BOOK REVIEWS

Impressive inhibitors

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Nucleosides as Biological Probes. By R. J. Suhadolnik. Pp.364. (Wiley: New York and Chichester, UK, 1979.) $50, £23.

THIS book is published by Wiley-Interscience as a sequel to *Nucleoside Antibiotics* which appeared in 1970. It describes the application of naturally occurring nucleoside and nucleotide analogues as biological probes in cellular reactions. The compounds listed and considered inhibit between them an impressive range of events including cell wall synthesis, protein synthesis, DNA and RNA synthesis, purine and pyrimidine interconversions, and the activities of both cyclic-AMP-phosphodiesterase and adenosine deaminase. Several of the compounds are of medical importance since they have limited use in the treatment of cancer and viral infections in humans.

It is of no surprise to find an old friend — puromycin — featured in the text. Many biochemists have successfully experimented with this most useful antibiotic to study the mechanism of peptide bond formation on ribosomes, the release of incomplete nascent polypeptide chains and the properties of the ribosomal binding sites for transfer RNA. What may be surprising to some, however, is the fact that there are 69 other compounds described here of which 40 or so have been discovered since the 1970 volume was published. The number of additional events inhibited has increased dramatically in line with the number of new compounds identified. Medical implications are also clearly indicated. In 1970, for example, only 5-azacytidine, of the nucleoside antibiotics, had been used to treat cancer, showing good activity against certain leukaemias and limited activity on some solid tumours, although predictably the drug frequently produces unpleasant side effects. Of the newer compounds described in the present volume, both the pyrrolopyrimidine nucleoside antibiotic tubercidin and 9-β-D-arabinofuranosyladenine (ara-A), the latter having low myelosuppressive activity in humans, have been cleared by the Federal Drugs Administration for the treatment of human basal cell carcinoma, herpes simplex keratitis and herpes simplex encephalitis. Tubercidin is also a potent anthelmintic agent, as is the pyrimidine nucleoside disaccharide analogue hikizimycin (anthelmycin).

The presentation in this book is fairly standard for each entry and usually covers discovery, production, isolation, physical properties, chemical and biological properties, structural elucidation, biosynthesis, toxicity and where known the mode(s) of action. The 'interest generation' is extremely variable. Some compounds come over as fascinating and remarkable inhibitors. Thus coformycin and 2′-deoxycoformycin inhibit adenosine deaminase, an important enzyme in purine metabolism, a deficiency of which produces an inborn error of metabolism associated with severe combined immunodeficiency disease. The role of these two compounds as immunosuppressants aids the success of tumour grafts and indicates a usefulness in organ transplantation. Other compounds, by contrast, come over as being somewhat boring but it is fair to say that in each case beauty, or lack thereof, will always be in the eye of the beholder.

All but two of the ten chapters end with a particularly valuable summary section drawing together many of the important facts in concise form. Of the two chapters lacking a summary one deals exclusively, albeit briefly, with clitidine and tells us very little of the biological properties of this pyrimidine nucleoside, although we do discover that it resides in the mushroom *Clitocybe acromelalga* and is a physiologically active substance. One presumes that little is, in fact, known about this compound. The remaining summary-less chapter deals equally briefly with the herbicidins A and B, 5′-O-glycosyl-*ribo*-nucleosides, raphanatin and 6-benzylamino-7-β-D-glucopyranosylpurine. Curiously we are told that the herbicidins show promise as weed killers but are not toxic to mice (or gardeners?).

The text is profusely illustrated not only with the chemical structures of the various compounds described but also with a large selection of diagrams and tables reproduced from original papers. I can understand the author's wish to underscore his factual writing with real experimental data but I found this aspect of the book very annoying on occasion. Certainly these entries fill out the volume but much of the original experimental data presented are, in my opinion, redundant. For example, I am prepared to accept the author's word that cordycepin (3′-deoxyadenosine) inhibits the synthesis of ribosomal RNA and if I found this observation of particular interest I should naturally read the relevant reference. I see little reason why the present text should labour the point by illustrating an experiment involving agarose gel electrophoresis of ribosomal RNA from L1210 cells treated with the inhibitor. Again, an illustration is hardly necessary to support the statement that whereas RNA polymerases isolated from either *Escherichia coli* or T3 bacteriophage are not affected by α-amanitin, the former enzyme is completely inhibited by the naturally occurring nucleotide analogue thuringiensin whereas the latter enzyme is not. There are many other such examples throughout the text.

Overall, however, this will be a useful volume for those who are interested in the subject area — although whether or not the number of such individuals represents a viable economic proposition for Wiley-Interscience, and hence for Professor Suhadolnik, is debatable. Certainly, though, the text makes the reader aware of the remarkable versatility of nucleoside and nucleotide analogues with respect to their inhibitory effects and allows for interesting speculation in the fascinating field of structure–function relationships.

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