Book Reviews

Computer Aided Drug Design. Methods and Applications
Edited by Thomas J. Perun and C. L. Propst
Published 1989 Marcel Dekker Inc, New York
516 pp $99.75 USA and Canada. $119.50 other

For quite some years now, drug researchers have been repeatedly told that new and improved drugs will come from an understanding of the disease processes at the molecular level and by subsequent rational drug design. This new book, edited by Perun and Propst, attempts to review the current state of play in the drive in this direction. As the subtitle suggests, the book is divided into two. The first half on "Methods" includes the approaches and ideas as well as the actual techniques that are available, and indeed necessary to elucidate structure and interaction of molecules; the second half, under the heading of "Applications" describes a number of case histories where the rational approach has guided the discovery effort towards successful drugs in the area of ACE inhibitors, renin inhibitors, dihydrofolate reductase inhibitors, antiviral drugs, opioid peptides and cholate uptake inhibitors. I use the word "guided" rather than "directed" as I am yet to be convinced that some of the rational decisions made in such case histories are not made retrospectively. Still, who wants to spoil a good story? This is not to say however, that the case histories do not illustrate the future of drug discovery and development.

A striking feature of the book is that, apart from the last chapter on cholate uptake inhibitors from the J. C. Goethe University in Frankfurt, all the contributions are from United States laboratories. Now it is entirely natural that the American editors should commission the work from colleagues they know best, but even the reference lists seem to be short of British and European influences. Are our American friends really so parochial, or are we on this side of the Atlantic—the originators of a healthy proportion of the world's successful drugs—unaware of the new era that is dawning in drug research? If the latter is true then our drug researchers would be well advised to purchase this book and begin the process of catching up.

The editors set the scene in an introductory chapter. One of the important points made early on in the book, in this chapter and the following one on Computer Graphics by O'Donnell, is the need to appreciate that drug molecules and their receptors are three-dimensional objects. In fact this is so vitally important that the conventional two-dimensional format of the printed page is rapidly exposed as inadequate for a full description of the topic. The chapter by O'Donnell describes the various methods of depicting realistic three-dimensional images on the computer screen. As the book is intended for students as well as established researchers, I would have liked to have seen a more detailed description of how to use the stereo views printed in several chapters in the book. After all, this would be more relevant to the book itself than the lists of commands available for specific modelling programs. In fact for those who can master the technique of going cross-eyed at will, the three-dimensional views are so spectacularly different to any two-dimensional representation the book can go a long way to overcoming the inadequacies of the flat page.

Such a book as this, with its wide range of intended readership, has to be aware of the needs and the tolerances of both the genuine newcomer who wants to know what it is all about and the researcher expert in some aspects but not in others. Generally the book succeeds in this respect although there are occasional lapses; for example, I could find no definitions of CNDO and MNDO and the chapter on NMR would appeal more to the knowledgeable spectroscopist than the modeller wishing to understand how NMR contributes to drug research. This all means of course that the book does not stand completely on its own and not unreasonably the reader will need to consult other texts—both less advanced and more advanced. Nevertheless the editors have produced a timely, useful and well-written contribution to the burgeoning field of rational drug design.

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Analytical Profiles of Drug Substances. Volume 18
Edited by K. Florey
Published December 1989 Academic Press Inc., San Diego
646 pp $69.95

This is the latest volume in a series familiar to analytical chemists involved in drug research and development, and which has appeared approximately once a year since the first volume in 1972. Like the others it contains information of analytical interest on a number of selected drug substances—sixteen in this volume. Although a format has evolved over the years and the contents pages of the monograph tend to be identical, what goes in to each monograph is entirely up to the author and is usually the information that is available rather than the information that is needed, i.e. most authors review the literature rather than set out to carry out new work to complete a comprehensive monograph. This is a great pity. To produce such a volume every year and to persuade contributors to produce their work on time is praiseworthy. This is partly achieved by the use of something called the Academic Press Rapid Manuscript Reproduction. This is also a great pity. Presumably the point of rapid manuscript reproduction is to convey the results of work to the scientific public as quickly as possible, whereas inspection of the reference lists in this volume reveals very little recently published information; in many cases the most recent references—i.e. less than two years old—are to other reference works.

The book relies on the submission of camera-ready copy, which undoubtedly is part of the rapid reproduction system. However, as George Orwell may have put it, some camera-ready copy is more ready than others. Despite there being an Editorial Board, there appears to be no refereeing, no language editing and no proof-reading. Some may accept that these can be sacrificed to the merits of rapid publication, but I do not think so. This series purports to be a reference work of high standing. Such non-words as "singulett" and "sixtet" when speaking of NMR (and not, I might add, in the same article) are unacceptable. "Flourine" appears twice in two lines in one chapter, followed later by "flourescence". "Categoration" isn't in my dictionary. These are not isolated examples, nor are they trivial: such a book will be consulted by many researchers for whom English is not their native language, and the editors have a responsibility to correct the errors and not comply in the propogation of them.

It is not impossible for one person, or a group of people, to have a sound grasp of the whole field of drug analysis and related topics but I am afraid that in many chapters the authors stray out of their depth. I am not convinced that clofazimine can be deduced to have a half-life in man of greater than 69 days on the basis of less than 1% of the dose being excreted in the urine in one day; and the monograph on clioquinol states "calculation of the area under the curve for blood plasma samples, determined by a GLC method, indicates a half-life of 11–14 hours with maximum concentration occurring at 4 hours." Such statements would surely have been challenged and clarification sought from a competent refereeing system. Again the editor has a responsibility to his readers seeking enlightenment for ensuring that anything in a work of reference is accurate and is sensibly interpreted.

In summary, Analytical Profiles of Drug Substances has lots of information, can possibly point the reader to the appropriate literature, but cannot be regarded as authoritative.

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