

Book reviews

Atta-ur-Rahman (Ed.), *Studies in natural products chemistry, in: Bioactive Natural Products (Part J)*, vol. 29, Pub: Elsevier, 2003, ISBN 0-444-51510-0, p. xiii+902, Cost: EUR 410/USD 410/GBP 273.50

Once again Atta-ur-Rahman has produced another excellent volume in the now extremely well established series “Studies in Natural Products Chemistry”. This is the 29th overall volume, and the ninth volume focused on “Bioactive Natural Products”; further groups of volumes are those on “Stereoselective Synthesis”, “Structure Elucidation”, and “Structure and Chemistry”.

Volume 29 contains fifteen chapters, embracing the isolation, synthesis and biological properties of a very diverse group of natural products from a variety of terrestrial, fungal, and marine sources. The topics include the structure–activity relationships of the ecdysteroids (Dinan), cancer chemopreventive and anti-inflammatory terpenoids (Akihisa, Yasukawa and Tokuda), drimane sesquiterpenoid synthesis (Suzuki, Takao, and Tadano), the synthesis of bioactive diterpenes (Banerjee, Ng, and Laya), unexplored microbial resources (Ishibashi), *p*-terphenyls from fungi (Cali, Spatafora, and Tringali), halogen-containing antibiotics from *Streptomyces* (Dezanka and Spidek), natural bridged biaryls (Baudoin and Guéritte), lactam building blocks in alkaloid synthesis (Toyooka and Nemoto), synthesis of carbasugars (Rassu, Auzzas, Pinna, Battistini, and Curti), biosynthesis of anti-carbohydrate antibodies (Pazur), protease inhibitors from plants (Polya), screening of natural products for cyclooxygenase and lipoxygenase activities (Jia), chemistry and biology of lapachol and derivatives (Ravelo, Estévez-Braun, and Pérez-Sacau), and the chemistry and pharmacology of the genus *Dorstenia* (Ngadjui and Abegaz). Refreshingly, these contributions

are truly global in scope, reflecting the efforts of groups in 11 countries.

The well-established quality of the series is certainly maintained in this volume, and, as in previous volumes, there is an excellent fusion of chemistry, structure elucidation, synthesis and biology in the various chapters, clearly aimed at engaging a diverse audience. A very comprehensive subject index (95 pages) concludes the volume. Perhaps the only detraction is that the series now needs a collective index of previous chapter topics in each successive volume.

In summary, this is another superb volume in a highly valuable series on natural products for which Professor Atta-ur-Rahman is once again to be congratulated. Although the volume should be an important and essential asset for those libraries supporting the efforts of natural product research groups, the price is way, way beyond the budget of many libraries these days, and certainly individual scientists will not have the resources to afford such a treatise. Yet it is these researchers and students around the world who most need access to the information. The publisher should very seriously consider making individual chapters from the volumes in this series downloadable for a reasonable price in order to enhance global accessibility to important review volumes such as this.

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Zhiqiang An. *Handbook of industrial mycology, in: Mycology*, vol. 22, Marcel Dekker, New York, 2005, ISBN 0-8247-5655-X, p. 763

I highly recommend this book. The volume is one in an impressive series with the two previous concerning other aspects of fungal biotechnology. Secondary metabolism is emphasised at a time when it is being ignored foolishly

in favour of “molecular biology”. However, in vivo biological efficacy and toxicity profiling are not tackled at all in the book. It is dominated by contributors from the USA, and Europe is represented poorly. There are 8 sections with 26 chapters: “The economic importance of fungi is almost impossible to exaggerate”.

Chapter 1 addresses the history, current situation and future trends in industrial mycology with Demain as

co-author. Future developments which are envisaged are, alternative hosts, production of non-fungal proteins, engineering of biosynthetic pathways, and analysis of gene expression. The phylogeny of fungi and “fungal-like eukaryotes” is discussed next. The decision needs to be made to drop “non fungi” in general. Eighteen different therapeutic areas comprising 718 references are reported in the chapter on biological activities. It is only a matter of time before “... fungal natural products eventually return to their rightful place at the core of industrial drug discovery programs.” The Nobel Prize was awarded to cell cycle researchers which is the field considered in Chapter 4. The key role of cyclin-dependent kinases in mitosis is mentioned. It will soon be demonstrated that cell cycle regulation plays an important role in secondary metabolism (and vice versa). Chapter 5 on *Agrobacterium* wins because it deals with the fungi as much as the biology of the bacterium.

A crucial chapter for those involved with culture collections follows and provides a paradigm for innovative thinking around genetic resources. Many organisations believed that natural product screening programmes are “capable of delivering lead structures beyond the imagination of synthetic chemists”. The DNA of a mysterious cranberry endophytic fungus was introduced into *Aspergillus nidulans* (Chapter 7). The transgenic strains produced compounds not observed in the controls. Harris’ paper on structure determining is extremely valuable: If you cannot isolate the compounds then they are not much use. Only a very few projects are extant on chemotaxonomy (Stadler and Hellwig). However, the chapter is let down by some sloppy proof reading (See tables 1 and 2). “Natural products, including fungal metabolites have yielded most of the clinically useful antimicrobial agents to date.” So say Schulman and McCallum in a very informative chapter on screening. By selectively impairing fungal protein synthesis the sordarins have utility in the fight against fungal infections. However, work is required to improve activity against the real threats such as *A. fumigatus*.

The evidence for horizontal transfer of genes is fascinating (Zhang et al.). Fungal lactam genes appear 1400 million years closer than expected in evolutionary time to the bacterial ones. In carotenoid biosynthesis, a single enzyme is responsible for all sequential dehydrogenase reactions in fungi in contrast to bacteria and plants where two are involved. Even now, the Holy Grail appears to be uncovering what the roles are of secondary metabolites. It is back to basic with aflatoxin genomics in Chapter 13. The use of “metabolic pathway analysis” may yield an explanation of why cultures produce different amounts of mycotoxins although grown under identical conditions. A small chapter follows on the indole-diterpene mycotoxins – the mammalian tremogens and anti-insect compounds. Common grasses are aided in survival by endophytic fungi and these are considered in the following piece. Many of the asexual *Neotyphodium* spp.

are interspecific hybrids capable of diversifying metabolic capability via this mechanism. The nonribosomal peptide synthetases are interesting – they totally avoid the normal route for peptides (Chapter 16). The enniatin and beauvericin exhibit insecticidal activity and enniatins appear to be wilt toxins. Polyketides lovastatin and/or compactin are taken by millions of people to inhibit cholesterol biosynthesis and are considered next. Unsurprisingly the use of cloned genes has been investigated to increase production. Just how well *A. nidulans* has been studied is presented which emphasises its white-spored wA polyketide synthetase capabilities. This is perhaps the most well studied fungal PKSs. However, there are still functions to be resolved, e.g. how do they stabilize chemically active polyketomethylene intermediates?

Antifungal agents are worth 4×10^9 and growing. The pneumocandins have been approved for life threatening infections. There follows an admirable chapter on optimisation of production of these compounds from *Glarea lozoyensis*. A piece on how to improve yields of secondary metabolites states wrongly that they are produced when rapid growth is completed – some are produced during rapid growth. Mutagenesis and screening remain successful methods despite being labour intensive and time consuming. Some possible future developments are discussed. Chartaina and Sturr immediately state, “Recent investigations have clearly demonstrated that enantiomers of racemic pharmaceutical drug mixtures can present different pharmacokinetic properties”! A gentler introduction would have made a verbose chapter more accessible.

I looked forward to the metabolomic chapter as I feel this is an area with the potential to redress a genomics bias. However, I was left a little bemused. Whereas, metabolomics is the “computing of emergent properties of biological systems...from kinetic models of DNA, RNA and protein”, what about the metabolites? Surely to the central dogma of DNA \gg RNA \gg protein must be added \gg metabolites? Nevertheless the huge scope of the chapter cannot be denied. Metabolomics was addressed more directly in the following chapter on metabolic engineering. A new term (to me) of fluxomics is introduced although is it necessary? More on fungal proteomics is merited.

No effective commercial vectors are available for filamentous fungi for heterogeneous protein expression (Zhang et al.) and more work is required. The chapter on mycotoxins per se appears somewhat out of place. The book ends with secondary metabolites from biological control agents: Some of the metabolites are important pathogenicity determinants. The authors rightly state that concerns are increasing about risks from the metabolites through their use.

In general, a well produced book, although proof reading is occasionally slack. Some chapters exhibit verbiage. A quick search indicated that references do not go much

beyond 2002. The book fills gaps in recent biotechnology publications especially in relation to natural product discovery. It will be of most use to scientists established in their careers, and so-called decision makers. It is an essential addition to the set. Natural product discovery from fungi is alive and well, at least in the USA. Indeed, underscoring this fact may be one of its most valuable functions.

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