

## Book Reviews\*

**Plant Cell Culture Secondary Metabolism: Toward Industrial Application.** Edited by Frank Di-Cosmo (University of Toronto) and Masanaru Misawa (Bio International, Inc.). CRC Press, Boca Raton, FL, 1996. vii + 232. 17.5 × 25.5 cm. \$169.95. ISBN 0-8493-5135-9.

Overall, this book lacks a unifying structure for the wide range of subject matter covered. In addition, the article quality between chapters makes this book come up short of the goal stated; i.e., to explore industrial applications. The omission of a chapter on product recovery and purification to compliment the excellent treatment of large-scale production in Chapter 2 is made more annoying by the addition of "filler", such as Chapter 5. Nonetheless, a handful of the articles, particularly Chapters 2, 7, and 8, do provide insightful treatments of the challenges that face any group attempting to move from research to the commercial realm and provide a needed dose of realism in a field where dreamy expectations are too often crushed by economic reality.

The lack of strong connections between the chapters necessitates providing a critique on a chapter by chapter basis to address specific points. Chapter 1 is a workable review on the subject of screening plant cell cultures for industrially interesting compounds. Information in this chapter provides a good review of assay methods, compound extraction, and industrial efforts to utilize callus-derived compounds together with results with callus extracts that usually have lower levels of interesting compounds than whole plant extracts. One problem with this chapter is that it is dated by referring to killing all of the yew trees to obtain Taxl (p 3).

Chapter 2 is well laid out and sequentially explores relevant topics in an understandable manner. The presentation of each step in order (economic analysis, scale-up principles, in-depth review of biomass and product formation, and resulting process strategies) can serve as a step-by-step checklist whether a project should be considered or scrapped. The (acknowledged) omission of recovery technologies and considerations is the only weakness. This is particularly true if the consideration is for compounds targeted at the pharmaceutical market: the major costs and technical challenges traditionally start after the cells are harvested from the bioreactor.

Chapter 3 provides a number of examples where the recent advances and dropping prices in computational power and visual processing components offer promise in bringing automation (and associated labor and cost savings) to a problematic area such as culture monitoring and quality control. The crux of this and related monitoring methods, automated off-line sampling of plant cell cultures, is the aspect likely to decide the practical success or failure of these systems. A more in-depth analysis of this topic by these authors possibly

as a separate chapter would provide the reader with a more realistic assessment of whether these technologies will remain esoteric research interests or play a major role in a future plant cell culture industry.

The majority of Chapter 4 focuses on a comprehensive review of plant biotransformation literature over the past 10 years, which is good. However, there is only a small section at the end of this chapter (half a page of a 35-page article) that discusses the potential for industrial applications and neglects to consider the nascent revolution now occurring in microbial biocatalysis.

As mentioned in the general review above, Chapter 5 appears to be only a filler article. This chapter is a minimal reworking of a published article by the author and coauthor 8 years ago and adds little to this book.

Chapter 6 provides an inclusive treatment of work done in both the authors' and others' labs on the production of taxol in *Taxus* cell culture. Using a model system highlighting the difficulties faced in commercializing a plant cell culture technology for the pharmaceutical market, the Taxol story is a prime case study. This article provides detailed information on efforts to increase the productivity to commercially competitive levels and optimistically state the possibility of a future role for commercial Taxol production from plant cell culture.

Chapter 7 gives a well-rounded treatment of a feasibility study for production of anthocyanin as a commercial product from plant cell culture. The blend is scientific, technical, and commercial aspects make this study a model for the range of factors that impact commercialization of a process. The specific numbers used for the cost estimation section (such as equipment costs) are unrealistically low and the breakdown of costs has significant gaps, but readers are left with a sense of the work required outside of the technical aspects necessary to move from the bench to the factory.

As the only nation with any notable commercial plant cell culture processes, Chapter 8 gives a realistic taste of the current state-of-the-art and an industrial perspective on the future of this industry. The author, as a researcher at the company with the first commercial plant cell culture process, brings an authority to predictions of technologies and systems that will be the focus in the near-, mid-, and long-term. This chapter provides a realistic assessment of plant cell technology's place in the commercial realm.

The information presented in this Chapter 9 is primarily drawn from work done 5–15 years ago. This chapter presents a historical record of university research done in the Netherlands with secondary metabolism and plant cell cultures. The era of this work corresponded with a government initiative to promote biotechnology; in an ironic way, this author documents in this specific case the generally poor record government/university collaborations have in creating any impact in the industrial sector, particularly when

\* Unsigned book reviews are by the Book Review Editor.

contrasted with the situation in Japan outlined in the previous article.

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**Progress in the Chemistry of Organic Natural Products, Vol. 63.** Edited by W. Herz (Florida State University), G. W. Kirby (The University, Glasgow), R. E. Moore (University of Hawaii), W. Steglich (University of Munich), and Ch. Tamm (University of Basel). Springer Verlag, Vienna and New York. 1996. viii + 498 pp. 15.5 × 23 cm. \$226.00 ISBN 3-211-82702-1.

Volume 68 of this respected series consists of a single chapter entitled "Naturally Occurring Organohalogen Compounds: A Comprehensive Review" by Gordon Gribble of Dartmouth College. Why might a review dealing with naturally occurring organohalogens be of interest to a larger and broader audience than a similar review, say, on organonitrogen or organosulfur compounds produced naturally? The answer can be found in the debate concerning the future of industries based on chlorine. There is a presumption, widely held, that organohalogen, particularly organochlorine, compounds are entirely man-made and alien to the natural world. However, the variety, quantity, and biogenic origin of such compounds, well exemplified in this timely review, should serve to demolish this presumption once and for all. Gribble has critically reviewed an extensive (and ever-growing) literature up to February 1995. There appear to be few serious omissions. However, in the 12 months between manuscript submission and going to press, Gribble records that a further 120 natural organohalogens were reported. It is clear that the area is a rapidly moving one.

By far the bulk of the work is taken up with a meticulous description and classification of the 2448 fully characterized naturally occurring organohalogen compounds containing fluorine (20 compounds), chlorine (1452), bromine (1290), and iodine (80). These are of astonishing variety and complexity and are sorted into 26 subgroups, including halogen-containing alkanes, terpenes, steroids, lipid and fatty acids, polyacetylenes, prostaglandins, alkaloids, aromatics, heterocycles, amino acids/peptides, and phenolics. Among the structural units represented one may be surprised to find carbonimidic dichloride, cyclopropane, cyclobutane, oxetane, allene, enal, enediyne, *N*-oxide, and 2-chlorovinyl sulfate moieties. Some materials are extensively halogenated: one cyclopentane derivative from the fungus *Mollisia ventosa* contains 69% by weight of chlorine. The range of compound types is matched only by the variety of organisms which produce them, from marine and terrestrial plants and animals, bacteria, fungi and insects, as well as from other nonbiogenic but natural processes, such as fires and volcanic eruptions. Parsley, pea, potato, cod, halibut, and salmon all produce such

compounds. Even humans produces an organobromine compound, isolated from cerebrospinal fluid.

It has taken many years for interest in the topic to grow, stimulated, in part, Gribble claims, by the activities of those seeking to ban chlorine. In addition, there has been a resurgence of interest from pharmaceutical companies interested in the pharmacological properties particularly of marine natural products, as potential antitumour, antibacterial, antifungal, and antiviral agents. Pharmacologically active organochlorine metabolites have, of course, long been known, including griseofulvin (reported in 1935), chloramphenicol (1948), aureomycin (1948), and vancomycin (1956). Organochlorines have also been isolated from a range of Japanese and Chinese folk medicines.

Many of the studies cited represent individual triumphs of isolation, analysis, and structural elucidation, with particular difficulties associated with multiple halogenation and determination of stereochemistry. Not surprisingly, structural revisions are commonplace. Although the possibility that some chlorine-containing compounds are artefacts or metabolites of chlorinated pollutants cannot be excluded in every case (and is, in fact, proposed by some authors to explain the isolation of halogen-containing compounds), it is clear that most chlorine-containing compounds are in fact natural products. Thus in some cases the procedures for compound manipulation were designed to avoid exposure to sources of chlorine, and in others, *de novo* biosynthesis was unequivocally demonstrated by the use of isotopically labeled halogen.

It is currently impossible to estimate with any accuracy the amounts of naturally occurring organohalogens that are produced annually. Some are present only in trace amounts, though others, such as the halogenated methanes, are much more abundant, having annual natural fluxes of millions of tons. It would also seem that the capability to produce organohalogens may be modified by local conditions, since species from one locality produce materials not found from identical species found in another locality. Gribble speculates that chlorination of humic acids in soil may prove to be a source of huge quantities of organochlorines. Because of the complexity and location of these materials, their isolation and characterization will provide further challenges to the chemists' skills.

Less is known about the processes by which organisms produce organohalogens, though the haloperoxidases responsible for some biohalogenations are widely distributed. Almost nothing is known about the function of naturally produced organohalogens, though their use in defense, as antifeedants, as plant growth regulators, and as sex and aggregation pheromones has been proposed in a limited number of instances.

Gribble's review, if nothing else, should provide a stimulus for more research on the biosynthetic pathways, functions, distribution and fate of a diverse group of fascinating natural products. However, it should do far more. Bearing in mind the widespread concern regarding the impact of anthropogenic organochlorine pollutants on humans and the environment, it should also inform a wider audience that halogenated, and particularly chlorinated, compounds have long been part of the natural universe. In Gribble's words, the review should "provide important background material for

regulatory and governmental agencies worldwide to facilitate informed decisions regarding the use of halogenated chemicals". Amen to that.

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**Soybeans: Chemistry, Technology, and Utilization.** Edited by Keshun Liu (Hartz Seed). Chapman and Hall, New York. 1997. xxvi + 532 pp. 22.5 × 14.5 cm. \$89.95. ISBN 0-412-08121-0.

This book provides an overview of the use of the soybean, primarily as a food in various forms. The chapter titles are as follows: 1. Agronomic Characteristics, Production, and Marketing; 2. Chemistry and Nutritional Value of Soybean Components; 3. Biological and Compositional Changes During Soybean Maturation, Storage, and Germination; 4. Nonfermented Oriental Soyfoods; 5. Fermented Oriental Soyfoods; 6. Soybean Oil Extraction and Processing; 7. Properties and Edible Applications of Soybean Oil; 8. Soybean Protein Products; 9. The Second Generation of Soyfoods; 10. Soyfoods: Their Role in Disease Prevention and Treatment; 11. Soybean Improvements Through Plant Breeding and Genetic Engineering.

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**Herbal Drugs Industry: A Practical Approach to Industrial Pharmacognosy.** Edited by R. D. Chaudhri (Consultant, Bombay, India). Eastern Publishers, New Delhi, India. 1996. xii + 648 pp. 18 × 23 cm. \$200.00. ISBN 0-532-42154-5.

The title of this book is misleading. It would have been more properly entitled Herbal Drugs Industry of India because it deals primarily with the medicinal herbs used in India and the production protocols for the Indian herb industry.

Most of the book is written in a confusing outline form that is divided into 13 chapters. Chapter I on the Pharmacological Classification of Medicinal Herbs comprises over one-third of the book. The classification is based on therapeutic categories such as adaptogens,

antifertility agents, and laxatives, to name a few. An herb is placed into one of these categories if there is a report in the literature that it has that purported activity in animal or human studies. The significance or validity of the particular study was not evaluated by the authors. The literature citations for these entries are not up-to-date with the latest being 1992. Many are incomplete, making it impossible to find the original article; a polyglot of different styles is used with numerous acronyms and abbreviations that are impossible to decipher; and after attempting to find several citations in the original literature, I found that they were rife with errors.

A sampling of other chapters that were covered in the book includes Chapter IV on the Suggested Dosage of Natural Plant Products, where a dose range is given for various types of preparations for each herb, e.g., dry extract, soft extract, infusion, etc., but no dosage regimen is supplied. Chapter V on the Key to Identification of Medicinal Plants simply gives references to the literature that could be used in identification. Chapter IX, entitled Quality Control and Standardisation, is extremely elementary. By way of illustration, the complete section on Spectroscopic Analysis reads as follows:

The electromagnetic vibrations utilized in spectroscopic analysis can be roughly divided, according to wavelength, into the ultra-violet (185-380 nm), the visible (380-780 nm), the near-infra-red (780-3000 nm) and the infrared (3-40 nm) regions. In spectroscopic analysis we are concerned with the capacity of certain molecules to absorb vibrations at specific wavelengths.

Chapter XI addresses Regulatory Requirements for India, China, The United Kingdom, Canada, and the United States. In the case of the United States, it is obvious that the authors have a poor understanding of the regulatory morass facing the herbal medicine industry in this country.

This book is poorly done, and I can see no redeeming value in any aspect that would allow me to recommend its purchase by any segment of the scientific community including industry, academics, libraries, or even individuals living in India.

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