Business as Usual

The Science and Business of Drug Discovery: Demystifying the Jargon

By *Edward D. Zanders.*

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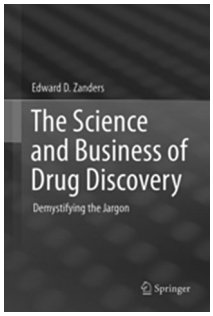

This book resulted from the many courses that the author has given to PhD students and professionals from diverse disciplines and backgrounds, in order to introduce them to the complexities of drug discovery, clinical development, pharmaceutical marketing and business. The author has 20 years of hands-on experience in pharmaceutical discovery and development in industry, an extensive network of collaborators and colleagues, and an excellent up-to-date overview and thorough insight into the many relevant activities, processes, and environments of the pharmaceutical business. He is thus in a unique position to convey a coherent picture of the most intrinsically complex matters and to facilitate both a digestible entry for the newcomer or interested outsider and a helpful overview for the expert professional or insider. This has been achieved in an outstanding fashion.

The book details the various stages of drug discovery and development, registration, marketing, and the post-launch activities. It is split into five parts, each containing a number of chapters, further divided into subchapters.

In Chapters 6–13, the various activities and processes, expectations and deliverables, as well as scientific (sub)disciplines or specific technologies are well described within the contexts of each discovery or development stage, with illustrative examples and short summaries at the end of each chapter. The interrelations to other stages are also clearly outlined. Thus, the highly complex matter of drug discovery and development is presented in an easily digestible format of eight short chapters, each subdivided into 3–6 subchapters. This central part of the book is complemented by two additional chapters: one focusing on diagnostics, the companion to pharmaceutical R&D, and its many opportunities to establish modern 'personalized medicine' (Chapter 14), and the other presenting a case history of drug discovery and development (Chapter 15), which provides a welcome example of the aspects discussed in the preceding chapters.

Prior to this central part, essential aspects of cardinal disciplines like chemistry, medicine, pharmacology, and parts of biotechnology are outlined with much emphasis on historical roots going back to ancient times to highlight constancy and breakthroughs in development, influences of philosophies and technological innovations, ultimately leading to today's rational drug discovery.

In Chapters 16 and 17, more general aspects of pharmaceutical business, such as the marketplace, intellectual property, generics, life-cycle management, or current challenges and responses by the biopharmaceutical industry are discussed. In the final section (Part V), aspects of successful and unsuccessful interactions with representatives from biopharmaceutical industry are highlighted in two short chapters. This part could be particularly useful for technology transfer officers or recruitment executives. A final chapter summarizes the challenges in translating official drug documents and provides hints and tips for translators.

The book is written in an easy style, without too much compromise or oversimplification in order to maintain the validity of key information. As each discipline and technology uses its specific terminologies, nomenclature, and in particular abbreviations, which often present difficult hurdles to any newcomer, interested outsider, or even inside specialist, this book provides an excellent guide to prevailing esotericisms and thus helps to 'demystify the jargon'. Nomenclature and abbreviations are well explained in the context of their use. A final Glossary at the end of the book summarizes some of them; but, perhaps this Glossary could have been extended, as many terms or abbreviations in the book are not recapitulated. However, some of the missing terms can be found in the subsequent Index.

Many important pieces of information are illustrated by figures. Most of the figures are well selected and serve as a clarifying or supporting complement to the text. Some figures, however, are oversimplified or do not really improve the textual content. Should a second edition of this book be considered, it would be good to see several illustrations exchanged for more informative ones.

It is unavoidable that a presentation by one single author of such diverse aspects as basics in chemistry, marketing policies, stem-cell biology, or business strategies, might not cover every aspect to the same accuracy or depth. Much assistance by colleagues in different disciplines and functions is well acknowledged by the author. Nevertheless, slight inaccuracies in various parts of the book are still recognized. However, these do not affect the overall mission of the book.

This book can be well recommended to anyone wishing to know more about the key activities and complex processes of modern drug discovery and development, the difficulties of pharmaceutical business, the challenging environment, or simply to get an answer to the provocative question stated at the beginning:

"Why can we put a man on the moon but still not cure cancer?". Furthermore, the book excellently highlights many scientific and technological developments, breakthroughs, and their impacts on pharmaceutical R&D at its various stages and thus provides interesting reading for students, professionals, and even experts in scientific disciplines relevant to drug discovery and development, who might still not have a full picture or overview of the complete pharmaceutical business. Finally, the book can also be recommended as excellent reading to all those who would like to break through the walls of esotericism of the many disciplines and technologies or expert circles involved in the pharmaceutical business.

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Chiral Drugs: Chemistry and Biological Action

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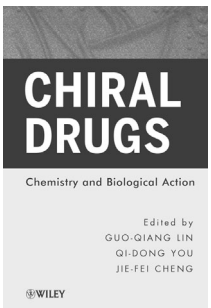

Our hands are mirror images of one another, but they are not identical, rather they are said to be chiral. This property is evident only when they interact with something else that is also chiral. When you shake hands with a friend, you do not use your right hand to reach for his left hand. Chirality becomes even clearer when you put on your gloves, the right-hand glove for the right hand, not the opposite. However, if you use disposable gloves when you work with greasy things under your car, you use very low-quality gloves. In this case, there is no difference between left- and right-hand gloves.

So, what does this have to do with chiral drugs? Molecules that constitute the active pharmaceutical ingredient (API) of drugs can also be chiral. If such molecules are mirror images of each other, they are called enantiomers. Our bodies are chiral because they consist of chiral molecules such as amino acids, carbohydrates, and oligomers and polymers of these. When a drug is administered to a patient, one enantiomer of the drug will act differently from the other enantiomer, just like gloves interact differently with your hands. It is important to have control of the handedness of the API. With good quality gloves, there is a big difference between right- and left-hand glove, and the same applies to drugs. When a drug is optimal, there is great difference between the right- and left-handed version of the drug. This difference is described by the eudismic ratio, which is the ratio of the activity of the active enantiomer, the eutomer, to that of the less active enantiomer, the distomer. Examples of this important feature of chiral drugs are discussed in several places of the book, but not given a separate chapter. In some cases, the distomer does not show a serious side effect but represents an isomeric ballast. The β-blockers are examples of this, where the therapeutic effect is due almost entirely to the (*S*)-enantiomer and the (*R*)-enantiomer is totally inactive. In contrast, ketamine and ethambutol are examples of where the distomers have very serious side effects.

The US Food and Drug Administration (FDA) very much focuses on the enantiopurity of chiral drugs. In principle, the drug should be enantiopure or at least the physiological effects of both enantiomers should be investigated.

The book covers all of the above-mentioned aspects. The Editors have chosen to divide the material into eleven chapters: 1. Overview of chirality and chiral drugs; 2. Chiral drugs through asymmetric synthesis; 3. Chiral drugs via biocatalytic approaches; 4. Resolution of chiral drugs; 5. Fluorine-containing chiral drugs; 6. Industrial application of chiral technologies; 7. Structural basis and computational modeling of chiral drugs; 8. Pharmacology of chiral drugs; 9. Pharmacokinetics of chiral drugs; 10. Toxicology of chiral drugs; 11. Representative chiral drugs.

The enantiomers of a chiral drug have identical physical properties, such as melting points, boiling points, spectra, etc. This makes their synthesis challenging. Only when such molecules interact with other chiral entities are their differences apparent.

Synthetic methodology is discussed in Chapters 2–4. In principle, there are three different ways to obtain enantiopure molecules: starting with enantiopure natural products like terpenoids, carbohydrates, amino acids, etc.; asymmetric synthesis; or chiral resolution. Asymmetric synthesis is most commonly performed using a chiral catalyst, and it has the advantage of resulting in material with 100% enantiomeric excess (*ee*). The authors have chosen to dedicate a separate chapter to biocatalysis, however, it should be noted that enzyme catalysis in principle is not different from nonbiological (chemical) catalysis, and moreover, that biocatalysts are used both in asymmetric synthesis and resolution. The final chapter gives an overview of 25 chiral drugs, their trade names, and synthesis.

The book can be recommended to all those who are interested in this important and fast-growing field of research at the interface of chemistry, pharmacy, and medicine.

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