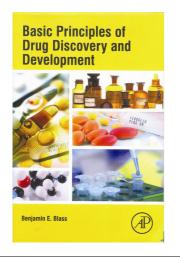
## **BOOK REVIEWS**



**Basic Principles of Drug Discovery and** Development. Benjamin E. Blass. Academic Press, An Imprint of Elsevier, 32 Jamestown Road, London NW1 7BY, UK. 2015. xv + 574 pp. Price: US\$ 99.95.

This book will be of interest to followers of medicinal chemistry, drug discovery and biologists working in collaboration with chemists in finding new scaffolds as better therapeutics. It lists various steps that form the basis of drug discovery and each chapter covers examples which illustrate the concept. The chapters are arranged covering topics in drug discovery like modern methods and principles, classical targets, in vitro screening, medicinal chemistry, in vitro ADME and in vivo pharmacokinetics, animal models, safety and toxicology, basics of clinical trials, translational medicine, trends in pharmaceutical industry, IP and patents, and some case studies. The book covers more than 900 references, 300 figures and 100 drug molecules and clinical candidates, thus giving access to the literature scattered in different areas at one point. The book defines various terms used regularly in drug discovery using simple definitions to make them comprehensible to even a layman. It can act as a starting point for beginners working in the area of drug discovery. It can also help those already working in this area to understand the steps that are to be completed towards taking a primary hit molecule to market, involving different disciplines. The author traces the steps and their significance in drug discovery up to clinical trials.

In the first chapter, the author gives a brief idea about drug discovery starting from target discovery to clinical trials. It also provides examples of a few diseases

such as HIV, cancer and cardiovascular diseases, wherein drug discovery and development significantly changed the clinical outcomes. There are several drug molecules listed in this part which are useful for students. The importance of natural products and natural product analogues is explained by giving the classical example of Taxol which has been used for cancer treatment.

The second chapter describes the evolution of drug discovery process from ancient times to the present day, which includes use of traditional medicines to advanced therapeutics. Various animal models are also described in detail. The importance of animal study in drug discovery is emphasized by giving the example of sulphonamide. The importance of chiral stability of a drug is explained with the story of thalidomide.

The third chapter deals with the classical targets in drug discovery. It describes about the four types of macromolecules which are most commonly targeted by majority of drugs, including enzyme, GCPR, ion channels and transporters. It also describes the protein structures, enzymes and their inhibition. Finally, emphasis is on the new dimensions of targets in drug discovery which include protein-protein, protein-DNA, protein-**RNA** interactions

The fourth chapter explains the development of in vitro screening system of modern drug discovery. It also summarizes the key language of screening which is essential to understand and interpret the resulting data. Different types of assay systems have been described which are employed for understanding of the nature, function and utility of the potential drug candidates.

The fifth chapter describes the importance of medicinal chemistry in drug discovery. Various important factors such as structure-activity and structure-property relationship play a vital role in medicinal chemistry, since change in the chemical structure of a compound leads to different binding potency, functional activity and selectivity of the drug. The importance of chirality is illustrated by giving examples of Darvon and Novrad, which are enantiomers having different biological activity. Information regarding how to develop SAR dataset is also provided

The sixth chapter describes the importance of pharmacokinetics and in vitro ADME properties in drug discovery. It includes studies of various factors such as absorption, solubility, permeability, distribution and excretion of drug candidate in the body. In 1991, 39% of clinical failures was reported due to poor pharmacokinetic properties, but this number decreased to 8% by 2000 showing the importance of these studies. The effect of structural changes on the solubility, permeability, distribution and stability of the drug molecule in the human body is well explained with the help of many useful examples.

The seventh chapter focuses on animal model studies in drug discovery process. Due to regulations of FDA, it becomes important to provide proof of efficacy and safety of any drug candidate in animals before it could be tested in the human body. From the viewpoint of drug discovery, it is important to choose the correct animal model and species (rat, mice or dog) that correlate with human condition or disease for successful outcome. Animal models for different diseases such as those for neurodegeneration, hypertension, cardiovascular disease, hyperlipidaemia, heart failure, infectious diseases and cancer have been systematically explained.

The eighth chapter is about safety and toxicology. In drug discovery and development, it is important to check safety parameters of the drug candidate on normal physiological functions. Aspects of toxicity discussed are acute and cytotoxicity chronic toxicity, and genotoxicity. Therefore, in order to minimize the risk of safety and toxicity issues, it becomes important to understand the safety of a drug candidate.

The ninth chapter is about basic clinical trials. Here, various factors such as drug delivery methods and formulations have been explained. Also, information regarding various important phases of clinical trials is given.

The tenth chapter deals with translational medicine and biomarkers. The use of biomarkers and their differentiation from surrogate end-point are defined. Advances in imaging technologies are discussed in detail, followed by examples of practical uses of biomarkers.

The eleventh chapter deals with trends in the pharmaceutical industry and organizational structures of the industry, which have an impact on the process of drug discovery. The comparison of academic research with industrial projects is also included.

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Transgenic insertion of the gene responsible for the production of green fluorescent protein (GFP) results in mice that fluoresce when exposed to ultraviolet light. The GFP gene has been successfully expressed in bacteria, fungi, plants, insects, and mammalian cells.

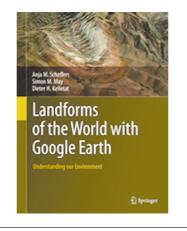
The twelfth chapter covers one of the most important issues in drug discovery – IP rights and patents. Finer nuances of what is patentable, obviousness, inventorship, assignment and ownership, patent application contents and classification are covered in this chapter.

Case studies in drug discovery are covered in the final chapter. Tamiflu, HDAC inhibitors, HIV protease inhibitors, nitrofurantoin, terbinafine, loratidine, MPTP, bupropion and COX-2 inhibitors are covered in this chapter. Details of how changes in the structure of the molecule impact their activity are provided. The chapter covers issues related to safety of the drug molecule, identification of the role of metabolite and challenges in finding selective COX-2 inhibitors.

The book is well written and is recommended for libraries or individuals who are interested or are working in the area of drug discovery. The readers will benefit if early discovery concepts such as 'biology-oriented synthesis', 'fragment-based drug discovery' or 'diversity-oriented synthesis' are included. Hopefully, the author will incorporate these in future editions.

S. CHANDRASEKHAR

Indian Institute of Chemical Technology, Uppal Road, Hyderabad 500 007, India e-mail: srivaric@iict.res.in



Landforms of the World with *Google Earth*: Understanding our Environment. Anja M. Scheffers, Simon M. May and Dieter H. Kelletat. Springer, Dordrecht, The Netherlands. 2015. 391 pp. Price: US\$ 129.00. ISBN 978-94-017-9712-2.

Google Earth's reach extends from the layman who pins his home to the Earth, to the professional scientific journals asking for KML files of study areas. A revolution to the power of ten would have been witnessed by mankind if Google Earth was available during the era of Alexander the Great or Charles Darwin. The popularity and utilization achieved by Google Earth since inception into the cyber world in 2004 is simply marvellous. This all embracing coverage of Google Earth, which has elevated the status of maps and images from esoteric collections housed in dusty libraries to cutting edge technology is brought out well in this book. The authors bring to life the agility of Google Earth, especially as related to the needs of the geoscientific community seeking to understand our environment through landforms. This book with a sparse, yet crisp narration and beautiful illustrations stands out in all aspects. At places, an oblique angle view of Google Earth images provides a digital elevation model which helps the reader to internalize the terrain. Google Earth's bird's-eye perspective images are also supported by classical terrestrial photographs by these authors. The Google Earth image of Joshua Tree National Park, California, USA and its corresponding terrestrial photograph (p. 68, figures 3.9 c and d respectively) are identical and prove the veracity of the high-resolution images.

Landforms on the Earth's surface are neither identical nor static – from the

majestic peaks of the mighty Himalayas to the deepest Mariana Trench and the spectacular Devils Tower to deep impact craters of Chicxulub - but are dynamic. Earth abhors static, its dynamism is what drives and sustains life, and this sense of fluidity in a solid Earth is elucidated well in this book with Google Earth efficiently capturing our planet in its brilliant hues. The book also provides a virtual field tour for both the professional as well as amateur geologists. It is split into four parts based on the geomorphic processes that carved out a particular landform. Abstract for each chapter, which is unusual in textbooks other than edited volumes, gives a glimpse of the tale that the chapter tells.

This highly illustrated textbook will be an asset to any geologist, and should be on the book shelves of geology libraries of all colleges and universities in India. This book will also help a geologist to rove over in the *Google Earth* platform to enjoy the spectacular landforms and identify them. It was Henry Hudson, the great English navigator and sea explorer who said, 'This land may be profitable to those that adventure it'. And this book leads you on a semi-adventure, if not on an adventure, all in itself.

K. S. SAJINKUMAR

Department of Geology, University of Kerala, Thiruvananthapuram 695 581, India e-mail: sajinks@gmail.com

Annual Review of Genetics, 2015. Bonnie L. Bassler, Michael Lichten and Gerturd Schüpbach (eds). Annual Reviews, 4139 El Camino Way, Palo Alto, CA 94303-0139, USA. Vol. 49. ix + 718 pp. Price: US\$ 99.

'HIGHLY ESTEEMED SIR:

The acknowledged pre-eminence your honour enjoys in the detection and classification of wild-growing plant hybrids makes it my agreeable duty to submit for your kind consideration the description of some experiments in artificial fertilization.'

Thus began the first of a series of letters addressed to the renowned Swiss botanist Carl Nägeli during 1866–1873. These