Drug Toxicity

J. W. GORROD (Editor)
Taylor and Francis, London, 1979, pp. 326, £12.50

Although scientific and legislative attention has only recently been focused on the possible toxicity of our chemical environment, the world literature is now large, and is growing rapidly. Even though *Drug Toxicity* deals with 16 different aspects of the field, these represent only a selection of topics. The 16 chapters are the papers read at the Pharmaceutical Society's Easter School in 1978. Naturally, even though the individual contributors are experts in their own subjects, the approach varies greatly in each section. For me the most useful chapter was by A. R. Boobis, in which the influence of genetic factors on the side effects of drugs was discussed. This contained everything I wanted in a review article; there was relatively brief mention of early work in the field and most attention was placed on recent findings. Also the recent amplifications of some of the older work was described. I was particularly happy to find references to the work indicating the genetic contributions to agranulocytosis following chloramphenicol and phenylbutazone and also to recent progress in unusual responses to drugs due to defects in the erythrocyte glutathione system.

Another excellent contribution was by Dennis Parke on toxicological consequences of enzyme induction and inhibition. By contrast, Robin Felix presented a paper on dermatological responses to drugs which was mainly clinical, descriptive and broadly ranging. This was packed full of interest and gave some advice on the investigation of drug reactions. Yet another type of article was by C. I. Levene on 'Prospects for the therapeutic control of fibrosis'. This was on the specialized field of the effects of drugs on collagen.

The book must not be missed by anyone interested in drug action. However, one wonders what sort of superman the new breed of toxicologist must be to span so many different aspects of biological science.

R. G. SPECTOR

Burger's Medicinal Chemistry, Fourth Edition, Part II

MANFRED E. WOLFF (Editor)
John Wiley and Sons, New York, 1979, pp. 1302, £48.80

This volume covers the fields of antimicrobial chemotherapy, anti-tumour drugs, sex hormones and peptide hormones, blood clotting, prostaglandins, cyclic nucleotide analogues, immunosuppressants and lipid-lowering agents.

The book is large (1302 pages) and the approach to each drug group is systematic. There is a full and detailed account of the chemical structure of the drugs and modifications within the group. The descriptions of the actions, uses and toxicity of each substance are remarkably fully dealt with, considering the book is purported to deal with chemical aspects of medicines. Where possible the chemical basis of the mode of action is discussed. This is usually also covered in detail, and I have read no other text to rival the wealth of original references in this field. Structure–activity relationships are discussed, and there is usually a separate section on relationships between physicochemical properties of drug groups and their chemotherapeutic activity. Some of the pharmacokinetic properties of the drugs described are also summarized.

The sections concerned with the peptide hormones are particularly well written and are spiced throughout with the biological importance of the structures discussed. In this chapter are excellent summaries of the endogenous opioid agonists and of the hypothalamic hormones.

Each chapter is written by specialists in their respective fields, but the style of presentation is pleasingly uniform.

This is an important book and deserves its place as a standard reference work in medicinal chemistry.

R. G. SPECTOR

Dielectric and Electronic Properties of Biological Materials

R. PETHIG
John Wiley and Sons, Chichester, 1979, pp. 376, £15

The measurement of dielectric properties of molecules achieved respectability with Peter Debye, and it was soon after the publication of his book (1929) that the first reliable measurements were made of dielectric dispersions for proteins. This biophysical work of the 1930's and 1940's was associated with workers such as Oncley and Wyman, who did much to establish the technique for recording rotational motions of whole, and parts of, molecules. Unfortunately, technical problems required the measurements to be made outside normal physiological limits (low ionic strengths) and these, when combined with theoretical difficulties in interpreting dielectric dispersions at the molecular level, made the technique fade in importance for Biophysical Chemistry. Recently, however, there has been a resurgence in interest in the method, largely because of improved techniques. This growth is reflected in the recent textbooks published on the subject; last year one came from Professor Grant and colleagues (*Dielectric behaviour of biological molecules in solution*), Oxford University Press, 1978), and now there is a text from Dr. Pethig. These two texts are fully complementary, because the present book makes no attempt to describe experimental techniques, whereas the earlier book devotes considerable space to these techniques.

Dr. Pethig has produced a very sound discussion of the molecular origin of dielectric and electronic effects, using classical and quantum mechanics to relate measurement to molecular motion. The relationships are made to look disarmingly simple through the many 'orders of magnitude' calculations given in the text. These examples give the text a readable quality which puts meat on the bones of the theory. I found the two chapters concerned with hydration of proteins and the role of water in dielectric measurements particularly interesting; I finished the book thinking that possibly it is in measuring these complex interactions between macromolecule and water that dielectric techniques will be most useful. I think it becomes clear from the complexity of the theory that dielectric measurements on macromolecules do not produce clear-cut interpretations (it is rare to obtain a single relaxation time for a protein or to calculate exact polarizabilities from the experimental records). Thus it is reassuring to find from this book that many empirical interpretations of results are possible, particularly when dealing with whole tissues or cells.

No. in Burger's Medicinal Chemistry, Part II, Wolff ed, 374,980, filed on Jul. 3, 1989 now U.S. Pat.Â rat mast cell protease II, human skin chymase, and group attached to the alkyl group, Ct-6 alkyl with an. human lung chymase. These compounds inhibit the serine proteases by reaction with the active site serine to form an acyl enzyme, which in some cases may further react with another active site nucleophile to form an additional covalent bond.