

## Discovery And Characterization Of Verinurad A Potent And

Concise and clinically focused, Gout, by Drs. Naomi Schlesinger and Peter E. Lipsky, provides a one-stop overview of recent developments regarding this common form of inflammatory arthritis. Impacting an estimated 8.3 million people in the U.S. alone, gout is seen frequently by both primary care physicians as well as rheumatologists. This resource provides detailed coverage of the epidemiology, causes, diagnosis, management, and treatment of patients with both acute and chronic gout. Addresses key topics such as genetics, hyperuricemia, comorbidities of gout, treatment guidelines for acute and chronic gout, classification and diagnosis, and imaging. Discusses future outlooks for improving pharmacological and nonpharmacological treatment options, including an overview of drugs in the pipeline. Consolidates today's available information on this timely topic into one convenient resource.

Reviews of Environmental Contamination and Toxicology attempts to provide concise, critical reviews of timely advances, philosophy and significant areas of accomplished or needed endeavor in the total field of xenobiotics, in any segment of the environment, as well as toxicological implications.

Exploration of stochastic control theory in terms of analysis, parametric optimization, and optimal stochastic control. Limited to linear systems with quadratic criteria; covers discrete time and continuous time systems. 1970 edition.

GoutElsevier Health Sciences

Aquaporin Regulation, Volume 112, the latest release in the Vitamins and Hormones series, highlights new advances in the field, with this new volume presenting interesting chapters highlighting Perspectives on the evolution of aquaporin superfamily, Structure and dynamics of aquaporin-1, Selectivity and Transport in Aquaporins from Molecular Simulation Studies, Aquaporin regulation in metabolic organs, Phosphorylation of human AQP2 and its role in trafficking, Regulation of Aquaporin-2 by RNA Interference, Aquaporin Regulation: Lessons from Secretory Vesicles, CFTR Regulation of Aquaporin-mediated Water Transport, Glucocorticoid Gene Regulation of Aquaporin-7, and much more. Provides the authority and expertise of leading contributors from an international board of authors Presents the latest release in the Vitamins and Hormones series Updated release includes the latest information on aquaporin regulation This book aims to guide and inspire drug researchers as they enter the 21st century. Stereochemistry is an essential dimension in pharmacology and should

be understood as such by all drug researchers whatever their background. When used as probes or medicines, stereoisomeric drugs offer invaluable insights or innovative therapeutic strategies. The book spans the subject from the molecular to the clinical. The first section on chemical aspects contains chapters on chemical synthesis, analysis, natural products, chiral stability (racemization) and physical properties. The second section is on experimental pharmacology, with chapters on drug-receptor interactions, chiral recognition, ion channels, and molecular toxicology. The third section focuses on drug disposition, with chapters on absorption, distribution, protein binding, metabolism and elimination. The final section is dedicated to regulatory and clinical aspects.

This issue of Clinics in Laboratory Medicine, Guest Edited by Nigel Clarke, MD, and Andrew Hoofnagle, MD, will focus on Mass Spectrometry, with topics including: Proteins; Peptides; Small Molecules: Toxicology; Small Molecules: Diagnostics; and Regulatory Considerations.

Paediatric Rheumatology is an indispensable resource for the identification and management of specific rheumatological disorders. As well as covering common and rare rheumatological problems, there are also chapters on investigations and emergencies, designed for quick reference. The handbook includes dedicated topics on systemic diseases affecting rheumatology; the relevant clinical

guidelines and information needed for a rheumatologist to successfully management a young patient; and, a coloured section for guidance on rash-related investigations. Paediatric Rheumatology is also fully endorsed by the British Society for Paediatric and Adolescent Rheumatology and the UK Paediatric Rheumatology Clinical Studies Group.

Almost six decades after its discovery, metformin still remains the gold standard drug for the management of type 2 diabetes mellitus, owing to its euglycemic property and cost-effectiveness. It is the most commonly prescribed and utilized oral antidiabetic drug worldwide. However, no two persons with the same phenotypical characteristics, such as age, gender, body weight and others, tend to respond similarly to equivalent doses of metformin. As such, The Pharmacological Guide to Metformin first focuses on the various genetic polymorphisms that influence the therapeutic effects of metformin. Physicochemical, pharmacological, and pharmacokinetic properties of metformin will also be reviewed. The side effects of this drug can be dangerous. Metformin-induced lactic acidosis is a lethal disorder. The first significant deviation is gastrointestinal tract involvement. Common infection or the effect of metformin itself causes vomiting and diarrhea, with subsequent hypovolemia causing pre-renal acute kidney injury, which in turn raises metformin levels up to toxic values. Development of kidney failure is often unexpected and fast. Following this, the authors explore the differences between healthy and cancer cells and how this may influence the metformin effect on these cells. In conclusion, the molecular mechanisms underlying the anticancer effects of metformin in breast and ovarian cancers are summarized, and the potential anticancer applications of

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metformin-based combinatorial chemotherapy are discussed.

This volume is an up-to-date examination of pediatric rheumatology, a relatively new and rapidly growing specialty. It includes information from expert contributors in the field, concentrating on recent advances and clinical studies, as well as possible future directions. The book is unique for its international perspective, is the most up-to-date work of its kind, and is an ideal guide for pediatricians, rheumatologists, immunologists, orthopedic surgeons, and ophthalmologists who need to keep up with the recent surge of research in this area.

*Plant-Based Functional Foods and Phytochemicals: From Traditional Knowledge to Present Innovation* covers the importance of the therapeutic health benefits of phytochemicals derived from plants. It discusses the isolation of potential bioactive molecules from plant sources along with their value to human health. It focuses on physical characteristics, uniqueness, uses, distribution, traditional and nutritional importance, bioactivities, and future trends of different plant-based foods and food products. Functional foods, beyond providing basic nutrition, may offer a potentially positive effect on health and cures for various disease conditions, such as metabolic disorders (including diabetes), cancer, and chronic inflammatory reactions. The volume looks at these natural products and their bioactive compounds that are increasingly utilized in preventive and therapeutic medications and in the production of pharmaceutical supplements and as food additives to increase functionality. It also describes the concept of extraction of bioactive molecules from plant sources, both conventional and modern extraction techniques, available sources, biochemistry, structural composition, and potential biological activities.

This book brings together the theoretical, commercial, and practical aspects of chirality and

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biological activity of drugs and acts as a ready reference for the effects of enantiomers of drug substances.

Based on topics presented at the Annual Japanese (Quantitative) Structure-Activity Relationship Symposium and the Biennial China-Japan Drug Design and Development conference, the topics in this volume cover almost every procedure and subdiscipline in the SAR discipline. They are categorized in three sections. Section one includes topics illustrating newer methodologies relating to ligand-receptor, molecular graphics and receptor modelling as well as the three-dimensional (Q)SAR examples with the active analogue approach and the comparative molecular field analysis. In section 2 the hydrophobicity parameters,  $\log P$  (1-octanol/water) for compound series of medicinal-chemical interest are analysed physico-organic chemically. Section 3 contains the examples based on the traditional Hansch QSAR approach. A variety of methodologies and procedures are presented in this single volume, along with their methodological philosophies.

Fundamentals of Renal Pathology is a compact and up-to-date resource on the basics of renal pathology that will be of particular value for residents and fellows in training in renal pathology, general pathology, and nephrology, but will also serve as a handy reference for the more experienced. This second, revised and updated edition of the book offers an integrated approach based on contributions from established experts in the field. Key diseases are discussed within the context of clinical presentations, with the emphasis on clinicopathological correlation and differential diagnosis. Topics discussed include glomerular diseases with nephrotic or nephritic syndrome presentations; systemic and vascular diseases affecting the kidney, including diseases affecting the renal transplant; tubulointerstitial diseases; and plasma

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cell dyscrasias and associated diseases. Well-chosen color illustrations and electron micrographs enhance and complement the text.

Following significant advances in deep learning and related areas interest in artificial intelligence (AI) has rapidly grown. In particular, the application of AI in drug discovery provides an opportunity to tackle challenges that previously have been difficult to solve, such as predicting properties, designing molecules and optimising synthetic routes. Artificial Intelligence in Drug Discovery aims to introduce the reader to AI and machine learning tools and techniques, and to outline specific challenges including designing new molecular structures, synthesis planning and simulation. Providing a wealth of information from leading experts in the field this book is ideal for students, postgraduates and established researchers in both industry and academia.

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for being an important part of keeping this knowledge alive and relevant.

This book provides a comprehensive overview of the unique challenges inherent in pediatric kidney transplantation. The text reviews the problems faced during each stage of the kidney transplantation process, including the occurrence of infections during the pre-transplant stage, surgical challenges during the actual transplantation, and medication issues during the post-transplant stage. The book also features high-yield case presentations of typical pediatric transplant scenarios, from the pre-transplant management of a child with CAKUT to the evaluation and treatment of antibody mediated rejection in children. Written by experts in the field, *Challenges in Pediatric Kidney Transplantation: A Practical Guide* is a valuable resource for clinicians, practitioners, and trainees who manage or are interested in this challenging group of patients. .

This book provides practical guidance for statisticians, clinicians, and researchers involved in clinical trials in the biopharmaceutical industry, medical and public health organisations. Academics and students needing an introduction to handling missing data will also find this book invaluable. The authors describe how missing data can affect the outcome and credibility of a clinical trial, show by examples how a clinical team can work to prevent missing data, and present the reader with approaches to address missing data effectively. The book is

illustrated throughout with realistic case studies and worked examples, and presents clear and concise guidelines to enable good planning for missing data. The authors show how to handle missing data in a way that is transparent and easy to understand for clinicians, regulators and patients. New developments are presented to improve the choice and implementation of primary and sensitivity analyses for missing data. Many SAS code examples are included – the reader is given a toolbox for implementing analyses under a variety of assumptions.

Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals. For the treatment of human diseases, nasal and pulmonary routes of drug delivery are gaining increasing importance. These routes provide promising alternatives to parenteral drug delivery particularly for peptide and protein therapeutics. Drugs have long been used to improve health and extend lives. Biomedical engineers have not only contributed substantially to our understanding of the physiological barriers to efficient drug delivery -- such as transport in the circulatory system and drug movement through cells and tissues -- they have contributed to the development of a number of new modes of drug delivery that have entered clinical practice. This book covers the physiological barriers controlling penetration and transport of substances in the body, strategies for drug

penetration across tissue compartments, and drug transport into cells and their compartments. It provides an overview of the current advances in this field, including considerations on the biological regulation and natural mechanisms overcoming these barriers, as well as drug delivery strategies assisting the transport of drugs and their carriers at the tissue, cell, and subcellular levels. The recent progress of nano drug delivery systems in breaking the physiological barriers for more effective in vivo anti-tumour effect, in order to shed a new perspective on the development of tumor-targeted nano drug delivery systems are reviewed. For any therapeutic agent to be effective, it must accumulate in target cells in optimal concentrations for a required duration of time.

Unfortunately, physicochemical and physiological barriers can lead to heterogeneous accumulation of various therapeutic molecules, particles, and cells in solid tumors. In a disease such as cancer, failure to treat a small fraction of cells can result in tumor regrowth. Thus, it is crucial to know which cells have been successfully treated and which have not. To determine this, high-resolution imaging of drug distribution and its physiological determinants is essential. Only with this knowledge can we improve drug delivery to all regions of a tumour. This handbook provides a comprehensive insight into how imaging techniques should be applied to particular clinical problems and how the results can be used

to determine the diagnosis and management of musculoskeletal conditions. Human Evolutionary Genetics is a groundbreaking text which for the first time brings together molecular genetics and genomics to the study of the origins and movements of human populations. Starting with an overview of molecular genomics for the non-specialist (which can be a useful review for those with a more genetic background), the book shows h

Wild Plants, Mushrooms and Nuts: Functional Properties and Food Applications is a compendium of current and novel research on the chemistry, biochemistry, nutritional and pharmaceutical value of traditional food products, namely wild mushrooms, plants and nuts, which are becoming more relevant in diets, and are especially useful for developing novel health foods and in modern natural food therapies. Topics covered will range from their nutritional value, chemical and biochemical characterization, to their multifunctional applications as food with beneficial effects on health, though their biological and pharmacological properties (antioxidant, antibacterial, antifungal, antitumor capacity, among others).

Pharmacogenomics supports personalized medicine by translating genome-based knowledge into clinical practice, offering enhanced benefit for patients and health-care systems at large. Current routine practice for diagnosing and treating

patients is conducted by correlating parameters such as age, gender and weight with risks and expected treatment outcomes. In the new era of personalized medicine the healthcare provider is equipped with improved ability to prevent, diagnose, treat and predict outcomes on the basis of complex information sources, including genetic and genomic data. Targeted therapy and reliable prediction of expected outcomes offer patients access to better healthcare management, by way of identifying the therapies effective for the relevant patient group, avoiding prescription of unnecessary treatment and reducing the likelihood of developing adverse drug reactions.

Presenting a wide-ranging view of current developments in protein research, the papers in this collection, each written by highly regarded experts in the field, examine various aspects of protein structure, functions, dynamics, and experimentation. Topics include dynamical simulation methods, the biological role of atom fluctuations, protein folding, influences on protein dynamics, and a variety of analytical techniques, such as X-ray diffraction, vibrational spectroscopy, photodissociation and rebinding kinetics. This is part of a series devoted to providing general information on a wide variety of topics in chemical physics in order to stimulate new research and to serve as a text for beginners in a particular area of chemical physics.

The Horizon Scientific Press titles focus on high-level microbiology and molecular biology topics. Written by internationally renowned and highly respected leaders in the field, titles in this series comprise of review manuals, practical manuals, and reference texts for research scientists, bioscience professionals and graduate students. Engineering living cells continues to pose immense challenges to the researcher. In fact many bioengineers have only just started to appreciate the full extent of the hierarchical control used by living systems: upon attempts to increase the activity of a "rate-limiting" step, the multiple feedbacks at the metabolic, signaling and genetic levels result in the rate limiting step shifting to elsewhere in that pathway or even to elsewhere in the whole organism. The advent of full-force genomics should enable preventing this response, however, it has been difficult for researchers to know where to turn for guidance. This book aims to help the reader understand and deal with the plasticity of living cell factories and to turn the plasticity into the desired rather than the adverse direction. The book brings together all the recent, most important breakthroughs in this exciting field: Internationally renowned key scientists have reviewed each topic in detail. In the Introduction, the editors give an overview of new approaches and spell out what the engineer and the industry may now really begin to aim for; they even adapt the definition of metabolic engineering to benefit

the post-genomics era. Other topics included are: the experimental approaches necessary to understand cellular regulation at all of its hierarchical levels, including proteomics [Chapter 2], metabolomics [Chapter 3] and fluxomics [Chapter 4]; new tools that help metabolic engineering [Chapters 5-7]; modeling of living cells, e.g. finding metabolic pathways [Chapter 8] and comparing the actual and predicted use of these in living organisms such as *E. coli* and *Corynebacteria* [Chapters 9, 10]; the optimization of cell factories as production organisms (e.g., use of whole cell models, silicon cells, and coordinate manipulation of multiple genes [Chapters 12-15]). A chapter on future perspectives directs further developments of the field in the near future. *Metabolic Engineering in the Post Genomic Eras* is an essential reading for everyone with an interest in engineering living cells including: Metabolic engineers, bioengineers, biotechnologists, molecular biologists, and pharmaceutical and biotechnology companies. Transport of pharmaceutical agents in the body is paramount to therapeutic efficacy. Advances in the past decades have rendered a remarkable improvement of drug delivery strategies, which has helped to increase the bioavailability of therapeutic agents by protecting them from degradation, targeting them to diseased sites, and controlling their circulation time and release

rate. Additionally, for most therapeutics, reaching the targets of action require penetration across tissues and/or entry within cells. The design of strategies to control the transport of therapeutic compounds through these physiological barriers has become an imperative and a challenging need in the quest for better therapeutics. This book provides an overview of the current advances in this field, including considerations on the biological regulation and natural mechanisms overcoming these barriers, as well as drug delivery strategies facilitating the transport of drugs and their carriers at the tissue, cell, and subcellular levels. Pharmacometrics is the science of interpreting and describing pharmacology in a quantitative fashion. The pharmaceutical industry is integrating pharmacometrics into its drug development program, but there is a lack of and need for experienced pharmacometricians since fewer and fewer academic programs exist to train them. Pharmacometrics: The Science of Quantitative Pharmacology lays out the science of pharmacometrics and its application to drug development, evaluation, and patient pharmacotherapy, providing a comprehensive set of tools for the training and development of pharmacometricians. Edited and written by key leaders in the field, this flagship text on pharmacometrics: Integrates theory and practice to let the reader apply principles and concepts. Provides a comprehensive set of tools for training and developing expertise in the

pharmacometric field. Is unique in including computer code information with the examples. This volume is an invaluable resource for all pharmacometricians, statisticians, teachers, graduate and undergraduate students in academia, industry, and regulatory agencies.

This monograph has been written to demonstrate to organic chemists and graduate students the strategies for controlling stereochemistry in carbon-carbon bond formations with borane intermediates. The boranes were initially found to be useful reagents by Nobel Laureate H.C. Brown. Their precursors are commercially available and derivatization is fast, clean and simple.

Axially Chiral Compounds Explore this comprehensive and current volume summarizing the characteristics, synthesis, and applications of axial chirality. Appearing widely in natural products, biologically active molecules, asymmetric chemistry, and material science, axially chiral motifs constitute the core backbones of the majority of chiral ligands and organocatalysts in asymmetric catalysis. In a new work of particular relevance to synthetic chemists, Axially Chiral Compounds: Asymmetric Synthesis and Applications delivers a clearly structured and authoritative volume covering the classification, characteristics, synthesis, and applications of axial chirality. A must read for every synthetic chemist practicing today, the book follows the development history, research

status, and applications of axial chirality. An introductory chapter familiarizes the reader with foundational material before the distinguished authors describe the different classes and the synthesis of axial chiral compounds used in asymmetric synthesis. The book concludes with a focus on the applications of chiral ligands, chiral catalysts, and materials. Readers will also benefit from the inclusion of: A thorough introduction to asymmetric synthesis, including biaryls atropisomers, heterobiaryls atropisomers, and non-biaryls atropisomers Explorations of chiral allene, spiro skeletons, and natural products Practical discussions of asymmetric transformation, chiral ligands, and chiral catalysts An examination of miscellaneous applications of axially chiral compounds Perfect for organic chemists, chemists working with or on organometallics, catalytic chemists, and materials scientists, Axially Chiral Compounds: Asymmetric Synthesis and Applications will also earn a place in the libraries of natural products chemists who seek a one-stop reference for compounds exhibiting axial chirality. Synthetic Methods in Drug Discovery Volume 1 focusses on the hugely important area of transition metal mediated methods used in industry. Current methods of importance such as the Suzuki-Miyaura coupling, Buchwald-Hartwig couplings and CH activation are discussed. In addition, exciting emerging areas such as decarboxylative coupling, and the uses of iron and nickel in coupling reactions

are also covered. This book provides both academic and industrial perspectives on some key reactions giving the reader an excellent overview of the techniques used in modern synthesis. Reaction types are conveniently framed in the context of their value to industry and the challenges and limitations of methodologies are discussed with relevant illustrative examples. Edited and authored by leading scientists from both academia and industry, this book will be a valuable reference for all chemists involved in drug discovery as well as postgraduate students in medicinal chemistry.

In the last decade there have been numerous advances in the area of rhodium-catalyzed hydroformylation, such as highly selective catalysts of industrial importance, new insights into mechanisms of the reaction, very selective asymmetric catalysts, in situ characterization and application to organic synthesis. The views on hydroformylation which still prevail in the current textbooks have become obsolete in several respects. Therefore, it was felt timely to collect these advances in a book. The book contains a series of chapters discussing several rhodium systems arranged according to ligand type, including asymmetric ligands, a chapter on applications in organic chemistry, a chapter on modern processes and separations, and a chapter on catalyst preparation and laboratory techniques. This book concentrates on highlights, rather than a

concise review mentioning all articles in just one line. The book aims at an audience of advanced students, experts in the field, and scientists from related fields. The didactic approach also makes it useful as a guide for an advanced course.

This one-stop reference systematically covers key aspects in early drug development that are directly relevant to the discovery phase and are required for first-in-human studies. Its broad scope brings together critical knowledge from many disciplines, ranging from process technology to pharmacology to intellectual property issues. After introducing the overall early development workflow, the critical steps of early drug development are described in a sequential and enabling order: the availability of the drug substance and that of the drug product, the prediction of pharmacokinetics and -dynamics, as well as that of drug safety. The final section focuses on intellectual property aspects during early clinical development. The emphasis throughout is on recent case studies to exemplify salient points, resulting in an abundance of practice-oriented information that is usually not available from other sources. Aimed at medicinal chemists in industry as well as academia, this invaluable reference enables readers to understand and navigate the challenges in developing clinical candidate molecules that can be successfully used in phase one clinical trials.

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This is the first book to examine the future opportunities and challenges in the development of drugs which target kinases

AMPK has emerged as an important integrator of signals that control energy balance through the regulation of multiple biochemical pathways in eukaryotes. This book focuses on the implications of AMPK as a master metabolic regulator in diseases, including new methods and animal models. The contributions are written by leading experts in the field and give an extensive overview of the current knowledge of AMPK biology and the role of AMPK in health and disease.

This issue of Heart Failure Clinics examines co-morbidities in patients with heart failure. Topics include hypertension, diabetes, pulmonary disorders, cardiorenal syndrome, anemia, depression, atrial fibrillation, obesity and cardiac cachexia, peripheral vascular disease, rheumatologic disorders, co-morbidities and polypharmacy, coronary artery disease, and clinical trials.

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.

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This book illustrates, in a comprehensive manner, the most crucial principles involved in pharmacology and allied sciences. The title begins by discussing the historical aspects of drug discovery, with up to date knowledge on Nobel Laureates in pharmacology and their significant discoveries. It then examines the general pharmacological principles - pharmacokinetics and pharmacodynamics, with in-depth information on drug transporters and interactions. In the remaining chapters, the book covers a definitive collection of topics containing essential information on the basic principles of pharmacology and how they are employed for the treatment of diseases. Readers will learn about special topics in pharmacology that are hard to find elsewhere, including issues related to environmental toxicology and the latest information on drug poisoning and treatment, analytical toxicology, toxicovigilance, and the use of molecular biology techniques in pharmacology. The book offers a valuable resource for researchers in the fields of pharmacology and toxicology, as well as students pursuing a degree in or with an interest in pharmacology.

The idea that the immune system may play a role in protecting against malignant disease is not new. Since the earliest days of immunology research, scientists have sought to understand the mechanisms by which the host immune system might recognise cancer cells, and to manipulate these responses for therapeutic gain. It has become clear that the key to immune recognition of tumours lies in the relationship between cells in the microenvironment of the tumour itself. This volume provides a

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comprehensive collection of techniques for establishing tumour cell lines, testing their immunogenicity, and characterising the major effector cells, leading to protocols for manipulating antibody and T-cell receptor structure, preparing cytokine-secreting tumour cells and testing the efficiency of these new agents in preventing tumour growth. Researchers in immunology as a whole in addition to those interested in cancer immunology will find *Tumour Immunobiology: A Practical Approach* to be an invaluable practical resource.

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