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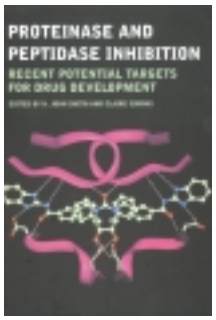

Proteinase and Peptidase Inhibition: Recent Potential Targets for Drug Development

Edited by H. John Smith and Claire Simons, Taylor and Francis, 2002, Price £95.00, 440 pages in hardback, ISBN 0-4152-7349-8

The book *Proteinase and Peptidase Inhibition: Recent Potential Targets for Drug Development* represents a useful and concise introduction to the current state of studies on proteinase and peptidase inhibition. Overall, the book is well organized and treats a diverse and complicated subject in a simple way that should make the subject accessible to a wide variety of readers. From undergraduates specializing in medicinal chemistry for the first time, to practicing medicinal chemists in industry wishing to rapidly assimilate the state-of-the art in an unfamiliar area, this book provides a readable introduction to the various proteinase targets of interest at present.

The book is organized into a series of chapters, with each chapter devoted to an area of major current interest in the pharmaceutical industry. Chapter 1 gives a clear and concise chapter on the types of proteolytic enzymes that are known, and progresses to discuss the various types of catalytic mechanisms that these enzymes employ to cleave peptide bonds, a necessary prelude to any discussion on the design and use of inhibitors. Chapter 2 then provides an account of the various mechanisms by which proteinase activity is regulated in a normal situation, as well as in various disease states. Subsequent chapters describe the following important proteinases, among others: matrix metalloproteinases (MMPs), proteasomes, human neutrophil elastase, factors VIIa, IXa and Xa, urokinase-type plasminogen activator (uPA), amyloid β-peptide-related proteinases, herpes virus and cytomegalovirus proteinase, aminopeptidases, hepatitis C virus NS3/4A proteinase and zinc metalloproteinases (ACE, NEP, ECE).

Chapter 17 is devoted to HIV aspartate proteinase, the target enzyme of several clinically approved drugs used in the treatment of HIV infection, and in particular, to the resistance to these agents that is starting to appear, based on mutations close to the active site. Potential strategies for overcoming this resistance, based upon improved inhibitor design, are also introduced. The final chapter describes proteases that are present in several medically important protozoan parasites, which could represent useful new ways to develop treatments for difficult to treat infections.

The organization of each chapter starts with an introduction to the physiological role and catalytic mechanism of action, followed by a description of the various types of known inhibitor. Finally, wherever information is available, the clinical developments in the area are briefly described. Although the coverage is not comprehensive, the useful references included at the end of each chapter provide a basis for further exploration and study, making each chapter useful in its own right. With the exception of ACE and HIV protease inhibitors, several of which have been marketed for a number of years, all proteinases described represent current important targets in the pharmaceutical industry, and as such the book is a timely review and should stimulate further developments in the area. As a final note, the preface points out that the discovery of novel inhibitors of new proteinases, based upon rational design concepts, is now well developed but the progression to the market is tortuous, as a result of problems with bioavailability, pharmacokinetics and toxicology. Although *Proteinase and Peptidase Inhibition* only touches on these subjects, the overall feeling gleaned from reading this book is that many advances remain to be made. The overall importance of the targets described to human disease certainly implies a continued major effort in the discovery of new therapeutic entities based upon inhibition of proteinases, and this book should provide stimulus for the generation of new ideas and approaches.

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