

## Pharmacology of the Renin-Angiotensin System (Farmakologija renin-angiotenzin sistema)

Author: Rajko Igić

Publisher: Medical Faculty, Banja Luka, 2014.

Book volume: 10 + 122 pages, illustrated

The renin-angiotensin system (RAS) and kallikrein-kinin systems (KKS) were discovered more than a century ago. Interestingly, both systems emerged from initial observations involving the urinary system. Renin was discovered when it was noted that extracts of rabbit kidney caused a hypertensive effect, while the hypotensive effect of intravenously injected urine led to discovery of kallikrein. Kallikrein was named according to the Greek name kallikréas (pancreas), where the highest concentration was found. The discovery of renin was dormant for several decades, until it was found that the occlusion of the renal artery in dogs caused hypertension. Soon afterwards it was discovered that renin releases an inactive decapeptide, angiotensin (Ang) I, from a substrate, angiotensinogen, and this peptide is further cleaved by Ang-converting enzyme (ACE) to octapeptide Ang II, a very strong hypertensive material.

The KKS participates in various vascular processes by the generation of two peptides: a nonapeptide, bradykinin (BK), and a decapeptide, lys-bradykinin (kallidin). Bradykinin causes hypotension, cough, and relaxation/contractions of smooth muscles. It is ten times more potent on a molecular basis than histamine. The enzyme, ACE, has a dual function – it activates Ang and inactivates BK. Thus, ACE inhibitors decrease formation of Ang II, and increase the level of BK. These effects contribute to both the therapeutic properties and the side effects of ACE inhibi-



tors. The first orally active ACE inhibitor, captopril, was discovered by the researchers of the Squibb Company, in 1977; today we have sixteen ACE inhibitors in clinical use.

The book *Pharmacology of the Renin-Angiotensin System* has eleven chapters. The introductory ones provide a short history of the RAS and KKS. Components of the RAS (prorenin/renin, synthesis and secretion of renin) are explained with emphasis on the fast synthesis and secretion of renin by sympathetic nerve stimulation, long-lasting renin release by renal baroreceptors, and the chronic adaptive system of renin release by the ions via the macula densa. Pharmacological and clinical data of ACE inhibitors, Ang receptor blockers, and renin inhibitors are presented in three longer chapters. Another chapter examines the vasopeptidase inhibitors, including omapatrilat,

ilepatril, bosentan, and inhibitors of endothelin-1-converting enzyme (ECE-1). The final chapter is devoted to future research on the RAS.

The appendix includes a discussion of the following medical conditions relative to the RAS: arterial hypertension, heart failure, myocardial infarction, and sleep apnea. These short chapters are prepared for the non-physicians, such as pharmacists, medical biochemists, and biomedical students. Perhaps the appendix should include a chapter on nephrology as well.

The original illustrations are simple and will help the reader follow the complex relationships of the various systems (the RAS, KKS and vasopeptidases). The book includes 92 references, 15 of which are in the appendices as footnotes, and after a short biographical note about the author, there are 57 references to his publications in various journals.

Clinicians, students, and biomedical investigators dealing with study or treatment of cardiovascular disease will find this book to be an excellent guide. It may also be useful to anyone who wants to review this complex subject of pharmacology and therapeutics.

*Academician Enver Zerem  
University Professor of Medicine*

Department of Medical Sciences  
The Academy of Sciences and  
Arts of Bosnia and Herzegovina  
Sarajevo  
Bosnia and Herzegovina  
zerem@live.com