Blood Brain Barrier In Drug Discovery Optimizing Brain Exposure Of Cns Drugs And Minimizing Brain Side Effects For Peripheral Drugs

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Advanced Drug Formulation Design to Optimize Therapeutic Outcomes Robert O. Williams 2007-09-25 This title demonstrates how advanced formulation designs and delivery technologies can be used to improve drug efficacy and treatment outcomes in particular therapeutic categories or disease states. It discusses nanoparticle systems for cancer treatments, and also presents cutting edge immono-regulation agents for transplantation and the local targ
Structure-Based Drug Design for Diagnosis and Treatment of Neurological Diseases

Rona R. Ramsay 2017-03-24 European Cooperation in Science and Technology (COST) supports the collaboration of nationally-funded science and technology research through the creation of networks. COST is the longest-running European framework enhancing cooperation among researchers, engineers and scholars across Europe. The COST Action CM1103 “Structure-based drug design for diagnosis and treatment of neurological diseases: dissecting and modulating complex function in the monoaminergic systems of the brain” is a good example of the advances possible through interdisciplinary collaboration on difficult problems. COST Action CM1103 brought together 28 research groups from 18 countries to collaborate for four years on multi-target drug design for complex neuropathologies. The interdisciplinary expertise of the members is spans the range from computational enzymology to human studies, providing outstanding opportunities for the interdisciplinary development of trainees, and is reflected in the articles in this e-book. This Research Topic covers progress in multi-target drug design for the complex neuropathologies of the monoamine system that are apparent, for example, in Alzheimer’s disease. After a mini-review to introduce the topic of multi-target drug design, the other articles review the Research topic from their own perspective, two from computational approaches, three from medicinal chemistry, two from molecular pharmacology, and two from studies in whole brain. This multi-faceted approach describes new compounds, new methodology, and advances in the basic science of understanding the brain. This Ebook is based upon work from COST Action (CM1103 “Structure-based drug design for diagnosis and treatment of neurological diseases: dissecting and modulating complex function in the monoaminergic systems of the brain"), supported by COST (European Cooperation in Science and Technology). COST (European Cooperation in Science and Technology) is a pan-European intergovernmental framework. Its mission is to enable break-through scientific and technological developments leading to new concepts and

products and thereby contribute to strengthening Europe's research and innovation capacities. It allows researchers, engineers and scholars to jointly develop their own ideas and take new initiatives across all fields of science and technology, while promoting multi- and interdisciplinary approaches. COST aims at fostering a better integration of less research intensive countries to the knowledge hubs of the European Research Area. The COST Association, an International not-for-profit Association under Belgian Law, integrates all management, governing and administrative functions necessary for the operation of the framework. The COST Association has currently 36 Member Countries. www.cost.eu

Translational Research in Traumatic Brain Injury Daniel Laskowitz 2015-12-01 Traumatic brain injury (TBI) remains a significant source of death and permanent disability, contributing to nearly one-third of all injury related deaths in the United States and exacting a profound personal and economic toll. Despite the increased resources that have recently been brought to bear to improve our understanding of TBI, the development of new diagnostic and therapeutic approaches has been disappointingly slow. Translational Research in Traumatic Brain Injury attempts to integrate expertise from across specialties to address knowledge gaps in the field of TBI. Its chapters cover a wide scope of TBI research in five broad areas: Epidemiology Pathophysiology Diagnosis Current treatment strategies and sequelae Future therapies Specific topics discussed include the societal impact of TBI in both the civilian and military populations, neurobiology and molecular mechanisms of axonal and neuronal injury, biomarkers of traumatic brain injury and their relationship to pathology, neuroplasticity after TBI, neuroprotective and neurorestorative therapy, advanced neuroimaging of mild TBI, neurocognitive and psychiatric symptoms following mild TBI, sports-related TBI, epilepsy and PTSD following TBI, and more. The book integrates the perspectives of experts across disciplines to assist in the translation of new ideas to clinical

practice and ultimately to improve the care of the brain injured patient.

Optimization in Drug Discovery Zhengyin Yan 2004 Recent reports of drug attrition rates have revealed that a significant number of drug candidates fail in the later stage of clinical development due to absorption, distribution, metabolism, elimination and toxicity issues. Lead optimization in drug discovery, a process of attempting to uncover and correct these defects, is highly beneficial in lowering the cost and time to develop therapeutic drugs by reducing drug candidate failures in development. This book provides the assays utilized in drug discovery to rapidly screen for compounds with favorable drug-like properties. A total of 25 chapters, contributed by many experts in the field, cover a wide spectrum of subjects including physicochemical properties, absorption, plasma binding, metabolism, drug interactions, and toxicity, making this an essential book for all pharmacologists and pharmaceutical scientists.

Encyclopedia of Psychopharmacology Ian Stolerman 2010-07-31 Here is a broad overview of the central topics and issues in psychopharmacology, biological psychiatry and behavioral neurosciences, with information about developments in the field, including novel drugs and technologies. The more than 2000 entries are written by leading experts in pharmacology and psychiatry and comprise in-depth essays, illustrated with full-color figures, and are presented in a lucid style.

Drug Transporters Martin F. Fromm 2010-11-19 It is increasingly recognized that various transporter proteins are expressed throughout the body and determine absorption, tissue distribution, biliary and renal elimination of endogenous compounds and drugs and drug effects. This book will give an overview on the transporter families which are most important for drug therapy. Most chapters will focus on one transporter family highlighting tissue expression, substrates, inhibitors, knock-out

mouse models and clinical studies.
Drug Discovery Efforts Targeting Mutant P53 for the Treatment of Glioblastoma Randa R. Barsoom 2014 Targeted approaches to treating cancers including glioblastoma multiforme (GBM) are limited and partially effective, at best. By attacking specific oncogenic drivers for a tumor, an on-target and effective drug might be possible. The transcription factor p53 is a cell control tumor suppressor protein responsible for maintaining the integrity of a cell's genome and eliminating cells with DNA mutations. Mutant p53 is found, and believed to be causative, in 50% of all human cancers. The oncogenic driver for a high percentage of GBM is thought to be mutant p53. In this thesis, a drug discovery effort that targets mutant p53 in GBM cells is described. The goal is to identify compounds that reactivate mutant p53 and allow normal biological function of p53 in the GBM cells. The process of identification of lead structures and efforts in developing new analogues that optimize potency, selectivity, metabolic stability and other drug-like properties, including the ability of the compounds to cross the blood brain barrier, BBB, are explained. Crossing the BBB is a critical step for drugs used in central nervous system (CNS) diseases. Here, seven synthesized compounds in two classes, quinoline and benzimidazoles, are discussed. Six of these compounds reactivate mutant p53 in the GBM cells and allow for production of proteins downstream of p53. Of these six active compounds, three cross the blood brain barrier. A structure activity relationship, SAR, regarding in-cell potency, selectivity, metabolic stability and the ability to cross the BBB is then developed. This SAR and drug discovery effort can be further expanded to develop compounds with an optimized biological profile that would lead to potential drug candidates for the treatment of glioblastoma multiforme.
Discovery and Development of Antibodies for Drug Delivery Across the Blood-brain Barrier Loukas Goulatis 2018 The cure and management of the majority of diseases affecting the brain is hampered by the blood-brain barrier (BBB). In the brain

endothelia adjacent endothelial cells are sealed together, redirecting molecular trafficking from the paracellular route to transcellular trafficking and preventing the vast majority of therapeutics from entering the brain from the blood. The lack of effective treatments for brain diseases motivates the development of non-invasive methods for brain drug delivery. A widely researched method for non-invasive delivery across the BBB is to target via antibodies the brain's endogenous transport mechanisms particularly transporters that utilize receptor mediated transcytosis (RMT) to ferry therapeutics into the brain. Current RMT systems suffer from low trans-BBB transport capacity, as well as ubiquitous expression throughout the periphery, necessitating the research for novel antibody-RMT pairs. In this work, we aim to discover and develop such brain penetrating antibodies. First, we describe a novel, combinatorial methodology to screen a phage display antibody library against a stem cell-derived model of the human BBB specifically for transcytosing antibodies that can traffic the BBB in vivo and target human antigens. We move forward to describe the production, purification, and validation for both in vitro and in vivo brain transport of our lead antibodies. A panel of novel antibodies able to transport across the BBB through RMT mechanisms is identified and evaluated. Next, we aim to develop an antibody functionalization platform to integrate our brain penetrating antibodies and enable further downstream in vivo evaluation. To this end, we describe the optimization of a semi-synthetic protein functionalization platform developed previously in our laboratory. Through fusing antibodies with an intein and secreting the fusion in yeast it is possible to append site-specifically a chemical handle to the protein of interest thereby enabling a controlled functionalization. By optimizing key amino acid residues at the protein-intein interface critical for cleavage and culture conditions we increase the total capacity of our system for site-specific protein functionalization. Thus, this body of work presents the discovery and development of brain penetrating antibodies as

potential vectors for drug delivery.
Neurological Disorders World Health Organization 2006 Although there are several gaps in understanding the many issues related to neurological disorders, we know enough to be able to shape effective policy responses to some of the most common. This book describes and discusses the increasing public health impact of common neurological disorders such as dementia, epilepsy, headache disorders, multiple sclerosis, neuroinfections, neurological disorders associated with malnutrition, pain associated with neurological disorders, Parkinson's disease, stroke and traumatic brain injuries. It provides information and advice on public health interventions that may reduce their occurrence and consequences, and offers health professionals and planners the opportunity to assess the burden caused by these disorders. The clear message that emerges is that unless immediate action is taken globally, the neurological burden is likely to become an increasingly serious and unmanageable.
Optimizing the "Drug-Like" Properties of Leads in Drug Discovery Ronald Borchardt 2007-12-31 This book arises from a workshop organized by the American Association of Pharmaceutical Scientists entitled "Optimizing the Drug-Like Properties of Leads in Drug Discovery," which took place in Parsippany, NJ in September 2004. The workshop focused on the optimization of the drug-like properties of leads in drug discovery. The volume outlines strategies and methodologies designed to guide pharmaceutical and biotechnology companies through the drug discovery and development process.
Drug-Like Properties Li Di 2015-12-17 Of the thousands of novel compounds that a drug discovery project team invents and that bind to the therapeutic target, only a fraction have sufficient ADME (absorption, distribution, metabolism, elimination) properties, and acceptable toxicology properties, to become a drug product that will successfully complete human Phase I clinical trials. Drug-Like Properties: Concepts, Structure Design and Methods from ADME to Toxicity Optimization, Second

Edition, provides scientists and students the background and tools to understand, discover, and develop optimal clinical candidates. This valuable resource explores physiochemical properties, including solubility and permeability, before exploring how compounds are absorbed, distributed, and metabolized safely and stably. Review chapters provide context and underscore the importance of key concepts such as pharmacokinetics, toxicity, the blood-brain barrier, diagnosing drug limitations, prodrugs, and formulation. Building on those foundations, this thoroughly updated revision covers a wide variety of current methods for the screening (high throughput), diagnosis (medium throughput) and in-depth (low throughput) analysis of drug properties for process and product improvement. From conducting key assays for interpretation and structural analysis, the reader learns to implement modification methods and improve each ADME property. Through valuable case studies, structure-property relationship descriptions, and structure modification strategies, Drug-Like Properties, Second Edition, offers tools and methods for ADME/Tox scientists through all aspects of drug research, discovery, design, development, and optimization. Provides a comprehensive and valuable working handbook for scientists and students in medicinal chemistry Includes expanded coverage of pharmacokinetics fundamentals and effects Contains updates throughout, including the authors' recent work in the importance of solubility in drug development; new and currently used property methods, with a reduction of seldom-used methods; and exploration of computational modeling methods

Absorption and Drug Development Alex Avdeef 2003-09-19 Many times drugs work fine when tested outside the body, but when they are tested in the body they fail. One of the major reasons a drug fails is that it cannot be absorb by the body in a way to have the effect it was intended to have. Permeability, Solubility, Dissolution, and Charged State of Ionizable Molecules: Helps drug discovery professionals to eliminate poorly

absorbable molecules early in the drug discovery process, which can save drug companies millions of dollars. Extensive tabulations, in appendix format, of properties and structures of about 200 standard drug molecules.

New Approaches to Drug Discovery Ulrich Nielsch 2016-03-30 This volume gives an overview of state of the art technologies and future developments in the field of preclinical pharmaceutical research. A balanced mix of experts from academia and industry give insight in selected new developments in the drug discovery pathway. The topics cover the different parts of the drug discovery process, starting with new developments in the target identification and validation area. The lead generation part as a next step focuses on the requirements and technologies to identify new small molecules as lead compounds for further optimization; in a second section the technologies to identify biologics as leads are addressed. The final part focuses on the pharmacological models and technologies to characterize new compounds and the impact of biomarkers to facilitate the transfer of drug candidates into the development phase.

The Blood-Brain Barrier and Drug Delivery to the CNS Michael Bradbury 2000-05-16 This timely and compact monograph addresses how to determine drug permeability across the blood-brain barrier more effectively. Focusing on the physiological mechanisms that influence the passage of agents into the brain, the book covers the latest research on the blood-brain barrier, the current problems of and solutions to drug delivery to the central nervous system (CNS), existing strategies, and prospects for future research. Avoid excessive in vivo experimentation and utilize timesaving in vitro techniques. A concise reference with reviews from nearly 40 international specialists in diverse fields, The Blood-Brain Barrier and Drug Delivery to the CNS assesses the properties of the blood-brain barrier to determine and measure drug permeability in animals and humans presents techniques to predict successful drug uptake through in vitro systems or by computation of physicochemical parameters

examines the multidrug resistance protein P-glycoprotein as a natural transporter analyzes current drug designs to known requirements for transport looks at drug delivery systems for the brain and much more! Densely packed with over 800 literature references, drawings, photographs, x-rays, tables, and equations, The Blood-Brain Barrier and Drug Delivery to the CNS is a vital addition to the bookshelves of biochemists, pharmacists, clinical and research pharmacologists, neuroscientists and neurologists, and graduate and medical school students in these disciplines.

The ADME Encyclopedia Alan Talevi 2022-05-20 The ADME Encyclopedia covers pharmacokinetic phenomena (Absorption, Distribution, Metabolism and Excretion processes) and their relationship with the design of pharmaceutical carriers and the success of drug therapies. It covers both basic and advanced knowledge, serving as introductory material for students of biomedical careers and also as reference, updated material for graduates and professionals working in any field related to pharmaceutical sciences (medicine, pharmaceutical technology, materials science, medicinal chemistry). Structured as alphabetically ordered entries with cross-references, the Encyclopedia not only provides basic knowledge on ADME processes, but also detailed entries on some advanced subjects such as drug transporters, last generation pharmaceutical carriers, pharmacogenomics, personalized medicine, bioequivalence studies, biowaivers, biopharmaceuticals, gene delivery, pharmacometrics, pharmacokinetic drug interactions or in silico and in vitro assessment of ADME properties

Inflammation and Cancer Bharat B. Aggarwal 2014-05-12 This volume examines in detail the role of chronic inflammatory processes in the development of several types of cancer. Leading experts describe the latest results of molecular and cellular research on infection, cancer-related inflammation and tumorigenesis. Further, the clinical significance of these findings in preventing cancer progression and approaches to treating the

diseases are discussed. Individual chapters cover cancer of the lung, colon, breast, brain, head and neck, pancreas, prostate, bladder, kidney, liver, cervix and skin as well as gastric cancer, sarcoma, lymphoma, leukemia and multiple myeloma.
Nanotechnology Methods for Neurological Diseases and Brain Tumors Yasemin Gürsoy Özdemir 2017-07-14 Nanotechnology Methods for Neurological Diseases and Brain Tumors: Drug Delivery across the Blood-Brain Barrier compiles the latest (and future potential) treatment strategies for brain tumors and neurological diseases, in particular Alzheimer's, Parkinson's and stroke, those that bypass the blood/brain barrier. The current understanding of brain drug delivery and access is discussed in Chapter One, with the next section focusing on the implementation of the nose-to-brain intranasal route in brain-targeted drug delivery. In addition, nanotechnology-based brain drug delivery is covered in Chapter Three. This avenue offers impressive improvement in the treatment of neurological diseases and brain tumors by using bio-engineered systems that interact with biological systems at a molecular level. In Chapter Four, emphasis is placed on the need for brain-targeted experimental models that mimic disease conditions. Final chapters discuss the very latest advances in targeted treatment strategies for neurological diseases and brain tumors. Comprehensive guide for up-to-date views on the latest advances in targeted treatment strategies for brain tumors and neurological diseases Designed with a multidisciplinary approach that links neurology, neuro-oncology and nanoscience to drug delivery to the brain with an emphasis on the blood-brain-barrier Written in a language that makes it easy to understand nanotechnology drug delivery techniques Presents a unique book that also covers advanced treatment approaches of neurological diseases and brain tumors
Blood-Brain Barrier in Drug Discovery Li Di 2015-02-02 Focused on central nervous system (CNS) drug discovery efforts, this book educates drug researchers about the blood-brain barrier

(BBB) so they can affect important improvements in one of the most significant – and most challenging – areas of drug discovery. • Written by world experts to provide practical solutions to increase brain penetration or minimize CNS side-effects • Reviews state-of-the-art in silico, in vitro, and in vivo tools to assess brain penetration and advanced CNS drug delivery strategies • Covers BBB physiology, medicinal chemistry design principles, free drug hypothesis for the BBB, and transport mechanisms including passive diffusion, uptake/efflux transporters, and receptor-mediated processes • Highlights the advances in modelling BBB pharmacokinetics and dynamics relationships (PK/PD) and physiologically-based pharmacokinetics (PBPK) • Discusses case studies of successful CNS and non-CNS drugs, lessons learned and paths to the market

Organotypic Models in Drug Development Monika Schäfer-Korting 2021-03-25 This book provides latest findings in organotypic models in drug development and provides the scientific resonance needed in an emerging field of research in disciplines, such as molecular medicine, physiology, and pathophysiology. Today the research on human-based test systems has gained major interest and funding in the EU and the US has increased over the last years. Moreover, so-called 3R (reduce, replace, refine animal experiments) centres have been established worldwide.

Encyclopedia of Drug Metabolism and Interactions Alexander Lyubimov 2012 This multi-volume, state-of-the-art encyclopedia discusses all preclinical, clinical, toxicological, regulatory and marketing perspectives of drug metabolism and interactions. Methods and detailed protocols describing how to perform studies of metabolism and drug interactions are presented in one of the volumes. All aspects of drug metabolism and interactions in silico, in laboratory animals and in humans, are backed with a range of examples. This reference is essential for researchers interested in all aspects of drug development, and chemists,

pharmacologists, pharmaceutical specialists, toxicologists, molecular toxicologists, and clinicians including practitioners and physicians.

Physiology and Pharmacology of the Blood-Brain Barrier Michael W.B. Bradbury 2012-12-06 The blood-brain barrier is still not completely understood and therefore the subject of fascinating study. How are endogenous substances transported through the blood-brain barrier? What are the known therapeutic and toxic agents? How are they transported across cerebral microvessels? The discussion of these and other questions with far-reaching consequences for all neuroscientists can be found in this volume. This authoritative and up-to-date review of the blood-brain barrier gives a proper understanding of the topic. The experimental principles, the results of very recent research, as well as the implications that experimental research has for clinical treatment are thoroughly covered. Information is given on: - new findings based on classical physiological and pharmacological techniques, - results obtained from brain capillaries in vitro and in culture, - results obtained from the new scanning techniques (PET and MRI), - the immunology of the blood-brain barrier, - trace metal transport, - the pathological breakdown of the barrier and - the modification of drugs to increase their entry into the brain. Here is a source of information that is invaluable to specialists concerned with basic research in the neurosciences, with the design of neuropharmacological agents, with the radiological diagnosis of cerebral pathology or with the treatment of cerebral lesions!

Drug-like Properties Li Di 2016-01-12 Of the thousands of novel compounds that a drug discovery project team invents and that bind to the therapeutic target, only a fraction have sufficient ADME (absorption, distribution, metabolism, elimination) properties, and acceptable toxicology properties, to become a drug product that will successfully complete human Phase I clinical trials. Drug-Like Properties: Concepts, Structure Design and Methods from ADME to Toxicity Optimization, Second

Edition, provides scientists and students the background and tools to understand, discover, and develop optimal clinical candidates. This valuable resource explores physiochemical properties, including solubility and permeability, before exploring how compounds are absorbed, distributed, and metabolized safely and stably. Review chapters provide context and underscore the importance of key concepts such as pharmacokinetics, toxicity, the blood-brain barrier, diagnosing drug limitations, prodrugs, and formulation. Building on those foundations, this thoroughly updated revision covers a wide variety of current methods for the screening (high throughput), diagnosis (medium throughput) and in-depth (low throughput) analysis of drug properties for process and product improvement. From conducting key assays for interpretation and structural analysis, the reader learns to implement modification methods and improve each ADME property. Through valuable case studies, structure-property relationship descriptions, and structure modification strategies, Drug-Like Properties, Second Edition, offers tools and methods for ADME/Tox scientists through all aspects of drug research, discovery, design, development, and optimization. Provides a comprehensive and valuable working handbook for scientists and students in medicinal chemistry Includes expanded coverage of pharmacokinetics fundamentals and effects Contains updates throughout, including the authors' recent work in the importance of solubility in drug development; new and currently used property methods, with a reduction of seldom-used methods; and exploration of computational modeling methods

Brain Drug Targeting William M. Pardridge 2001-05-31 This challenging 2001 book reviews modern neurotherapeutics from the point of view of drug targeting.

Improving and Accelerating Therapeutic Development for Nervous System Disorders Institute of Medicine 2014-02-06 Improving and Accelerating Therapeutic Development for Nervous System Disorders is the summary of a workshop

convened by the IOM Forum on Neuroscience and Nervous System Disorders to examine opportunities to accelerate early phases of drug development for nervous system drug discovery. Workshop participants discussed challenges in neuroscience research for enabling faster entry of potential treatments into first-in-human trials, explored how new and emerging tools and technologies may improve the efficiency of research, and considered mechanisms to facilitate a more effective and efficient development pipeline. There are several challenges to the current drug development pipeline for nervous system disorders. The fundamental etiology and pathophysiology of many nervous system disorders are unknown and the brain is inaccessible to study, making it difficult to develop accurate models. Patient heterogeneity is high, disease pathology can occur years to decades before becoming clinically apparent, and diagnostic and treatment biomarkers are lacking. In addition, the lack of validated targets, limitations related to the predictive validity of animal models - the extent to which the model predicts clinical efficacy - and regulatory barriers can also impede translation and drug development for nervous system disorders. Improving and Accelerating Therapeutic Development for Nervous System Disorders identifies avenues for moving directly from cellular models to human trials, minimizing the need for animal models to test efficacy, and discusses the potential benefits and risks of such an approach. This report is a timely discussion of opportunities to improve early drug development with a focus toward preclinical trials.

Nanomedicines for Brain Drug Delivery Javier O. Morales 2021

Virtual Drug Design Daniela Schuster 2020-01-13 In the current drug research environment in academia and industry, cheminformatics and virtual screening methods are well established and integrated tools. Computational tools are used to predict a compound’s 3D structure, the 3D structure and function of a pharmacological target, ligand-target interactions, binding energies, and other factors essential for a successful drug. This

includes molecular properties such as solubility, logP value, susceptibility to metabolism, cell permeation, blood brain barrier permeation, interaction with drug transporters and potential off-target effects. Given that approximately 40 million unique compounds are readily available for purchase, such computational modeling and filtering tools are essential to support the drug discovery and development process. The aim of all these calculations is to focus experimental efforts on the most promising candidates and exclude problematic compounds early in the project. In this Research Topic on virtual activity predictions, we cover several aspects of this research area such as historical perspectives, data sources, ligand treatment, virtual screening methods, hit list handling and filtering.

An Introduction to Deep Reinforcement Learning Vincent Francois-Lavet 2018-12-20 Deep reinforcement learning is the combination of reinforcement learning (RL) and deep learning. This field of research has recently been able to solve a wide range of complex decision-making tasks that were previously out of reach for a machine. Deep RL opens up many new applications in domains such as healthcare, robotics, smart grids, finance, and many more. This book provides the reader with a starting point for understanding the topic. Although written at a research level it provides a comprehensive and accessible introduction to deep reinforcement learning models, algorithms and techniques. Particular focus is on the aspects related to generalization and how deep RL can be used for practical applications. Written by recognized experts, this book is an important introduction to Deep Reinforcement Learning for practitioners, researchers and students alike.

Ketogenic Diet and Metabolic Therapies Susan A. Masino 2016-10-14 Ketogenic diets have been used to successfully treat epilepsy and stop seizures for nearly a century. When more traditional therapies, such as pharmacology, reach their limitations for treatment, the metabolic approach surpasses, targeting the overall physiology and homeostatic functions of the

patient. Ketogenic Diet and Metabolic Therapies is the first comprehensive scientific resource on the ketogenic diet, covering the latest research including the biomedical mechanisms, established and emerging applications, metabolic alternatives, and implications for health and disease. Experts in clinical and basic research share their research into mechanisms spanning from ion channels to epigenetics, their insights based on decades of experience with the ketogenic diet in epilepsy, and their evidence for emerging applications ranging from autism to Alzheimer's disease to brain cancer. Research in metabolic therapies has spread into laboratories and clinics of every discipline, and is yielding to entirely new classes of drugs and treatment regimens. The book's editor, Susan A. Masino, brings her unique expertise in clinical and research neurology to the overall scope of this work. To further enhance the scope and quality of this one of a kind book, section editors Eric Kossoff, Jong Rho, Detlev Boison, and Dominic P. D'Agostino lend their oversight on their respective sections.

Advances in Neuropharmacology Md. Sahab Uddin 2020-01-31 Here is a comprehensive overview of the drugs that act on the central and peripheral nervous systems. This volume thoroughly describes the diseases associated with the nervous system and the drugs used for their treatment while also looking at the current status of these drugs and their future potential and challenges. Divided into three sections, the book first focuses on the drugs that affect the functions of the autonomic nervous system to produce therapeutic effects. These drugs may act presynaptically by manipulating the genesis, storage, and secretion, and by blocking the action of neurotransmitters. Some drugs may trigger or impede postsynaptic receptors. Section 2 focuses on drugs that affect the central nervous system, including antianxiety drugs, sedative and hypnotic drugs, antidepressant drugs, antipsychotic drugs, antiepileptic drugs, and many more. It covers the pharmacological management of various diseases, including Alzheimer’s, Parkinson’s,

Huntington's, and others. The last section offers explanations of neurochemical interactions with the aim to develop drugs that have beneficial effects on neurochemical imbalances. This section demonstrates models to assess the transport of drugs across the blood-brain barrier and nanomedicine to treat brain disorders. This rich compilation provides thorough and extensive research updates on the important advances in neuropharmacological drugs and drug therapy from experienced and eminent academicians, researchers, and scientists from throughout the world.

Pharmacokinetic Challenges in Drug Discovery O. Pelkonen 2013-03-09 Despite increased spending on research and development, the number of new medicines marketed successfully continues to decline. The Pharmaceutical industry is therefore focussing on ways to reduce attrition by addressing frequent reasons for clinical drug failures very early in the drug discovery process. One of the biggest challenges is the pharmacokinetic (PK) optimisation of drug candidates tailored and predicted to have appropriate absorption, distribution, metabolism and excretion (ADME) characteristics in human. This book describes how traditional pbarmacokinetic approaches and methods are being re-invented' to meet specific needs dictated by the dynamics of the drug discovery process. The book gives an overview of state-of-the-art tools and their use in the decision-making process is discussed by a number of scientists from leading pharmaceutical companies.

Solubility, Delivery and ADME Problems of Drugs and Drug Candidates Karoly Karoly Tihanyi 2011-09-20 "This comprehensive ebook covers all the aspects of ADME/PK modeling including solubility, absorption, formulation, metabolic stability, drug-drug interaction potential and a special delivery tool of drug candidates. The book provides an integrated view of"

Retrometabolic Drug Design and Targeting Nicholas Bodor 2012-08-29 Innovative approach to drug design that's more likely to result in an approvable drug product Retrometabolic drug design

incorporates two distinct drug design approaches to obtain soft drugs and chemical delivery systems, respectively. Combining fundamentals with practical step-by-step examples, Retrometabolic Drug Design and Targeting gives readers the tools they need to take full advantage of retrometabolic approaches in order to develop safe and effective targeted drug therapies. The authors, both pioneers in the fields of soft drugs and retrometabolic drug design, offer valuable ideas, approaches, and solutions to a broad range of challenges in drug design, optimization, stability, side effects, and toxicity. Retrometabolic Drug Design and Targeting begins with an introductory chapter that explores new drugs and medical progress as well as the challenges of today's drug discovery. Next, it discusses: Basic concepts of the mechanisms of drug action Drug discovery and development processes Retrometabolic drug design Soft drugs Chemical delivery systems Inside the book, readers will find examples from different pharmacological areas detailing the rationale for each drug design. These examples set forth the relevant pharmacokinetic and pharmacodynamic properties of the new therapeutic agents, comparing these properties to those of other compounds used for the same therapeutic purpose. In addition, the authors review dedicated computer programs that are available to support and streamline retrometabolic drug design efforts. Retrometabolic Drug Design and Targeting is recommended for all drug researchers interested in employing this newly tested and proven approach to developing safe and effective drugs.
Prodrugs Valentino Stella 2007-03-12 These volumes represent a comprehensive guide to prodrugs. They guide the reader through the current status of the prodrug concept and its many applications and highlight its many successes in overcoming formulation and delivery of problematic drugs. Replete with examples of approved and marketed prodrugs, these volumes introduce the topic to the novice as well as professional in the

design of prodrugs.
Drug-like Properties: Concepts, Structure Design and Methods Li Di 2010-07-26 Of the thousands of novel compounds that a drug discovery project team invents and that bind to the therapeutic target, typically only a fraction of these have sufficient ADME/Tox properties to become a drug product. Understanding ADME/Tox is critical for all drug researchers, owing to its increasing importance in advancing high quality candidates to clinical studies and the processes of drug discovery. If the properties are weak, the candidate will have a high risk of failure or be less desirable as a drug product. This book is a tool and resource for scientists engaged in, or preparing for, the selection and optimization process. The authors describe how properties affect in vivo pharmacological activity and impact in vitro assays. Individual drug-like properties are discussed from a practical point of view, such as solubility, permeability and metabolic stability, with regard to fundamental understanding, applications of property data in drug discovery and examples of structural modifications that have achieved improved property performance. The authors also review various methods for the screening (high throughput), diagnosis (medium throughput) and in-depth (low throughput) analysis of drug properties. * Serves as an essential working handbook aimed at scientists and students in medicinal chemistry * Provides practical, step-by-step guidance on property fundamentals, effects, structure-property relationships, and structure modification strategies * Discusses improvements in pharmacokinetics from a practical chemist's standpoint
Drug Delivery to the Brain Margareta Hammarlund-Udenaes 2013-12-03 The development of new CNS drugs is notoriously difficult. Drugs must reach CNS target sites for action and these sites are protected by a number of barriers, the most important being the blood –brain barrier (BBB). Many factors are therefore critical to consider for CNS drug delivery, e.g. active/passive transport across the BBB, intra-brain distribution, and central/systemic pharmacokinetics, to name a few. Neurological

disease and trauma conditions add further complexity because CNS barriers, drug distribution and pharmacokinetics are dynamic and often changed by disease/trauma. Knowledge of all these factors and their interplay in different conditions is of utmost importance for proper CNS drug development and disease treatment. In recent years much information has become available for a better understanding of the many factors important for CNS drug delivery and how they interact to affect drug action. This book describes small and large drug delivery to the brain with an emphasis on the physiology of the BBB and the principles and concepts for drug delivery across the BBB and distribution within the brain. It contains methods descriptions for studying drug delivery, routes and approaches of administering drugs into the brain, the influence of disease, and drug industry perspectives. Therewith, it contributes to an in-depth understanding of the interplay between brain (patho)-physiology and drug characteristics. Furthermore, the content is designed to be both cutting-edge and educational, so that the book can be used in high-level training of academic and industry scientists with full references to original publications. ?

Brain Targeted Drug Delivery Systems Huile Gao 2018-09-20

Brain Targeted Drug Delivery Systems: A Focus on Nanotechnology and Nanoparticulates provides a guide on nanoparticulates to both academic and industry researchers. The book discusses key points in the development of brain targeted drug delivery, summarizes available strategies, and considers the main problems and pitfalls evidenced in current studies on brain targeted drug delivery systems. As the brain is the most important organ in the human body, and disorders of the central nervous system (CNS) are the most serious threat to human life, this book highlights advances and new research in drug delivery methods to the brain. Provides an overview of brain targeting drug delivery that is useful to both academic and industry-based researchers Discusses key points in developing brain targeting drug delivery systems Summarizes and presents currently

available strategies for brain targeting drug delivery Covers not only current studies and their strengths, but also gives insight into the pitfalls of current research

The Blood Brain Barrier (BBB) Gert Fricker 2014-10-24 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.

The Medicinal Chemist's Guide to Solving ADMET Challenges Patrick Schnider 2021-08-20 The Medicinal Chemist’s Guide to Solving ADMET Challenges summarizes a series of design strategies and tactics that have been successfully employed across pharmaceutical and academic laboratories to solve common ADMET issues. These are exemplified with a curated collection of concrete examples displayed in a highly visual “table-of-contents” style format, allowing readers to rapidly identify the most promising approaches applicable to their own challenges. Each ADMET parameter is introduced in a concise yet comprehensive manner and includes background, relevance and

screening strategies. Medicinal chemistry knowledge of how best to modify molecular structure to solve ADMET issues is challenging to retrieve from the literature, public databases and even corporate data warehouses. The Medicinal Chemist's Guide to Solving ADMET Challenges addresses this gap by presenting state-of-the-art design strategies put together by a global group of experienced medicinal chemists and ADMET experts across academia and the pharmaceutical industry.
Pharmacokinetic Optimization in Drug Research Bernard Testa 2001-03-26 In this age of combinatorial chemistry and high-throughput technologies, bioactive compounds called hits are discovered by the thousands. However, the road that leads from hits to lead compounds and then to pharmacokinetically optimized clinical and drug candidates is very long indeed. As a result, the screening, design, and optimization of pharmacokinetic properties has become the bottleneck and a major challenge in drug research. To shorten the time-consuming develop-ment and high rate of attrition of active compounds ultimately doomed by hidden pharmacokinetic defects, drug researchers are coming to incorporate structure-permeation, structure-distribution, structure-metabolism, and structure-toxicity relations into drug-design strategies. To this end, powerful biological, physicochemical, and computational approaches are being developed whose objectives are to increase the clinical relevance of drug design, and to eliminate as soon as possible compounds with unfavorable physicochemical properties and pharmacokinetic profiles. Toxicological issues are also of utmost importance in this paradigm. There was, hence, an urgent need for a book covering this field in an authoritative, didactic, comprehensive, factual, and conceptual manner. In this work of unique breadth and depth, international authorities and practicing experts from academia and industry present the most modern biological, physicochemical, and computational strategies to optimize gastrointestinal absorption, protein binding and distribution, brain permeation, and metabolic profile. The biological strategies

emphasized in the book include cell cultures and high-throughput screens. The physicochemical strategies focus on the determination and interpretation of solubility, lipophilicity, and related molecular properties as factors and predictors of pharmacokinetic bahavior. Particular attention is paid to the lipophilicity profiles of ionized compounds, to lipophilicity measurements in anisotropic media (liposomes/water, IAM columns), and to permeability across artificial membranes. Computational strategies comprise virtual screening, molecular modelling, lipophilicity, and H-bonding fields and their importance for structure-disposition relations. This book is both about theoretical and technological breakthroughs. Thus, molecular properties are contemplated from a dual perspective, namely a) their interpretation in biological and/or physicochemical terms, and b) their value in screening, lead optimization, and drug-candidate selection. In addition to its 33 chapters, the book includes a CD-ROM containing the invited lectures, oral communications and posters (in full version) presented at the Second LogP Symposium, 'Lipophilicity in Drug Disposition—Practical and Computational Approaches to Molecular Properties Related to Drug Permeation, Disposition and Metabolism', held at the University of Lausanne in March 2000.

Nanomedicines for Brain Drug Delivery Javier O. Morales 2021-12-04 This volume explores the latest research in central nervous system (CNS) targeted nanocarriers, methods for their synthesis, and its characterization process. Chapters in this book cover topics such as polymeric nanoparticles and liposomes; self-assembled peptide-based scaffolds for lesions of the nervous system; use of peptides as CNS drugs and as potential carriers to optimize brain-targeted delivery; ways to model and assess blood brain barrier absorption of drugs; and the role of neurodegeneration progress of nanomaterials and their potential toxicity concerns. In the Neuromethods series style, chapters include the kind of detail and key advice from the specialists

needed to get successful results in your laboratory. Thorough and cutting-edge, Nanomedicines for Brain Drug Delivery is a valuable resource that will help researchers guide and advance the field of nanomedicines for the brain and nervous system.