Contact Angles on Human Skin

Keyphrases □ Contact angles—human skin, previously developed equations discussed □ Skin, human—determination of contact angles, equations

To the Editor:

Several reports of contact angle measurements of various liquids on human skin have appeared in recent years (1–4). Although these papers differed in the reported values of the contact angles, especially for water, there was general agreement that human skin behaves as a low energy solid. Rosenberg *et al.* (3) made their measurements on specially cleaned viable and excised skin and calculated the surface energy of skin due to dispersion forces (γ_S^D) using Eq. 1:

$$\cos\theta = \frac{-\gamma_L + 2\sqrt{\gamma_S^D\gamma_L^D} - \pi_S}{\gamma_L - \pi_L} \qquad \text{(Eq. 1)}$$

where θ is the contact angle, γ_L is the surface tension of the liquid, γ_L^D is the dispersion force component of the surface tension of the liquid, π_S is the reduction in surface energy of the solid due to adsorption of vapor from the liquid drop, and π_L is the reduction in surface tension of the liquid due to spreading of the solid. The investigators assumed π_S and π_L to be negligible, as is often done when dealing with low energy surfaces.

Similarly, El-Shimi and Goddard (4) neglected these spreading terms in their analysis of the dispersion force (γ_S^D) and polar (γ_S^P) contributions to the surface energy of skin, using Eq. 2:

$$\cos\theta = \frac{-\gamma_L + \dfrac{4\gamma_S^D\gamma_L^D}{\gamma_S^D + \gamma_L^D} + \dfrac{4\gamma_S^P\gamma_L^P}{\gamma_S^P + \gamma_L^P}}{\gamma_L} \qquad \text{(Eq. 2)}$$

In addition to the symbols previously defined, γ_L^P is the polar contribution to the surface tension of the liquid.

Skin presents a complex surface whose properties are influenced by a variety of endogenous, secreted, and excreted substances. Mono-, di-, and triglycerides and free fatty acids are among the lipids found most abundantly on the skin (5); these substances are known to spread on water, lowering its surface tension significantly (6). According to a recent report, sweat collected from thermally stimulated subjects had surface tension values lower than that of water by about 13–19 dynes/cm, depending on the skin region used (7).

There is, therefore, good reason to think that π_L may have a value other than zero in many cases. The value of π_L will be a function of the liquid, the nature of the skin area, the history (or pretreatment) of the skin sample, and the area of contact between the liquid drop and the skin. If the spreading process is time dependent, then the contact angle will decrease with time, an effect observed by one investigator (1). The large variation found in the contact angle of water on skin (1–4) is probably related to differences in lipid adsorption at both the water–air and skin–water interfaces.

Unfortunately, neither Eq. 1 nor 2 is adequate for quantitating the effect of skin surface lipids on the contact angle. Equation 2 does not contain π_L. Equation 1 does contain π_L, but no provision is made for changes in adsorption at the solid–liquid interface. For liquids whose contact angles are greater than 90°, Eq. 1 predicts that a rise in π_L will cause an increase in the value of the contact angle. Actually, the opposite takes place (8).

Thus, it appears that approaches that have been successful in characterizing other low energy surfaces are of only limited usefulness when applied to skin. More data on the adsorption of surface lipids would be helpful in understanding wetting and spreading on skin.

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Received March 3, 1975.
Accepted for publication April 4, 1975.

Variability in System for Automated Determination of Dissolution Rate

Keyphrases □ Dissolution rates—automated determination, analysis of data, variability □ Automated analysis—dissolution rates, analysis of data, variability

To the Editor:

Recently, Johnson *et al.* (1) described a continuous-flow system for the automated determination of dissolution rates. The major obstacle encountered in any continuous system, *i.e.*, assuring the measurement of a clear solution free of extraneous particles which cause turbidity in the solution and cloud the surfaces of the flow cells, was overcome by the incorporation of filter units into the system, utilizing disposable Teflon or polyvinyl inserts.

The authors (1) reported excellent agreement between the dissolution rates obtained by an automated system and by manual measurements. According to these investigators, their instrumentation can

Table I—Range of Individual *In Vitro* Dissolution[a]

	USP—NF[b]				500-mg Levodopa Tablet[c]			
	500-mg Levodopa Tablet		2-mg Benzodiazepine Tablet		USP—NF		Levy	
Minutes	Average, %	Range, %	Average, %	Range, %	Average, %	Range, %	Average, %	Range, %
2.5	48	17	22	21	17	17	16	17
5	85	11	69	11	38	43	30	22
10	97	11	83	9	78	27	53	43
15	99	7	91	12	87	12	67	51
20	100	5	100	11	90	8	73	50
30	100	4	—	—	94	5	81	30

[a] Data from Ref. 1. [b] Table V of Ref. 1. Speed of agitation and number of determinations not specified. [c] Table VI of Ref. 1. Agitation speed of 60 rpm; six determinations.

Table II—Dissolution Rate of Salicylic Acid Tablets

	Percent Salicylic Acid Dissolved													
	Experiment												Average	
Minutes	1	2	3	4	5	6	7	8	9	10	11	12	%	Range, %
2.5	22	21	20	23	25	27	29	24	23	25	24	21	24	20—29 = 9
5	36	38	40	44	39	38	36	37	32	38	44	38	38	36—44 = 8
10	66	58	68	67	57	60	62	56	68	68	56	58	62	56—68 = 12
15	80	80	83	81	75	77	73	70	85	77	73	72	77	70—85 = 15
20	90	92	95	90	89	85	83	82	93	92	89	87	89	82—95 = 13
30	100	99	103	102	99	98	95	95	100	102	103	102	100	95—103 = 8

measure real differences in the dissolution rate of unit doses within a batch if these differences exceed ±2.8% of the average assay. However, analysis of their data (Table I) indicates that the intertablet variations gave rather large-range values. This study was undertaken to investigate the nature of the large-range values obtained with the automated apparatus.

Since the authors claimed the accuracy and reproducibility of the instrumentation by showing negligible variation caused by the electrical imbalance (<1%) and instrumentation, possible explanations for the large intertablet variation may be: (*a*) differences in the active ingredient content of the tablets, (*b*) differences in the disintegration properties of the tablets, and/or (*c*) uneven distribution of drug particle size among tablets.

An examination of Table I reveals that the range values were much higher in the period represented by 20–80% dissolution. This finding indicates that the disintegration properties, rather than content uniformity, of the tablets were largely responsible for the variations observed. For example, if some tablets in a given batch disintegrated much faster than the others, the faster disintegrating tablets would tend to yield faster dissolution rates as compared to the slower disintegrating tablets. Thus, the "average" dissolution rate of this batch of tablets would exhibit large intertablet variations.

To minimize differences due to content uniformity and manufacturing variables, a batch of 200-mg salicylic acid tablets was prepared by individually weighing 200 mg of salicylic acid for each tablet and compressing the tablets using a hydraulic press[1]. All tablets were prepared using identical compression force for the same time period, thus assuring that the tablets were uniform. Quick checks of the disintegration and hardness revealed that the tablets were identical in these respects.

Dissolution was followed in an automated apparatus[2] similar to the one described by Johnson *et al.* (1), using 900 ml of simulated gastric fluid (without enzymes), according to the USP–NF method (2, 3). A 1.9-ml/min flow rate[3] through a flow cell[4] and a recording spectrophotometer[5] were used. From the results (Table II), it is evident that the intertablet variations were somewhat greater than the accuracy and reproducibility claimed for the apparatus. Therefore, the large variations found by Johnson *et al.* could be due to differences in disintegration and other physical properties of the tablets as well as to the nonreproducibility of the apparatus. Further work is in progress to determine the factors responsible for these variations.

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(2) "The United States Pharmacopeia," 18th rev., Mack Publishing Co., Easton, Pa., 1970, p. 934.

(3) "The National Formulary," 13th ed., Mack Publishing Co., Easton, Pa., 1970, p. 802.

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Received January 23, 1975.
Accepted for publication March 21, 1975.

[1] P-30 hydraulic press, Research and Industrial Co. Ltd., London, England.

[2] Model T1045-20x/53, Vanderkamp tablet dissolution tester, Van-Kel Industries, Chatham, N.J.

[3] Model 1201, Harvard Apparatus Co., Millis, Mass.

[4] Type 42 flow cell, Luminon, Inc., Irvington, N.J.

[5] Hitachi-Perkin-Elmer UV-VIS recording spectrophotometer model 139, Coleman Instruments Division, Maywood, Ill.