Abstract

The pathophysiology of hypertension is yet unknown. Vasoconstrictive substances are generally accepted to play a central role in the physiology and pathology of vascular regulation. In this thesis, a vasoconstrictive substance derived from human lymphocytes should be, isolated, identified and characterized.

Pilot experiments revealed a vasoconstrictive substance in supernatants of human lymphocytes after incubation at room temperature. Therefore, the aim of this study was the isolation, identification and characterization of this substance. Mononuclear leukocytes were obtained from healthy subjects according to established techniques. Immediately after incubation, the supernatant was chromatographed using a cation exchanger and reversed-phase-chromatography.

After chromatographic purification structural analysis by matrix-assisted laser desorption/ionisation and electrospray ionization mass spectrometry revealed a peptide with a mass of 1003 Da. Structural analysis by matrix-assisted laser desorption/ionisation and electrospray ionization mass spectrometry revealed an angiotensin octapeptide with the sequence Asp-Arg-Val-Tyr-Ile-His-Pro-Phe, which differs from Ang II in Ala^1 instead of Asp^1.

des[Asp^1]-[Ala^1]-Ang II may be generated from angiotensin II by transformation via a lymphocyte-derived aspartate decarboxylase. des[Asp^1]-[Ala^1]-Ang II had the same affinity to the AT_1-receptor as Ang II, but was a weaker vasoconstrictor, suggesting partial AT_1-receptor agonist, and showed a higher AT_2 receptor affinity.

These findings indicate that des[Asp^1]-[Ala^1]-Ang II has a specific profile of actions and may modulate the Ang II effects on vasculature. des[Asp^1]-[Ala^1]-Ang II is a further active angiotensin peptide, which II may be synthesised from Ang II by decarboxylation of Asp, and which is a further member of renin-angiotensin-system.

The findings indicate that in addition to Ang II another novel vasoconstricitive angiotensin peptide occurs in human leukocytes. The actions of des[Asp^1]-[Ala^1]-Ang II may be an important additional component of vasoregulation in humans.