1. Record Nr. UNINA9910876995303321

Titolo	Molecular drug properties : measurement and prediction / / edited by Raimund Mannhold
Pubbl/distr/stampa	Weinheim, : Wiley-VCH, c2008
ISBN	1-282-01059-X 9786612010590 3-527-62128-8 3-527-62129-6
Descrizione fisica	1 online resource (503 p.)
Collana	Methods and principles in medicinal chemistry ; ; v. 37
Altri autori (Persone)	MannholdRaimund <1948->
Disciplina	615.7
Soggetti	Drug development Drugs - Design
Lingua di pubblicazione	Inglese
Formato	Materiale a stampa
Livello bibliografico	Monografia
Note generali	Description based upon print version of record.
Nota di bibliografia	Includes bibliographical references and index.
Nota di contenuto	Molecular Drug Properties; Contents; List of Contributors; Preface; A Personal Foreword; Part I Introduction; 1 A Fresh Look at Molecular Structure and Properties; 1.1 Introduction; 1.2 Core Features: The Molecular "Genotype"; 1.2.1 The Argument; 1.2.2 Encoding the Molecular "Genotype"; 1.3 Observable and Computable Properties: The Molecular "Phenotype"; 1.3.1 Overview; 1.3.2 Equilibria; 1.3.3 Stereoelectronic Features; 1.3.4 Recognition Forces and Molecular Interaction Fields (MIFs); 1.3.5 Macroscopic Properties 1.4 Molecular Properties and their Adaptability: The Property Space of Molecular Entities1.4.1 Overview; 1.4.2 The Versatile Behavior of Acetylcholine; 1.4.3 The Carnosine-Carnosinase Complex; 1.4.4 Property Space and Dynamic QSAR Analyses; 1.5 Conclusions; 2 Physicochemical Properties in Drug Profiling; 2.1 Introduction; 2.2 Physicochemical Properties and Pharmacokinetics; 2.2.1 DMPK; 2.2.2 Lipophilicity - Permeability - Absorption; 2.2.3 Estimation of Volume of Distribution from Physical Chemistry; 2.2.4 PPB and Physicochemical Properties; 2.3 Dissolution and Solubility 2.3.1 Calculated Solubility2.4 Ionization (pK(a)); 2.4.1 Calculated pK(a); 2.5 Molecular Size and Shape; 2.5.1 Calculated Size Descriptors; 2.6 H-

bonding; 2.6.1 Calculated H-bonding descriptors; 2.7 Lipophilicity; 2.7.1 Calculated log P and log D; 2.8 Permeability; 2.8.1 Artificial Membranes and PAMPA; 2.8.1.1 In Silico PAMPA; 2.8.2 IAM, Immobilized Liposome Chromatography (ILC), Micellar Electrokinetic Chromatography (MEKC) and Biopartitioning Micellar Chromatography (BMC); 2.8.3 Liposome Partitioning; 2.8.4 Biosensors; 2.9 Amphiphilicity; 2.10 Drug-like Properties
2.11 Computation versus Measurement of Physicochemical Properties2.11.1 QSAR Modeling; 2.11.2 In Combo: Using the Best of two Worlds; 2.12 Outlook; Part II Electronic Properties and H-Bonding; 3 Drug Ionization and Physicochemical Profiling; 3.1 Introduction; 3.1.1 Absorption, the Henderson-Hasselbalch Equation and the pH-partition Hypothesis; 3.1.2 "Shift-in-the-pK(a)"; 3.2 Accurate Determination of Ionization Constants; 3.2.1 Definitions - Activity versus Concentration Thermodynamic Scales; 3.2.2 Potentiometric Method; 3.2.3 pH Scales; 3.2.4 Cosolvent Methods
3.2.5 Recent Improvements in the Potentiometric Method Applied to Sparingly Soluble Drugs3.2.6 Spectrophotometric Measurements; 3.2.7 Use of Buffers in UV Spectrophotometry; 3.2.8 pK(a) Prediction Methods and Software; 3.2.9 Tabulations of Ionization Constants; 3.3 "Octanol" and "Membrane" pK(a) in Partition Coefficients Measurement; 3.3.1 Definitions; 3.3.2 Shape of the Log D(oct)-pH Lipophilicity Profiles; 3.3.3 The "diff 3-4" Approximation in log D(oct)-pH Profiles for Monoprotic Molecules
3.3.4 Liposome-Water Partitioning and the "diff 1-2" Approximation in log D(MEM)-pH Profiles for Monoprotic Molecules

Sommario/riassunto

This first systematic overview for more than a decade is tailor-made for the medicinal chemist. All the chapters are written by experienced drug developers and include practical examples from real drug candidates. Following an introduction to global drug properties and their impact on drug research, screening and combinatorial chemistry libraries, this handbook demonstrates the best and fastest way to estimate those properties most relevant for the efficiency and pharmacokinetic performance of a drug molecule: lipophilicity,solubility, electronic properties and conformation.