From the Beginning . . .

Fundamentals of Early Clinical Drug Development: From Synthesis Design to Formulation

Edited by *A. F. Abdel-Magid* and *Stéphane Caron*.

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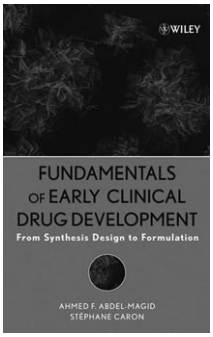

When historians record the key scientific achievements of the 21st century, they surely will note that the role of pharmaceuticals in extending life expectancy and improving our quality of life. They undoubtedly will highlight the pharmaceutical industry's brilliant discoveries and the creative chemical and biological insight that led to them. An interesting question is whether or not historians will recognize the critical role that process chemistry has played in bringing these discoveries to the patient. This part of the new drug story is often less visible than the discovery part. The translation of a laboratory method for making an organic chemical on a milligram scale to a safe production process on a kilogram to ton scale while maintaining high quality, reproducibility, and minimum cost, is an extremely challenging task.

Chemical development shifted its focus from the long development of the "perfect" chemical process and the production of large quantities of drug substance, and adopted a faster approach to quickly improve the existing synthesis and produce smaller quantities of product. Because all development activities do not start until sufficient quantities of drug substance are produced, chemical process research maintained its central role in the early decision to continue or discontinue the development of potential drug candidates. The key stage in the development of new drugs requires the preparation of 2–10 kg of drug substance under current good manufacturing practice (cGMP) conditions. The development process of today is more a highly interdisciplinary process than it was in the past.

The idea of this book project originated from the symposium "The Role of Organic Synthesis in Early Clinical Drug Development II", which was held by the Organic and Medicinal Divisions of the American Chemical Society on September 8, 2003. However, this book is different from symposia proceedings because it does more than merely gather several recent synthesis examples of development candidates, or highlight new synthetic methodologies or applications of new techniques such as automation in selecting the optimal reaction conditions. This book expands its scope beyond process chemistry to present a more comprehensive look at other aspects of drug development and to cover additional subjects of interest such as formulation development, the importance of solid-phase properties of a drug candidate, the development of analytical methods, and patent issues.

This book contains 15 chapters. The first six highlight some of the most recent advances in synthetic process chemistry written by lead researchers in the field from different pharmaceutical companies. The following nine chapters discuss other aspects of the early drug-development process such as automation, chemical engineering, solid form selection, and formulation. The editors also included chapters on the use of radioisotopes and the current trends of the growing outsourcing activities that are generating a new business of contract research companies in this field. There are excellent chapters on patents and intellectual property, explaining in a simple way what is subject for a patent filing and what is not patentable. A chapter highlighting the important role of chemical engineering for process scale-up is also included. The process of drug formulation and solid-phase properties, including the importance of the correct salt form and the emerging role of different polymorphic forms, are well addressed in chapters that cover the selection of drug forms, strategies to achieve the appropriate particle size of the drug substance, and challenges in turning a drug substance into the formulated drug product. The only aspect I miss is the role of metabolic and kinetic investigations supporting the search for the optimal final formulation.

Exciting case studies of synthetic pathway optimization dealing with various types of problems such as chirality provide an excellent source for medicinal and organic chemists. The list of chapters shows the diversity of topics presented by experts in their field. The balance is good between real process chemistry, which does not make an appearance until 100 fascinating pages of synthetic organic and medicinal chemistry is read, and pharmaceutical development. Very well-prepared figures, synthetic pathways illustrating the organic and medicinal chemistry behind process development, as well as well-selected references enhance the value of the book chapters.

None of these chapters was intended for experts in these fields, because for all the topics, more specialized reference books are available. This book is written for organic chemists in general and process chemists in particular to increase their awareness of these important topics and to facilitate the interaction with other professionals contributing to the same challenge, the development of a new drug candidate.

This book will give a lot of pleasure and valuable information to synthetic organic chemists including process and medicinal chemists in the pharmaceutical industry, as well as those in academia who develop new synthetic methods. It will also be of interest to all chemists who want to learn and understand the multidisciplinary drug-development process beyond synthesis. The book also provides a reference for current topics in chemical process research and the application of new and different techniques.

The only thing a bit misleading is the title, in that this book is more about process chemistry providing kilogram-scale batches for early clinical studies than it is about the clinical aspects of a drug development. However, this book is recommended, as it simultaneously provides a lot of pleasure and information for any chemist who would like to learn more about the complexity of the drug-development process.

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Protein–Carbohydrate Interactions in Infectious Diseases

Edited by *Carole A. Bewley.*

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In 1993 Varki asserted that "Biological roles of oligosaccharides—all of the theories are correct" (*Glycobiology* **1993**, *3*, 97–130). Now, nearly 2500 citations later, we are finally beginning to appreciate this earlier insight. In relation to microbial pathogenesis, in particular, the role of carbohydrates in the infection process, and hence the scope for therapeutic intervention, is becoming clear. The publication of a text in this area is therefore timely.

This recent addition to the Royal Society of Chemistry Biomolecular Science series sets out to make the glycobiology of protein–carbohydrate interactions in infectious diseases accessible to the chemist. Providing a balance of contemporary chemistry and glycobiology in a coherent fashion is a big task, but this text achieves its objective very well indeed. The book, which comprises eleven chapters written by leading experts in the field, contains a good range of background information on the fundamentals of protein–carbohydrate interactions in the context of pathogen recognition and moves on to survey specific topics: mycobacterial glycolipids, *Pseudomonas aeruginosa* lectins, enterobacterial infections, antiviral retrocyclins, and targeting microbial sialic acid metabolism for new drug development. Further chapters deal with the development of synthetic carbohydrate-based antimalarial vaccines and rationally designed conjugate vaccines for cholera. In addition, the chemistry necessary to develop glycomimetics is considered in relation to inhibition of bacterial enterotoxins. The final chapter deals with the explosion of interest in carbohydrate microarrays for high-throughput analysis of carbohydrate–protein interactions. The book is well produced, chapters are uniformly well written, diagrams and schemes are clear and accurate throughout. All chapters provide an extensive bibliography that enables the reader to dig a little deeper into the relevant literature. Dr. Bewley has very successfully compiled a readable account of topical issues associated the glycobiology of infectious diseases. The selection of articles is somewhat eclectic in nature, but this book does much more than merely reproduce the standard or expected content. The book offers the chemist an entree to both the chemistry and biology associated with the study and exploitation of protein–carbohydrate interactions. There is much new information in this book for the experienced glycoscientist. However, I must reiterate that this text is also accessible: a very useful addition to the bookshelf of the informed but non-expert chemist wishing to engage with glycobiology in general, and microbial pathogenesis in particular.

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Metabolomics: Methods and Protocols

Edited by *Wolfram Weckwerth.*

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This book forms part of an extensive and successful series from *Methods in Molecular Biology* published by Humana Press. Metabolomics comprises the analysis of all small-molecule metabolites within a biological sample, and the term was coined in analogy with transcriptomics and proteomics. Currently it is not possible to analyse the entire range of metabolites by a single analytical method, and so a combination of techniques is required. One of the strengths of this book is the contribution of prominent researchers in this field to the varied and, on the whole, comprehensive protocols. A wide range of analytical approaches for metabolomics are covered over seven sections, including gas chromatography mass spectrometry (GC–MS), capillary electrophoresis mass spectrometry, liquid chromatography mass spectrometry (LC–MS), and nuclear magnetic resonance (NMR) spectroscopy. One topic covered in detail is data analysis, a key part of metabolomics and an area where many researchers may need guidance, although readers more experienced in bioinformatics may not find this sufficiently comprehensive.

However, with contributions from many authors, the overall result is a lack of cohesiveness that is evident in different writing styles, varied chapter formats, and a fair amount of information redundancy. Although some of the protocols contain enough detail to enable the reader to follow easily, some sections are disappointingly brief. For example, more detail concerning LC–MS technologies would be beneficial, as key topics such as ultra performance liquid chromatography (UPLC) and tandem mass spectrometry are missing. In addition, the flow of the book could be improved by grouping the types of sample analysis techniques together, followed by data handling, as many of the statistical approaches will be common to all data collection techniques.

