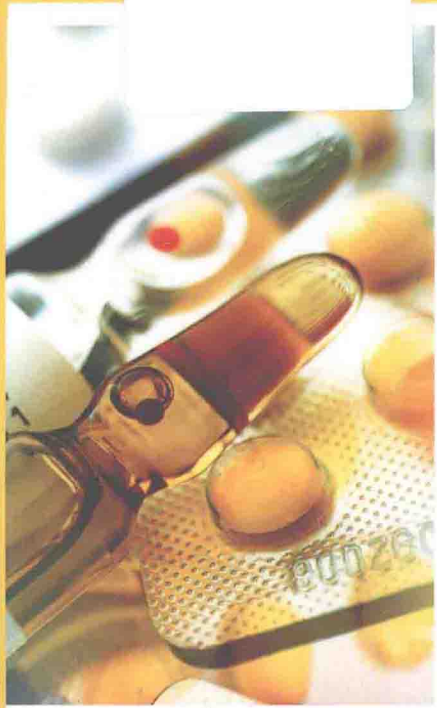
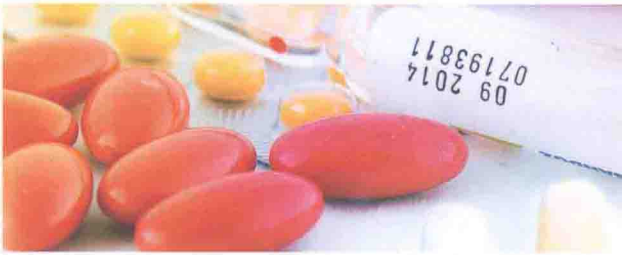
Basic Principles of Drug Discovery and Development





Benjamin E. Blass

BASIC PRINCIPLES OF DRUG DISCOVERY AND DEVELOPMENT

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Dedication

Sir Isaac Newton, one of the greatest scientists of his time, wrote "If I have seen further it is by standing on ye shoulders of Giants." Although he was almost certainly referring to his scientific achievements, the underling concept of learning from our forbearer is true in any endeavor. Indeed, this concept can be further extended to include those who are there in the present day, supporting the activities of an individual as he or she attempts to accomplish that which they view as important. With this thought in mind, I have dedicated this book to the scientists who came before me, those who mentored me, and those who work with me on a daily basis. In addition, and perhaps more importantly, this text is dedicated to the loving and supportive family that has helped me become the person that I am today. Special thanks are offered to my mother, father, sister, brother, my three children, and of course, my wife Kathleen. These are the giants on whose shoulders I have stood upon.

Foreword

The last three decades have witnessed a revolution in the drug discovery and development process. Medicinal chemistry and in vitro screening that were once major bottlenecks in the process of identifying novel therapeutics have been dramatically accelerated through the incorporation of automation and the development of enabling technologies such as recombinant DNA and transfection technology. High-throughput screening (HTS), parallel synthesis, and combinatorial chemistry have facilitated the synthesis and biological evaluation of large numbers of potentially useful compounds. These activities, in turn, have generated vast amounts of data that can be analyzed to develop structure–activity relationships and structure–property relationships useful for the optimization of lead compounds. At the same time, new techniques, technological advances, and a greater understanding of the importance of pharmacokinetics, animal models, and safety studies have dramatically altered how new molecules are selected for clinical study. Design strategies of clinical trials, biomarkers, translational medicine, the regulatory landscape, intellectual property rights, and the business environment have also changed dramatically over the course of the last 30 years.

The complexities of the drug discovery and development process cannot be overstated, nor can the wide range of expertise required for the successful development of new, marketable therapeutics. In order to thrive in this every changing landscape, individuals interested in a career in the pharmaceutical industry or related fields must be more than simply experts in their chosen field of study. They must also have an understanding of the numerous, overlapping fields of their colleagues. *Basic Principles in Drug Discovery and Development* has captured the critical information on the disparate processes, technologies, and expertise required for modern drug discovery and development and presents it in a logical and concise manner for students, practicing scientists, and nonscientists with an interest in the pharmaceutical industry. Dr Benjamin E. Blass, an experienced educator and scientist with foundational knowledge in medicinal chemistry, drug design, biological targets, and over 20 years of experience in industrial and academic drug discovery and development, provides a comprehensive account of the many functions involved in drug discovery and development, from initial medicinal chemistry conceptualization and in vitro biological evaluation to clinical trials and beyond.

There are many aspects of this book that will help practicing scientists, graduate students, and future drug discovery researchers to develop a strong foundation in the concepts that govern the multidisciplinary process of drug discovery. Through this unique text, they will acquire an understanding of key aspects of drug discovery and development. The organization of the subject material was chosen to allow the readers to incrementally increase their knowledge in the wide range of disciplines required to identify new, marketable therapeutic agents. The book is thoroughly written and includes 13 chapters with over 300 figures and 900 references. Throughout the text, the reader will become familiar with more than 100 drugs and clinical candidates that exemplify important theories and practices.

Each chapter contains examples of drugs pertaining to the material in the chapter. The opening chapter provides an overview of drug discovery and development. This serves as the foundation for the following 10 chapters which describe the various functions involved in drug discovery and development. The early phases of drug discovery are described in detail through discussions of important topics such as target identification, target validation, lead identification, multidimensional lead optimization, pharmacokinetics, preclinical pharmacodynamics, and early toxicology. This is followed by discussions of preclinical activities, clinical trial design, biomarkers, and translational medicine. Each chapter builds on the previous chapters and this approach provides the readers with an integrated view of the various, multidisciplinary functions required for the drug discovery and development process.

Chapters 11 and 12 describe two important topics essential for running an effective pharmaceutical R&D business: organizational structure and patent protection. These chapters give the reader a true understanding of the organizational structure required for the successful management of research and development organizations and the importance of protecting intellectual property to ensure a good return on investment. Patent protection is the life blood of the pharmaceutical and biotech industries, and at the same time a source of innovation for new discoveries. Patents ensure the sharing of discoveries and innovations that might otherwise be kept as trade secrets. In the final chapter, case studies demonstrating the practical application of the concepts and principles described in the previous chapters are provided. These vignettes also describe important lesson learned in each case, some of which changed the way modern drug discovery research and development programs are executed.

Although there are numerous textbooks that discuss various aspects of the drug discovery and development process, none of them provides a comprehensive view of the process. *Basic Principles in Drug Discovery and Development* is unique in its comprehensive approach to this

complex endeavor. In writing this textbook, Dr Blass has provided an important new tool for the education of the next generation and a valuable resource for people with a vested interest in the identification and commercialization of novel medications.

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