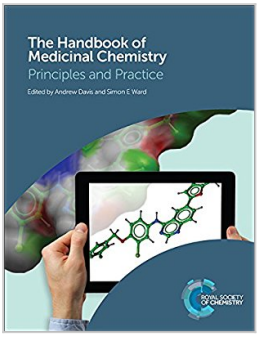

The Handbook of Medicinal Chemistry: Principles and Practice

From Royal Society of Chemistry

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Drug discovery is a constantly developing and expanding area of research. Developed to provide a comprehensive guide, the Handbook of Medicinal Chemistry covers the past, present and future of the entire drug development process. Highlighting the recent successes and failures in drug discovery, the book helps readers to understand the factors governing modern drug discovery from the initial concept through to a marketed medicine. With chapters covering a wide range of topics from drug discovery processes and optimization, development of synthetic routes, pharmaceutical properties and computational biology, the handbook aims to enable medicinal chemists to apply their academic understanding to every aspect of drug discovery.

Each chapter includes expert advice to not only provide a rigorous understanding of the principles being discussed, but to provide useful hints and tips gained from within the pharmaceutical industry. This expertise, combined with project case studies, highlighting and discussing all areas of successful projects, make this an essential handbook for all those involved in pharmaceutical development.

A free iPad app has been created in collaboration with the editors of the book. The Medicinal Chemistry Toolkit provides a suite of resources to support the day to day work of a medicinal chemist. Search for "Medicinal Chemistry Toolkit."

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Editorial Review

Review

"it looks like we have another, excellent, newcomer in the form of The Handbook of Medicinal Chemistry, edited by Andrew Davis and Simon Wood."

"The book is very nicely designed."

"this is an excellent addition to the (limited) range of medicinal chemistry textbooks and will no doubt become a must-have for many bookshelves."

(Professer Mark Searcey, University of East Anglia *ChemMedChem*)

Review

For a medicinal chemist in academia, it is relatively hard to find a textbook that is advanced enough to satisfy faculty, postdoctoral workers, and postgraduate students, but that can also be dipped into when developing an undergraduate programme. For many years, for me, the “go-to” text has been Foye’s Principles of Medicinal Chemistry, although the primarily US focus can be problematic when talking to UK pharmacists and chemists. Now, it looks like we have another, excellent, newcomer in the form of The Handbook of Medicinal Chemistry, edited by Andrew Davis and Simon Wood. This is a book that has its heart on its sleeve?drugs should be small (MW<500) and natural products, antibodies, or polymers have no place in this world. The argument against drugs that don’t conform to the Lipinski rules is set out even in the readable and immensely interesting introduction by Simon Campbell, formerly of Pfizer, who ends by suggesting a meeting of minds between industry-trained medicinal chemists moving into academia alongside (presumably nonindustrytrained) biologists and clinicians. As a nonindustry-trained chemist, I can see the benefits and the disadvantages to this approach. In academia, we can benefit from the knowledge and experience that comes from an industrial perspective, but we also have the potential to explore the blue skies of molecules and targets that would be ignored in the pharmaceutical industry. This is a book that is focussed on the realism of medicinal chemistry research on synthetic small molecules, and it dives straight in to a discussion of physicochemical properties and compound quality in its first chapter. This ends with a very useful table of tips that, at least in part, boils down to the notion that optimisation of small molecules for drug development should be a multivariate rather than serial concern, and that target affinity and selectivity must be assessed alongside molecular properties and pharmacokinetics. The next few chapters focus on techniques that aid in molecular design to find that elusive lead compound: computational chemistry, parallel synthesis, fragment- and structure-based drug design, and quantitative structure–activity relationship (QSAR) before delving in to the world of drug metabolism and pharmacokinetics? the latter could be an extremely dry subject but is enlivened by the inclusion of some nice real-world case studies. One of the real strengths of this new addition to medicinal chemistry textbooks then comes to light and really shines. This is the section on biology and the development of assays. To a chemist working in the laboratory to make new molecules, the beauty is in the design of the synthetic route and the resulting pure molecule. For many years, the pharmaceutical industry has focussed its efforts on the recruitment of pure organic chemists, with a

multistep total synthesis behind them, as this demonstrates that they can make molecules and they can then learn the “rest”?i.e. the very essence of this book?on the job. This ignores the huge importance in being able to understand, and even help to develop, molecular biology and/or cell-based assays that are the first steps in demonstrating the efficacy of your new molecule and can point you in the right direction for the synthesis of the next one. Many medicinal chemistry textbooks ignore these aspects and the following preclinical development of molecules entirely, and this, of course, is the place where all the attrition occurs. This one takes you all the way to the clinic, with a slight (but enlightening) detour to discuss the patent process and its associated pitfalls. Another strength is the inclusion of case studies written by those at the coalface, and these can be really inspirational in the development of teaching tools for undergraduate students. Several years ago, I was looking for some way to enhance the “drug metabolism” (DM) lectures I was giving to second-year pharmacy students. While at a medicinal chemistry meeting in Horsham, I happened to see a beautiful talk on the development of ezetimibe, in which an understanding of the metabolism of a lead compound led to the development of the clinically used agent. With the permission of the speaker (Duane Burnett), this story has formed the centrepiece for those DM lectures ever since (now given by one of my colleagues!). The stories here?aleglitazar, lapatinib, ticagrelor? give wonderful insights into the thought processes and the pitfalls of drug development and will undoubtedly be transformed in a similar way and across chemistry, pharmacy, and pharmacology departments into examples as to how clinical agents come to be. I was particularly taken with the section that begins “I wouldn’t start there” as part of the ticagrelor story and the assertion by the authors that the location of the (then) Fisons pharmaceuticals, in Loughborough and within reach of cardiology groups in Leicester and Nottingham, played a pivotal role in the development of the drug. Perhaps this is something that CEOs should reflect upon when closing or moving sites?local knowledge can be hugely beneficial. The book is very nicely designed. My only minor quibble might be the order of the chapters. I would perhaps have started with Chapters 18–20 and followed these with some of the early techniques chapters which further reinforce the concepts introduced. Overall, though, this is an excellent addition to the (limited) range of medicinal chemistry textbooks and will no doubt become a must-have for many bookshelves. It will sit on my desk for a long time, becoming somewhat dog-eared, no doubt, as I dip into it both for relevant information and also for a good read.

(Professor Mark Searcey, University of East Anglia *ChemMedChem*)

From the Back Cover

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