

machinery – showed that glutamate and lysine residues in the LBD form a ‘charge clamp’ to allow SRC-1 to bind.

According to Colin Palmer, a ‘PPAR-ligand hunter’ at the University of Dundee, UK, ‘The binding of ligand changes the shape of the PPAR allowing SRC-1 to bind. This represents the molecular basis of how the PPAR ‘switches on’ transcription in response to drugs,’ he explains. The charge clamp is needed for SRC-1 binding and this clamp is not in the right position unless the PPAR is bound by ligand.

Increasing interest

Palmer points out that the pharmaceutical companies are investing a lot of money on PPARs, in general. With two percent of the British population currently diagnosed as having non-insulin dependent diabetes and an increasing incidence of the disease as a result of a lack of exercise and poor diet, PPAR research is likely to become more important. Now that a crystal ‘snapshot’ has been taken, there is likely to be a flurry of experiments looking for its ligands and potential new drugs for the disease, he says.

In addition, Rosenfeld says that ‘The data also imply there are flanking amino acids that must provide specificity and constitute a ‘code’ in which both receptor-specific and ligand-specific use of coactivators are likely to act.’ He points out that this may underlie the diverse biological actions of nuclear receptors and act in development, regulation, and control of proliferation in all mammalian genes.

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<http://www.camsoft.com/elemental/>

Book review

Natural Products Isolation

edited by Richard J.P. Cannell, Humana Press, 1998. \$89.50 (x + 473 pages, hardback) ISBN 0-89603-362-7

Nature exhibits unique structure-activity relationships and has a proven ability to produce diverse and novel chemical prototypes with drug potential. There is also an accelerated interest in the areas of herbal drugs and functional foods. However, in drug discovery the application of combinatorial chemistry together with high-throughput screening is an obvious challenge to research aimed at the discovery of new bioactive molecules from natural sources. The consequences may be that the need for natural products in lead generation will decrease, especially for compounds of low molecular weight.

If natural products should play a continuing important role in the discovery of potential and innovative leads in drug development and in the development of high quality herbal drugs with proven efficacy, improvements and development of new research strategies and in-depth studies are needed. The selection of organisms for improving diversity and increasing dereplication to avoid known molecules, and the development of faster and more efficient isolation procedures are thus routine chal-

lenges for a natural product scientist. Moreover, a broad knowledge and experience is needed to avoid the pitfalls in dealing with a complex biomass and to reach the objective of discovering novel bioactive molecules. It was therefore of great interest to have read the excellent and comprehensive book *Natural Products Isolation* edited by Richard J.P. Cannell, which summarizes this type of experience.

Consisting of 15 chapters written by experienced research scientists from both the pharmaceutical industry and academia, this book provides detailed descriptions of novel and classical methods for extraction and purification of natural products from a wide range of biological sources and discusses the potentials and limitations of these methods in drug discovery.

Strategic planning

The first, very useful, chapter of the book, written by the editor, explains how a research scientist should approach the isolation of a natural product and it provides a detailed understanding of how to build up a strategy for isolating a bioactive compound. This basic theory is supplemented with examples from the research literature and also with useful comments. Furthermore, the limitations and possibilities for extraction, isolation and assay procedures are summarized in

protocols based upon the experience of the authors.

Many text books on natural product research focus on isolation and structure elucidation of natural products; however, selection and collection of starting materials and extraction from such materials are usually not discussed. It is therefore of the utmost importance that several of the chapters are focused on these details and include, for example, special problems of extraction, product capture of fermentation broths and filtration procedures together with pictures showing the set-up of necessary equipment. One section that is particularly useful is devoted to supercritical fluid extraction (SFE), which is a general extraction strategy for a wide range of bioactive compounds from plant and microbial samples. This section provides the basic theory behind SFE, the equipment required and also the pros and cons of the method compared with conventional extraction procedures and applications.

Isolation of natural products

About 150 pages of the book deal with isolation of natural products using low pressure column chromatography, ion-exchange methods, HPLC, planar chromatography and high-speed counter-current chromatography. The different techniques are introduced without a

complex theory but, instead, a detailed description is given of how to use the techniques, including data for selecting the optimal conditions and experimental protocols. The examples taken from the literature showing strategy and isolation schemes with the chemical structures are very useful for preparing a research scientist for new challenges. Advantages and disadvantages using the different methods are also discussed, and in the chapter describing planar chromatography, several examples are summarized from literature showing the compound name, chemical structure and TLC conditions.

An important step in the purification procedure is the crystallization process from a concentrated solution. Experience of crystallization in the field of natural product research, especially among young scientists, is, in my opinion, very limited and it is often difficult to find information about the practical aspects of crystallization. It is therefore highly appropriate that one chapter focuses on the problems and solutions for crystallization as a final stage of purification.

To date, most natural products isolated have been lipophilic; the purification of small water-soluble molecules has been avoided by most research groups. A chapter is focused on this subject, which is very important as the ability to isolate hydrophilic compounds promises to be of greater interest in the future. The content and literature citations within this chapter,

however, could have been more comprehensive.

The special problems of isolation of bioactive compounds from marine organisms are described in one chapter, where illustrative tables present the taxonomic origin of source organisms and the types of compounds extracted from such species versus the purification methods required.

Highlights

An outstanding chapter in the book is focused on dereplication; it has been well researched and includes 92 literature references. The authors address the important problem of bioassay-interfering nonselective natural products in the isolation process and provide the methods used to localize and characterize such compounds quickly. Also, the problem of artefact formation is described, together with information on how to create a biological profile of a compound by using different types of bioassay. Moreover, the authors explain how to use the available databases in the process of dereplication and how to deal with prioritization of natural product extracts for further studies.

Another highlight of the book is the final chapter, concerning how to follow-up the isolation of a natural product and maximize chemical diversity. The authors describe different methods such as blocked biosynthesis, directed biosynthesis, combinatorial biosynthesis and biotransformation to maximize

chemical diversity based on the knowledge achieved in the isolation of the original compound. Also included in the book is information on how to scale up the isolation process of a natural product using standard laboratory equipment.

Overview

As a research aid, all chapters include literature references for further in-depth studies, however, a list of contents at the beginning of each chapter would have been useful for the reader. Another use of the book is as a handbook in the laboratory, as basic information about solvent properties, chromatographic materials, methods for assays and commercial sources is summarized in tabulated form. However, the information regarding methods for purifying water-soluble compounds, especially macromolecules, could have been expanded.

I wholeheartedly recommend this book to all academic and industry research groups as a multilevel textbook in natural product research and also as a comprehensive handbook for solving problems in daily research.

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