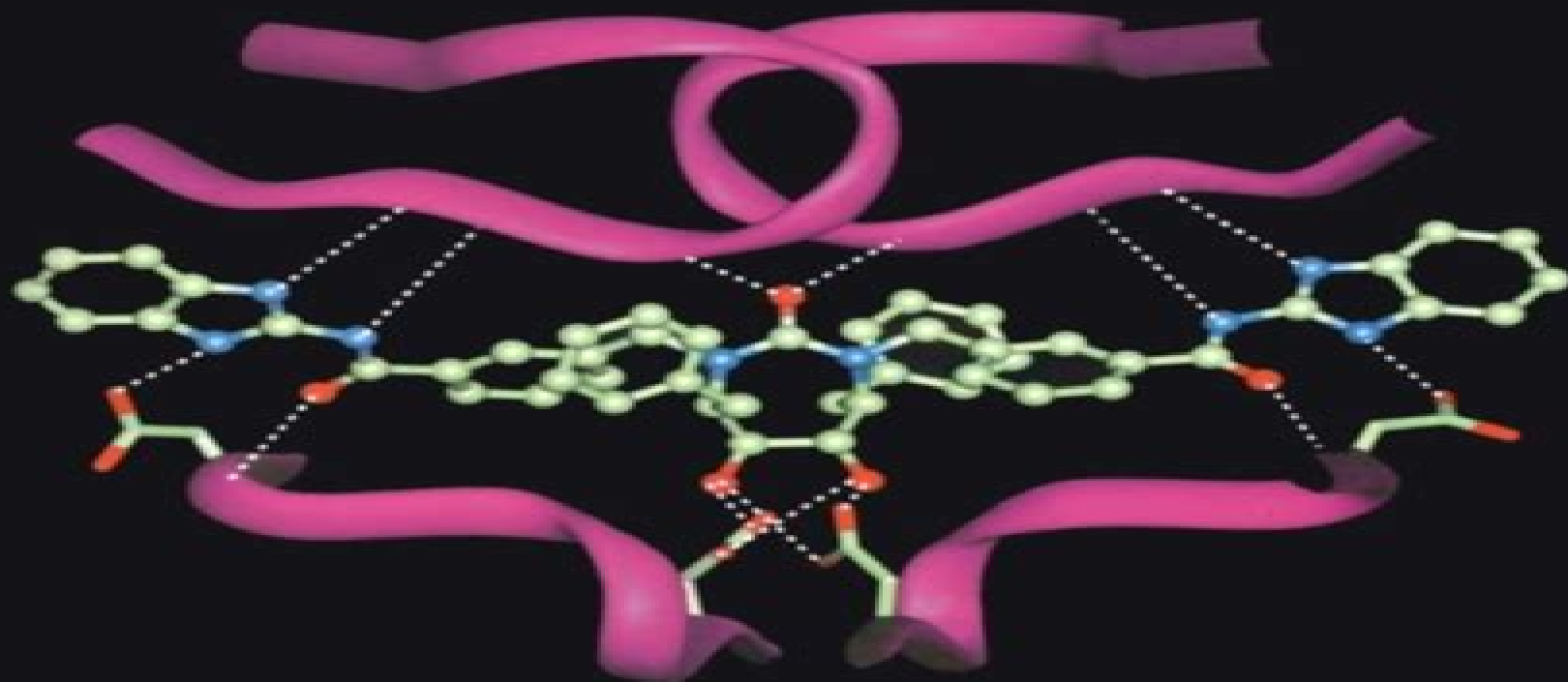


PROTEINASE AND PEPTIDASE INHIBITION

RECENT POTENTIAL TARGETS FOR DRUG DEVELOPMENT

EDITED BY H. JOHN SMITH AND CLAIRE SIMONS



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Proteinase and Peptidase Inhibition H. John Smith, Claire Simons, 2002-03-28 Cellular proteinases and their physiological role in normal and disease states have been the subject of great interest recently Proteinase and Peptidase Inhibition presents new reports on a wide range of cellular proteinases whose inhibitors may hold the key to the development of new drugs It deals with enzyme classes inhibitor types and regulatory mechanisms governing proteinase activity Target enzymes are fully described and classified by structural similarity rather than by pharmacological effects This is a valuable reference for academic and industrial researchers in medicinal chemistry drug design and development pharmacology biochemistry and molecular and cell biology

Proteinase and Peptidase Inhibition Senior Lecturer in Medicinal Chemistry H John Smith, Claire Simons, 2019-12-02 Cellular proteinases and their physiological role in normal and disease states have been the subject of great interest over recent decades At present specific protease inhibitors are exploited both as tools in unraveling the role of individual proteinases in particular cellular processes and for the development of chemotherapeutic agents for the treatment of various disorders Proteinase and Peptidase Inhibition presents updated progress reports on the characterization of a wide range of cellular proteinases whose inhibitors may hold the key to the development of new drugs Introductory chapters deal with the broad enzyme classes inhibitor types and regulatory mechanisms governing proteinase activity The target enzymes themselves together with all aspects of their inhibition and inhibitor design are comprehensively described The classification of target enzymes by structural similarity rather than by pharmacological effects provides a new and coherent platform for understanding how inhibition of different targets can lead to the same therapeutic outcomes This is a valuable reference book that will appeal to both academic and industrial researchers in the fields of medicinal chemistry drug design and development pharmacology biochemistry and molecular and cell biology

Enzymes and Their Inhibitors H. John Smith, Claire Simons, 2004-11-29 Focusing on the development of enzyme inhibitors as therapeutic drugs Enzymes and Their Inhibitors Drug Development provides a concise overview of the chemistry of major types of enzymes and their inhibitors The opening chapters introduce readers to the structure functions mechanisms and kinetics of enzymes including their use as disease markers
Smith and Williams' Introduction to the Principles of Drug Design and Action H. John Smith, H. John Williams, 2005-10-10 Advances in knowledge and technology have revolutionized the process of drug development making it possible to design drugs for a given target or disease Building on the foundation laid by the previous three editions Smith and Williams Introduction to the Principles of Drug Design and Action Fourth Edition includes the latest information

Drug Design of Zinc-Enzyme Inhibitors Claudiu T. Supuran, Jean-Yves Winum, 2009-10-22 Brings together functional and structural information relevant to the design of drugs targeting zinc enzymes The second most abundant transition element in living organisms zinc spans all areas of metabolism with zinc containing proteins offering both established and potential drug targets Drug Design of Zinc Enzyme Inhibitors

brings together functional and structural information relevant to these zinc containing targets With up to date overviews of the latest developments field this unique and comprehensive text enables readers to understand zinc enzymes and evaluate them in a drug design context With contributions from the leaders of today s research Drug Design of Zinc Enzyme Inhibitors covers such key topics as Major drug targets like carbonic anhydrases matrix metalloproteinases bacterial proteases angiotensin converting enzyme histone deacetylase and APOBEC3G Roles of recently discovered zinc containing isozymes in cancer obesity epilepsy pain management malaria and other conditions Cross reactivity of zinc enzyme inhibitors and activators The extensive use of X ray crystallography and QSAR studies for understanding zinc containing proteins Clinical applications An essential resource for the discovery and development of new drug molecules Drug Design of Zinc Enzyme Inhibitors gives researchers professionals students and academics the foundation to understand and work with zinc enzyme inhibitors and activators

Non-peptide Inhibitors of Proprotein Convertase Subtilisin Kexins (PCSKs) Utpal Chandra De, Priyambada Mishra, Prasenjit Rudra Pal, Biswanath Dinda, Ajoy Basak, 2012

The Ca²⁺ dependent mammalian Proprotein Convertase Subtilisin Kexins PCSKs or Proprotein Prohormone Convertases PCs are a family of endoproteases that play critical roles not only in normal development and metabolism but also in various physiological and pathological conditions These were initiated by the proteolytic processing of large inactive proproteins into their shorter bioactive mature forms by the PCSK enzymes These events take place in a highly selective orchestrated and stepwise manner Among the various proprotein substrates of PCSK enzymes particularly important are the precursor growth factors that include proPDGF A B proIGF 1 2 and proVEGF C because of their strong implications in neoplasia initiation progression and metastasis As a result of these findings PCSK enzymes particularly furin or PCSK3 became a major target for possible interventions of cancer via the use of their selective inhibitors Significant progress has been accomplished in the development of peptide and protein based PCSK inhibitors However non peptide PCSK9 inhibitors are more preferable because of their drug like and other characteristics So far a few non peptide inhibitors of PCSK enzymes of various types of chemical structures have been described in the literature These include i Carbocyclic compounds of diterpene and streptamine class ii Nitrogen N based heterocyclic compounds of various types and chemical structures such as a pyrrolidine bis piperazines b Cu Zn chelating terpyridine derivatives iii Oxygen O based Heterocyclic compounds of varying types of chemical structures such as a Flavonoids b Coumarins of simple and dimeric types c Quinonoids d Iridoids iv Aromatic compounds such as a Aryl guanidino and amidino derivatives b Naphthyl fluorescein derivative and c Phenyl Arsonic acids and v C₂ symmetrical aromatic azo compounds When measured against a small peptidyl MCA fluorogenic substrate these inhibitors displayed IC₅₀ values ranging from nM to M A number of these inhibitors exhibited significant anti PCSK activity when tested in ex vivo or cell culture conditions This article provides an overall review of all non peptide PCSK inhibitors so far reported in the literature along with those we identified recently for the first time and not yet published The potential implications of these molecules

as biochemical therapeutical or clinical agents will also be discussed

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Animal Study with Non peptide PCSK Inhibitors

Future Perspectives of Non peptide PCSK Inhibitors and Concluding Remarks

Acknowledgments

References

Proteases in Health and Disease Sajal Chakraborti, Naranjan S. Dhalla, 2013-12-04

In view of rapidly growing research in the deregulation of proteases and their impact in human health and diseases this book will highlight existing and emerging research in this exciting area

In depth critical state of the art reviews will be written by established investigators on proteases dysfunctions associated with pathogenesis of different diseases that are known to occur due to deregulation of proteolytic systems

Multidisciplinary approaches demonstrating biochemical and signal transduction mechanisms associated with deregulation of proteases leading to manifestation of the diseases will be discussed

The book highlights the roles of both intracellular and extracellular proteases in health and disease

Matrix Metalloproteinase Inhibitors Satya Prakash Gupta, 2012-04-07

Matrix metalloproteinases MMPs are proteolytic enzymes that are involved in many physiological and pathological processes

The field of MMP research is very important due to the implications of the distinct paralogs in both human physiology and pathology

Over activation of these enzymes results in tissue degradation producing a wide array of disease processes such as rheumatoid arthritis osteoarthritis tumor growth and metastasis multiple sclerosis congestive heart failure and others

Thus MMP inhibitors are candidates for therapeutic agents to combat a number of diseases

The present book discusses the design and development of different classes of inhibitors of important classes of MMPs such as gelatinases and collagenases

The articles focus specifically on structure activity relationships of all classes of compounds and on their modes of action and specificity of binding with the receptors based on experimental and theoretical studies

These studies constitute a valuable asset for all those involved in drug development

Viral Proteases and Their Inhibitors Satya Prakash Gupta, 2017-07-03

Viral Proteases and Their Inhibitors provides a thorough examination of viral proteases from their molecular components to therapeutic applications

As information on three dimensional structures and biological functions of these viral proteases become known unexpected protein folds and unique mechanisms of proteolysis are realized

This book investigates how this facilitates the design and development of potent antiviral agents used against life threatening viruses

Users will find descriptions of each virus that detail the structure and function of viral proteases

discuss the design and development of inhibitors and analyze the structure activity relationships of inhibitors

This book is ideal for biochemists virologists and those working on antiviral agents

Provides comprehensive state of the art coverage of virus infections the virus lifecycle and mechanisms of protease inhibition

Analyzes structure activity relationships of inhibitors of each viral protease

Presents an in depth view of the structure and function of viral proteases

Carbonic Anhydrase Claudiu T. Supuran, Andrea

Scozzafava, Janet Conway, 2004-05-27 *Carbonic Anhydrase Its Inhibitors and Activators* provides a state of the art overview of the latest developments and challenges in carbonic anhydrase research Authors describe the mechanisms of action of specific inhibitors in relation to physiological function and present previously unpublished research on CA activators Written by a team of in Hydroxamic Acids Satya P. Gupta, 2013-09-30 Satya P Gupta's *Hydroxamic Acids* is the first book to compile invited articles written by international experts on the class of compounds hydroxamic acids Found to possess a wide spectrum of biological activities the hydroxamic acids are of interest to theoretical and experimental chemists who can study and make use of them in drug design and development Chapters in this book provide a diverse and comprehensive coverage of this compound class and consequently this publication is a valuable resource for researchers in chemical pharmaceutical and biological sciences

Molecular Staging of Cancer H. Allgayer, M.M. Heiss, F.W. Schildberg, 2012-12-06 An explosion of information has occurred since scientists began to define the molecular events that describe the malignant transformation and progression of cells and their development towards a life threatening metastatic disease The First International Congress on Molecular Staging of Cancer held in Munich in December 2001 aimed to establish an international platform of exchange among molecular biologists cell biologists tumor immunologists and clinical and surgical oncologists This network approach should be fruitful for both clinicians and researchers The highlighted topics included tumor associated proteolysis minimal residual disease new approaches for molecular diagnosis and targeting and the first molecular staging models One session focused on technology transfer opening up a new field of funding for innovative concepts Finally the impact of molecular staging on clinical strategies was discussed

Metalloenzymes Claudiu T. Supuran, William Alexander Donald, 2023-08-30 *Metalloenzymes From Bench to Bedside* offers a thorough overview of metalloenzymes spanning biochemical and structural features pharmacology and biotechnological applications After a brief overview international experts in the field discuss a wide range of magnesium calcium zinc manganese nickel iron copper cadmium molybdenum and tungsten enzymes along with catalytic roles within their active sites With a uniform approach throughout each chapter includes the structure and function of the enzyme physiologic and pathologic roles inhibitors and activators of the enzyme and their design and clinical agents or compounds applied in medicine and drug discovery This book enables scientists across academia and industry to adopt ongoing metalloenzyme research and continuous discovery of novel metalloenzymes in new life science studies and clinical applications Examines a range of metalloenzymes from biochemistry to pharmacology and drug design Each chapter examines enzyme structure and function physiologic and pathologic roles inhibitors and activators and clinical application Features chapter contributions from international experts in the field

Special Topics in Drug Discovery Taosheng Chen, Sergio Chai, 2016-11-30 Drug discovery involves multiple disciplines technologies and approaches This book selects important topics related to drug discovery including emerging tool Chapter 1 cutting edge approaches Chapters 2 3 and 4 examples of specific therapeutic area Chapter 5 quality control in drug development Chapter 6 and job and career

opportunities in the pharmaceutical sector a topic rarely covered by other books Chapter 7 This book draws knowledge from experts actively involved in different areas of drug discovery from both industrial and academic settings We hope that this book will facilitate your efforts in drug discovery

Proteases in Human Diseases Sajal Chakraborti, Tapati Chakraborti, Naranjan S. Dhalla, 2017-07-13 This book bridges the gap between fundamental research and biomedical and pharmacological applications on proteases It represents a comprehensive overview of the multifaceted field of proteases in cellular environment and highlights the recently elucidated functions of complex proteolytic systems in different diseases Several established investigators have elucidated the crucial role of proteases in biological processes including how proteolytic function and regulation can be combined to develop new strategies of therapeutic interventions Proteases form one of the largest and most diverse families of enzymes known It is now clear that proteases are involved in every aspect of life functions of an organism Under physiological conditions proteases are regulated by their endogenous inhibitors however when the activity of proteases is not regulated appropriately disease processes can result in So there is absolute need for a stringent control of proteolytic activities in cells and tissues Dysregulation of proteases may cause derangement of cellular signalling network resulting in different pathophysiological conditions such as vascular remodelling atherosclerotic plaque progression ulcer and rheumatoid arthritis Alzheimer disease cancer metastasis tumor progression and inflammation Additionally many infective microorganisms require proteases for replication or use proteases as virulence factors which have facilitated the development of protease targeted therapies for a variety of parasitic diseases

Cancer-Leading Proteases Satya Prakash Gupta, 2020-01-09 Cancer Leading Proteases Structures Functions and Inhibition presents a detailed discussion on the role of proteases as drug targets and how they have been utilized to develop anticancer drugs Proteases possess outstanding diversity in their functions Because of their unique properties proteases are a major focus of attention for the pharmaceutical industry as potential drug targets or as diagnostic and prognostic biomarkers This book covers the structure and functions of proteases and the chemical and biological rationale of drug design relating to how these proteases can be exploited to find useful chemotherapeutics to fight cancers In addition the book encompasses the experimental and theoretical aspects of anticancer drug design based on proteases It is a useful resource for pharmaceutical scientists medicinal chemists biochemists microbiologists and cancer researchers working on proteases Explains the role of proteases in the biology of cancer Discusses how proteases can be used as potential drug targets or as diagnostic and prognostic biomarkers Covers a wide range of cancers and provides detailed discussions on protease examples

Burger's Medicinal Chemistry, Drug Discovery and Development, 8 Volume Set, 2021-04-20 Burger's Medicinal Chemistry Drug Discovery and Development Explore the freshly updated flagship reference for medicinal chemists and pharmaceutical professionals The newly revised eighth edition of the eight volume Burger's Medicinal Chemistry Drug Discovery and Development is the latest installment in this celebrated series covering the entirety of the drug development and discovery

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Human Drug Targets Edward D. Zanders,2015-12-14 The identification of drug targets in a given disease has been central to pharmaceutical research from the latter half of the 20th century right up to the modern genomics era Human Drug

Targets provides an essential guide to one of the most important aspects of drug discovery the identification of suitable protein and RNA targets prior to the creation of drug development candidates The first part of the book consists of introductory chapters that provide the background to drug target discovery and highlight the way in which these targets have been organised into online databases It also includes a user's guide to the list of entries that forms the bulk of the book Since this is not designed to be a compendium of drugs the emphasis will be on the known or speculated biological role of the targets and not on the issues associated with pharmaceutical development The objective is to provide just enough information to be informative and prompt further searches while keeping the amount of text for each of the many entries to a minimum Human Drug Targets will prove invaluable to those drug discovery professionals in both industry and academia who need to make some sense of the bewildering array of online information sources on current and potential human drug targets As well as creating order out of a complex target landscape the book will act as an ideas generator for potentially novel targets that might form the basis of future discovery projects

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