

Preface

As is now well known, the matrix metalloproteinases (MMPs) are proteolytic enzymes that are involved in many physiological and pathological processes associated with inflammatory reactions. The over-activation of these enzymes results in tissue degradation, leading to a wide array of disease processes, such as rheumatoid arthritis, osteoarthritis, tumor growth and metastasis, multiple sclerosis, congestive heart failure, and a host of others. Therefore, the studies on MMPs and their inhibitors have evoked a great interest among the scientists, and hence the objective of this book is to present some important aspects of such studies, which may be of great value to develop potential therapeutic agents against a number of diseases. The book may be of high interest to medicinal and pharmaceutical chemists as well as to those working in the areas of biotechnology.

The book contains seven chapters in all. The very first chapter entitled “Matrix Metalloproteinases (MMPs)” and written by Viola et al. discusses about MMPs, their different families, their functions, diseases resulting from their over-activations, and their regulations. This chapter may arouse enough interest in those who are less familiar with MMPs and their functions. For the design of effective MMP inhibitors, it is essential that we should have enough knowledge about binding sites in MMPs, their structures, and specificity of binding. Chapter 2 “Specificity of Binding with Matrix Metalloproteinases” authored by Gupta and Vaishali discusses these aspects of MMPs. The article presents the X-ray crystallographic and NMR studies on three-dimensional structures of a number of MMPs to reveal their catalytic sites, subsites, specificity of binding with substrate and inhibitors, and catalytic mechanism.

Among MMPs, gelatinases constitute an important class as they have been found to be massively upregulated in malignant tissues. They are expressed during carcinogenesis and angiogenesis and it has become clear that they are involved at almost all stages of tumor progression—from initial tumor development, growth, and angiogenesis to invasion, metastasis, and growth at secondary sites. In Chap. 3 entitled “The Gelatinases and Their Inhibitors: The Structure–Activity

Relationships”, Snehasikta et al. present a description of this class of MMPs covering their structure, specific functions, over-activations, and inhibitors.

Collagenases constitute another important class of MMPs, which are currently being investigated as drug targets for rheumatoid arthritis and osteoarthritis. Chapter 4 “Advances in Studies on Collagenase Inhibitors” authored by Yadav et al. discusses in detail the role of collagenases in the pathophysiology of arthritis and their different classes of inhibitors with two- and three-dimensional QSARs thereof.

Among the various classes of MMP inhibitors, the hydroxamic acid-based inhibitors—the compounds containing hydroxamate moiety (CONHOH)—have been most widely studied. In Chap. 5, Verma describes several groups of this class of compounds and their SAR and QSAR in detail. Another important class of MMP inhibitors has been the sulfonamide-based inhibitors that have been studied to inhibit varying members of MMP family. In Chap. 6, Vaishali and Gupta have presented QSAR studies on several groups of this class of MMP inhibitors and discussed their implications.

In the last chapter (Chap. 7), Benjamin and Khalil have described MMP inhibitors as investigative tools in the pathogenesis and management of vascular disease. MMPs play an important role in the regulation of numerous physiological processes including vascular remodeling and angiogenesis. MMPs may also be involved in vascular diseases such as hypertension, atherosclerosis, aortic aneurysm, and varicose veins. Because there are no specific activators of MMPs, MMP inhibitors are often used to investigate the role of MMPs in different physiologic processes and in the pathogenesis of specific diseases. Such role of MMP inhibitors is of great interest and has been vividly described by Benjamin and Khalil in this last chapter entitled as “Matrix Metalloproteinase Inhibitors as Investigative Tools in the Pathogenesis and Management of Vascular Disease.”

Thus, an attempt has been made to compile the articles of varying taste and useful to those involved in research on MMPs and their inhibitors. As an editor of this book, I have greatly enjoyed reading all the articles and hope so will do all the readers. I gratefully acknowledge the interest and zeal of all the authors for contributing such interesting and useful articles in this book.

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