



Medicinal Chemistry – An Introduction

by Gareth Thomas,
John Wiley & Sons,
2000. 539 + 17

pages; paperback (Internet price \$45.00),
ISBN: 0-471-48935-2; hardback (Internet
price \$98.00), ISBN: 0-471-98807-3

Books on medicinal chemistry have historically been focused towards the lucrative pharmaceutical/biotechnology industry market. Some are outstanding reference works such as *Burger's Medicinal Chemistry* and *Comprehensive Medicinal Chemistry*; others address in great detail a particular pharmaceutical class or reproduce papers presented at medicinal chemistry symposia. Few have attempted to provide a comprehensive description of this vast subject in a format suitable for undergraduate education so it is appropriate to ask the question 'What should the contents and the level of detail of such a book be?'

Expectations

I would expect to see coverage of most of the major pharmaceuticals as case histories, some historical perspective with examples, a biochemically and pharmacologically detailed description of the major therapeutic targets, some mention of genomics and proteomics, and a description of screening processes (including an understanding of how one selects a handful of compounds for preclinical evaluation from *in vitro* HTS hits). I would also expect coverage of pharmacokinetics and pharmacodynamics, toxicology, the FDA, the role of organic synthesis, combinatorial chemistry, structure determination and computer graphics, modern QSAR in drug discovery and so on. The level of detail of the book should be well beyond the teaching

requirements, so that the brightest and most curious students are stimulated further and the tome might find its way into the offices of graduate students and industry researchers.

Reality

Medicinal Chemistry – An Introduction provides excellent coverage of some of these topics. For example, 59 pages of drug design includes 17 pages on the newer methodologies in combinatorial chemistry. The section on biological membranes includes antibiotics and drug resistance, there are 35 pages of pharmacokinetics with some of the underlying mathematics, enzymes, receptors, metabolism, DNA and RNA, and a chapter on nitric oxide with over 30 pages of interesting narrative including the mechanism of action of Viagra.

In other areas, however, the book falls short on many of these desires. Some of the most prominent drugs in recent times, such as the cholesterol-lowering HMG-CoA reductase inhibitors, the HIV protease inhibitors, the COX2 inhibitors, cimetidine and ranitidine, omeprazole, the β -blockers and other adrenergics, dopamine and serotonin-receptor agonists and antagonists, channel blockers, and the anti-cancer drugs taxol and tamoxifen are either skimmed over or completely missing. Other topics, which have been the backbone of recent medicinal chemistry research, such as the role of peptides as neurotransmitters, peptidergic hormones, and computer-based drug design, are barely mentioned. Where are the orphan receptors, the immune system, the antibodies, the chemokines and their receptors, the cyclin-dependent kinases (CDKs), etc.? Many of the examples used in different parts of the book are of historical interest only. Topliss trees and Craig plots are largely obsolete today: there are now computers that select compounds using Lipinski's 'rule of 5', along with a

synthetic capability to make, in parallel, all of the substituents possible on a template. In the year 2001, one really does not need a re-run of Erlich's Salvarsan, probably one of the least safe drugs ever used in the clinic! The organic synthesis chapter is too brief and incomplete to be of value to a medicinal chemist.

Conclusions

In conclusion, this book has some shortcomings. However, the softback price of \$45 might be cheap enough for teachers of medicinal chemistry to use the good parts of the text. Wiley should have based their format on the major biochemistry textbooks of the century such as Lehninger *et al.* or Voet *et al.* They should have taken note of the excellent content, and mix of text and high-quality diagrams (some of which are in colour) in these books, and commissioned a textbook capable of becoming the worldwide standard for medicinal chemistry teaching.

Nigel R.A. Beeley

Vice-President and Chief Chemical Officer

Arena Pharmaceuticals

6166 Nancy Ridge Drive

San Diego

CA 92121, USA

tel: +1 858 453 7200 ext. 276

fax: +1 858 453 7210

e-mail: nbeeley@arenapharm.com

Student subscriptions

Students may take out a subscription to *Drug Discovery Today* and receive a 50% discount on the Personal subscription rate. To qualify for this discount please use the bound-in card contained within this journal.