Angiotensin, Bradykinin and the Endothelium

C. Dimitropoulou · A. Chatterjee · L. McCloud · G. Yetik-Anacak · J. D. Catravas
Vascular Biology Center and Department of Pharmacology and Toxicology, Medical College of Georgia, Augusta GA, 30912-2500, USA
jcatrava@mcg.edu

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Abstract  Angiotensins and kinins are endogenous peptides with diverse biological actions; as such, they represent current and future targets of therapeutic intervention. The field of angiotensin biology has changed significantly over the last 50 years. Our original understanding of the crucial role of angiotensin II in the regulation of vascular tone and electrolyte homeostasis has been expanded to include the discovery of new angiotensins, their important role in cardiovascular inflammation and the development of clinically useful synthesis inhibitors and receptor antagonists. While less applied progress has been achieved in the kinin field, there are continuous discoveries in bradykinin physiology and in the complexity of kinin interactions with other proteins. The present review focuses on mechanisms and interactions of angiotensins and kinins that deal specifically with vascular endothelium.

Keywords  Angiotensin receptors · Bradykinin receptors · Angiotensin-converting enzyme · Angiotensin receptor blockers · Angiotensin-converting enzyme inhibitors

1 Angiotensin

The octapeptide angiotensin (ANG) II (Asp\(^1\)-Arg\(^2\)-Val\(^3\)-Tyr\(^4\)-Ile\(^5\)-His\(^6\)-Pro\(^7\)-Phe\(^8\)) stimulates the release of catecholamines from the adrenal medulla and sympathetic nerve endings, increases sympathetic nervous system activity, stimulates thirst and appetite, and regulates sodium and water homeostasis by stimulating aldosterone release from the adrenal cortex (Luft et al. 1989; Mitchell and Navar 1989; Ferrario and Flack 1996). It regulates endothelial function and stimulates inflammatory, proliferative, fibrotic and thrombotic processes in the vasculature. It has potent effects on vascular tone, constricts smooth muscle cells, regulates vascular cell growth, apoptosis, fibrosis, matrix metalloproteinase production and extracellular matrix degradation (Griendling et al. 1997; Tomita et al. 1998; Yoo et al. 1998). ANG IV, the (3–8) hexapeptide fragment of ANG II (Swanson et al. 1992), and ANG-(1–7) can be formed metabolically by peptidase or protease cleavage from either ANG II or ANG I (Wright and Harding 1995). ANG IV interacts specifically with the AT4R subtype (Harding et al. 1992).