physiological saline and given 10–15 min before intravenous antigen challenge. For intravenous dosing, the compounds were dissolved in the saline/ovalbumin/Evans blue solution and given with the antigen. If necessary, the compounds were first dissolved in a slight molar excess of sodium bicarbonate and then diluted into the antigen solution. Groups of five animals were used for all dose levels and control groups.

To quantitate the PCA test, the mean diameter of each spot was graphed as a function of the relative antiserum concentration. The line, fitted by least-squares equation, was extrapolated to the value at "zero" antiserum concentration (base value). The following equation was then used to calculate the percent inhibition:

$$\% \text{ inhibn} = \left[1 - \left(\frac{\text{diameter of drug} - \text{base value}}{\text{diameter of control} - \text{base value}}\right)\right] \times 100$$

The statistical significance of the results was determined by Student's $t$ test ($p \leq 0.05$). An inhibition of 15% was significant.

Melting points were taken in open capillary tubes on a Mel-Temp and are uncorrected. Each analytical sample was homogeneous by TLC and had IR, UV, and NMR spectra compatible with its structure. Combustion analysis for C, H, N, and Cl gave results within 0.4% of theory.

The procedures for the preparation of the reported compounds are listed as methods A–C and may be considered as general methods of preparation. The reported yields for the products obtained were not maximized.

**Method A. 8-Chloro-10-oxo-10*H*-pyridazino[6,1-*b*]quinazoline-2-carboxylic Acid (4).** A mixture of 5-chloroanthranilic acid (5.4 g, 31.6 mmol) and 6-chloro-3-pyridazinecarboxylic acid[3] (5.0 g, 31.6 mmol) was heated in refluxing glacial acetic acid[4] (50 mL) for 80 h. The mixture was cooled and the precipitate which formed was collected, giving 4.73 g (54.6%) of crude **4**, mp 253–300 °C dec. Recrystallization of this material from pyridine gave 1.3 g (15%) of the analytical sample, mp 260–262 °C.

**Method B. 8-(Carboxymethyl)-2-chloro-10-oxo-10*H*-pyridazino[6,1-*b*]quinazoline (7).** Dimethyl 4-aminoisophthalate[5] (4.2 g, 20 mmol) and 3,6-dichloropyridazine (3.0 g, 20 mmol) were heated at 155–160 °C as a melt for 0.5 h. The resulting dark solid was recrystallized from pyridine, giving 2.6 g (45%) of **7** as a red powder. The crude **7** was further recrystallized from pyridine to give 0.4 g (7%) of the analytical sample as yellow crystals, mp 241–245 °C.

**Method C. 2-Chloro-10-oxo-10*H*-pyridazino[6,1-*b*]quinazoline-8-carboxylic Acid (6).** A mixture of 2.6 g (9.0 mmol) of **7** and 150 mL of 6 N HCl was refluxed for 18 h. The solution was cooled and the gray solid which formed was collected. The crude **6** was recrystallized from pyridine, giving 1.32 g (53%) of a yellow solid, mp 287–290 °C. Further recrystallizations from pyridine yielded 0.63 g (25%) of the analytical sample, mp 290–295 °C.

# Book Reviews

**Handbook of Experimental Pharmacology. Volume 25. Supplement. Bradykinin, Kallidin and Kallikrein.** Edited by E. G. Erdös. Springer-Verlag, New York. 1979. xxii + 817 pp. 17 × 24.5 cm. $198.00.

This encyclopedic volume on bradykinin, kallidin, and kallikrein, which was published in 1979, nearly 1 decade following the previous "handbook" on this subject, is truly a supplement to the previous volume; it is not a revised edition of the 1970 text. This supplement reflects the ever increasing interest, knowledge, and range of experimental and therapeutic applications, all related to the kallikrein–kinin system. Among the many areas of experimental or clinical studies, the following are emphasized: (1) how kallikreins and kinins can affect (a) coagulation of blood, (b) activation of complement, (c) formation of angiotensin II, (d) release or modulation of effect of mediators such as prostaglandins, histamine, catecholamines, etc.; (2) how can inhibitors of kallikreins or of kininase II (identical to "angiotensin-converting enzyme") find cardiovascular applications. The former can be tried in extracorporeal circulatory systems and the latter have demonstrated efficacy as antihypertensive agents.

Twenty-four eminent authors including the editor have contributed to the vast scope of the text in this supplement volume. A total of about 3250 references have been cited in the 17 chapters. In Chapter 1, H. Z. Movat reviews in great detail "The Plasma Kallikrein–Kinin System and Its Interrelationship With Other Components of Blood". L. M. Greenbaum discusses "Kininogenases of Blood Cells (Alternate Kinin Generating Systems)" in Chapter 2. F. Fiedler presents a chapter on "Enzymology of Glandular Kallikreins" (Chapter 3). "Kallikrein Inhibitors" are reviewed in Chapter 4 by R. Vogel.

The ensuing seven chapters deal with kinins. Thus, in Chapter 5, J. M. Stewart summarizes and discusses "Chemistry and Biologic Activity of Peptides Related to Bradykinin". J. J. Pisano discusses "Kinins in Nature" in Chapter 6. "Bradykinin Receptors" are reviewed by C. E. Odya and T. L. Goodfriend in Chapter 7. The current status of "Bradykinin Radioimmunoassay" is described in Chapter 8 by R. C. Talamo and T. L. Goodfriend. W. G. Clark discusses "Kinins and the Peripheral and Central Neurons Systems" in Chapter 9. The "Effects of Kinins on Organ Systems" are reviewed by A. R. Johnson in Chapter 10. Chapter 11 presents the "Release of Vasoactive Substances by Kinins", authored by N. A. Terragno and A. Terragno.

The twelfth chapter entitled "Kininases" is written by the editor E. G. Erdös. Kininases I and II, as well as other kininases, are discussed with reference to their distribution, specificity, properties, inhibition, etc.

Three chapters are allocated to glandular, renal, and urinary kallikreins. K. D. Bhoola, M. Lemon, and R. Matthews review "Kallikrein in Exocrine Glands" in Chapter 13 (pancreatic, salivary, and submandibular kallikreins). "Renal and Urinary Kallikreins" are discussed by P. E. Ward and H. S. Margolius in Chapter 14. I. H. Mills reports on "Renal Kallikrein and Regulation of Blood Pressure in Man" in Chapter 15. R. W. Colman and P. Y. Wong review the "Kallikrein–Kinin System in Pathologic Conditions" (including deficiency of proteins necessary for kinin formation and disorders leading to increased kinin formation) in Chapter 16. The last chapter (17) is a survey of the Russian literature on "Bradykinin, Kallidin, and Kallikreins" by T. S. Paskhiva and A. P. Levitskiy.

The price of this supplement may, in some instances, tend to restrict its acquisition by some individual researchers, but it should be acquired by all libraries in chemical and life science oriented research centers. This valuable supplement (1979) is recommended very highly as a reference text to chemists, biochemists, enzymologists, physiologists, pharmacologists, and medical investigators with more than a passing interest in the kinin system. It is quite likely that research investigations of the kallikrein–kinin system will continue at an unabated pace, and volumes like the present one will always be needed to summarize the status of the field at regular intervals.

*The Squibb Institute for Medical Research* **Bernard Rubin**

**Atlas of the Three-Dimensional Structure of Drugs. Janssen Research Foundation Series. Volume 1.** Edited by J. P. Tollenaere, H. Moereels, and L. A. Raymaekers. Elsevier/North-Holand, Amsterdam. 1979. xii + 322 pp. 17 × 24.5 cm. $36.50.

This volume is the outgrowth of the authors occupation with three-dimensional aspects of drug molecules and related substances by compiling crystallographic data from their own file, as well as that of the Cambridge Crystallographic Data Center file. During the last 10 years a growing awareness of the need and importance of structural information on molecules going beyond the classic structural information has been recognized. Crystal structure analyses of conformationally flexible molecules do not necessarily lead to information about the conformational preferences in solution or at the site of the receptor. However, such information is extremely valuable, since the solid-state conformation represents at least one of the possibly many minimum-energy conformations a molecule can adopt. Furthermore, the solid-state conformation can be used for comparison with the conformation in solution and as primary input for quantum chemical calculations. The latter constitutes a valuable tool for the exploration of the entire conformational profile of a molecule. The authors intended this volume to serve as a bridge between crystallographers and structural chemists and those engaged in drug research.

The 260 compounds covered in this volume include high-quality color reproductions of the computer-drawn molecules, accompanied by bibliographic data on the structure determination and the main pharmacological and clinical properties. The crystallographic literature references are comprehensive through the middle of 1978. A generic name index, formula index, and trade mark index are also included.

This volume will appeal not only to the crystallographers but even more to the medicinal chemists and pharmacologists interested in the representation of molecular structures. The multicolor three-dimensional representations of the drug molecules make this volume a worthwhile investment for institutional and for personal purchase by medicinal chemists.

**Staff**

**Vitamin K Metabolism and Vitamin K-Dependent Proteins.** By J. W. Suttie. University Park Press, Baltimore, Md. 1979. xi + 592 pp. 16 × 23 cm. $39.50.

"Vitamin K Metabolism and Vitamin K-Dependent Proteins" contains the proceedings of the 8th Steenbock Symposium held at the University of Wisconsin, Madison, in June 1972. This volume focuses on recent developments in research concerning vitamin K and presents more than 90 papers by active researchers. The recent progress made since the discovering in 1974 of the molecular role of vitamin K as a cofactor for an enzyme that carboxylates peptide-bound glutamyl residues and converts them to γ-carboxyglutamyl residues is reported. The papers presented also cover investigations in a number of related areas. No author index is included; however, a rather inadequate subject index can be found.

**Staff**

**Selective Toxicity. Sixth Edition. The Physico-Chemical Basis of Therapy.** By Adrien Albert. Wiley, New York. 1979. xiii + 662 pp. 17 × 24 cm. $42.50.

The sixth edition of this classic text, first published by Professor Albert in 1951, preserves the general format of the previous editions and has taken into account recent developments in the field since the publication of the fifth edition in 1973. New sections in this edition include a discussion of psychotherapeutic agents and their receptors and the repair of membranes by active agents; their is a new short chapter on steps available for the perfection of a discovery. A multiple regression analysis, the Free–Wilson method, molecular orbital calculations, and molecular connectivity are briefly discussed.

**Staff**

**Asymmetry in Carbohydrates.** Edited by R. E. Harmon. Marcel Dekker, New York. 1979. vii + 253 pp. 15 × 23.5 cm. $26.50.

This book contains ten manuscripts of lectures which, although not acknowledged, appear to have been a symposium. One author states the symposium started as "History and Modern Research Related to Asymmetry in Carbohydrates" and later became "Modern Research Related to Asymmetry in Carbohydrates". As is usual for books which are collections of lectures, there is little, if any, coordination of materials from one chapter to the next. In this case, the book is reproduced from the original manuscripts which have numerous typographical errors, varying size type, and varying quality of illustrations. Editing appears to have been limited to the production of a good subject index. The usual reason for direct reproduction from manuscripts is to obtain rapid publication. This book, which was copyrighted in 1979, contains only a few references from 1977 and most of the references are prior to 1977.

The first manuscript, "Development of Concepts of Ring Conformation and Neighboring Group Effects Prior to 1940", is primarily of historical value since it summaries the contributions of carbohydrate chemists in the area of stereochemistry.

Chapter 2, "The composition of Reducing Sugars in Solution", is an interesting short article on the numerous difficulties of dealing with the composition of reducing sugars in solution.

The third manuscript, "Prochirability and Pseudoasymmetry in Carbohydrate Biochemistry", is an excellent treatment of the biological conversion of prochiral molecules to chiral molecules.

Chapter 4, which is titled "Influence of Configuration Upon Reactivity in Nitro Carbohydrates", is a good review through about 1975 of research on nitro carbohydrates. This chapter is valuable in that it brings together much of the available material on a subject which has not been broadly discussed.

Chapter 5 deals with CD spectra of cuprammonium complexes of diols and amino alcohols and Chapter 6 is a discussion of the synthesis of chiral tertiary alcohols by Grignard addition to glycosulose derivatives.

Chapter 7 is a review of the reactions of ribose and ribosides containing a carbonyl group.

Chapter 8 is a discussion of the conformational requirements for biological activity of poly(L-lysine) adducts of reducing sugars. The helical content of these adducts in the presences of calcium ion and sialic acid was studied by CD and by carbon-13 NMR.

"Lock and Key Chemistry with Crown Compounds", is the title of Chapter 9, which describes the synthesis of chiral crown ethers from carbohydrates. The ability of chiral crown ethers to bind primary ammonium cations is also discussed.

The final chapter of this book is titled "Chiral Sulfur in Carbohydrate Chemistry". It is a review of chiral sulfur compounds of which a few are carbohydrates. The overall discussion of chirality in organic sulfur compounds is valuable.

This book is of value to those doing research in carbohydrate chemistry or in stereochemistry; however, it is of limited value to those who need an organized approach to asymmetry in carbohydrate chemistry.

*University of Mississippi* **W. Franklin Gilmore**

**Recent Advances in Phytochemistry. Volume 13. Topics in the Biochemistry of Natural Products.** Edited by Tony Swain and George R. Waller. Plenum Press, New York and London. 1979. x + 253 pp. 16 × 23.5 cm. $29.50.

This volume constitutes the record of an international symposium held jointly by the Phytochemical Society of North America and the American Society of Pharmacognosy at Oklahoma State University in August, 1978. By way of introduction to what will be, perhaps, the trend of plant biochemistry during the next decade, it goes beyond biosynthetic pathways, isolation, and chemotaxonomic significance of natural compounds and addresses problems of the enzymes involved in biosynthesis, the modification of compounds through food chains, and the potential changes in chemical events during the course of plant evolution. There are eight chapters, two each devoted to the "Stereochemistry of Enzyme Action, Alkaloids, Terpenoids, and Marine Natural

Products". There are relatively few typographical errors and the editors are to be congratulated in producing a photooffset volume in which the typeface is uniform throughout.

**Staff**

**Antiepileptic Therapy. Advances in Drug Monitoring.** Edited by S. I. Johannessen, P. L. Morselli, C. E. Pippenger, A. Richens, D. Schmidt, and H. Meinardi. Raven Press, New York. 1979. xxvi + 425 pp. $39.00.

Forty-eight extended abstracts from the June, 1979, "Fourth Workshop on the Determination of Antiepileptic Drugs in Body Fluids" are printed here with minimal editing but extensive discussions. For those who monitor treatment of epilepsy, this volume will provide interesting preliminary data at a price of $0.04/gram and 64 words per penny. The abstracts generally lack summaries and vary in quality, so this is a koldtbord to sample selectively. The discussions are incisive and evoke an aura of the meeting as crisp as the gustatory effluvium of the herring of its site in Oslo. The reader will learn details of kinetics of one drug or another, often from studies using elegant techniques. Blood concentrations of a single drug are related to seizure control, and the effects of a second drug on the kinetics of another are documented. But when several drugs are given together, how do concentrations of these drugs and their metabolites relate to effect? This $64 question is not even 61% answered by this anthology. Emphasis is given to newer drugs, e.g., carbamazepine, dipropylacetate, clonazepam, clorazepate, and phenylethylacetylurea, and to unusual seizures, e.g., myoclonus, temporal lobe epilepsy, partial complex seizures, and the Lennox syndrome. Although most authors are German or Scandinavian, this proceeding is published in two languages. The English is understandable, but the "kineticspeak" may require a translation of monotherapy, cotherapy, polytherapy, undertreatment, comedication, dosedependent, institutionalised, polypharmacy, receptorplace, phenytoinindex, compartment, and "volume" of distribution. In German such constructions may dextrously bridge scientific crevasses, but in English they more often engulf precision in a sticky babel of jargon.

*Case Western Reserve University* **W. Leigh Thompson**

**Chemical Diagnosis of Disease.** Edited by Stanley S. Brown, Frederick L. Mitchell, and Donald S. Young. Elsevier/North Holland Biomedical Press, New York. 1979. xviii + 1383 pp. 17 × 24.5 cm. $74.75.

This new text prepared by British and American clinical laboratory scientists contains 24 chapters covering most aspects of chemical laboratory testing. Along with the usual subjects are included informative chapters on more unusual aspects of laboratory practice, such as biological variability, body fluids other than blood, abnormal hemoglobin, and cancer. Each chapter is well referenced and the indexing appears to be excellent. Since the emphasis of this text is on interpretation of test results, there is no presentation of specific methods. While this work is a good general reference to clinical laboratory testing, it suffers overall from the amount of time which elapsed between manuscript preparation and publication. Topics of great interest at the current time, such as HDL cholesterol measurement, glycosylated hemoglobin, and prostatic acid phosphatase radioimmunoassay, are only fleetingly mentioned in addenda paragraphs.

*Lahey Clinic Foundation* **Ann Warner**

**Advances in Enzymology. Volume 50.** Edited by Alton Meister. Wiley, New York. 1979. xxxii + 437 pp. 16 × 24 cm. $32.00.

The latest volume of "Advances in Enzymology" contains several chapters that would be of particular interest to medicinal chemists. One article by R. O. Brady and P. H. Fishman deals with the molecular basis for the "social behavior" of cells, where "social behavior" refers to the ability of cells to communicate with one another either as a result of contact or indirectly through humoral factors. The majority of this chapter is devoted to the mechanism of action of cholera toxin, which interacts with a membrane-transducing substance (ganglioside $GM_1$) and activates adenylate cyclase through a NAD-dependent ADP ribosylation. Comparisons are made between the mechanism of action of cholera toxin and trophic hormones (e.g., thyrotropin and lutropin). The mechanism of action of tetnus toxin and interferon are also discussed, since they are thought to interact with similar membrane ganglioside transducing systems.

Another chapter in this volume reviews the enzymological properties of two protein kinases, phosphorylase kinase and cAMP-dependent protein kinase. These enzymes are involved in the intracellular biochemical "cascade" initiated by epinephrine and other hormones that function through adenylate cyclase and cAMP. The cAMP-dependent protein kinase catalyzes the phosphorylation of many proteins in addition to phosphorylase kinase. In this chapter, the authors carefully analyze what is known about these kinases with the objective being to develop some general concepts concerning the chemical and regulatory aspects of protein phosphorylation.

This volume also contains several interesting chapters which deal with the mechanisms of enzymatic catalysis. A chapter by D. E. Metzler reviews what is known about tautomerism in pyridoxal phosphate, with the intent being to point out the magnitude of the electronic effects underlying tautomerism and to convince the reader that tautomeric effects in enzymes probably play decisive roles both in catalysis and in regulation. Another chapter by H. G. Floss and M. D. Tsai describes how chiral methyl groups can be used as stereochemical probes to study enzyme-catalyzed reactions. The chapter provides an excellent discussion of the theory, methodology, and application of using chiral methyl groups to study the stereochemistry of enzymatic reactions involving the formation, conversion, and transfer of methyl groups. In a related chapter, I. A. Rose describes how the technique of positional isotope exchange can be used to study group transfer reactions. The majority of the chapter is devoted to studies of ATP reaction mechanisms where the torisonal symmetry of the $\beta$-phosphoryl group of ADP is utilized to carry out positional isotope exchange studies. The theory, methodology, and recent applications of this very powerful technique are clearly and concisely described in this chapter.

Other chapters in this volume deal with the mechanism of mandelate racemase, the biosynthesis, regulation, and function of creatine, and the existence of nonprotein amino acids in plants.

This being the 50th volume in this series, the editor has provided a listing of the contents of the earlier volumes of "Advances in Enzymology". Inspection of this listing reveals that the series has continuously had the pioneers in biochemistry and enzymology as contributing authors. The topics reviewed are consistently of current interest to a broad group of biological scientists. This 50th volume will continue the high level of excellence achieved in the proceeding volumes.

*University of Kansas* **Ronald T. Borchardt**

**The Anticancer Drugs.** By W. B. Pratt and R. W. Ruddon. Oxford University Press, New York and Oxford. 1979. 323 pp. 16 × 23.5 cm. $18.95.

Written for scientists and clinicians in the fields of biochemistry, medicinal chemistry, molecular biology, pharmacology, toxicology, and clinical oncology, this relatively small book contains a surprisingly large amount of useful information with respect to anticancer drugs. In the opinion of this reviewer, the book can be considered as one of the best written summaries of this type during the past 2 decades.

The book contains ten chapters. The incidence of neoplastic disease (data collected only up to 1970), general characteristics of the malignant cell, and the role of drugs in cancer treatment are adequately provided in the initial chapter. Proper historical background and credits are given for the development of more important drugs in the second chapter. This is followed by a third chapter wherein tumor and host determinants, including total tumor burden and cell cycle phase, are discussed. With this background, the fourth chapter, "Choice of Drugs for Cancer

Chemotherapy" (coauthored with R. H. Wheeler), naturally comes into reality. The next few chapters consist of a detailed discussion of anticancer drugs: the alkylating agents, the antimetabolites, the antibiotics, the steroid hormones, and plant alkaloids, enzymes, and miscellaneous anticancer drugs. The last chapter is devoted to information of newer drugs and comments on new directions in cancer chemotherapy.

For each anticancer agent or every group of agents, the mechanism of action, the pharmacology and clinical application, the resistance problem, as well as the biochemical and pathophysiological basis for drug toxicity and side effects, together with many unsolved problems, are discussed (this reviewer, however, does not believe that DNA intercalation can be considered as the ultimate mechanism of action for some anticancer agents or agents possessing other clinical usefulness such as antimalaria or antischistosomiasis). For the steroid hormones, the rationale for steriod therapy and a discussion of steroid receptors are also properly provided. The reasoning behind single and combined therapeutic schedules and adjuvant therapy, in connection with cell and tumor growth kinetics, has been explained in detail. References are sufficiently up to date. In addition, the authors never fail to supply existing review literature for important anticancer drugs if readers wish to explore additional information in a certain area.

One of the outstanding features which makes the book a valuable reference is in the collection and compilation of many useful tables. These tables provide the readers with a convenient guide and comparison for certain agents or problems at a glance.

For a book of this kind not written by chemists, the chemical structures are extraordinarily clear and cleanly printed without noticeable mistakes. The structure for bleomycin (pages 179 and 182), however, has not been corrected from recent literature. Instead of a $\beta$-lactam ring connecting carbon atom 35 and nitrogen atom 36, the structure should have carbon atom 35 as part of a carboxamide group and nitrogen atom 36 as a secondary amine, and there is no linkage between atoms 35 and 36 [T. Takita, T. Muraoka, T. Nakatani, A. Fryii, Y. Umezawa, H. Naganawa, and H. Umezawa, *J. Antibiot.*, **31**, 801 (1978)]. Also, although the structures of VM-26 (NSC-122819) and VP 16-213 (NSC-141540) are shown on page 233, the structure for the parent compound, podophyllotoxin, should be included to illustrate the relationship with the aforementioned two semisynthetic derivatives. Information on many newer drugs under development has been added in the last chapter. Some derivatives, such as 1,4-dihydroxy-5,8-bis[[2-[(2-hydroxyethyl)amino]ethyl]amino]-9,10-anthracenedione (DHAQ, NSC-279836), eventually have shown clinical promise. Most compounds discussed have been developed in the United States in connection with the National Cancer Institute drug development programs. Inclusion of agents developed in other countries, as well as other agents developed in this country, such as methylglyoxal bis(guanylhydrazone) (Methyl-GAG) and interferon, could increase the value of this already valuable book even more. Interferon, which belongs to a class of glycoproteins, certainly has a promising future and would also substantiate the authors' opinion on "Some approaches to drug design" (page 290).

This concise and comprehensive book is recommended to all the scientists and clinicians who are dedicated in the field of oncology.

*University of Kansas Medical Center* **C. C. Cheng**

**Advances in Experimental Medicine. Volumes 120A and 120B. Kinins II.** Edited by S. Fujii, H. Moriya, and T. Suzuki. Plenum Press, New York and London. 1979. 17 × 25 cm. Volume A: xii + 610 pp. $59.50. Volume B: xiv + 719 pp. $69.50.

Although our knowledge of the enzymes known as kallikreins begins early in this century, the elucidation of the structure of bradykinin 20 years ago initiated the modern era of kinin research. During the past 2 decades kinins have been implicated in physiological regulation such as functional vasodilation, modulation of blood pressure, and control of vascular permeability, as well as their pathological counterparts of shock, inflammation, and pain production. The 1970's have been marked by new insights into the interrelationship of blood coagulation, fibrinolysis, and kinin formation both through experimental studies and the discovery of two new hereditary deficiencies of proteins central to kinin formation—prekallikrein and high-molecular-weight kininogen. The interaction of kinins and prostaglandins in inflammation has also been delineated.

These two volumes are the complete Proceedings of the International Symposium on Kinins held in Tokyo, Japan, November 6-9, 1978, comprising 120 papers and three special lectures. The photooffset process has allowed publication of these articles within 14 months after the meeting. This procedure has obviated the dated material which may accompany publication of symposium in printed form and has made these volumes more valuable. The chapters of Volume 120A cover the chemistry, assays, biochemical characterization, physiological, pathological, and clinical significance of kinins. The role of kallikrein and kininogen in plasma proteolysis, kallikrein inhibitory therapy, and the regulation of blood pressure and salt metabolism are presented in Volume 120B. The papers, except for the plenary lectures, are mostly specialized contributions. Like most volumes of this kind, no critical review is attempted, and thus the contributions tend to be very uneven. Some present new data, while others summarize published papers of the authors. The reports vary from 4 to 22 pages and are sometimes too brief to be of value. Unfortunately, the provocative discussions that characterized the symposium are not presented.

These volumes will be useful as a reference to investigators in the field who did not attend the symposium or wish to consider the data presented in an unhurried fashion. Judging by previous experience, the book will have a useful life of about 2 years, during which time most of the worthwhile data will be published in more critically reviewed journals. These volumes cannot be recommended to other scientists seeking a perspective of this rapidly advancing field but serve admirably to indicate the breadth of kinin research.

*Temple University Health Sciences Center* **Robert W. Colman**

**Modern Size-Exclusion Liquid Chromatography. Practice of Gel Permeation and Gel Filtration Chromatography.** Edited by W. W. Yau, J. J. Kirkland, and D. D. Bly. Wiley, New York, Chichester, Brisbane, and Toronto. 1979. xv + 476 pp. 16 × 23.5 cm. $24.95.

Modern or high-performance liquid chromatography was developed by applying practical and theoretical findings of gas chromatography to classical column chromatography. It is hoped that the size-exclusion processes commonly known as gel filtration and gel permeation will get a similar promotion by transferring this knowledge to that separation technique.

This book, written by experts both in modern liquid chromatography as well as in gel permeation chromatography, is the first that integrates classical gel chromatography with the high-performance technique. In every chapter the personal experience and the practical know-how of the authors with this separation method can be realized. The newcomer will especially appreciate the chapters on equipment and detectors, separation columns, operating variables, and on laboratory techniques including some remarks on trouble-shooting and on calibration. The more experienced practitioner for whom the chapters on retention, on resolution, and on band broadening are devoted will get some practical hints or new insights from these chapters. An additional chapter deals with data handling. Special techniques, such as recycling, vacancy, or prepscale exclusion chromatography, are also described. The two final chapters are devoted to the application of the method to the characterization of various kinds of synthetic polymers and to water-soluble polymers.

The book is recommended to all those dealing with any kind of chromatographic technique based on size exclusion and to speed up separations. It is hoped that in the future a variety of stationary phases for modern or high-speed size-exclusion chromatography may also become available for the separation of naturally occurring water-soluble polymers.

*University of Saarland* **H. Engelhardt**

**Clinical Neuropharmacology. Volume 4.** Edited by H. L. Klawans. Raven Press, New York. 1979. x + 228 pp. 16 × 23.5 cm. $22.50.

This is the fourth in a series of volumes on clinical neuropharmacology. Like the three previous volumes, it is a compilation of diverse topics on neurological disease, with emphasis on biochemical mechanisms and pharmacological intervention. The authors are generally well known, and the chapters are lucidly written. Although the "major focus" of the volume is purportedly on the pharmacology of epilepsy, the subject is basically limited to the first two of the ten chapters.

The available data on nonepileptic uses of antiepileptic drugs are most cohesively presented. The review of the effect of carbamazepine on mania is especially good, as are discussions of the use of phenytoin in myotonia, diazepam in stiff-man syndrome, and acetazolamide for periodic paralysis. Clonazepam is mentioned in the treatment of myoclonus. Since we do not understand the mechanisms by which antiepileptic drugs act against seizures, it is useful to be cognizant of the effects of these compounds in other conditions. As we learn more about their actions and uses in epileptic and nonepileptic conditions, perhaps a convergence of our understanding of these drugs will occur. This volume emphasizes the likelihood of such convergence and contributes to our clinical understanding of the uses of these drugs.

*National Institute of Neurological and Communicative Disorders and Stroke* **Roger J. Porter**

**Plants of the Gods.** By Richard Evans Schultes and Albert Hofmann. McGraw-Hill, New York, St. Louis, and San Francisco. 1979. 192 pp. 20 × 27 cm. $34.95.

Much has been and will continue to be written by the folklorists, the anthropologists, and the ethnobotanists in an effort to jog the medicinal chemists and the pharmacologists into a serious consideration of the medicinal value, if any other than as an aid in psychotherapy, of the broad class of compounds we call the hallucinogens. This book summarizes our present knowledge of the origins and traditional uses in the religious rites and shamanistic practices of many peoples, primitive or otherwise, to whom these substances or at least the plants containing them are sacred. And not without reason, for while we in our sophistication may recognize that the round-trip ticket to Elysium lies in the powerful CNS effects of these drugs, the mechanism of the conveyance eludes us still.

Fourteen of the old standbys are discussed here in considerable detail: opium, cannabis, mandrake, the nightshades, the cacti, and the mushrooms. There are, however, about 80 other lesser known plants to which the epithet "hallucinogen" might be applied based on suspected or reported use. The attention of the chemist and the pharmacologist might be directed to at least some of these, though the notion that a drug, e.g., *Lycoperdon*, will allow the partaker to approach others without detection is difficult to accept. As might be expected, several of the plants have reported medicinal uses beyond their mind-altering properties.

The book is intended for the general reader. Nonetheless, botanical descriptions (at times rather technical), notions of chemical structure, and a brief introduction to the biochemistry of the brain are included. It is lavishly illustrated, and the few typographical errors in no way detract from a highly readable account of one of the time-honored methods man has used in the search for his gods.

*Northeastern University* **Robert F. Raffauf**

**Progress in Drug Research. Volume 23.** Edited by Ernst Jucker. Birkhäuser, Boston, Basel, and Stuttgart. 1979. 320 pp. 17 × 24.5 cm. $78.00.

Volume 23 includes six contributions, as well as the index for Volumes 16–23. The key-word index, and the Author Index for Volumes 1–23, like those of Volumes 11 and 15, provides the reader with a simple cross-reference to all fields of possible interest to drug researchers. The present volume, as well as its predecessor, has broken the tradition of 500–600 page volumes in the hope that more rapid publication of individual volumes will better meet the needs and wishes of readers. Unfortunately, this very desirable goal has not been met in this volume. Criticism could be directed to the Editor of this series by printing a talk by L. H. Sarett presented before the Society for Drug Research Symposium in April 1977 without including the illustrations or references as part of this lecture. The editor in this instance has fallen short of providing current information useful to the reader of these volumes. The 233 pages of text treat the following topics: "Some Useful Problems with Vaccines" (N. N. Preston); "Adverse Reactions of Sugar Polymers in Animals and Man" (G. B. West); "The Impact of Natural Product Research on Drug Discovery" (L. H. Sarett); "On the Relation Between Chemical Structure and Function in Certain Promoters and Antitumor Agents" (J. R. Smythies); "Lipophilicity and Drug Activity" (H. Kubinyi); "Quantitative Structure–Activity Relationships" (Saxena and Ram). The last two articles, which comprise 126 pages, particularly meet the objectives of this series in that the topics reviewed provide the reader with a useful and current orientation in this rapidly developing field.

**Staff**

**Trace Metals in Health and Disease.** Edited by N. Kharasch. Raven Press, New York. 1979. xix + 315 pp. 16 × 24 cm. $29.50.

Dedicated to Dr. Klaus Schwartz, this volume contains the proceedings of the 12th annual Intra-Science Research Foundation Symposium (held in Nov 1978, in Santa Monica, Calif.) concerning new roles of metals in biochemistry, the environment, and clinical studies. Approximately half of the 20 papers bear on the role of metals in carcinogenesis with special attention given to the possibility of metal-induced mutagenesis in the initiation of cancer.

The lead article summarizes the toxic effects of chromium (introduced as chromate) on soil bacteria and points out that the metal is chemically modified by the bacteria. The second entry by J. B. Nielands succinctly reviews the importance of bacterial siderophores and their potential uses in medicine. A group from the Freshwater Biological Institute cogently presents the known mechanisms for methylation of metal ions by cobalamins. The next two articles deal with mammalian cell culture models for screening metal compounds for carcinogenicity and toxicity.

The problems associated with the valid evaluation of metals as carcinogens are considered by A. Furst. G. L. Fisher reviews trace elements as antagonists or synergists of both metal and organic chemical carcinogenesis together with carcinogenesis-linked alterations in trace element levels. Possible mechanisms for the initiation of cancers by metal ions are discussed by C. P. Flessel with particular emphasis on chromates, for which there is substantial epidemiological and biochemical data. This is followed by a concise review of metal ion interactions with nucleic acids and a discussion of potential modes of metal-induced genetic miscoding. Michael Beer surveys methods for heavy-metal labeling of specific sites on nucleic acids and proteins as an aid to structure determination by electron microscopy in light of recent developments in scanning electron microscopy.

Two papers are devoted to the role of zinc in cell and body development. A series of four papers discuss calcium metabolism with regard to regulation by vitamin D and the mechanism of pharmaceuticals which are calcium antagonists.

The final series of articles focuses on Dr. Schwartz's pioneering work on selenium, the functioning of glutathione peroxidase, and possible modes of cancer protection conferred by antioxidant systems.

In general, the entries are well-written, critical, and concise. The set of articles dealing with metals and carcinogenesis provides an excellent starting point for those considering research in this area. However, the inclusion of the five papers on the metabolism of calcium (which can hardly be considered to be a trace element) somewhat disperses the focus of the volume. A final minor, but troubling, criticism is the tendency to refer to carcinogenic properties by element rather than by element and oxidation state. Since only a few compounds of a particular element are normally carcinogenic, at least the oxidation state of the element should always be stated so as not be be misleading.

The book is cleanly presented with sharp printing on quality paper. The editor is to be congratulated for compiling a valuable reference text which broadly surveys an emerging and important field at a price which is less than exorbitant.

*Boston College* **Michael J. Clarke**

**Biological/Biomedical Applications of Liquid Chromatography. II. Chromatography Science Series. Volume 12.** Edited by Gerald L. Hawk. Marcel Dekker, New York. 1979. xiv + 504 pp. 15.5 × 23.5 cm. $45.00.

This book consists of a selected group of papers contributed to the second Liquid Chromatography Symposium sponsored by Waters Associates in Fall, 1978. Essentially, it is a continuation of Volume 1 which was reviewed in November, 1979, and many of the comments directed toward Volume 1 also apply to this one. As denoted by the title, the 24 presentations are all of a practical nature, in many cases almost to the point of "how to do it". The work addresses several areas of biomedical research, including proteins and smaller fragments derived therefrom, carbohydrates, lipids, and other naturally occurring substances such as purines, pyrimidines, steroids, neurotransmitters and their metabolites, enzymes, and vitamins. There is also limited coverage of some drugs and their metabolites. Overall, the book has a distinctly clinical flavor, with 13 of the articles clinically based and several others having obvious clinical extendability. This book is quite useful when one needs to analyze a class of compounds addressed by one of the chapters, but a potential drawback is that some of the material may be outdated, depending on the specific chapter and application. The ideas and experiences presented will soon be approaching 2 years of age, and some applications have improved dramatically during this interval.

With the potential obsolescence of parts of the book in mind, one can say that it is a well-written, well-edited, practical book covering a variety of clinical high-performance LC applications. It will provide a ready reference to selected methods and approaches, as well as a basis for searching the more recent literature on a given topic. While the work itself is worthy of inclusion in the libraries of those concerned with biomedical high-performance LC applications, the publisher has made its distribution more difficult by pricing it at an unreasonable level. At a cost of over 11 cents a page for photooffset, camera-ready copy, one has to weigh its value most carefully.

*University of Connecticut* **James G. Henkel**

**Submolecular Biology and Cancer. Ciba Foundation Symposium. Number 67 (New Series).** Edited by G. E. W. Wolstenholme, D. W. Fitzsimons, and Julie Whelan. Excerpta Medica, Amsterdam, Oxford, New York. 1979. ix + 349 pp. 17 × 24.5 cm. $42.50.

A 3-day symposium with this title was held in September 1978 at the Ciba Foundation in London, in honor of Albert Szent-Györgyi on the occasion of his 85th birthday. Twenty-five investigators, mostly from the British Isles and the United States, are listed as participants; 17 of them presented formal papers, usually followed by a more or less extensive floor discussion recorded in these pages.

After brief introductory remarks by the conference chairman, R. J. P. Williams of Oxford University, the elements of the bioelectronic concept of the living state—charge transfer and permittivity, the central role of methylglyoxal, the $\alpha \leftrightarrow \beta$ transformation, and the function of ascorbic acid—are succinctly stated by Szent-Györgyi. In a further lecture designed to set the stage for the symposium, a general discussion of the nature of cancer is presented by S. Reslova-Vasilukova and Williams.

There follow papers on energy bands and charge transfer in proteins (K. Laki and associates); solid-state aspects of the electronic structure of proteins and DNA (J. J. Ladik); the mechanisms of conduction in proteins (T. J. Lewis); electronic and dielectric properties of protein–methylglyoxal complexes (S. Bone and R. Pethig); free radicals in cancer (H. M. Swartz); whole-body nuclear magnetic resonance scanning as applied to tumor cells (R. Damadian and collaborators); quantum chemical investigations of charge-transfer interactions in relation to the electronic theory of cancer (C. Thomson and J. R. Ball); search for new cancerostatic agents related to methylglyoxal (G. Fodor and co-workers); thermal copoly(amino acids) as inhibitors of glyoxalase I (S. W. Fox and associates); interactions of methylglyoxal with methylamine (S. F. Abdulnur); methylglyoxal production in human blood (R. B. Brandt and S. A. Siegel); formation and properties of reactive aldehydes such as 4-hydroxyalkenals (E. Schauenstein and H. Esterbauer); biological activity of methylglyoxal and related aldehydes (M. U. Dianzani); carcinostatic activity of methylglyoxal and related substances in tumor-bearing mice (P. J. Conroy); and biochemical studies of transient intermediates in relation to chemical carcinogenesis (T. F. Slater).

As these titles suggest, the presentations range from the general to the detailed, from the theoretical to the applied, from physical chemistry to biology. Each paper is preceded by a useful abstract and includes a list of cited references. Figures and tables abound throughout the volume, ranging from NMR or ESR spectra to detailed protocols of mean tumor weights in treated animals. The book is well edited, adequately indexed, and handsomely produced.

To this reviewer, the volume exhibits both the strengths and weaknesses of the published record of this kind of gathering by invitation. The participants are well acquainted, as shown by the frequent citations of each others publications and the tenor of the floor discussion, and are joined by a common interest in and general acceptance of the formulations and experimental findings on which the bioelectronic theory of cancer is based. For the noninitiate, however, who looks to this book to provide a systematic introduction to and critical evaluation of the theory and its supporting evidence, a more cohesive and integrated presentation would have been more helpful and instructive.

*CMDNJ-New Jersey Medical School* **Erich Hirschberg**

**The Chemistry of Heterocyclic Compounds. Volume 34. Thiazole and Its Derivatives. Part 3.** Edited by Jacques V. Metzger. Wiley-Interscience, New York. 1979. xii + 407 pp. 16 × 23.4 cm. $70.00.

This is the final volume of a three part set, edited by Professor J. V. Metzger of the University of Aix-Marseilles, concerned with the chemistry of the thiazole ring system. Included therein is a cumulative author index which constitutes over 30% of the monograph. The balance consists of Chapter 8, devoted to a discussion of mesoionic thiazoles (by M. Begtrup and C. Roussel); Chapter 9 (by H. Larivé and R. Dennilauler), which gives the chemistry of cyanine dyes derived from thiazolium salts; and Chapter 10 (by R. Guglielmetti), which reviews selenazole and its derivatives. As is the case with most chapters in this set of monographs, the textual matter is supplemented with tables listing fairly comprehensively the physical properties of pertinent compounds and references to their synthesis.

The chapter on mesoionic thiazoles appears to be the first review on this subject. It is brief (22 pp.), well written, and informative. The discussion of cyanine dyes stresses their synthesis, spectroscopic properties, and theories which attempt to correlate structure with color. The chapter on selenazole and its derivatives is an amplification of Bulka's two earlier works on the subject. (The author mistakenly attributes the authorship of Bulka's later review to the co-editors of the monograph in which it appears.) Guglielmetti's chapter is well organized and covers the literature until 1976. It alludes to the special problems of dealing with selenium-containing starting materials. Not surprisingly, one concludes that that chemistry of selenazole is very similar to that of thiazole and even more challenging. Guglielmetti states that "... selenamides are more instable than thioamides; so $P_2Se_5$ was replaced with $Al_2Se_3$. In that case the cycle is less broken but the yield of the reaction is not as good." To my knowledge, $Al_2Se_3$ has not been used successfully to directly affect the conversion of a carbonyl to a selenocarbonyl group. As for nomenclature, the author uses superfluous deltas and uses them inconsistently as in "2-amino-$\Delta_2$-selenazoline", "... 4-phenyl-$\Delta$4-selenazoline", or "2-methyl-$\Delta$-2-selenazoline".

Once again I must chide the copy editor for not aiding the French authors by his allowing such terms as "obtention",

"composant", "methode", and "alcoxyalcene" to remain in the text. Inattention to details is also responsible for such lapses as the three consecutive listings in the subject index for "2-(2-thienyl)selenazole". A check of the unlikely listing in the author index, "Maatschappij, B. V." (meaning "company, incorporated" in Dutch) revealed that the reference was to a patent issued to Shell Internationale Research Maatschappij B.V. Under the letter "S" one finds "Sir, Robinson, R". A cumulative subject index would have been far more useful than a cumulative author index.

Despite its minor failings, the final volume in the thiazole series is a worthwhile acquisition for libraries, especially those wishing to complete the set and for chemists involved in heterocyclic chemistry.

*Walter Reed Army Institute of Research* **Daniel L. Klayman**

**Ethnopharmacologic Search for Psychoactive Drugs.** Edited by Daniel H. Efron, Bo Holmstedt, and Nathan S. Kline. Raven Press, New York. 1979. xviii + 468 pp. 15.5 × 23.5 cm. $24.00.

This volume contains the proceedings of a symposium held in San Francisco on January 28–30, 1967. Introduction, discussions, and comments are well-organized. The book contains 27 papers with usable bibliographies. Although some of the 27 chapters are difficult to follow, most are well-organized, easily understood, informative, and just plain fun to read.

This book contains much general and specific data on the natural chemistry of many plants used by man for their psychoactive constituents, for example, Kava (*Piper methysticum*), nutmeg (*Myristica fragrans*), and Fly Agaric (*Amanita muscaria*). Many articles have excellent photos (black and white) illustrating methods, effects, geographical distribution, and artifacts from previous and present cultures. Articles on South American snuffs make excellent use of these methods. These articles alone are well worth the price of the book.

In general, this book is a must for anyone interested in naturally occurring psychoactive drugs. The book could be used as the basic text for a course in ethnopharmacology. The extensive indexing gives good coverage of the contents and thus eliminates the arduous task of trying to ascertain all esoteric possibilities. This reviewer recommends this book highly. The greatest weakness is—the book ends!

*University of Mississippi* **Carlton E. Turner**

**Books of Interest**

**Behavioral Analysis and Treatment of Substance Abuse. Research Monograph Series. No. 25.** National Institute on Drug Abuse, Department of Health, Education, and Welfare. 1979. viii + 256 pp. 15 × 23 cm. $5.00.

**The Behavioral Aspects of Smoking. Research Monograph Series. No. 26.** National Institute on Drug Abuse, Department of Health, Education, and Welfare. 1979. vii + 192 pp. 15 × 23 cm. $5.00.

**The Pendulum and the Toxic Cloud (The Course of Dioxin Contamination).** By Thomas Whiteside. Yale University Press, New Haven, Conn. 1979. 205 pp. 13 × 23 cm. $4.95 (paper); $15.00 (cloth).

**Current Developments in Psychopharmacology. Volume 5.** By W. B. Essman and L. Valzelli. SP Medical & Scientific Books (a division of Spectrum Publications, Inc.), Jamaica, N.Y. 1979. 491 pp. 23 × 16 cm. $50.00.

**Antiviral Agents and Viral Diseases of Man.** By George J. Galasso, Thomas C. Merigan, and Robert A. Buchanan. Raven Press, New York. 1979. xii + 719 pp. 16 × 24 cm. $49.50.

**Histamine Receptors.** By Tobias O. Yellin. SP Medical & Scientific Books. 1979. 418 pp. 16 × 23 cm. $35.00.

**Complex Carbohydrates of Nervous Tissue.** By Richard U. Margolis and Renee K. Margolis. Plenum Press, New York. 1979. xviii + 401 pp. 16 × 23 cm. $39.50.

**Claude Bernard Memorial Symposium and the International Environment.** By Eugene Debs Robin. Marcel Dekker, New York. 1979. xvi + 299 pp. 15.5 × 23.5 cm. $34.50.

**Advances in Ophthalmology. Anti-Herpes Virus Chemotherapy. Experimental and Clinical Aspects.** By K. K. Gauri. S. Karger Publishing Co., Basel, Switzerland. 1979. ix + 300 pp. 18 × 24 cm. $89.25.