

Camille Georges Wermuth (Ed.)  
*The Practice of Medical Chemistry*

Academic Press, London, 1996,  
42 chapters, xi + 968 pages.  
ISBN 0-12-744640-0.

In the foreword to the book, the editor says that it is »one more book on medical chemistry«, but every book in this field is new, not only because of the different approach of the author(s), but more due to the new developments in this very rapidly growing field of applied chemistry. In its essence, the book is a collection of review papers written by 44 authors, but the diligence of the editor (author and coauthor of 13 chapters!) made the book – in spite of its mosaic structure – a well composed, systematically guided and competently written piece of work, which should be interesting to everybody that deals, directly or indirectly, with medical chemistry.

In the first part of the book (four chapters), general aspects of medical chemistry are presented (drug and disease classification, general strategy in discovering new drugs, measurement of drug effect and main phases of drug activity). The second part of the book deals with the strategies for discovery of lead compounds (from discovery by chance to systematic search in the »libraries« of new compounds or compounds described in computer data bases). There is a very interesting chapter written by S. Hobbs de Witt on finding a pharmaceutically active compound in the peptide mixtures and the chapter by V. J. Hruby on automatic preparation of these mixtures (»libraries«). There are also two chapters on the molecular action of drugs (J.-P. Gies, A. N. Hobden), which should be particularly interesting to the chemist not very familiar with biochemistry and biophysics.

The next two parts (III and IV) are devoted to the relationship between structure and activity. The editor, C. G. Wermuth, gave in four chapters very systematic accounts of the influence of chemical modifications on physiological activity (isosteric replacement, ring transformations, specific substituent effects, effects of vinylogue and benzologue derivatizations). J.-J. Borguignon wrote a chapter on twin drugs, *i.e.* drugs containing two pharmacophoric groups, and described the methods for their »construction«, along with a discussion of the advantages and disadvantages of such drugs. The

chapter written by H. van de Waterbeemd is devoted to quantitative approaches to structure-activity relationships.

The fifth part is entirely devoted to molecular modelling. After two introductory chapters on stereochemical aspects of drug action, explaining the basic spatial factors which influence the action of the drug (conformational restriction, steric hindrance, hydrophobic collapse, optical isomerism), the next chapters address more practical aspects. H.-D. Höltje wrote an article on pharmacophore identification and receptor mapping, in which he described methods of molecular modelling (conformational analysis, calculations of molecular electrostatic potentials and molecular interaction fields). The methods are illustrated by the case study of the mapping of 5-HT serotonergic receptor. Y. C. Martin and C. T. Lin wrote the chapter about 3D-QSAR and illustrated the method by its application on designing D2 dopamine agonists.

The sixth part deals with the chemical modification influencing the pharmacokinetic properties. After the three introductory chapters on the fate of the xenobiotic in living organisms (F. M. Belpaire and M. G. Bogaert), biotransformation reactions (C. G. Wermuth and B. Testa) and biotransformations which lead to toxic metabolites (A. Picot and A.-C. Macherey), the next three chapters are devoted to carrier prodrugs and macromolecular carriers for drug targeting, in which the covalent binding of drug molecules to biopolymers is described.

The seventh part of the book deals with the pharmaceutical aspects of drug design, *i.e.* with the chemical formulation problems. The chapter written by B. D. Anderson and K. P. Flora presents the problem of drug solubility (dependence on pH, crystal modification, ionic strength of the surrounding electrolyte *etc.*). In the next chapter (C. G. Wermuth), the chemical modification of parent compound made in order to enhance the drug solubility is described. Finally, virtually insoluble organic compounds can be dispersed by colloidal processes (micelle formation) – this is the topic of the chapter written by K. H. Bauer. The pharmacodynamic properties of a drug can be modified by its binding to cyclodextrins, which are the new »hit« of pharmaceutical industry, and to their numerous derivatives. Therefore, chapter 37 (K. Uekama and F. Hirayama) is devoted to this class of compounds.

In the last, seventh part of the book, legal and economic aspects of development and production of new drugs are presented. There is, first, an introductory chapter describing all the steps leading from the discovery to market availability (J. A. Dangoumau). The next two chapters teach the chemist how to name his new drug and obtain a patent protection. The last chapter (B. G. Reuben) deals with the consumption and production of pharmaceuticals; you can learn, for instance, that the best business is to develop new ulcer or heart drug. Also, if somebody is interested in developing a drug for a rare disease (»orphan drug«), he will have to seek government support, or he would be forced to try curing the rare disease with the existing drugs.

At the end, I cordially recommend this excellent book to every chemist that is engaged or will be engaged in drug business. The book is conceived practically, not theoretically; therefore, the reader should find many reports from the practice at the expense of detailed description of the methods or broad generalizations (which are very dubious in this field of research!). Due to the mosaic structure of the book, there is a slight redundancy among some chapters, but it is a good property if the book should be viewed as a textbook. If the reader needs the book as a reference book, he will not be disappointed because he will be helped by rich cross-references, many titles and subtitles and, most of all, with the thirty index pages at the end of the book.

*Nenad Raos*