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Study on Novel Vasorelaxing Peptide Derived from Food Proteins and Its Physiological Functions

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Summary

A number of low-molecular-weight bioactive peptides have been found from the protease hydrolysate of various food proteins. In the current study, we found that Arg-Phe (RF), a simple dipeptide consisting of two L-amino acids, exhibits vasorelaxing activity (EC_{50}=580 nM). RF had no ACE-inhibitory activity. To the best of our knowledge, RF-induced vasorelaxing activity seems to be more potent than that of previous reported bioactive peptides derived from food proteins. The retro-sequence dipeptide FR was inactive, suggesting that the RF sequence is important for potent vasorelaxing activity. RA and AF were also inactive. Nitric oxide (NO) and prostaglandins (PGs) are known to be vasorelaxing factors; however, the vasorelaxing activity of RF was inhibited by neither *N*G-nitro-L-arginine methyl ester (L-NAME), a NO synthase inhibitor, nor indomethacin, a COX inhibitor. Interestingly, this activity of RF was blocked by lorglumide, an antagonist of the cholecystokinin $(CCK)_1$ receptor; however, RF had no affinity for CCK_1 and CCK_2 receptors, suggesting that RF stimulates CCK release. Orally administered RF decreased blood pressure in SHRs, and this anti-hypertensive activity of was also blocked by a CCK_1 antagonist. Taken together, a novel CCK-dependent vasorelaxing RF decreases blood pressure in SHRs.