Book Reviews

Drug Design For Neuroscience. Edited by Alan P. Kozikowski. Raven Press, New York. 1993. xiii + 480 pp. 16 × 23.5 cm. ISBN 0-7817-0061-2. $110.00.

The situation normally found in contemporary drug discovery research is aptly stated by the editor of the present volume in the introduction: The question is one of "what to make" rather than "how to make it." The modern practice of discovery and development of new therapeutic agents is an intensively multidisciplinary one, requiring that its practitioners be versed in organic chemistry, molecular biology, pharmacology, cell biology, immunology, biochemistry, and computational chemistry, among others. Rather than attempt to provide tutorials on these myriad skills, the volume presents case studies from various laboratories which illuminate the practice of modern drug design by example.

The book is organized according to the common therapeutic targets in the mammalian nervous system. The continuing importance of research in the area of excitatory amino acid neurotransmission is underscored by the fact that glutamate receptors and their pharmacological manipulation are the focus of five chapters, nearly one-third of the volume. Other chapters deal with approaches to Alzheimer's disease (three chapters), serotonin receptors (two chapters), dopaminergic agents (two chapters), and benzodiazepine receptors (one chapter). Following this tour of the commonly targeted enzymes and cell-surface receptors, two chapters are devoted to the relatively new approach of manipulating intracellular second messenger systems, specifically inositol cell signalling. A final chapter discusses approaches for enhancing the blood-barrier penetrability of centrally active agents.

The disciplinary mix varies from chapter to chapter. Some contain a great deal of interesting synthetic chemistry and describe in detail the chemical thinking underlying the drug discovery process; in others the focus is on biology and pharmacological characterization. The emphasis throughout is on traditional small molecule drugs. The chapters are generally well-referenced with up-to-date citations, many from the 1990s. The subject index is regettably incomplete. For example, molecular modeling is discussed in six chapters, only one of which is indexed. Other problems result from inconsistent use of stereochemical terminology between chapters. The unfortunately common (and incorrect) designation of the 1*S*,3*R*-isomer of ACPD as "*trans*" is perpetuated, and in general the descriptors "*cis*" and "*trans*", rather than "*R*" and "*S*", are frequently used as stereochemical descriptors for glutamate agonists and antagonists, further confusing the already-complex area of glutamate receptor stereochemistry.

Despite a few minor quibbles, this book is an extremely useful "snap-shot" of contemporary drug design in neuroscience by leading practitioners. It should be a worthwhile addition to the bookshelves of most medicinal chemists.

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