

1. Record Nr.	UNINA9910298633703321
Titolo	Tactics in Contemporary Drug Design // edited by Nicholas A. Meanwell
Pubbl/distr/stampa	Berlin, Heidelberg : , : Springer Berlin Heidelberg : , : Imprint : Springer, , 2015
ISBN	3-642-55041-X
Edizione	[1st ed. 2015.]
Descrizione fisica	1 online resource (400 p.)
Collana	Topics in Medicinal Chemistry, , 1862-2461 ; ; 12
Disciplina	54 611.01816 615 615.19
Soggetti	Medicinal chemistry Molecular biology Pharmacology Medicinal Chemistry Molecular Medicine Pharmacology/Toxicology
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	Preface to the Series; Preface; Contents; Physical Properties in Drug Design; 1 Introduction: The Realisation of Physical Property Issues; 1.1 Molecular Obesity and Obsession with Potency; 1.2 Med Chem Inflates Properties: The Body Doesn't Change; 2 Physical Properties: What Are They and Which Are Important?; 2.1 Lipophilicity/Hydrophobicity; 2.1.1 Small Hydrophilic Molecules: A Forgotten Strategy for Oral Medicines?; 2.1.2 Methods for the Measurement and Prediction of Lipophilicity; 2.1.3 Octanol Water Methods: Issues with Overly Lipophilic Compounds 2.1.4 Measurements Using Chromatographic Methods 2.2 Acid/Base Strength: pKa; 2.2.1 Measurement and Calculation of pKa; 2.3 Solubility; 2.3.1 The General Solubility Equation; 2.3.2 Simulated Gastrointestinal Fluids; 2.4 Escape from Flatland and the Impact of Aromatic Ring Count; 2.4.1 Lipophilicity and Aromaticity Act in Unison; 3 How the Physical Environment of a Drug Changes from

Administration to Target; 3.1 The Passage Through the Body for an Oral Medicine; 3.2 Oral Developability Classification System: Dose, Solubility and Permeation
4 Impact of Physical Properties on Developability and DMPK Parameters
4.1 General Aspects of Lipophilicity-Dependent Behaviour; 4.2 Impact of logP, logDpH and Aromaticity on Particular Parameters; 4.2.1 Permeability; 4.2.2 Cytochrome P450s; 4.2.3 hERG Binding; 4.2.4 Promiscuity; 4.2.5 Human Serum Albumin Binding; 4.2.6 Intrinsic Clearance; 4.3 The Composite Risks of Poor Physical Profiles; 5 Efficiency Metrics and Their Interrelationship with Physical Properties; 5.1 Drug Efficiency; 5.1.1 Physical Estimates of Drug Efficiency; 5.2 Ligand Efficiency and Related Measures
5.3 Ligand Lipophilicity Efficiency Measures
5.4 The Combined Influence of Efficiency Metrics and Physical Property Measures; 5.5 The Thermodynamics of Efficient Binding; 6 Conclusions; References;
Improving Solubility via Structural Modification; 1 Introduction; 2 Description of Aqueous Solubility; 2.1 Definition of Solubility; 2.2 General Solubility Equation; 2.3 Solvation of Organic Molecules; 2.3.1 Effect of Molecular Size and Shape on Solvation; 2.3.2 Water-Solute Hydrogen Bonding; 2.4 Crystal Lattice Stability and Packing Efficiency; 2.4.1 Effect of Molecular Shape on Packing Efficiency
2.4.2 Intermolecular Interactions in the Solid State
2.4.3 The Effect of Molecular Symmetry on Crystal Packing; 3 Tactics for Improving Solubility; 3.1 Reducing LogP; 3.1.1 Introducing a Solubilizing Appendage; Introducing Basic Appendages; Introducing Acidic Appendages; Introduction of Neutral Appendages; 3.1.2 Template and Substituent Modifications; Substituent Modifications; Analysis of Substituent Effects on Solubility; The Dual Nature of Fluorine; Intramolecular Interactions; Examples of Substituent Modifications; Template Modifications; 3.2 Disrupting Crystal Lattice Stability
3.2.1 Disruption of Intermolecular H-Bonding Interactions

Sommario/riassunto

Medicinal chemistry is both science and art. The science of medicinal chemistry offers mankind one of its best hopes for improving the quality of life. The art of medicinal chemistry continues to challenge its practitioners with the need for both intuition and experience to discover new drugs. Hence sharing the experience of drug research is uniquely beneficial to the field of medicinal chemistry. Drug research requires interdisciplinary team-work at the interface between chemistry, biology and medicine. Therefore, the topic-related series Topics in Medicinal Chemistry covers all relevant aspects of drug research, e.g. pathobiochemistry of diseases, identification and validation of (emerging) drug targets, structural biology, drugability of targets, drug design approaches, chemogenomics, synthetic chemistry including combinatorial methods, bioorganic chemistry, natural compounds, high-throughput screening, pharmacological in vitro and in vivo investigations, drug-receptor interactions on the molecular level, structure-activity relationships, drug absorption, distribution, metabolism, elimination, toxicology and pharmacogenomics. In general, special volumes are edited by well known guest editors.
