

pentapeptide, L-histidyl-glycyl-L-glutamyl-L-seryl-L-phenylalanine, had a much lower catalytic activity ($93 \text{ l. mole}^{-1} \text{ min.}^{-1}$) when compared with the corresponding pentapeptide containing aspartic acid in the sequence. The same observation was true in the case of two tetrapeptides, L-histidyl-L-aspartyl-glycyl-L-serine (catalytic coefficient $150 \text{ l. mole}^{-1} \text{ min.}^{-1}$) and L-histidyl-L-glutamyl-glycyl-L-serine (catalytic coefficient $63 \text{ l. mole}^{-1} \text{ min.}^{-1}$). The importance of aspartic acid in the peptide esterase models was further confirmed by comparing two pentapeptides, L-histidyl-L-alanyl-L-aspartyl-glycyl-L-serine (catalytic coefficient $210 \text{ l. mole}^{-1} \text{ min.}^{-1}$) and L-histidyl-L-alanyl-L-glutamyl-glycyl-L-serine (catalytic coefficient $87 \text{ l. mole}^{-1} \text{ min.}^{-1}$). The increased catalytic activity of peptide esterase models containing aspartic acid may be justified on the basis that, in the case of chymotrypsin, aspartic acid occupies position 194, which is adjacent to the postulated active serine at position 195. The same is true of trypsin, where aspartic acid is at position 184 adjacent to active serine at position 183.

The catalytic activity of the peptide esterase models was determined by the liberation of *p*-nitrophenol from *p*-nitrophenylacetate following the procedure used by Sheehan *et al.* (4). The synthesis of the pentapeptide, L-histidyl-L-alanyl-L-aspartyl-glycyl-L-serine, which has the highest catalytic coefficient of reported peptide esterase models, is outlined in Scheme I. To limit the degree of racemization, the peptide chains were extended from the C-terminal residues of amino acids, and all peptide bonds, except histidine, were formed using the pentachlorophenyl active ester method (8, 9). Histidine residues were incorporated in the peptide chain using the azide method (10). All the protecting groups used for unreacting functionalities during the reaction sequences were acid labile or removable by hydro-

genolysis. This approach excluded the use of alkali treatment during the synthesis, thereby further limiting the degree of racemization and problems of transpeptidation (11). The elemental analyses of the intermediates and final peptides reported in this work were within experimental tolerance, and they were homogeneous to paper chromatography and paper electrophoresis under a variety of conditions.

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BOOKS

REVIEWS

Antitussive Agents, Volumes I, II, and III. Section 27, International Encyclopedia of Pharmacology and Therapeutics. Edited by H. SALEM and D. M. AVIADO, Pergamon Press Inc., Maxwell House, Fairview Park, Elmsford, NY 10523, 1970. li + 833 pp. 16×23.5 cm.

All but three of the 15 chapters in this three-volume series are authored by the editors. In this ambitious undertaking, the authors have extensively reviewed the pharmacological and clinical literature pertaining to antitussives up through 1966 and systematically organized their findings into a readily usable format. The first portion of Volume I, an exhaustive tabular listing of patents issued for antitussive compounds, should be of great assistance to medicinal chemists as well as patent lawyers interested in searching for new chemical entities with this activity. The 453 entries include names of consignees, countries issuing, and references. A comprehensive review of antitussive testing methods in humans and animal species is also presented in tabular form. Pharmacologists should find the 100 referenced entries most useful because each includes information about the cough stimulus used, the method

of assessing the cough, as well as other pertinent specifications. The last part of Volume I consists of two chapters. The first discusses physiology of the cough reflex as a basis for understanding factors causing cough and pharmacologic approaches to alleviating cough. The last chapter is an interesting historical review of the changing concepts of causes and approaches to treating pathological cough.

Volumes II and III of this series present a review of the experimental and clinical literature about specific antitussive compounds. Volume II deals with derivatives of opium (three chapters on codeine, *d*-methorphan, and miscellaneous opiates) and four chapters on classes of nonopiates with central action. Volume III considers nonopiates with peripheral actions (chapters on local anesthetics, bronchodilators, expectorants, and mucolytic agents). The format of each chapter includes chemistry and dosage, pharmacodynamics, and clinical usefulness of the compound in question, as well as a tabular listing of all domestic and foreign commercially available preparations containing those particular compounds.

The carefully designed format of these three volumes provides a comprehensive look at the presently available experimental and clinical information about antitussive compounds. Areas needing further study are clearly identified so that these volumes provide a

valuable point of departure for experimental or clinical pharmacologists with interests in this field. Unfortunately, this series will be of less value to the clinician who is looking for a critical appraisal of currently available antitussive compounds. Questions relating to clinical efficacy and untoward effects are left dangling in some cases. It would have been helpful to the clinician-reader if the authors had included a critique of conflicting reports presented based on their own expertise and assessment of the literature.

Each volume concludes with a complete subject index. In addition, Volume III contains an index to names of preparations and an index to authors cited in the series.

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Permeability and Function of Biological Membranes. Edited by L. BOLIS, A. KATCHALSKY, R. D. KEYNES, W. R. LOEWENSTEIN, and B. A. PETHICA, North-Holland/American Elsevier, New York, NY 10017, 1970. vii + 364 pp. 15.5 × 22.5 cm. Price \$16.25.

The papers included in this book are based on material reported at the 1969 International Conference on Biological Membranes.

While the title of the book might suggest it would have broad appeal to pharmaceutical scientists, this is not entirely accurate. The individual papers are restricted to very specific fields; the reader would have to have in-depth knowledge of many fields to benefit greatly from this book as a whole.

However, for the scientist working specifically in this area, the book does cover much of the recent work in this field and might be a useful reference source.

Staff Review ■

Advances in Drug Research, Vol. 5. Edited by N. J. HARPER and A. B. SIMMONDS, Academic Press, London, England, 1970. vii + 278 pp. 15.5 × 23.5 cm. Price \$13.00.

This volume contains six comprehensive articles that summarize the progress made in certain areas of drug research.

Topics included in this volume are: Biologically Active Benzo[b]-thiophene Derivatives; Spectroscopic Techniques for the Study of Drug Interactions with Biological Systems; Endogenous Broncho-Active Substances and their Antagonism; The Role of Slow Reacting Substance in Asthma; Disodium Cromoglycate (Intal); and Recent β -Adrenoreceptor Stimulants.

Staff Review ■

Alkaloid-Bearing Plants and Their Contained Alkaloids, 1957-1968, Supplement of Lloydia—The Journal of Natural Products. By J. J. WILLAMAN and H. LI, The Lloyd Library and Museum and The American Society of Pharmacognosy, Storrs, Conn., 1970. vii + 286 pp. 17 × 25 cm. Price \$6.00. (Available from The Lloyd Library and Museum, P. O. Box 484, Cincinnati, OH 45201)

This supplement to *Lloydia* contains one article that is a continuation of the compilation "Alkaloid-bearing Plants and Their Contained Alkaloids," by J. J. Willaman and Bernice G. Shubert, pub-

lished in 1961 by Agricultural Research Services, Technical Bulletin No. 1234, U. S. Department of Agriculture.

The purpose of this supplement and the original compilation was to assemble in one place all the scattered information of the occurrence of alkaloids in the plant world.

The supplement is organized into two cross-referenced tables, one entered by the plant name and the second entered by using the specific alkaloid name.

Staff Review ■

Late Effects of Radiation. Edited by R. J. M. FRY, D. GRAHN, M. L. GRIEM, and J. H. RUST, Van Nostrand Reinhold, 450 West 33rd St., New York, NY 10001. 1970. ix + 298 pp. 18 × 26 cm. Price \$10.95.

This book contains the proceedings of a colloquium held at the University of Chicago in May 1969. This colloquium represents the climax of a ten-year effort to study the impact of the peaceful uses of atomic energy on public health.

The concluding chapter in the book, "The degradation of our environment," was written by Lord Ritchie-Calder.

Staff Review ■

NOTICES

Teeanalyse. By L. HORHAMMER, Springer-Verlag, 1 Berlin 33, Heidelberger Platz 3, Germany, 1970. 74 pp. 21 × 29.5 cm. Price \$13.00. (German)

Hexoprenalin: Pharmakologie und Therapeutische Anwendung Beim Asthmatischen Formendreis. Edited by E. DEUTSCH, K. IRSIGLER, and O. KRAUPP, Springer-Verlag, New York, NY 10010, 1970. viii + 127 pp. 15 × 22.5 cm. Price \$5.20. (German)

British Veterinary Codex, Second Edition (Supplement). Prepared by The Department of Pharmaceutical Sciences of the Pharmaceutical Society of Great Britain, The Pharmaceutical Press, 17 Bloomsbury Square, W. C. 1, London, England, 1970. xxiii + 317 pp. 14.5 × 22 cm. Price 3 Pounds, 10 Shillings.

Medicaments Organiques De Synthèse III. By G. VALETTE, Masson Et C^{ie}, 120 Boulevard Saint-Germain, Paris VI, France, 1970. 341 pp. 15.5 × 22 cm. Price 120 f. (French)

Drug Abuse and What We Can Do About It. Edited by J. C. BENNETT and G. D. DEMOS, Charles C Thomas, Springfield, IL 62703, viii + 138 pp. 15.5 × 24 cm. Price \$8.50.

Lehbuch der Pharmazeutischen Chemie. By H. AUTERHOFF, Wissenschaftliche Verlagsgesellschaft MBH, Stuttgart, Germany, 1970. xii + 536 pp. 17 × 25 cm. Price DM 54. (German)

Encyclopedia of Industrial Chemical Analysis. Edited by F. D. SNELL and L. S. ETTRE, Wiley, 605 Third Ave., New York, NY 10016, 1970. xiv + 680 pp. 18.5 × 26 cm. Price \$35.00 for subscription; \$45.00 for single copy.

NEW JOURNAL

Pharmacology and Therapeutics in Dentistry. Edited by A. H. KUTSCHER, Association of Pharmacology and Therapeutics Teachers in Dentistry, 630 West 168th St., New York, NY 10032, 1970.