Induction of vasorelaxation through activation of nitric oxide synthase in endothelial cells by brazilin

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Abstract

The vasorelaxant activity of Caesalpinia sappan L., a traditional Chinese medicine, and its major component brazilin were investigated in isolated rat aorta and human umbilical vein endothelial cells. In isolated rat aorta, C. sappan L. extract and brazilin relaxed phenylephrine-induced vasocontraction and increased cyclic guanosine 3',5'-monophosphate (cGMP) content. Induction of vasorelaxation of brazilin was endothelium-dependent and could be markedly blocked by pretreatment with nitric oxide synthase (NOS) inhibitor, N(G)-nitro-L-arginine methyl ester (L-NAME); N(G)-monomethyl-L-arginine acetate (L-NMMA) and guanylyl cyclase inhibitor, methylene blue; 1H-[1,2,4]oxadiazolo[4,3-a]quinoxalin-1-one (ODQ) and nitric oxide (NO) scavenger, hemoglobin. The increasing cGMP content induced by brazilin was also blocked by pretreatment with L-NAME, methylene blue, and the removal of extracellular Ca(2+). In human umbilical vein endothelial cells, brazilin dose-dependently induced an increase in NO formation and NOS activity, which were greatly attenuated by either the removal of extracellular Ca(2+) or the chelating of intracellular Ca(2+) chelator, 1,2-bis(2-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid (BAPTA-AM). Moreover, brazilin dose-dependently induced the influx of extracellular Ca(2+) in human umbilical vein endothelial cells. Collectively, these results suggest that brazilin induces vasorelaxation by the increasing intracellular Ca(2+) concentration in endothelial cells of blood vessels and hence activating Ca(2+)/calmodulin-dependent NO synthesis. The NO is released and then transferred into smooth muscle cells to activate guanylyl cyclase and increase cGMP content, resulting in vasorelaxation.