

Book reviews

Progress in Medicinal Chemistry, Vol. 31

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Elsevier, Amsterdam, London, New York, etc.
Available from Elsevier, Amsterdam; in USA/
Canada, from Elsevier Science Inc., P.O. 945,
Madison Square Station, New York, NY 10160-
0757. 1994, viii + 465 pages ISBN: 0-444 –
81807-3 Dfl 375. US\$214.25

This latest issue of a long-running series presents reviews covering important advances in the chemistry and biology of a broad spectrum of medicinal topics. Seven of the nine reviews are contributed by industrial scientists; the other two by experienced academics.

The first, a review on 'New Hypoglycaemic Agents' (B. Hulin, Pfizer Central Research, USA), deals with the emergence of new insulin variants and some new hypoglycaemic drugs and their role in the treatment of diabetes mellitus. After a long period of stagnation, new molecules for the treatment of non-insulin dependent diabetes are starting to emerge; they have new molecular modes of action which differ from those of the established sulphonylureas and biguanides.

The second review on 'Inhibitors of Human Leukocyte Elastase' (P.R. Bernstein, P.D. Edwards and J.C. Williams, ZENECA Pharmaceuticals, USA) discusses selective inhibitors of the degrading effect of human leukocyte elastase (HLE) on elastin. The promiscuous nature of HLE and the variety of biological activities expressed by it has led to the hypothesis that an imbalance in the delicate equilibrium between

HLE and its endogenous inhibitors may result in, or exacerbate, cystic fibrosis, chronic bronchitis and several other pathological states. Selective suppression of these undesirable characteristics may provide valuable therapy. The focus of the review is on compounds which have been evaluated both in vitro and in vivo and which have been considered as potential clinical candidates.

The azido group has, in recent years, become a feature of several drugs (including AZT) which are showing considerable clinical potential. The medicinal chemical significance of this function group is reviewed in the third chapter (R.J. Griffin, Department of Chemistry, University of Newcastle, UK).

Gastric H^+/K^+ -ATPase (gastric proton pump) inhibitors are the subject of the fourth review (A.W. Herling and K. Weidmann, Hoechst AG, Germany). Reversible and irreversible inhibitors provide an alternative and, it is believed, superior treatment to the H_2 -receptor antagonists for gastric and duodenal ulcers.

The fifth review, 'Semi-Synthetic Derivatives of 16-Membered Macrolide Antibiotics' (H.A. Kirst, Eli Lilly, USA), complements a survey of semi-synthetic erythromycins which appeared in the preceding volume of this series. The present review relates how new antibiotics of greater efficiency and a lower level of side effects are likely to emerge. Research with a similar therapeutic goal is discussed in the sixth review: ' β -Lactamases: Targets for Drug Design' (S. Coulton and I. Francois, SmithKline Beecham Pharmaceuticals, UK). β -lactamases severely limit the efficacy of some β -lactam antibiotics and the dis-

covery of inhibitors of these enzymes has restored the usefulness of several penicillins.

The 'Antimicrobial Activity and Actions of Silver' are reviewed in the seventh chapter by two academics (A.D. Russel, Welsh School of Pharmacy, and W.B.Hugo, Nottingham) who have lengthy experience in antimicrobial research. They trace the pedigree, describe their uses, and discuss in depth the mechanisms of action and bacterial resistance against the silver compounds that have been introduced into antimicrobial therapy.

'Inhibition of the Pharmacological Effects of Endothelin' is the title of the eighth review (C. Wilson and R.B. Hargreaves, ZENECA Pharmaceuticals, UK). This amino-acid peptide is one of the most potent vasoconstrictors known and its effect on the vasculature are characterised by an unusually long duration of action. It is also a potent cellular mitogen and a constrictor of non-vascular smooth muscle. Other effects are on the airways, the gastrointestinal tract, the kidneys and the central nervous system. With such profound biological actions, it is not surprising that, as this review relates, a vast amount of research has been aimed at establishing its physiological or pathological role and inhibiting its actions.

Finally, a review on 'Potassium Channel Activators; Pharmacological Methods, Models and Structure-Activity Relationships' (J.M. Evans and S.G. Taylor, SmithKline Beecham Pharmaceuticals, UK) describes the significance and therapeutic potential of this relatively new type of pharmacological agent.

As with the previous editions of this series, the present volume presents an up-to-date, state of the art account of important topics currently being researched. Each review has a comprehensive reference list and it will obviously be of interest to medicinal and pharmaceutical chemists and also to others, like myself, who like to keep abreast of what is going on in medicinal chemistry. The book is very well presented by its two editors and the only criticism that I have is the price, which I think is excessive and will undoubtedly restrict its sales.

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SSDI 0378-5173(95)04266-D

Validation Compliance Annual, 1995

International Validation Forum, Inc., Marcel Dekker, New York, 1995, ISBN: 0-8247-9459-1, Price US\$195.00.; 1120 pages.

This weighty annual is essentially a compendium of government regulations relating to the manufacture of pharmaceuticals, medical devices and similar regulated manufacturing activities. On reading the book, 'government' clearly refers to the United States and, in particular, its statutory authorities, the Food and Drug Administration (FDA) and the Environmental Protection Agency (EPA). Indeed, much of the book consists of a reproduction of general regulations issued by the FDA and EPA, together with those regulations promulgated by the European Union (EU) in respect of pharmaceuticals and medical devices manufacturing. In addition, the entire FDA regulatory framework relating to inspections of drugs, biologics and devices manufacturing is also reproduced in the context of setting validation within the overall GMP framework. The regulatory documentation is published with a relatively small amount of comment, included as an 'overview' to each relevant chapter. There is also an extensive section summarising recent FDA adverse findings in the form of brief case histories. These are, in fact, so brief as to be of rather limited value. Perhaps of greater use is the extensive glossary of QA and related terminology.

Although 'validation' is the object of the book, the reader will find that, on closer inspection, the overall emphasis is specifically on computer systems validation, now vitally important in modern mass manufacturing of pharmaceuticals and medical devices but something of a speciality in itself. I found it confusing at times that computer sys-