number of spontaneously active dopamine neurons in both the A9 (nigrostriatal) and A10 (mesolimbic) dopamine pathways in the brain. In contrast, agents with reduced EPS liability selectively deactivated only the A10 pathway. Like haloperidol and clozapine, 1 increases the number of spontaneously active dopamine neurons on acute administration vs vehicle control (Figure 1). However, on chronic administration (Figure 2), haloperidol reduces the number of active neurons vs control in both the A9 and A10 pathways, while clozapine decreases activity selectively in the A10 pathway. Compound 1 also produces a selective decrease in the A10 dopamine neuron activity, displaying a clozapine-like profile indicative of atypical antipsychotic activity. In preliminary safety studies, 1 shows no prohibitive toxicological or cardiovascular effects.

In summary, the pharmacological profile of development candidate 1 both in vitro and in vivo suggests that this agent may prove to be an effective treatment for schizophrenia with reduced propensity for extrapyramidal side effects.[19]

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Supplementary Material Available: The procedure for the dopamine single unit electrophysiology assay (1 page). Ordering information is given on any current masthead page.

(19) Portions of this work were presented at the 202nd American Chemical Society Meeting, New York, NY, August 1991; Abstract MEDI 85.

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Book Reviews

Clinical Applications of TGF-β. Ciba Foundation Symposium 157. Edited by Gregory R. Bock and Joan Marsh. John Wiley & Sons, Chichester, U.K. 1991. x + 254 pp. 15.5 × 23.5 cm. ISBN 0-471-92811-9. $69.50.

This volume is a collection of presentations and discussions deriving from a Ciba Foundation Symposium on the clinical applications of TGF-β held in London on June 12–14, 1990. The symposium focused on the clinical applications of transforming growth factor-β (TGF-β) in the control of cell differentiation and proliferation with special emphasis on the unique role of this group of peptides in the formation, remodeling, and destruction of the extracellular matrix. Particular attention is directed to the role of TGF-β in the pathogenesis of disease and as a mediator of inflammation and the repair of tissue injury. The important implications of the use of TGF-β or its antagonists in human therapeutics are stressed.

Topics addressed include the multiple forms of TGF-β; TGF-β receptors; mechanisms in TGF-β action; regulation of epithelial proliferation by TGF-β; molecular structure and mechanisms of action of latent forms of TGF-β; the role of TGF-β in the nervous system; the possible role of TGF-β in autocrine immune regulation and in wound healing; a stimulatory effect of TGF-β in tumor development; and the effects of TGF-β on bone, cardiac muscle cells, cell proliferation, fibrogenesis, glomerulonephritis, pulmonary fibrosis, normal and neoplastic hemopoiesis, and glioblastoma.

The book contains an adequate author and subject index. The volume should provide the reader with abundant evidence, obtained from molecular, cellular, and in vivo studies, to support the prediction of important clinical applications of TGF-β in medicine and surgery in years to come.

Staff

Drugs in Gastroenterology. Edited by P. C. Braga, M. Guslandi, and A. Titabello. Raven Press, New York. 1991. xi + 533 pp. 16 × 24 cm. ISBN 088167-864-3. $60.00.

This book reviews the pharmacology of various experimental and marketed drugs used to treat disorders of the gastrointestinal tract. The text is unique in that it brings under one cover a detailed compilation of both animal and clinical studies. Its intended purpose is to provide an information link between academic, pharmaceutical, and clinical scientists in the area of drug development for digestive disease.

The book is divided into 18 chapters primarily on the basis of pathophysiology. Chapters 1 and 2 review agents that are involved in the treatment of upper gastrointestinal disorders. Prokinetic drugs such as metoclopromide and cisapride are covered here. Chapters 3–6 deal with antiulcer and gastroprotective medications. A number of the top selling histamine(H_2)-receptor antagonists (e.g. cimetidine and ranitidine) are extensively reviewed in Chapter 4. In Chapter 7, the cytoprotective actions of misoprostol (a prostaglandin E_1 analog) against gastroduodenal lesions induced by nonsteroidal antiinflammatory drugs are examined. The remaining chapters review agents used to treat a variety of ailments including diarrhea (Octreotide), irritable bowel syndrome (hyoscine-N-butyl-bromide, cimetropium bromide), and inflammatory bowel disease (5-aminosalicyclic acid). Over 30 drugs in all are discussed.

Each chapter is dissected into several concise drug reviews. The general pharmacology of each drug is organized as follows: introduction, chemistry, animal studies (pharmacology, pharmacokinetics, metabolism), clinical studies, and safety. Tables are frequently used to summarize the literature of each compound and serve as a good reference source for dose selection. References as late as 1990 are noted, although some chapters appear more timely than others. An adequate subject index is included. One drawback of this text is that it contains numerous typographical, grammatical, and technical errors. Another limitation is that few of the authors appear to have been intimately involved with the research.

Overall, the book is a valuable source of information for those engaged in the study of gastrointestinal drugs. It is best suited for industrial and academic libraries as a reference book.

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Ring Enlargement in Organic Chemistry. By Manfred Hesse. VCH Verlagsgeselshaft mbH, Weinheim (Germany) and VCH Publishers, Inc., New York, NY. 1991. xi + 235 pp. 18 × 24.5 cm. ISBN 3-527-28182-7 (Weinheim), ISBN 0-89573-991-7 (New York). $85.00.

The ring enlargement reaction is a challenging concept in a complex field. Yet chemists who master the theory and the

practice are masterfully armed to contribute creatively to organic chemistry and also well-girded against fateful blunders where seemingly straightforward transformations lead to unexpectedly complicated changes. For ring enlargement chemistry seems to embody much of the essence of understanding organic chemistry and is without close analogy outside of organic chemistry. We are therefore greatly indebted to Manfred Hesse for his book *Ring Enlargement in Organic Chemistry*. His work is a "concept book" where the reader is presented with the carefully digested heart of each ring enlargement concept, mechanistically well-founded but also reaching back to the classic origins (including name-reaction references) of the understanding of the reaction. While brief (the book is 235 pages), nevertheless depth is maintained by masterful inclusion of discussion of retrograde chemistry and non ring enlargement chemistry where this is critical to the overall picture. The bias of the book is toward natural products, where much of the understanding and use of ring enlargement chemistry had its genesis. Missing is significant reference to commercially important ring enlargement chemistry. Medicinal chemists will be disappointed that, for example, the rearrangement reaction leading to the antianxiety agent Librium is not included. The book is well-organized, proceeding from the more easily understood one-atom phases of the concept to the more complex and far-reaching ones. The numerous schemes are easily viewed and stereochemistry is carefully shown. Hesse's writing is succinct and clear. Two indices, compound and subject, are included, the compound index utilizing an instructive arrow notation. Careful proofreading has produced a nearly error-free work. Diligent literature reading has provided a limited but up-to-date selection of references; many are from 1989. Manfred Hesse confesses in the preface that this work is a labor of love. Readers will appreciate the depth of his emotion and congratulate themselves on their selection and investment of their time in the study of it.

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The Status of Differentiation Therapy of Cancer. Edited by S. Waxman, G. B. Rossi, and F. Takaku. Serono Symposia Publications, Raven Press, New York. 1991. xx + 451 pp. 16 × 24 cm. ISBN 0-88167-792-2. $135.00.

Most anticancer drugs exert antitumor activity by inhibiting the cellular processes required for cell proliferation. Such drugs lack selectivity, however, and affect neoplastic cells as well as rapidly proliferating normal cells. A relatively new and potentially selective means of cancer treatment involves the use of agents which bring about differentiation of the neoplastic cells. This volume, which is the 82nd in a series of Serono Symposia Publications, describes the proceeding of the fourth conference on the important and growing field of differentiation therapy held in Japan on November 4–9, 1990. The conference was dedicated to Professor Fumimaro Takaku on the occasion of his retirement from the University of Tokyo.

The 50 papers presented in this volume are organized under the following topics: regulatory mechanisms for growth and differentiation in normal and malignantly-transformed cells, gene expression as targets for differentiation therapy, growth and differentiation factors as targets for tumor suppression, membrane events regulating differentiation and terminal cell division, biological modification as an approach to differentiation therapy design, normal and abnormal retinoic acid metabolism in growth and differentiation, mechanisms of action and novel differentiation inducers, the incorporation of differentiation therapy into combination cancer treatment programs, and clinical trials of differentiation therapy. The individuals papers average approximately eight pages in length (camera-ready as submitted by the authors) and are for the most part well-written. Many of these papers had not appeared in refereed journals at the time of the conference. Literature citations are generally from the late 1980s and 1990. Thus, the reader is assured of literature coverage in the field up to 1990. An edition dealing with the preceedings of the fifth conference on differentiation therapy is expected to appear in 1993.

Should a medicinal chemist purchase this volume? There is little to be found therein in the way of traditional medicinal chemistry, such as the elucidation of structure–activity relationships with hundreds of analogues. The papers tend to have clinical and molecular biological themes. Nevertheless, the volume has much of interest to the medicinal chemist devoted to cancer research. An example is the induced differentiation by polar/apolar compounds such as hexamethylenebisacetamide (HMBA), a drug which induced a clinical cure in a patient with metastatic non-small cell adenocarcinoma of the lung (from Marks, Richon, and Rifkind, pp 295–303). Medicinal chemists interested in the area of differentiation therapy should definitely purchase this book. Others, who cannot afford the $135 price tag and have a superficial interest in the topic, should ask their institution's library to order the volume.

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