Contact Angles and Wettability of Human Skin

HANS SCHOTT

Abstract □ The contact angles of several liquids on human skin were measured before and after extraction of surface lipids with acetone. The critical surface tension of the skin was determined by extrapolating the cosines of the contact angles of the liquids as a function of their surface tensions to unity. The critical surface tensions for untreated and extracted skin were in the range of 22–30 dynes/cm. These low values are probably caused by reductions in contact angles resulting from furrows in the skin and by small amounts of air trapped at the furrows underneath the drops rather than by low free energy or polarity of the skin surface. Application of benzalkonium chloride and of a hand lotion reduced the contact angles of water on the skin.

Keyphrases □ Skin, human—measurement of contact angles of liquids before and after extraction of surface lipids □ Contact angles and wettability—liquids on human skin, critical surface tension determined □ Surface tension, critical—correlation to contact angles, human skin □ Wettability and contact angles—several liquids on human skin, critical surface tension determined

The surface properties of human skin are important in connection with the spreading of topically applied drugs and cosmetics. Measurements of the contact angles of various liquids were undertaken in view of the paucity of available data (1, 2).

THEORY

The spreading of a drop of liquid (*L*) placed on a solid horizontal surface (*S*) in air (*A*) is described by the equation:

$$\gamma_{SA} = \gamma_{SL} + \gamma_{LA}\cos\theta \qquad 0° \leq \theta < 180° \qquad \text{(Eq. 1)}$$

where γ represents interfacial tension, and θ is the contact angle measured in the liquid. This equation applies to the equilibrium condition, when the difference between the solid–air and solid–liquid interfacial tensions equals the adhesion tension. Strictly speaking, γ_{LA} refers to the interfacial tension between the liquid and its vapor (3).

Zisman (4) and his coworkers uncovered the linear relationship:

$$\cos\theta = a - b\gamma_{LA} \qquad \text{(Eq. 2)}$$

In the limit, $\cos\theta = 1$, and $\gamma_{LA} = \gamma_C$ equals the critical surface tension of the solid. Liquids with surface tensions equal to and smaller than γ_C will spread indefinitely on the solid surface, while liquids with $\gamma_{LA} > \gamma_C$ will make a finite contact angle (4). From Eq. 2:

$$\cos\theta = 1 + b(\gamma_C - \gamma_{LA}) \qquad \text{(Eq. 3)}$$

The critical surface tension has been identified with the surface tension of the solid (5, 6) but, more likely, it is somewhat smaller (7).

EXPERIMENTAL

Methods—Contact angles were measured by projecting the image of the drop against a vertically held piece of paper at a magnification of 20–30×, tracing the drop profile, drawing the tangent to the profile at the point where it intersects the baseline, and measuring the angle formed by the two. The light source, finger support, and lens were mounted on an optical bench.

Water drops were placed on the dorsal surface of the middle sections of the middle and ring fingers. The two joints of the fingers were bent to stretch the skin and smooth out its surface as much as possible. Additional measurements were made on the underside of the forearm. The drop profiles were traced within 3 sec. after placing the drops on the skin so that the advancing contact angles were measured. Due to the ridges and furrows and the nonuniformity of the skin, the hysteresis between the advancing and receding angles was considerable.

The hands and arms were those of females in the 20–28-year-old age group. In view of the large variation between individual subjects, more detailed work was done on a single subject. The mean of 64 measurements of the contact angles of water on the untreated skin of her two middle and ring fingers, made over a period of 3 months, was 87.8°, and the standard deviation of the mean was 1.3°.

This excellent reproducibility was obtained despite the lack of temperature control. Since the drop profiles were traced within 3 sec. of depositing the drops, and since the drop size was fairly uniform, the drops presumably warmed to approximately the same extent on contact with the skin. Neglecting the effect of temperature on γ_C, the difference between the contact angle of water on untreated skin between 18 and 37° of temperature is only about 3° according to Eq. 3.

The extensive measurements on a single subject were extended over 3 months to permit the skin to regenerate, between measurements, any lipids or other constituents removed by the drops of organic liquids in contact with it. The areas of the fingers and forearms used for contact angle measurements were not washed with soap for at least 20 hr. prior to the measurements to prevent precipitation of the hydrophobic lime soaps (8).

Surface tensions were measured at 19 ± 1° by means of a Wilhelmy balance equipped with a sand-blasted platinum blade.

Materials—The liquids chosen were doubly distilled water, reagent grade benzyl alcohol, absolute ethyl alcohol, and aqueous solutions of propylene glycol USP. The latter solutions bridge the gap between the surface tension of water (73 dynes/cm.) and of propylene glycol (36 dynes/cm.). This range is covered by few if any pure liquids of pharmaceutical importance.

RESULTS AND DISCUSSION

Contact Angles—For 13 subjects, the mean contact angles of pure water on the untreated skin of the fingers, averaged from six values measured on three drops, varied between 60 and 91°, with an overall mean value of 74°. Comparable reported values are 58° (2) and 75° (1). When lipids were removed from the skin by a 2-min. immersion in acetone followed by wiping dry with towels and drying in air, the range of contact angles for eight subjects was from 48 to 90°, with a mean of 64°. Lipid extraction reduced the contact angle of water in every instance, by amounts varying between 1 and 27°, with a mean reduction of 13°.

For the single subject, the contact angles of water were as follows: untreated skin of the fingers, 87.8 ± 1.3° (64 measurements); extracted skin of the fingers, 81.5 ± 2.0° (20 measurements); untreated skin of the forearms, 84.3 ± 1.3° (30 measurements); and extracted skin of the forearms, 91.8 ± 1.2° (30 measurements). For comparison, the contact angle of water on a defatted wool fiber, which also consists of keratin, was 85°. The effect of lipid extraction on the contact angles of 43% propylene glycol was less consistent: increases were observed for three subjects and reductions for four. In two additional instances, the difference was 1° or less.

The reported values (2) of the contact angles of water on solvent-extracted skin, 134° for acetone or 139° for hexane, are unusually high. For comparison, the contact angle of water on Teflon, one of the solids of lowest surface free energy known, is 108° (4) or 106° (9). One might attribute the high value reported to increased roughness of the extracted skin resulting from the removal of lipids, which leaves a somewhat porous surface. For contact angles greater than

Table I—Average Cosines of Contact Angles Obtained with Different Liquids on One Subject

Liquid		Finger				Forearm			
		Untreated Skin		Acetone-Extracted Skin		Untreated Skin		Acetone-Extracted Skin	
Composition	Surface Tension, dynes/cm.	cos θ	σ^a $(N)^a$	cos θ	σ^a $(N)^a$	cos θ	σ^a $(N)^a$	cos θ	σ^a $(N)^a$
Water	73.0	0.038	0.022(64)	0.148	0.035(20)	0.100	0.024(30)	−0.032	0.022(30)
11% PG^b	61.8	0.373	0.025(24)	0.352	0.035(12)	0.287	0.040(22)	0.101	0.037(18)
43% PG	48.6	0.437	0.026(30)	0.419	0.020(16)	0.505	0.019(18)	0.427	0.030(18)
90% PG	39.8	0.658	0.031(12)	0.721	0.014(12)	0.776	0.011(16)	0.727	0.025(16)
Benzyl alcohol	40.9	0.790	0.016(12)	0.750	0.033(20)	0.827	0.015(14)	0.868	0.015(16)
Ethyl alcohol	23.0	1.000	—	1.000	—	1.000	—	1.000	—
Critical surface tension, dynes/cm.		24.7		22.2		29.4		30.6	

^{a} Standard deviation of mean (number of angles measured). ^{b} Propylene glycol.

90°, increasing surface roughness increases the value of the apparent contact angle (3). However, an increase of the order of 70° would require a high degree of roughness, or a large amount of air pockets on the skin, unlikely to be present in viable human skin.

Critical Surface Tension—Cosines of the contact angles of different liquids on untreated and extracted skin of one subject are listed in Table I; they are plotted against surface tension in Fig. 1. The constants in Eq. 2, obtained from the linear dependence of cos θ on γ_{LA} by the method of least squares, have the following values: for untreated skin of the fingers, $a = 1.475$ and $b = 0.01924$; for acetone-extracted skin of the fingers, $a = 1.379$ and $b = 0.01707$; for untreated skin of the forearm, $a = 1.630$ and $b = 0.0214$; and for extracted skin of the forearm, $a = 1.798$ and $b = 0.0261$. The corresponding critical surface tensions are 24.7, 22.2, 29.4, and 30.6 dynes/cm., respectively. They are in fair agreement with the reported value of 26.8 dynes/cm. (2). Ethyl alcohol was not included in the calculations because it spread indefinitely on untreated and extracted skin.

These critical surface tensions are suspiciously low. By comparison, the γ_C values for smooth plastic surfaces are 16–18 dynes/cm. for Teflon (4, 5), 29 dynes/cm. for polypropylene, and 31 dynes/cm. for polyethylene (5). The presence of a dipole, in polyvinyl chloride, increases the critical surface tension to 39 dynes/cm. (5). For 66-nylon, the value is 46 dynes/cm. (10). These values are based on contact angles measured mostly with polar liquids capable of hydrogen bonding and are, therefore, directly comparable with the present data (11). Based on the nature and concentration of polar groups, the critical surface tension of the skin keratin should be at least as great as that of 66-nylon. The two polymers are similar in gross chemical composition inasmuch as both are rich in amide groups.

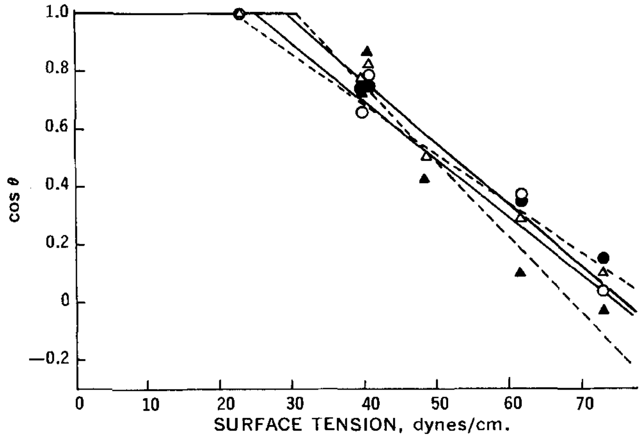

Figure 1—*Cosines of contact angles measured on one subject as a function of surface tension of the wetting liquids. Key:* △, *untreated forearm;* ▲, *acetone-extracted forearm;* ○, *untreated finger;* ●, *acetone-extracted finger;* —— *untreated skin; and* - - -, *acetone-extracted skin.*

Physical Factors Affecting Critical Surface Tension—It is unlikely that the critical surface tension of smooth skin would be smaller than that of solid hydrocarbons. Some factors which could affect the value of γ_C are discussed here.

1. Taking into account noncoherent surface roughness, *i.e.*, isolated elevations and depressions, would reduce γ_C further. If a roughness factor r is defined as the ratio between the actual area of the rough surface and the apparent or geometric area of the smooth surface (3):

$$r = \cos \theta_{\text{app}} / \cos \theta_{\text{true}} \geqslant 1 \qquad \text{(Eq. 4)}$$

Therefore, the cosines of the true contact angles, *i.e.*, the contact angles which would be observed on smooth skin, are smaller than the cosines of the corresponding apparent contact angles since the angles are smaller than 90°. Using the former in Fig. 1 would lower the lines, so their intercept with the horizontal line for cos $\theta = 1$, namely, γ_C, would become smaller. Even for the very low value of $r = 1.25$, γ_C drops from 23 to 11 dynes/cm.

2. Skin contains relatively deep furrows. If these furrows make an angle of inclination, ϕ, with the horizontal skin surface, the liquid front of the drop advancing perpendicularly to them has an apparent contact angle equal to the true contact angle plus ϕ. If $\phi = 15°$, $\theta_{\text{true}} = \theta_{\text{app}} - 15$. Subtracting 15° from the apparent contact angles measured with the five liquids on acetone-extracted fingers increases γ_C from 22 to 32 dynes/cm. For $\phi = 30°$, γ_C becomes 38 dynes/cm.

3. An alternative explanation is based on the assumption that the liquid drops trap pockets of air in the furrows of the skin surface as they advance. This process makes the skin a composite surface. A fraction, f_{SL}, of the area of the total apparent solid–liquid interface consists of true solid–liquid interface. The remainder, the fraction f_{LA}: consists of liquid–air interface. Neglecting hydrostatic pressure (12),

$$\cos \theta_{\text{app}} = f_{SL} \cos \theta_{\text{true}} - f_{LA} \qquad \text{(Eq. 5)}$$

Therefore, cos $\theta_{\text{true}} >$ cos θ_{app}, and the lines of Fig. 1 are displaced toward higher cosines if the measured contact angles are replaced by the true contact angles. This results in higher values for the true critical surface tension of skin, *i.e.*, for skin without adhering air pockets trapped beneath the liquid. If only 5% of the total apparent liquid–skin interface consisted of liquid–air interface for all five liquids, the true critical surface tension of the untreated skin would increase from 24.7 to 29.8 dynes/cm. according to Eq. 5.

Optical examination of drops of liquids on skin at low magnification with a grazing incident light beam showed the presence of minute air bubbles trapped beneath the drops, most of them attached to the furrows of the skin. This effect probably also accounts for the small difference in wettability of untreated and acetone-extracted skin.

The combination of Factors 2 and 3 seems adequate to account for the difference in critical surface tension between smooth 66-nylon and human skin, which amounts to about 19 dynes/cm.

Effect of Added Materials—When a commercial hand lotion was applied to the untreated skin of the fingers of one subject, followed by a 30-min. drying period, the contact angle of water decreased from 87 ± 3° (16 measurements) to 52 ± 2° (24 measurements)[1]. Application of the hand lotion reduced the mean contact angles of water on seven other subjects by 20–32°, with an average decrease of 28°. The angles were always measured after a 30-min. drying period. The moisturizing effect of the lotion includes the skin surface, possibly because some portion of the lotion was not absorbed by the skin but remained on the surface.

In another experiment, hands were immersed in a 1:1000 benzalkonium chloride solution USP for 10 min. Excess solution was then rinsed off by holding the hands for 5 sec. under running tap water and for 1 sec. under running distilled water. The contact angles of water were measured after drying with towels and in air. On placing drops on the skin, the initial contact angles were near 90°. After about 1 sec., the water drops suddenly began to spread and the contact angles decreased. Evidently, benzalkonium chloride which had been physically adsorbed on the skin was desorbed and dissolved by the drop, reducing its interfacial tension against skin as well as its surface tension. The mean value of the contact angles was lowered from 86 ± 3 to 48 ± 3° (18 measurements).

When hands treated with benzalkonium chloride were washed by 5-min. immersions in running lukewarm tap water, followed by rinsing with distilled water and drying with towels and in air, the average contact angle of water from 24 measurements increased to 84 ± 3°. Within the precision of the measurements, this value does not differ significantly from the initial value of 86 ± 3°, indicating that most if not all of the benzalkonium chloride was removed by immersion in water. Apparently, its adsorption by the skin is largely physical and reversible. This conclusion is made with some reservation, because chemisorption of a monolayer of alkyltrimethylammonium halides by glass, with the headgroups oriented toward the surface and the hydrocarbon tails away from it, produced sizable increases in the contact angles of water (13). Since the contact angles of water on untreated skin are already high, chemisorbed benzalkonium cations might not increase them at all.

REFERENCES

(1) V. A. Bandarin, V. G. Kolb, Y. M. Ostrovskii, and A. S. Chizh, *Estonsk. Biokhim. Obshchestvo, Tartu*, **1960**, 135; through *Chem. Abstr.*, **58**, 7233(1963).

(2) M. E. Ginn, C. M. Noyes, and E. Jungermann, *J. Colloid Interface Sci.*, **26**, 146(1968).

(3) N. K. Adam, "The Physics and Chemistry of Surfaces," 3rd ed., Oxford University Press, London, England, 1941, chap. 5.

(4) W. A. Zisman, in "Contact Angle, Wettability and Adhesion," F. M. Fowkes, Ed., Adv. Chem. Series 43, American Chemical Society, Washington, D. C., 1964.

(5) E. Wolfram, *Kolloid-Z. Z. Polym.*, **182**, 75(1962).

(6) V. R. Gray, *Chem. Ind.*, **1965**, 969.

(7) P.-J. Sell and A. W. Neumann, *Angew. Chem., Int. Ed.*, **5**, 301(1966).

(8) F. van V. Vader and H. Dekker, *J. Phys. Chem.*, **68**, 3556 (1964).

(9) H. Schott, to be published.

(10) A. H. Ellison and W. A. Zisman, *J. Phys. Chem.*, **58**, 503 (1954).

(11) J. R. Dann, *J. Colloid Interface Sci.*, **32**, 302(1970).

(12) A. B. D. Cassie and S. Baxter, *Trans. Faraday Soc.*, **40**, 546 (1944).

(13) L. Ter Minassian-Saraga, *J. Soc. Chim. Phys.*, **57**, 10(1960).

ACKNOWLEDGMENTS AND ADDRESSES

Received May 10, 1971, from *Temple University School of Pharmacy, Philadelphia, PA 19140*

Accepted for publication September 7, 1971.

---

[1] The ± sign precedes the standard deviation of the mean.

Physical Properties of Quaternary Ammonium Salts of Phenothiazine Derivatives

C. L. HUANG* and C. T. CHANG†

Abstract □ Physical constants, including melting points and IR and NMR spectra, and analytical data of the quaternary ammonium salts of nine clinically used phenothiazines are presented. Assignments for the spectral peaks were made and are discussed. These compounds were prepared in good yields, so the formation of quaternary ammonium salt may serve as a convenient method for the isolation and identification of these phenothiazines.

Keyphrases □ Phenothiazine derivatives, quaternary ammonium salts—synthesis, physical properties □ Quaternary ammonium salts of phenothiazine derivatives—synthesis, physical properties □ NMR spectroscopy—identity □ IR spectrophotometry—identity

Quaternary ammonium salts of phenothiazine neroleptics have been demonstrated to have a wide variety of biological activities. It was indicated in a previous study (1) that all of the quaternary ammonium salts of these compounds possess antimicrobial activities on Gram-positive and Gram-negative organisms and have a toxicity higher than the corresponding parent compound. Evidence was presented to show that the ^{14}C quaternary ammonium salts of phenothiazines were able to cross the blood–brain barrier to reach the brain tissues (2). The metabolic pathways of the quaternary ammonium salts of phenothiazines (mepazine, promethazine, promazine, chlorpromazine, triflupromazine, prochlorperazine, and trifluoperazine) are quite different from the corresponding hydrochloride salts; the quaternary ammonium salt is found predominantly in the feces (3) while the majority of the hydrochloride salt is excreted through the kidneys (4) and the lungs (5).

Although spectra–structure correlation of tertiary phenothiazines was reported (6), there is paucity of information concerning the physical properties of the quaternary ammonium salts of phenothiazines. The purpose of this paper is to present physical data, including melting points and UV, IR, and NMR spectra, of 11 quaternary ammonium compounds of nine clinically used phenothiazine derivatives: mepazine, promethazine, promazine, chlorpromazine, triflupromazine, prochlorperazine, trifluoperazine, perphenazine, and fluphenazine. Since all of these compounds form