

Foreword

The initial observations that led to the identification of kinins was discovered on the basis of the hypotensive action of normal human urine by J. E. Abelous and E. Bardier in 1909 (*CR Soc Biol* 66:511–520).

In 1926, the surgeon Emil Karl Frey, a German scholar, injected human urine into dogs while searching for the substance inducing anuria in newly operated patients. At that time, he could not imagine the significance of the hypotension that the urine produced and what this observation would lead to. His experiments, the first of a series of studies performed together with the physiologist, Prof. Heinrich Kraut, in the basement of the Department of Surgery of the University at Nußbaumstraße, was the birth of kinins.

How kinins appear and disappear unrivaled, was later discovered by the chemist, Dr. Eugen Werle, the third of the German pioneers in the field of kinins. Later, Werle was the first to become head of the Department of Clinical Chemistry in Germany, again located at the Surgical Department at the University of Nußbaumstraße. In 1930 Frey, Kraut, and Werle observed and documented the majority of the biological effects of kinins (*Hoppe-Seylers Z Physiol Chem* 189:97–106). During the 1950s, kinins became progressively recognized worldwide. From about 1940, the Brazilian scientist, Prof. Rocha e. Silva, contributed significantly to the understanding of kinins, which he termed as bradykinin because they produced slow contraction of the guinea-pig ileum. Early studies on the kinin system were reviewed by Sir Ashley Miles, Secretary of the Royal Society from the Lister Institute of Preventive Medicine, London (*Proc Roy Soc B*, 173:341–349). More recently, comprehensive historical and current status of kinins has been reviewed by one of the leading workers in the field, Prof. Dr. Michael Bader of the Charité-Universitäts Medicine, Berlin (*Kinins*, Michael Bader, De Gruyter, Berlin).

Kinins are recognized as the Kallikrein-Kinin system or the bradykinin system that includes the enzymes, precursors, and inactivating enzymes involved in the formation and inactivation of bradykinin. Kinins are straight chain polypeptides having 9–11 amino acids.

Kinins contribute significantly in numerous pathophysiological processes such as cancer, inflammatory, cardiovascular, diabetic, renal, and gastrointestinal. In a recent development, bradykinin receptor antagonists have provided great advancement in the therapy of various diseases where kinins are hyperactive. In addition, bradykinin agonist may have great values in treating pathological states caused by hypoactivity of bradykinin. Details about the kinin-forming system, receptors, and molecular mechanisms involving the actions of kinins can be found in the IUPHAR review by L. M. Frederik Leed-Lundberg et al. 2005; *Pharmacological Reviews* 57:27–77.

Recent research advances in the kinins field has necessitated to provide these developments in a book that can update these advancements in kinins.

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Preface

Kinins are pharmacologically active polypeptides, which are formed in the tissues and body fluids as a result of the enzymatic action of kallikreins of kininogens. The kinin family includes bradykinin (BK) (Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg), kallidin (Lys-Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg), and methionyl-lysyl-BK (Met-Lys-Ard-Pro-Pro-Gly-Phe-Arg). Kallidin and methionyl-lysyl-BK are converted into BK by circulation aminopeptidases in plasma and urine. BK is rapidly inactivated by circulating kininases (Kininase I and Kininase II, known as angiotensin converting enzyme (ACE)). The development of ACE inhibitors has provided a significant contribution to the treatment of hypertension. BK can cause hypotension, vasodilation, increased vascular permeability, pain, cell proliferation, and glucose transport. It is known to cause release of important mediators such as nitric oxide, prostaglandins, and prostacyclin. Kinins interact with two specific G-protein-coupled receptors known as B1-receptor (B1R) and B2R to produce various pathophysiological processes.

This book entitled “Recent Developments in the Regulation of Kinins” presents key topics of current interest in the field of several pathophysiological conditions including (a) the basic and clinical aspects of bradykinin receptor antagonists, (b) the Kallikrein-Kinin pathways in hypertension and diabetes, (c) tissue Kallikrein-Kinin therapy in hypertension and organ damage, (d) renal (tissue) Kallikrein-Kinin system in the kidney and novel potential drugs for salt-sensitive hypertension, (e) the Kallikrein-Kinin system in diabetes retinopathy, and (f) genetic manipulation and genetic variation of the Kallikrein-Kinin system; impact on cardiovascular and renal disease.

The book has been written by internationally reputed scientists with the aim to provide an overview of the recent developments that have occurred in the kinins field of research. It is intended for postgraduate students in medicine, pharmacy, physiology, pharmacology, and research organizations. Furthermore, it will be a great asset to endocrinologists, nephrologists, cardiologists, pharmacologists, physiologists, ophthalmologists, and rheumatologists.

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