

Inhibition of cyclic strain-induced endothelin-1 secretion by tetramethylpyrazine

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摘要

Abstract

1. Chuanxiong is a Chinese herb that has been used widely in China to treat vascular disorders. 2,3,5,6-Tetramethylpyrazine (TMP) is one of the major components purified from chuanxiong. Many studies have demonstrated that TMP is effective in the treatment of cardiovascular diseases. However, the mechanism of action by which TMP exerts relaxation in vascular vessels remains unclear. 2. Endothelin (ET)-1 is a potent vasopressor synthesised by endothelial cells both in culture and in vivo. The aims of the present study were to test the hypothesis that TMP may alter strain-induced ET-1 secretion and to identify the putative underlying signalling pathways in endothelial cells. 3. We showed that TMP inhibits strain-induced ET-1 secretion. 2,3,5,6-Tetramethylpyrazine also inhibits the strain-induced formation of reactive oxygen species (ROS) and phosphorylation of extracellular signal-regulated kinases (ERK) 1/2. Furthermore, pretreating cells with TMP or the anti-oxidant N-acetyl-cysteine decreased strain-induced increases in ET-1 secretion and ERK1/2 phosphorylation. Using a reporter gene assay, TMP and N-acetyl-cysteine were demonstrated to also attenuate the strain-induced activity of the activator protein-1 reporter. 4. In summary, we have demonstrated, for the first time, that TMP inhibits strain-induced ET-1 gene expression, in part by interfering with the ERK1/2 pathway via attenuation of ROS formation. Thus, the present study provides important new insights into the molecular pathways that may contribute to the proposed beneficial effects of TMP in the vascular system.