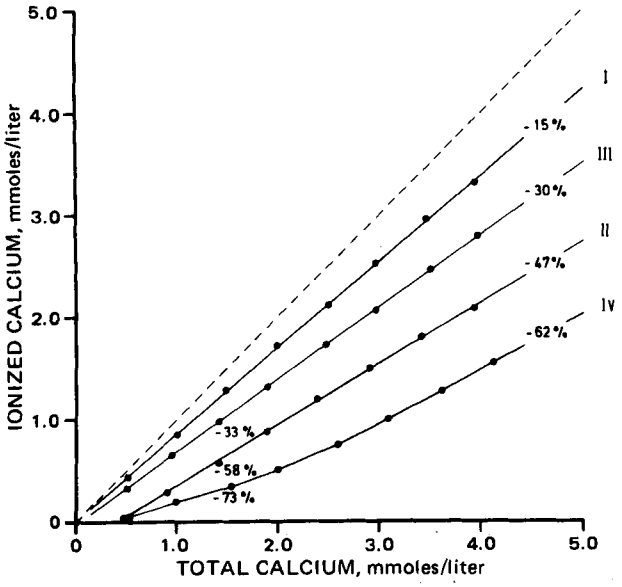

Figure 1—*Binding of added ionized calcium by contrast media (two parts) in a physiological saline solution (0.9% NaCl, seven parts). The roman numerals refer to contrast media (see text). Percentage values denote the reduction of ionized calcium levels below the total calcium content of 1.5 and 4.0 mmoles/liter. The expected line (i.e., no binding of ionized calcium) is shown as a dashed line with a slope of 1.*

The presence or absence of additives and their amounts were not analyzed; the compositions are given as presented in the manufacturer's data.

Total calcium content was determined by the fluorometric method[5] with correction for any edetate disodium present. Ionized calcium levels were measured by a calcium-sensitive flow-through electrode[6]. The reduction of ionized calcium levels below the expected line (Fig. 1) is consistent with calcium binding.

The shift in the lysine diatrizoate (II) titration curve, as well as the shift and the bend at 2 mmoles of total calcium/liter in one of the diatrizoate meglumine sodium (IV) curves, is believed to be due to the saturation of the calcium-chelating additives present in these contrast media (*e.g.*, 3.2 mg of citrate/ml and 0.4 mg of edetate disodium/ml in IV). The near-zero intercepts on the abscissa of the titration curves for ioxaglate meglumine sodium (I) and diatrizoate meglumine sodium (III) suggest a lack of large amounts of potent calcium-binding ligands in these contrast media. Deviations of the slopes of individual titration curves from the expected line after saturation of disodium edetate and citrate binding sites, or without any chelating additives present, indicate that calcium chelation is primarily an inherent property of ionic contrast media and not that of the additives.

The association constants (K_0) of radiopaque ligands (L) with calcium have been calculated on the basis of a 1:1 association by:

$$K_0 = \frac{[CaL]}{[Ca][L]} \qquad \text{(Eq. 1)}$$

Log K_0 values were 0.36 for the diatrizoate–calcium complex and 0.28 for the ioxaglate–calcium complex. However, the calculations do not necessarily signify the stability constants for well-defined chemical structures since the stoichiometry is not known. Values are below the known stability constants of human plasma protein–calcium complexes [log $K_0 \simeq$ 2–7 (4)]. Nevertheless, when the opacifying bolus is injected intracoronarily, the contrast molecules are more concentrated than the protein fraction in plasma and thus cause a marked reduction of plasma ionized calcium levels.

[5] Corning calcium analyzer 940, Vogel, Giessen, West Germany.
[6] Nova 2, Union Carbide, Newton, Mass.

(1) J. B. Caulfield, L. Zir, and J. W. Harthorne, *Circulation*, **52**, 119 (1975).
(2) C. B. Higgins and W. Schmidt, *ibid.*, **58**, 512 (1978).
(3) R. S. Frech, *Invest. Radiol.*, **10**, 323 (1975).
(4) R. J. P. Williams, in "Calcium-Binding Proteins and Calcium Function," R. H. Wasserman, R. A. Corradino, E. Carafoli, R. H. Kretsinger, D. H. MacLennan, and F. L. Siegel, Eds., North-Holland, New York, N.Y., 1977, pp. 3–12.

H. G. Wolpers ˣ
D. H. Hunneman
M. Stellwaag
G. Hellige
Physiological Institut I
Department of Experimental Cardiology
University of Göttingen
Humboldtallee 7, D-3400 Göttingen
Federal Republic of Germany

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Effect of Sampling Probe Size on Dissolution of Tableted Drug Samples

Keyphrases □ Dissolution rates—effect of sampling probe size on dissolution rate of tableted drug samples, USP paddle method □ Dissolution testing systems—various sampling probe sizes evaluated for effect on dissolution rate of tableted drug samples □ Hydrodynamics—dissolution rates affected by sampling probe size, USP paddle method

To the Editor:

When *in vitro* dissolution rates were determined using the USP paddle method (1), some tablet formulations consistently gave higher dissolution rates when sampled with an automated sampling system than when sampled manually. This difference was traced to turbulence caused by the filter-tipped probes used in automated sampling. With the automated system used in this laboratory, the probes are suspended in the dissolution medium during the entire test.

Table I—Effect of Sampling Probes on Dissolution Rate

Probe	Probe Volume, mm^3	Dissolution[a], % of label claim	Increase in Dissolution, %
None	—	41.4	—
1	44	41.4	0
2	177	43.0	1.6
3	466	45.1	3.7
4	706	46.4	5.0
5	877	48.4	7.0

[a] Average of 12 tablets.

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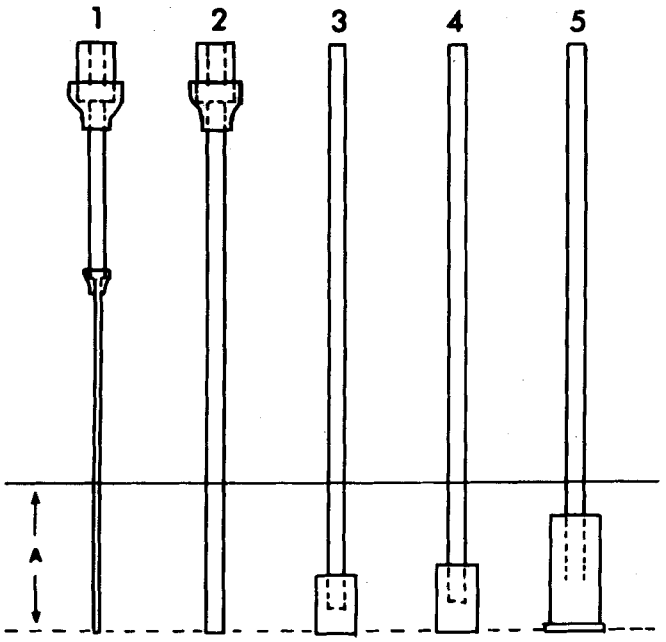

Figure 1—*Sampling probes, showing immersion depth (A).*

To reduce probe interference, five probe designs (Fig. 1) were tested with a six-place dissolution apparatus. All of the probes were constructed in this laboratory. Probes 3 and 4 were used early in the dissolution work. Probe 5 was designed to be similar to probes used in some commercial dissolution equipment. Probe 1 was the result of the laboratory's search for a probe with minimum interference in the dissolution test. Probe 2 was chosen to give an intermediate size between Probes 1 and 3. All probes were constructed from 3-mm o.d. glass tubing. The tip of Probe 1 was a 1.3-mm o.d. melting-point capillary. Commercially available filters were used. The 5-mg prednisone tablets used for the test were from a sample known to give different results depending on the presence or absence of a sample probe during the test.

One probe was suspended in each of five dissolution vessels, and the sixth vessel was used without a probe. The probes were placed halfway between the vessel wall and the paddle shaft, with the probe tip 25 mm below the liquid surface (approximately halfway between the liquid surface and the top of the paddle). The dissolution test was conducted for 30 min; samples then were withdrawn with a syringe for analysis by the USP (2) procedure. The test was repeated, and then the probes were moved to different vessels. This procedure was repeated until all probes were tested in duplicate in each vessel. This experimental design eliminated interference from sources other than the probes.

The data (Table I) show that there was a direct relationship between the displacement volume of the sampling probe and the increase in dissolution rate for the sample used. With the tablets used in this study, no effect on the observed dissolution rate was noted from Probe 1. However, the presence of any foreign object disturbs the hydrodynamics of the dissolution medium, and it is possible that the results from other, more sensitive samples could be influenced by the use of Probe 1.

The results show that the displacement volumes of sampling probes used with automated samplers should be as small as possible to reduce interference with the dissolution test.

(1) "The United States Pharmacopeia," 20th rev., United States Pharmacopeial Convention, Rockville, Md., 1980, p. 959.
(2) *Ibid.*, p. 655.

Clyde E. Wells
National Center for Drug Analysis
1114 Market Street
St. Louis, MO 63101

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BOOKS

REVIEWS

Pharmacy: A Profession in Search of a Role. By JACK ROBBINS. Navillus Publishing Corp. 1979. 143 pp. 15 × 23 cm. Price $14.95. (Available from Technomic Publishing Co., 265 Post Rd. W., Westport, CT 06880.)

The title of this book is both provocative and ambiguous. Readers seeking a definitive statement of the professional status or role of the pharmacist will not find it, nor will they find an expression of the need for clinical pharmacy, specialists, or new directions for the future.

Most of this book (large type, liberal white space) is devoted to an objective presentation of a 1975 mail survey of pharmacists. The study attempts to "correlate the dynamic changes in pharmacy during the past half century with the various modes which pharmacists have adopted to make their role expectations more consonant with their performance" and "to incorporate social–psychological theory in order to better understand the motivations underlying pharmacists' various adaptation modes." Theories (including role theory, role conflict and adaptation, and professionalization) are presented in easily understood language and context. Although a more in-depth discussion might be preferred, this approach is rational, laudable, and worthwhile in an area that too often is merely descriptive.

Chapter 5, Generational Effects: Younger *versus* Older Pharmacists, is especially intriguing to the reader seeking insight into the direction of future change. Chapter 8, Role Conflict and Social Change, is excellent and expands on the familiar business–professional conflict, reporting both the extent and direction of conflict within the context of practice changes.

Given the emphasis and style, chapter titles, acknowledgments, and cautious conclusions and projected future trends, one suspects that the book originally was a dissertation, a suspicion heightened by a citation of the same title by the same author in *Dissertation Abstracts* (1977). The dissertation subtitle, Functional and Psychological Adaptations of Pharmacists to Technological and Social Changes During the Past 50 Years, is descriptive of the contents. Exclusion of the survey instrument and the inadequate literature search (for example, no citations after 1976) will disappoint the researcher.

The foreword indicates that the book should be read by social scientists, pharmacy educators, individual pharmacy practitioners, pharmacy association executives, other health-care practitioners and organizations, members of Congress, and health-care planners and administrators. Such a broad appeal is unlikely to satisfy anyone completely.

The book should be of interest to pharmacy school administrators and pharmaceutical industry executives and employees whose market is practicing pharmacists. Chapter 4, Opinions About the Industry and