanol–water mixtures on a pure hydrocarbon surface such as paraffin and on surfaces with both polar and nonpolar forces such as poly(ethylene terephthalate) and poly(methylmethacrylate) yield curves that very nearly approximate straight lines between cos θ values of 0.7–1. The error introduced by this assumption would be well within the error due to variation in contact-angle measurements, which he puts at $\pm 3°$ in his work on polar polymers.

The surface tension of an organic compound can be estimated from its chemical structure using parachor values (13). The estimated surface tension of acetylsalicylic acid using this method is 34.0 ± 1.7 dynes/cm. This value is fairly close to the estimates obtained from γ_c value data, 30.7 ± 0.8 dynes/cm. and 29.8 ± 0.9 dynes/cm. The discrepancy may well be due to an imbalance of polar and dispersion forces between the tablet surface and the test liquids used.

The addition of magnesium stearate considerably reduces the γ_c of the tablet surface. The slopes of both lines, cos θ *versus* γ_L for methanol–water and 1-butanol–formamide, become steeper (more negative) by the addition of magnesium stearate to the acetylsalicylic acid. This signifies increasingly poorer wetting properties as the surface tension of the test liquids in contact with the tablet surface is increased.

The addition of talc does not significantly affect the γ_c of the tablet surfaces, although it does alter the slopes of the curves so that the curves do not intersect as they do for pure acetylsalicylic acid. The significance, if any, of these changes has not yet been established.

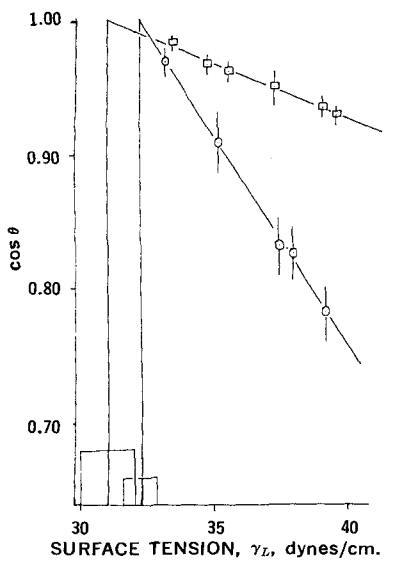

Figure 6—*Tablets of acetylsalicylic acid with 5% microcrystalline cellulose; cos θ versus γ_L plots of two liquid series. Key: ⊡, 1-butanol–formamide; and ⊙, methanol–water.*

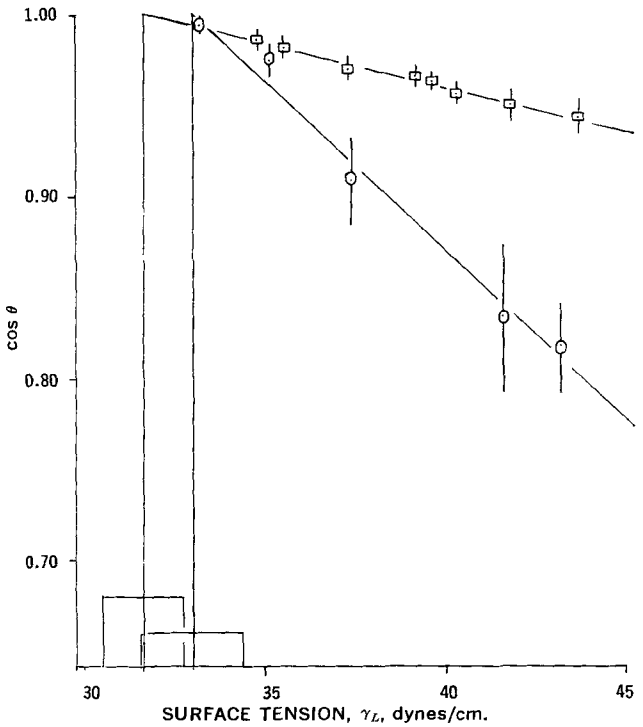

Figure 7—*Tablets of acetylsalicylic acid with 10% starch; cos θ versus γ_L plots of two liquid series. Key: ⊡, 1-butanol–formamide; and ⊙, methanol–water.*

Table V—Summary of Data Analysis from Plots, cos θ *versus* γ_L

Tablet Composition	Methanol–Water Data: Estimate γ_c, dynes/cm.	Methanol–Water Data: Slope	Methanol–Water Data: Correlation	1-Butanol–Formamide Data: Estimate γ_c, dynes/cm.	1-Butanol–Formamide Data: Slope	1-Butanol–Formamide Data: Correlation
Acetylsalicylic acid–1% magnesium stearate	21.6 ± 0.4	−0.060	0.96	22.2 ± 0.9	−0.017	0.96
Acetylsalicylic acid pure	30.7 ± 0.8	−0.025	0.94	29.8 ± 0.9	−0.013	0.77
Acetylsalicylic acid–1% talc	30.4 ± 0.6	−0.026	0.98	30.5 ± 0.8	−0.010	0.89
Acetylsalicylic acid–5% cellulose	32.2 ± 0.6	−0.031	0.96	31.0 ± 1.0	−0.008	0.96
Acetylsalicylic acid–10% starch	33.0 ± 1.4	−0.019	0.94	31.6 ± 1.1	−0.005	0.92
Acetylsalicylic acid–10% starch USP	32.9 ± 0.8	−0.025	0.97	32.1 ± 1.3	−0.008	0.85

The addition of microcrystalline cellulose and starches results in surfaces somewhat richer in hydroxyl groups, a consequent higher surface energy, and a surface more prone to polar bonding with polar materials. The experimental γ_c values are increased by the addition of these materials. The fact that for all three tablets the γ_c values obtained with the more polar methanol–water test liquids are greater than that obtained with the 1-butanol–formamide test liquids tends to indicate greater interaction of polar forces.

The attractive forces present in the surface layers and the extent and manner of interaction of these intermolecular forces have been discussed by Dann (12). When a liquid (L), with a surface tension (γ_L) made up of components (γ_L^W) due to dispersion forces and (γ_L^P) due to polar forces, is in contact with a surface made up of saturated hydrocarbons (S) where the surface tension (γ_S) is due to dispersion forces only ($\gamma_S = \gamma_S^W$), the relationship between the contact angle (D) the liquid makes with the hydrocarbon surface is given by the Good–Girifalco–Fowkes–Young equation (14):

$$\cos\theta = 2\sqrt{\gamma_S^W}\left(\frac{\sqrt{\gamma_L^W}}{\gamma_L}\right) - 1 \qquad \text{(Eq. 1)}$$

If the surface has both dispersion forces and polar forces present and the polar forces are mainly due to hydrogen bonding whose interaction across the interface can also be expressed by a geometric mean relationship, then Eq. 1 becomes:

$$\cos\theta = 2\sqrt{\gamma_S^W}\left(\frac{\sqrt{\gamma_L^W}}{\gamma_L}\right) + 2\sqrt{\gamma_S^P}\left(\frac{\sqrt{\gamma_L^P}}{\gamma_L}\right) - 1 \qquad \text{(Eq. 2)}$$

Since γ_L and cos θ are measurable, γ_S^W for paraffin is known to be 25.5 dynes/cm. (12). Moreover, since $\gamma_L = \gamma_L^W + \gamma_L^P$, the polar and dispersion forces operative in a liquid with mixed attractive forces can be determined (14). The same method could be applied to solid surfaces with mixed attractive forces to determine the individual polar and dispersion forces operative. A knowledge of the breakdown of these forces would permit adjustment of either or both the solid surface or the liquid applied to yield a balanced interface with optimum interaction and, therefore, optimum adhesion. It would also permit the intelligent application of the Zisman technique (15) in determining γ_c values of solid surfaces with mixed attractive forces.

By examining Eq. 2, one sees that if γ_S and γ_L are constant and $\gamma_S^W > \gamma_S^P$, an increase in the γ_L^P will cause a comparable decrease in the γ_L^W and an overall decrease in cos θ, *i.e.*, a larger contact angle. This would account for the difference in slopes of the plots of cos θ *versus* γ_L for the two different test liquid series.

The extent to which the γ_c values obtained represent the surface energies or attractive forces in the tablet surfaces depends on the extent to which the polar and dispersion forces in the test liquid balance the polar and dispersion forces in the solid surface, since cos $\theta \rightarrow 1$ when the test liquid only just wets the surface. Figure 9, taken from Dann (12), illustrates the effects of an unbalanced system. A solid surface, which yields a γ_c^W of 39 dynes/cm. when determined using a nonpolar liquid with only dispersion forces interacting, will yield a critical surface tension with a polar series of liquids (γ_c^{PL}), similar to the 1-butanol–formamide, of 31 dynes/cm. When an even more polar series of liquids, ethanol–water, similar to the methanol–water, is used, an even lower γ_c^{PL} value of 26 dynes/cm. is obtained. The use of highly polar liquid series to determine the

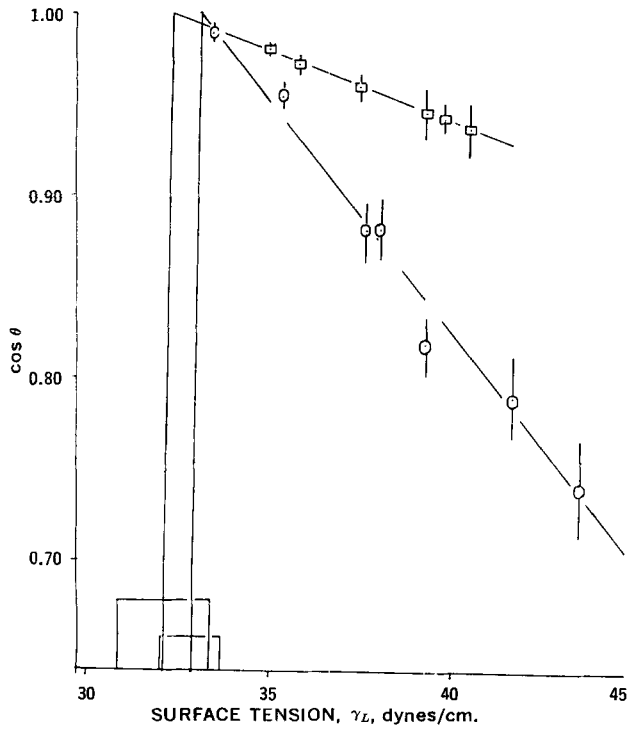

Figure 8—*Tablets of acetylsalicylic acid with 10% starch USP; cos θ versus γ_L plots of two liquid series. Key: ⊡, 1-butanol–formamide; and ⊙, methanol–water.*

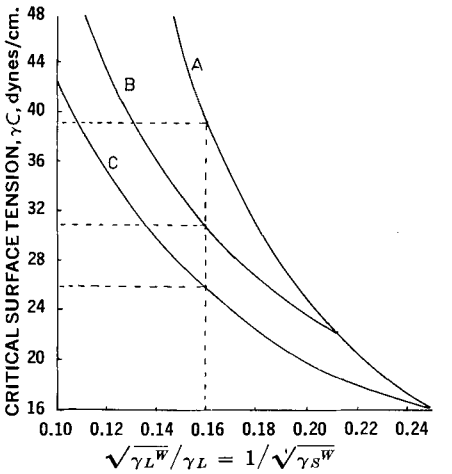

Figure 9—*Critical surface-tension conversion curves. Key: A, hydrocarbon liquid series with dispersion forces only; B, liquid series with moderate polar forces; and C, ethanol–water series with greater polar forces.*

surface energy level of surfaces with only moderate polar forces would result in a very misleading estimate of at least the dispersion forces present in that surface.

CONCLUSIONS

It is possible to characterize tablet surfaces according to their CED by using contact-angle data and applying a modification of the Zisman (15) technique. However, caution must be exercised in the interpretation of the γ_c values obtained. Particular attention should be paid to the possible effects of unbalanced polar and dispersion forces between the test liquids and surfaces investigated.

The surface energy of a tablet, as well as the types of forces present, can to some extent be predicted by studying the types of chemical components that would be present at the surface.

More work needs to be done in determining the presence and relative roles of polar and dispersion forces as they influence wetting, contact-angle data, adsorption, and adhesion.

A knowledge of the types of forces acting across the interface between the tablet surface and a film coating, their relative intensities, and the degree of interaction should greatly advance the understanding of processes involved in the formation of an adequate film coating.

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Rotating-Flask Method for Dissolution-Rate Determinations of Aspirin from Various Dosage Forms

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Abstract □ The dissolution of aspirin from different commercial dosage forms was evaluated by the rotating-flask method, and the data were correlated with previously reported absorption data. Regardless of agitation intensity, over a range from 0.9 to 2.4 r.p.m., dissolution rate was found to decrease in the following order: buffered tablets > plain tablets > timed-release tablets. The data were linearized by means of log-normal probability plots and interpreted accordingly. Aspirin dissolves from the buffered tablet about twice as rapidly as from the plain tablet and about eight times as rapidly as from the timed-release tablets. Once disintegration and deaggregation take place, the dissolution of aspirin from the capsule formulation proceeds as rapidly as from the buffered tablet. Surfactant decreased the dissolution rate of aspirin from certain formulations, in contrast to the enhanced dissolution effects observed using the beaker method where mound formation occurred. Excellent single- and multiple-quantitative correlations were observed between the dissolution data and absorption data in man.

Keyphrases □ Aspirin in dosage forms—dissolution rates □ Dissolution rates—aspirin dosage forms □ Surfactant effect—aspirin dissolution from dosage forms □ Rotating-flask method—dissolution-rate determination

A number of methods designed to measure the dissolution rate of drugs from solid dosage forms are presently available (1, 2). Interest has been particularly focused on the beaker method (3) and its variants, including the rotating-basket assembly (4) and the flask and stirrer method (5), since these methods have consistently provided data which permit some correlation with *in vivo* data (5–8).

A shortcoming of the beaker method is observed at relatively low agitation intensities, *i.e.*, <40–50 r.p.m., where the geometry of the system combined with the nature of the agitation forces the granules or particles into a mound at the bottom of the flask or beaker. The mound is more or less compact, depending upon the formulation of the dosage form, and may or may not present a markedly reduced surface area to the dissolution medium. This problem was exemplified by Levy *et al.* (6), who were concerned with the quantitative correlation of dissolution data with the gastrointestinal absorption in man of aspirin from different types of dosage forms. Clinical studies indicated that aspirin was absorbed about three times more rapidly from "plain tablets" of the drug than from a timed-release preparation. Dissolution data obtained at 50 r.p.m. gave virtually perfect correlation with respect to differences between the two dosage forms observed *in vivo*, but the dissolution rate of the drug from the plain tablet was about twice the absorption rate of the drug from the same dosage form. At 45 r.p.m., where the dissolution rate of aspirin from the plain tablet was comparable to the absorption rate of drug from this dosage form, there was only a 50% difference between the timed-