Figure 1—*Relationship between the rate of recovery from the neuromuscular blocking effects of fazadinium and the calculated $k_{app\ 25-75}$. Individual patient data are shown as solid circles while the solid line represents the linear regression line ($r^2 = 0.897$, $p < 0.005$).*

$$t \times R = m(\log A^0 - \log A_{min}) \qquad (Eq.\ 3)$$

where k_{10} is the apparent first-order rate constant for drug elimination from its site of action, A_{min} is the minimum effective dose, and m is the slope of the log dose (A^0) response relationship for the relaxant. Thus, according to the above three equations, four pharmacokinetic factors determine the duration and rate of decline of effect, with three of these terms (m, A^0, and A_{min}) appearing on the right side of Eq. 3, while k_{10} is implicit on the left-hand side but cancels out as such. Thus, in a group of patients given the same drug dose but showing different durations of effect, the product of duration (t) and rate of decline (R) of effect will yield a constant value if the differences in the observed time course of effect are solely the result of differences in k_{10}, the elimination rate constant. If, however, the values of $t \times R$ differ between the patients, then it must be concluded that these patients differ with respect to m and/or A_{min} and/or k_{10}.

The results obtained from the six patients in the study by D'Hollander et al. (3) are listed in Table I, with the numerical designations used by these authors but in order of increasing duration of effect. It can be seen that although the six patients differed in the duration (t) and the rate of decline (R) from the effects of fazadinium, the $t \times R$ values were identical for all the patients, implying that the differences in the rate of recovery from the neuromuscular effects of fazadinium in these six patients were solely due to a difference in the rate of elimination of the relaxant from the body. This claim is further supported by the finding that $k_{app\ 25-75}$, the apparent rate of decline of the (log) plasma concentration, which is a measure of the elimination rate of the relaxant during the linear (25–75%) phase of recovery, was different in each of the six patients and there was an excellent linear relationship between the rate of recovery from fazadinium and the calculated $k_{app\ 25-75}$ (Fig. 1).

(1) G. Levy, *Anesthesiology*, **32**, 551 (1970).

(2) G. Levy, *Br. J. Anaesth.*, **42**, 979 (1970).

(3) A. A. D'Hollander, P. Duvaldestin, D. Henzel, C. Delcroix, and J. M. Desmonts, *Br. J. Anaesth.*, **53**, 853 (1981).

(4) B. Srinivasan, C. Wahdi, and B. Pleuvry, *J. Pharm. Pharmacol.*, **25**, 657 (1973).

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BOOKS

REVIEWS

Pharmacokinetics, 2nd Ed. By MILO GIBALDI and DONALD PERRIER. Marcel Dekker, 270 Madison Avenue, New York, NY 11016. 1982. 494 pp. 16 × 23 cm. Price: $34.50 (20% higher outside the U.S. and Canada).

The second edition of this now classic text detailing the mathematical description of pharmacokinetics has been greatly expanded and updated over the previous edition. One of the most important new aspects to be presented is the comprehensive discussion of clearance concepts, flow models, and physiological modeling, which has given the new text a much broader scope while at the same time introduces the reader to new concepts presented over the last few years. In addition, an overview depicting the usefulness of statistical moments in pharmacokinetics is presented, a concept being explored extensively in the pharmacokinetic literature today which should prove useful to both the established researcher and the student. The new material added to the text is, in general, approached (as is the mark of these authors) in a detailed, step-by-step procedure that renders the work especially useful to novices and subsequently makes it an important teaching tool.

It is important to note that not only have new chapters and topics been added, but that the majority of the original text has undergone revision, expansion, and addition of new material. The majority of the equations have been generalized, thereby making them useful in a variety of models. Although the generalization makes the edition slightly less useful as a reference book for pharmacokinetic relationships, it is most illustrative for teaching purposes in demonstrating the generalities of kinetic models. Without too much effort, the generalized equations can readily be converted to relationships that can be applied in specific situations. The authors have also added a more philosophical overview to the various concepts that increase the understanding of many of the equations and relationships presented.

Other interesting additions to the second edition are the kinetics of irreversible pharmacological response, product inhibition aspects of nonlinear kinetics, and various aspects of protein binding in relation in pharmacokinetics. Although the discussion dealing with protein binding is often divergent from what this reviewer believes to be a rational development of the relationship between protein binding and pharmacokinetics, it is a valuable and instructive addition, especially in lieu of the paucity of such discussions.

After extensive scrutinization this reviewer can find only a few areas that may be considered for changes in future editions: 1. The use of natural logarithms instead of log to the base of 10. This will remove the always difficult task by students of deciding when to use the correction factor 2.303. 2. The use of the current concept of clearance throughout the book, not just in segments; *i.e.*, treating clearance as a fundamental pharmacokinetic parameter throughout the book rather than being dependent on volume of distribution and fractional rates (*i.e.*, elimination rate constant).

In summary, this is a substantially expanded version of the first edition, and as a comprehensive and logically developed text, it will probably enjoy an even higher readership than its predecessor. A must for all pharmacokineticists.

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Chromatography and Mass Spectrometry in Biomedical Sciences 2. (Analytical Chemistry Symposia Series 14). Edited by A. FRIG-ERIO. Elsevier/North Holland, 52 Vanderbilt Avenue, New York, N.Y. 10017. 1983. 506 pp. 16 × 24 cm. Price $106.50 (Dfl. 250).

This book contains the proceedings of the International Conference on Chromatography and Mass Spectrometry in Biomedical Sciences, held in Bordighera, Italy, in June 1982. There are five plenary lectures on five topics. Three of these lectures are on techniques such as combined gas chromatography–Fourier transform infrared spectroscopy, quantitative ion-exchange thin-layer chromatography, and tandem mass spectrometry (MS–MS). They represent the state of the art on each of the techniques and are well written. The other two plenary lectures are on "Recent Applications of Mass Spectrometry to Cannabinoid Studies" and "Chromatographic Techniques for Determination of Some Calcium Antagonist Drugs in Biological Fluids." Both of these presentations, as well as the previous three lectures, are worth reading. The rest of the papers presented or given as poster sessions at this meeting are widely varied, from drug studies to environmental analysis, where the techniques applied include the use of radioimmunoassay, high-performance liquid chromatography, thin-layer chromatography, gas chromatography, and combined techniques of gas chromatography–mass spectrometry. Like any other conference there are some good papers, some average in quality, and some which do not add anything new to the use of chromatography and mass spectrometry in the biomedical or environmental fields.

Since this book covers a very broad spectrum of techniques and subjects, it can not be recommended for anyone seeking an in-depth discussion on any particular subject. It certainly can be recommended for those who want an overview of the state of the art and current thinking of chromatography and mass spectrometry.

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New Drug Parade: A Historical Minireview 1954–1982. By PAUL DE HAEN. Paul de Haen International, Inc., 2750 S. Shoshone Street, Englewood, CO 80110. 1983. 22 × 28 cm. Price $25.00.

New Drug Review: A Historical Minireview offers a statistical and descriptive tabulation of major new drug introductions in the United States from 1954 to present, including single chemical entities, duplicate single products, combination products, and new dosage forms. Major drugs introduced each year are listed by trade name, generic name,

manufacturer, therapeutic use, chemical class, and foreign developer. The listed drugs have been selected on the basis of chemical innovation and therapeutic advantages.

In addition to the statistical and descriptive information, the publication includes brief comments for each year on such significant events as the state of research, trends in the pharmaceutical industry, and the relationship between the industry and governmental agencies. Also included are pertinent references to the original reports in *Drug and Cosmetic Industry* and secondary citations of the press comments, editorials, and reprint history. Following the individual information for each year is an overview of the entire period, including summary statistics.

—*Staff Review*

NOTICES

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Cancer Incidence in Singapore 1968–1977. By K. SHANMUGARATNAM, H. P. LEE, and N. E. DAY. World Health Organization, International Agency for Research on Cancer, Singapore Cancer Registry, Lyon, France. 1983. 171 pp. 21 × 29.8 cm. Price $15.00 (Sw. Fr. 30).

Catalog of Teratogenic Agents, 4th Ed. By THOMAS H. SHEPARD. The Johns Hopkins University Press, Baltimore, MD 21218. 1983. 529 pp. 16 × 24 cm. Price $35.00.

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Complying With FDA Good Manufacturing Practice Requirements: How to Develop Your GMP/QA Manual. By JOHN J. RIORDAN and WILLIAM COTLIAR. Association for the Advancement of Medical Instrumentation, 1901 N. Fort Myer Drive, Arlington, VA 22209. 1983. 201 pp. 22 × 28 cm. Price $65.00 ($50.00 for AAMI members.)

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