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ACKNOWLEDGMENTS AND ADDRESSES

Received July 27, 1976, from the *Faculty of Medicine, Division of Pharmacy, University of Dar Es Salaam, Dar es Salaam, Tanzania.*

Accepted for publication October 12, 1976.

The author acknowledges the Department of Pharmacy, University of Aston, Birmingham, England, for providing facilities for carrying out this work and the Tanzania Government for financial aid.

Contact Angles of Pharmaceutical Powders

C. F. LERK ˣ, M. LAGAS, J. P. BOELSTRA, and P. BROERSMA

Abstract □ Contact angles of pharmaceutical powders were determined by measuring the maximum height of a drop of a saturated solution on a presaturated compact of the material. The results for a series of drugs are presented.

Keyphrases □ Powders, various pharmaceutical—contact angles, densities, and surface tensions □ Contact angles—various pharmaceutical powders □ Densities—various pharmaceutical powders □ Surface tensions—various pharmaceutical powders

The wetting of solid dosage forms is an important initial step in the process of drug dissolution both *in vitro* and *in vivo*. Determination of contact angles of solids gives a measure of their wettability, but problems arise when the solid is finely divided as a powder. Recently (1), a method that consists essentially of measuring the maximum height of a drop of a saturated solution formed on a presaturated compact of the material was used successfully. This report presents the results of contact angle determinations for an additional series of pharmaceutical powders.

EXPERIMENTAL

Materials—The materials and standards are listed in Table I.

Methods—The contact angles were determined using a technique described earlier (1). The densities and surface tensions of the saturated solutions and the densities of the solids were determined with a balance[1], a tensiometer[2], and an air comparison pycnometer[3], respectively. The liquid measurements were carried out at 23°. Saturated solutions were prepared by allowing excess solid to equilibrate with distilled water at a constant temperature of 23°.

RESULTS AND DISCUSSION

Table I lists the contact angles of more than 50 drugs and excipients. The values vary between 21° (ampicillin trihydrate) and 124° (aceto-

[1] Mohr, G. Kern, Ebingen, West Germany.
[2] Du Noüy K 8600 Krüss, Hamburg, West Germany.
[3] Model 930, Beckman Instruments Ned. N.V., Amsterdam, The Netherlands.

Table I—Measured Values of Contact Angles of Pharmaceutical Powders [a]

Material	Standard	Surface Tension, dynes/cm	Density Solid, g/cm³	Contact Angle, θ°
Acetohexamide[b]	—	70.7	1.25	124
Adipic acid[c]	Laboratory grade	58.3	1.38	72
Allobarbital[c]	Ph. Ned. VI	69.4	1.28	61
Aluminum stearate[d]	—	69.4	1.05	120
Aminophylline[e]	—	71.5	1.44	47
Aminophylline (anhydrous)[c]	Ph. Ned. VII	65.5	1.44	40
Aminopyrine[c]	Ph. Ned. VI	57.5	1.19	60
Amobarbital[f]	USP XVII, BP 1973	55.7	1.17	102
Ampicillin (anhydrous)[g]	—	47.9	1.37	35
Ampicillin trihydrate[g]	—	38.6	1.37	21
Aprobarbital[c]	NF XII	57.8	1.28	75
Barbital[c]	Ph. Ned. VI	63.5	1.24	70
Boric acid[c]	Ph. Ned. VI	68.0	1.51	74
Butabarbital[f]	BP 1973	62.0	1.26	82
Butalbital[f]	NF XIII	58.8	1.25	87
Butethal[c]	BP 1968	51.0	1.18	78
Calcium carbonate[c]	Ph. Ned. VI	72.4	2.68	58
Calcium stearate[d]	—	70.7	1.03	115
Calcium sulfate dihydrate[c]	Laboratory grade	44.5	2.32	64
Cyclopentobarbital[f]	—	60.6	1.29	76
Diazepam[h]	BP 1973	64.0	1.37	83
Digoxin[i]	Ph. Eur.	68.1	1.28	49
Ephedrine hydrochloride[c]	Ph. Ned. VI	48.3	1.20	51
Heptobarbital[c]	Ph. Ned. VI	71.3	1.47	74
Hydrochlorothiazide[j]	USP XVIII	72.4	1.69	51
Indomethacin[j]	NF	71.5	1.39	90
Isoniazid[h]	Ph. Ned. VI	61.6	1.42	49
Isoxsuprine hydrochloride[k]	—	66.0	1.28	50
Lithium carbonate[c]	Laboratory grade	71.2	2.08	50
Lithium chloride[d]	Analytical grade	94.7	2.08	51
Mephobarbital[c]	Ph. Ned. VI	68.3	1.38	74
Meprobamate[c]	Ph. Ned. VI	51.9	1.24	83
Nitrofurantoin[h]	USP XVIII	70.6	1.69	69
Oxalic acid[l]	Laboratory grade	70.7	1.66	31

Table I—*(Continued)*

Material	Standard	Surface Tension, dynes/cm	Density Solid, g/cm^3	Contact Angle, θ°
Pentobarbital[c]	Codex Francais	51.5	1.21	86
Phenylbutazone[h]	Ph. Ned. VII	66.2	1.19	109
Phthalylsulfathiazole[m]	—	69.6	1.55	48
Prednisolone[n]	—	68.5	1.30	43
Prednisone[h]	Ph. Ned. VII	65.8	1.41	63
Procaine hydrochloride[c]	Ph. Ned. VI	42.5	1.23	55
Salicylamide[c]	NF XIII	64.0	1.37	70
Secobarbital[c]	USP XVII	48.2	1.19	82
Sodium stearate[c]	—	37.1	1.10	84
Stearic acid[c]	—	62.5	1.01	98
Succinylsulfathiazole[h]	Ph. Ned. VII	71.2	1.55	64
Sulfacetamide[c]	—	68.9	1.37	57
Sulfamerazine[o]	—	69.0	1.32	58
Sulfamethazine[c]	Ph. Ned. VI	71.7	1.44	48
Sulfamethizole[c]	—	69.8	1.52	57
Sulfanilamide[c]	Ph. Ned. VI	66.9	1.46	64
Sulfathiazole[c]	Ph. Ned. VI	69.8	1.61	53
Sulfisoxazole[h]	BP 1973	68.2	1.41	57
Theophylline[c]	Ph. Ned. VI	72.0	1.45	48
Tolbutamide[p]	—	67.9	1.24	72
Vinbarbital[f]	—	60.5	1.25	94
Vinylbital[r]	—	43.3	1.20	71
Chloramphenicol palmitate	β-Form (mp 92–93°)	72.4	1.20	108[q]
Chloramphenicol palmitate	α-Form (mp 87–88°)	72.4	1.20	122[q]

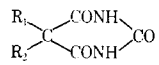
[a] The liquid density of the saturated solutions was 1.00 g/cm^3 except for aminopyrine (1.01), butalbital (1.01), cyclopentobarbital (1.01), aminophylline (Euphyllin) (1.01), amobarbital (1.02), boric acid (1.02), isoniazid (1.03), ephedrine hydrochloride (1.04), oxalic acid (1.05), lithium chloride (1.10), aminophylline anhydrous (1.12), and procaine hydrochloride (1.13 g/cm^3). [b] Lilly Research Centre, Windlesham, Surrey, England. [c] Interpharm, 's-Hertogenbosch, The Netherlands. [d] Merck, Darmstadt, West Germany. [e] Euphyllin, Byk, Zwanenburg, The Netherlands. [f] Siegfried, Zofingen, Switzerland. [g] Gist Brocades, Delft, The Netherlands. [h] Nogepha, Alkmaar, The Netherlands. [i] Boehringer Mannheim, Mannheim, West Germany. [j] Merck Sharp & Dohme, Haarlem, The Netherlands. [k] Philips-Duphar, Weesp, The Netherlands. [l] Brocacef, Maarssen, The Netherlands. [m] Sigma, St. Louis, Mo. [n] Organon, Oss, The Netherlands. [o] A.C.F., Amsterdam, The Netherlands. [p] Hoechst Holland, Amsterdam, The Netherlands. [q] Water contact angle. [r] Byk, Zwanenburg, The Netherlands.

hexamide). The reproducibility of contact angle values was better than 2° for most of the chemicals studied. Chemicals exhibiting poor compressibility (calcium carbonate) or showing swelling and softening of the compact formed (isoniazid and sulfisoxazole) had a reproducibility of contact angle values that was no worse than 4°.

Table I includes all drugs for which a dissolution test for tablets or capsules is required in USP XIX. A great number of these drugs are slightly hydrophobic, including nitrofurantoin, tolbutamide, and meprobamate, or even strongly hydrophobic, such as phenylbutazone and acetohexamide.

A correlation between chemical structure and hydrophobicity is illustrated in Table II for a series of 5,5-substituted barbituric acid derivatives. The results demonstrate the effect of chain length, positional changes in branching, and double bonds on the contact angle of the drugs.

Table II—Chemical Structure and Contact Angle of a Series of Barbiturates



Compound	R_1	R_2	Contact Angle, θ°
Barbital	CH_2CH_3	CH_2CH_3	70
Butethal	CH_2CH_3	$CH_2CH_2CH_2CH_3$	78
Butabarbital	CH_2CH_3	$CH(CH_3)CH_2CH_3$	82
Pentobarbital	CH_2CH_3	$CH(CH_3)CH_2CH_2CH_3$	86
Vinbarbital	CH_2CH_3	$C(CH_3)=CHCH_2CH_3$	94
Amobarbital	CH_2CH_3	$CH_2CH_2CH(CH_3)_2$	102
Aprobarbital	$CH(CH_3)CH_3$	$CH_2CH=CH_2$	75
Butalbital	$CH_2CH(CH_3)CH_3$	$CH_2CH=CH_2$	87
Secobarbital	$CH(CH_3)CH_2CH_2CH_3$	$CH_2CH=CH_2$	82
Vinylbital	$CH(CH_3)CH_2CH_2CH_3$	$CH=CH_2$	71

The wettability of a solid is also affected by its crystallographic structure. This fact is illustrated in Table I for two chloramphenicol palmitate polymorphs. The β-form, mp 92–93°, showed a water contact angle of 108°; the α-form, mp 87–88°, had a water contact angle of 122°. The technique thus provides a sensitive measure of the surface characteristics of chemicals. Variations in contact angle values may be found for different lots from different suppliers of a given chemical, depending on the preparation process. The effect of changes in the wettability of drugs and excipients upon the release from tablets and capsules will be reported later.

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ACKNOWLEDGMENTS AND ADDRESSES

Received August 4, 1976, from the *Laboratory for Pharmaceutical Technology, The University, Antonius Deusinglaan 2, Groningen 8004, The Netherlands.*

Accepted for publication November 26, 1976.

The authors thank Boeringer Mannheim, Gist Brocades, Hoechst Holland, Lilly Research, Merck Sharp & Dohme, Nogepha, and Organon for supplying digoxin, ampicillin, tolbutamide, acetohexamide, hydrochlorothiazide, indomethacin, diazepam, and prednisolone.

[x] To whom inquiries should be directed.