

From Natural Products to Sodium Channels

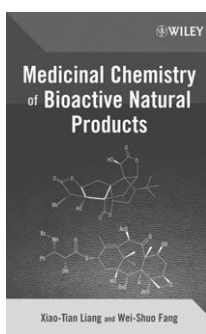
Medicinal Chemistry of Bioactive Natural Products

Edited by Xiao-Tian Liang and Wei-Shuo Fang.

Wiley InterScience, Hoboken 2006. XIX + 460 pp., hardcover \$ 90.00.—ISBN-13: 978-0-471-66007-1

Natural products are most important sources for bioactive compounds. This holds especially true today, as ten years of combinatorial synthesis coupled to high-throughput screening have not led to the expected increase in the identification of novel lead compounds. In the same time period, progress in analytical methods that facilitate the isolation and identification of low-molecular-weight compounds as well as molecular biology that enables in vivo modifications of complex natural product pathways has made natural products attractive targets for drug development. Different aspects of several natural products are currently under investigation by numerous research groups worldwide; this is expected to speed up our general understanding of natural products even more, and will hopefully lead to the development of new biologically active compounds.

As mentioned in the title, this book focuses on the medicinal chemistry of natural products. It is composed of 10 chapters; each is dedicated to one specific natural product class and was written by well-known experts in the field. The first chapter reviews a natural product success story that deals with the chemistry and biology of the anticancer agents epothilone and their role as lead struc-



tures for the discovery of microtubule inhibitors. Since their isolation from the myxobacterium *Sorangium cellulosum* in 1993 and the elucidation of their mode of action, which is similar to that of taxol, several epothilone analogues have been synthesized and tested for their biological activity. The chapter provides the current state of epothilone research, with a focus on the synthesis and modification of the natural compound by the Novartis research group, and thereby offers interesting insight into a real-life industrial project. The second chapter on the chemistry and biology of glycopeptide antibiotics such as vancomycin and teicoplanin discusses the synthesis and chemical modifications possible within this compound class. Moreover, the elucidation of the biosynthetic principles leading to these complex structures offers biotechnological methods to produce specific derivatives which are presented in detail. Furthermore, a brief chapter is dedicated to the use of these compounds as chiral selectors in chromatography and capillary electrophoresis, which opens new possibilities for natural products apart from their use as pharmaceuticals. Chapter three presents a concise review of the medicinal chemistry of taxol, one of the most important anticancer compounds currently in clinical use, with special emphasis on taxoids overcoming multidrug resistance and the concept of prodrugs.

Chapters four and five review the progress in medicinal chemistry of huperzine A, an acetylcholine esterase inhibitor with promising activity for the treatment of Alzheimer's disease, and artemisinin for malaria treatment. Both compounds have been used for several hundred years in traditional Chinese medicine and have attracted much recent interest due to their unusual biological activities.

Natural cembranoids from soft corals, reviewed in chapter six, represent the rap-

idly growing area of marine natural product chemistry, whereas the last four chapters describe the current state of research related to *Ginkgo biloba*, *Calophyllum*, coumarins, and other anti-HIV compounds from plants as well as acetogenins.

This book summarizes recent progress in a rapidly progressing field. This holds especially true for some of the compounds described, such as epothilones, taxol, artemisinins, and glycopeptides, which are still hot topics in natural product chemistry. One would expect to find the most recent results included, but a scan of the reference lists for all chapters shows no citations from 2005 or 2006.

Clearly, the book is dedicated to medicinal chemistry and it describes the current status of research of several natural product classes, some of which are generally not well known. However, highly detailed descriptions of synthetic routes for some of the compounds leads to an overrepresentation of synthetic chemistry in these chapters. In a book such as this, we would expect the different chapters to be more comprehensive. Furthermore, the influence of molecular biology and computational chemistry on natural product chemistry, as mentioned in the editorial, is hardly reflected by the book. We would have expected to read more about these areas in the chapters on epothilone, artemisinin, and taxol, where a lot of data is available (as described for the glycopeptides).

As mentioned by the editors, the primary intention in producing this book is to attract graduate students to the field of medicinal chemistry by giving examples of what can be done with various types of molecules. With respect to pure medicinal chemistry, this has been well done. However, with respect to the related fields that influence medicinal chemistry and drug development in general, a less detailed but more comprehensive perspective in some chapters might have added further value.

In summary, the title states exactly what can be expected from the book. It represents a very good overview of the different compound classes chosen. For newcomers to the medicinal chemistry of these various compounds, the book will be most valuable. For those readers that are interested in a comprehensive overview of all aspects of medicinal chemistry and drug development from natural products, it may rather be regarded as "nice to have".

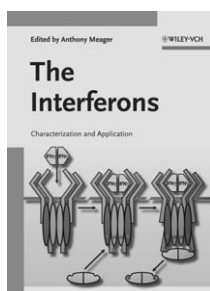
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DOI: 10.1002/cmdc.200600202

The Interferons: Characterization and Application

Edited by Anthony Meager.

Wiley-VCH, Weinheim 2006. L + 410 pp.,
hardcover € 169.00.—ISBN 3-527-31180-7

At the same time I was reading through *The Interferons: Characterization and Application* (edited by Anthony Meager) I happened to watch John Ford's movie version of *Arrowsmith*. After 80 years, Sinclair Lewis' saga still rings so very true, capturing the idealism and realities of our efforts to bring biomedical discoveries to bear on human disease. A central theme, of course, is the search for a "silver bullet". In Martin Arrowsmith's time it was the promise of bacteriophage as an agent to lyse bacteria that were actively infecting patients. When I was a graduate student, I first heard the interferons described in *Time* magazine (the cover story, no less!) in just the same magical terms. Even the name itself connoted the promise of a new silver bullet. Of course, there are no silver bullets (alas!), and indeed the interferons, although still very useful in treating multiple sclerosis,



hepatitis, and some cancers, are certainly no longer hyped that way. Nonetheless, in part because of the ability to induce the production of these clinically useful molecules (and therefore purify the interferons for clinical use) and also because of their early production as recombinant proteins, the biological functions of the interferons have been intensively studied. Thus, interferons and various associated molecules have become invaluable models for the study of a slew of biological and biochemical phenomena ranging from signaling, gene structure, transcription, and production of recombinant protein, to understanding the complexities of the immune system.

The various chapters are authored by experts in different niches of interferon biology. One shortcoming of the book is the lack of input from a number of the more prominent researchers in the interferon field. In a crowded field of top-notch researchers and given the limit to the length of a monograph, this seems inevitable. A second shortcoming of the book is the failure to integrate the color plates into the text. This seriously undercuts the utility of these well-crafted schemes, as the reader is unlikely to flip to the section of the book with the color plates (having paid for a real book, the reader deserves better treatment).

A wide array of topics are covered, ranging from the various interferon gene families, to signaling, to protein structure, physiologic function, and clinical utility. The book is an up-to-date reference critical to researchers focused on one or another aspect of interferon biology. It also offers a comprehensive introduction with a good bit of historical perspective to researchers, including graduate students, who are new to the field. Many chapters will also appeal to those investigators whose research only partly overlaps with the interferons. What does this monograph offer in comparison with our now routine perusal of Pubmed to find relevant reviews? The key advantage is that the monograph brings these various reviews together in one place. Plus, there is a consistent and comprehensive quality to the chapters, indicating a strong editor and/or a very enthusiastic group of contributors.

There are 13 chapters in the monograph. Although my comments focus on a few representative chapters, this is not meant to slight the remaining chapters. Hertzog and colleagues open the book with a thorough account of genomics of the largest family of interferons: the type I interferon gene family. The chapter by Platis and Foster provides a thorough review of the production of natural and recombinant type I IFN, a succinct and historically relevant overview of this important advance in drug development. This chapter provides wonderful perspective to the beginning graduate student. Meager's chapter on measuring interferon activities is clearly written, addressing a variety of technical issues (such as international activity standards) and contains brief methods sections for each of the leading bioassays for interferons. This is an excellent account for the investigator new to the field and who needs operational knowledge. Kotenko and Donnelly provide a timely overview of the recently discovered type III (lambda) interferons that is as comprehensive and up-to-date as anything in the available periodical literature. Pestka and Krause provide a thorough account of the many years of contributions from the Pestka laboratory that have helped to illuminate our understanding of the interferons. Fish and colleagues have written a very comprehensive appraisal of type I interferon signaling, including a thorough review of the important structural studies of the interferons and their cognate receptors as well as a detailed description of what is known about the corresponding signaling pathways. This includes not only the canonical JAK-STAT pathway, but also a number of ancillary pathways that are becoming better understood by investigators. Another brief but valuable chapter is that from Clemens and Jeffrey, detailing what we know about the apoptotic effects of the interferons.

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