Book review

Farmakologija renin-angiotenzin sistema
[Pharmacology of the Renin-Angiotensin System]

Enver Zerem, Corresponding Member of ANUBiH
Professor of Medicine, University of Tuzla, Tuzla, Bosnia and Herzegovina

The renin-angiotensin system (RAS) and the kallikrein-kinin system (KKS) were discovered more than a century ago. It is interesting that both systems were defined after initial observations from experiments on the urinary system. Renin was discovered when extracts of rabbit kidney caused a hypertensive effect, while hypotension due to intravenous injection of urine led to the discovery of kallikrein. Kallikrein got its name from the Greek *kallikréas* (pancreas), where the highest concentration was found. Renin was rediscovered several decades later when it was found that occlusion of the renal artery in dogs caused hypertension. Soon it was revealed that renin releases an inactive decapeptide, angiotensin (Ang) I, from a substrate, angiotensinogen, and this peptide is further cleaved by angiotensin converting enzyme (ACE) to the strongly hypertensive octapeptride Ang II.

The KKS participates in various vascular mechanisms releasing two peptides: a nonapeptide, bradykinin (BK), and a decapeptide, Lys-bradykinin (kallidin). Bradykinin causes hypotension, cough, and relaxation/contarctions of smooth muscles. It is 10 times stronger than histamine on a molar basis. ACE has a dual function; it activates Ang I and inactivates BK. The antihypertensive ACE inhibitors decrease the formation of Ang II and increase the level of BK. These effects have therapeutic importance, but they also contribute to side effects of the ACE inhibitors. The first orally active ACE inhibitor, captopril, was discovered in 1977 by the researchers of the Squibb Company. Today 16 ACE inhibitors are in clinical use.

In the book "Pharmacology of the Renin-Angiotensin System", Professor Rajko Igić has integrated his extensive research experience, focusing on biochemical, pharmacological, clinical, toxicological and epidemiological aspects of the RAS blockade. In addition, the book also gives an overview of current pharmacological, immunological

and genetic research in the field of RAS. The book is divided into eleven chapters, organised in methodical and logical order.

The introductory chapters of the book give a short history of the RAS and KKS. The components of the RAS and their physiological and pharmacological importance are described in chapters on prorenin and renin, (pro)renin receptor, angiotensinogen, ACE, Ang I, Ang II, genetic polymorphysms of ACE, sarcoidosis and ACE, chymase, ACE2, angiotensin receptors, and angiotensinases. The synthesis and release of prorenin/renin, the essential steps for the RAS activation, are described in detail. The release is controlled by three mechanisms: sympathetic nerve stimulation (fast release), renal baroreceptors (long lasting release), and influence of ions via macula densa (chronic release). Pharmacological and clinical data for ACE inhibitors, Ang receptor blockers, and renin inhibitors are presented in separate chapters. Another chapter is devoted to vasopeptidase inhibitors, including omapatrilat, ilepatril, bonsetan, and inhibitors of endothelin-1 converting enzyme (ECE-1). The final chapter discusses future research on the RAS.

The appendix describes arterial hypertension, heart failure, myocardial infarction, and sleep apnea in short chapters prepared for non-physicians, such as pharmacists, medical biochemists, and biomedical students. Perhaps the appendix should include a chapter on nephrology, as well.

Each chapter is concise, giving clear learning outcomes, enabling the reader to consolidate their gained knowledge. The simple, original illustrations help the reader to follow the complex relationships of the RAS and KKS and vasopeptidases. The book is well referenced and guides the enthusiast towards further reading. It includes 92 references; 15 appear in the appendices as footnotes. A short biographical note about the author includes 56 references to his publications in various journals.

This well-written book is aimed at clinicians, students, and biomedical investigators who study or treat cardiovascular diseases and who may use it as an excellent guide. The book is also useful to those who wish to review the pharmacology and therapeutics of this complex subject.