Drug generalisations

Drug Actions on Cholinergic Systems. (Pharmacology Monographs.) By R. W. Brimblecombe. Pp. 227. (Macmillan: London and Basingstoke, January 1975.) £9.95.

THE first third of this book is devoted to a discussion of the action of acetylcholine like substances and their antagonists on peripheral receptors. Although it would be fatuous to deny that there must be some relationship between the chemical structures of such drugs and their pharmacological activity, it remains a secret relationship and structure-activity data have not provided the insights, perhaps over-optimistically hoped for 20 or so years ago. Some important advances, it is true, have been made, but these have been mainly in relation to the variation in the actions of different members of homologous series: at present it seems altogether too much to hope that the structures of receptors can be deduced from those of known agonists and antagonists. Unfortunately, however, it is precisely the not very convincing attempts to do just this, that the author has chosen to stress in his introductory chapters. One particular difficulty, of which the reader is not made sufficiently aware, is that in so far as agonists are concerned, biological activity is only partly related to affinity. The situation is in principle simpler with antagonists, but in practice the diversity of effective structures is discouraging.

The greater part of the book is devoted to a survey of effects which have been attributed to the actions of drugs on acetylcholine receptors in the central nervous system. Here too, I wonder if the selected literature, much of it concerned with behavioural changes which are not too well established is really worth summarising in book form. Perhaps statements like (p. 202) "... considered that it was not inconsistent with the hypothesis that nicotine stimulates the brain-stem activating system to produce behavioural arousal" cause arousal in some minds, but they are not likely to convey much to readers with a more general interest in cholinergic systems.

It is also difficult to accept that there is evidence to justify, even as a simple working hypothesis, the idea that all acetylcholine receptors in the central nervous system may be categorised as muscarinic or nicotinic, or that drug actions on behaviour may be described simply as stimulant or depressant (or of course biphasic); or (p. 194) that "nicotinic action is primarily on the brain stem and hippocampus while the muscarinic action is directly on cortical neurones".

The author is certainly well aware of the confusions and the controversies and the uncertainties of the present state of affairs. This does not, however, deter him from making rather large generalisations of the kind that are useful in elementary text-books. This seems to be a question of policy, since an extract from his general conclusions (p. 215) reads "... it would be premature at the present state of knowledge to attempt to explain the role of central cholinergic systems in anything more than the most general terms". Evidently the author does not agree that in pharmacology the particular must precede the general.

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Polypeptides

The Chemistry of Polypeptides. Edited by P. G. Katsoyannis. Pp. xiii+417. (Plenum: New York and London, 1973.) $34.20.

THIS book is a collection of essays on different aspects of peptide chemistry, written by eminent scientists in honour of Leonidas Zervas. Appropriately, the opening chapter by P. G. Katsoyannis describes the life and scientific work of Leonidas Zervas, from his being awarded the degree of PhD in Chemistry at the University of Berlin, to his retirement from the Chair of Organic Chemistry at the University of Athens in 1968.

Zervas's most remembered contribution to peptide chemistry is the use of carbobenzoxy protecting groups in peptide synthesis and this epoch-making discovery is stressed in the opening paragraphs of several chapters.

J. Rudinger, in discussing the relative merits of the even older tosyl protecting group (originally described by Emil Fischer in 1915), emphasises that peptide chemists should perfect the use of each available protecting group rather than abandoning it when an apparently better one comes along. Hirschmann and Veber contribute an interesting chapter on the concept and advantages of minimal protection in peptide synthesis, including the thiol group of cysteine. Bricas appropriately describes, in view of Zervas's pioneering work on the synthesis of a glycopeptide, the present state of knowledge on the structure and synthesis of peptidoglycans and an unusual and interesting inclusion in a book of this kind is written by H. Hanson, on the mechanisms of intracellular proteolysis.

This book provides an historical review of assorted aspects of peptide chemistry with an extensive bibliography, but is not designed as laboratory text.

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