Book Reviews

Annual Review of Pharmacology. Vol. XIII. Edited by H. W. Elliott, R. Okun, and R. George with 37 contributors. Annual Reviews, Palo Alto, Calif. 1973. 520 pp. 15.6 × 23 cm. $10.00.

The scope of pharmacology has increased and is still increasing at such a rate that it is not possible for any one person to keep up with all the advances published in the current literature. The purpose of these reviews is to enable individuals involved with research and teaching in pharmacology to keep up to date with recent advances and problems in this area. Thus this latest volume, in a series of 25 articles, attempts to summarize the most recent advances in research, new problems arising from the orientation of this research, and the ability of newer and more sophisticated analytical procedures, which have become more generally available, to serve as tools to probe more deeply into pharmacological problems. Also, several of the reviews indicate where deficiencies exist and where the most significant progress may be expected in the near future.

Two reviews in this volume especially illustrate the role of the medicinal chemist in pharmacology. The first, titled Synthetic Analogs of Oxytocin and the Vasopressins, by Sawyer and Manning, describes the role of the synthetic chemist in the demonstration of structure-activity relationships of these peptides. The second, Stereoisomerism and Drug Action, by Sastry, discusses structure-activity aspects of adrenergic and cholinergic agonists. Other reviews, which offer insight into the power of the newest in analytical procedures for the investigation of biological problems, include Applications of Integrated Gas Chromatography/Mass Spectrometry in Pharmacology and Toxicology, by Jenden and Cho, and Application of New Analytical Techniques to Pharmacology, by Watson.

However, the reviews are generally short, about 20 pp, and cannot hope to thoroughly encompass the topic. Thus, it is found that the authors concentrate on the most recent literature, generally within the past 3-5 years, with selective citations from numerous published articles. For the most part, areas of omission are indicated with reference to more thorough reviews of specific areas within the general topic. Several authors include data from ongoing research which are not yet published. This serves to show the direction of current research and indicates somewhat the progress to be expected in the near future. The diversity of topics covered in this latest volume makes the 1973 Annual Review of Pharmacology a valuable reference for the teacher and investigator in the health sciences who wish to find a concise presentation of some of the most recent pharmacological research without having to resort to an extensive and time-consuming literature survey. This volume represents one of the few remaining bargains in this time of inflationary book pricing.

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Fundamentals of Chemotherapy. By William B. Pratt. Oxford University Press, London-Toronto. 1973. 332 pp. 13.5 × 21 cm.

This excellent text attempts successfully to introduce an understanding of chemotherapy on the molecular level. It comprises the therapy of bacterial and parasitic diseases as well as viral and neoplastic diseases. It is directed at the medical chemist but also useful for students and practitioners of medicine and veterinary medicine. Yet it is not and does not claim to be a clinical pharmacological guide. Thus, one does not find dosage suggestions or guidelines for administration in renal failure or hemodialysis.

One may disagree with some minor points of the text. For instance, in the case of a patient's sensitivity to penicillin this reviewer would prefer clindamycin to gentamicin or kanamycin as drugs of second choice for staphylococcal infections.

In the therapy of tuberculosis streptomycin still is given as a primary drug, whereas it appears to be replaced by rifampicin to an increasing degree.

Each chapter is followed by an excellent selective bibliography. The index is regrettably brief and not very helpful to the disease-oriented clinician.

In spite of such minor shortcomings, the book conveys an excellent understanding of chemotherapy and does so in remarkably clear and concise language.

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Drug Design. Vol. II. Edited by E. J. Ariens with 17 contributors. Academic Press, New York, N. Y. xviii + 645 pp. 15 × 23 cm. $37.50.

In the first chapter of this book (127 pp), entitled "Modulation of Pharmacokinetics by Molecular Manipulation," Ariens presents an excellent discussion of the rational approach and limitations in drug design. Using examples from diverse bioactive agents ranging from therapeutics to pollutants, he describes the manipulation of the "mother" compound to achieve the most useful activity. In contrast to the specific emphasis in *Molecular Modification in Drug Design [Advan. Chem. Ser.*, **No. 45** (1964)], Ariens presents an overview based on design, not therapeutic activity.

The remainder of the book deals with specific therapeutic classes with emphasis on the author's contributions in the area. H. Schaeffer illustrates reversible and irreversible enzyme inhibitors with 6-mercaptopurine, allopurinol, and studies on adenosine deaminase (32 pp). Cholinesterase receives the attention of R. D. O'Brien (52 pp) and I. B. Wilson and H. C. Froede (17 pp). The former deals with design of organophosphate and carbamates; the latter describes results achieved in reactivation of blocked cholinesterase approaching the problem from the chemistry of the inhibited enzyme. In a related chapter (78 pp, 644 ref), M. M. Smith brings the reader up to date with current views on the design of agents for neuromuscular blockade.

A. Grollman has a brief chapter on the inhibition of protein biosynthesis with a refreshing review of the molecular biology as it relates to the site of action of currently available agents. Together with S. B. Horwitz he, again, presents a logical approach to the design of antiviral agents. While both of these chapters are brief they are sufficiently informative and, more important, utilize current understanding of viral infection.

J. Rudinger has an extensive discussion on the design of peptide hormone analogs (100 pp, 649 ref). With a clear emphasis on design the chapter analyzes the structural and biological aspects important in this field.

J. A. Stock presents the design of tumor-inhibiting alkylating agents in a logical sequence; based on the chemistry of alkylating groups, the chapter progresses through design attempts to meet biological requirements.

Additional chapters on penicillins (A. E. Bird and J. H. C. Nayler), steroid design (G. A. Overbeek, J. van der Vies, and J. de Visser), and diuretic advances (G. deStevens) are included. The discussion by M. H. Richmond (Enzymes and Their Synthesis as a Target for Antibiotic Action) was the only useless chapter. Considering that these 10 pp constitute only 1.5% of the book the editor has done a fine job.

Overall the book is excellent; the abundance of references, almost 2500, suggests a catalog or compilation of the literature together with tables of compounds. However, this is not the case; most authors have maintained the goals of the editor and direct

the reader through the specific problems encountered in development of superior agents in the various classes of drugs. If the distinction can be made this book is instructional and in some cases an excellent review of selected topics.

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Catecholamines. Edited by L. L. Iversen with 17 contributors. British Medical Bulletin, British Council, London. 1973. 89 pp. 28.5 × 22 cm. $6.50.

The May 1973 issue of *British Medical Bulletin* (Vol. 29, No. 2) is a symposium on the physiology and pharmacology of catecholamines. A number of contributors are prominent figures in the field and are well qualified to discuss the various topics included in this symposium. Some of the contributions may be of particular interest to medicinal chemists. Among these are "Prostaglandins at Adrenergic Nerve Endings" by E. W. Horton and "Dopamine in the Basal Ganglia: Its Therapeutic Implications" by O. Hornykiewicz. Catecholamine biosynthesis is discussed by H. Blaschko and recent studies on catecholamine catabolism are presented by D. F. Sharman. D. S. Jenkinson presents a discussion entitled "Classification and Properties of Peripheral Adrenergic Receptors" which reviews the progress in the development of evidence for subclassification of adrenergic receptors. There are two chapters on antihypertensive drugs.

A very active area of medicinal chemistry in recent years has been the design and synthesis of selective β-adrenergic receptor agonists and antagonists. The many medicinal chemists working in this field may enjoy the physiologically oriented presentation entitled "Activation and Blockade of β-Adrenoreceptors in Common Cardiac Disorders" by J. W. Black and B. N. C. Prichard.

All of the reviews are short, but most of them contain numerous recent references. Somewhat disappointing is the absence of a chapter devoted to recent work which implicates cyclic nucleotides in adrenergic mechanisms. However, there is little doubt that this issue should be of considerable use to anyone interested in catecholamine physiology or pharmacology.

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Selective Toxicity. 5th ed. By Adrien Albert. Chapman and Hall, London. 1973. xv + 597 pp. 16.2 × 24.1 cm. $19.75.

This text presents a philosophy of drug action not often afforded the student of medicinal chemistry. The author considers most drug therapy as a form of selective toxicity.

The first four chapters are devoted to the definition of selective toxicity and a discussion of the three principles the author has established as the physical basis for selectivity. These three principles are: differences in distribution; comparative biochemistry; and comparative cytology. The next chapter is a discussion of the history and principles of chemotherapy and is followed by a chapter on pharmacodynamics.

The remainder (nine chapters) of the text concerns the relationship between chemical structure and biological activity. These chapters discuss: structure–activity relationships, chemical bonds, and adsorption; enzymes, substrates, and metabolites; the effects of ionization on biological activity; metal-binding substances; covalent bonds in selective toxicity; steric factors involved in biological activity; the modification of membranes by surface-active agents; free radicals in selective toxicity; and biological activity unrelated to structure.

There is a four-part Appendix containing a brief summary of the use of partition coefficients and regression analysis in quantitative structure–activity relationships. Appendix IV is a brief discussion of the use of nmr spectroscopy in medicinal and biological chemistry. The author has provided an excellent bibliography containing 1977 references. The index appears to be adequate.

This text is well organized for easy, rapid reading. Professor Albert has provided good balance between general information and detail. The text provides a good background for the reader seeking general information on the subject, and there is sufficient detail to provide the active research worker with new approaches to a particular problem.

Inasmuch as the author has not attempted a complete survey of all therapeutic classes of drugs, this text would not serve as a singular source for an undergraduate course in medicinal chemistry. However, the first six chapters are recommended reading for such students. The entire text should be required reading for graduate students and all other research workers in the field of organic medicinal chemistry.

This book will also be of interest to people involved in research with agricultural chemicals and environmental pollution. In this regard, Professor Albert has utilized insecticides, fungicides, and herbicides as examples of agents that exhibit selective toxicity.

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