

# **Tetramethylpyrazine Downregulates Angiotensin II-Induced Endothelin-1 Gene Expression in Vascular Endothelial Cells**

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摘要

## **Abstract**

1. Tetramethylpyrazine (TMP) is one of the active ingredients of the Chinese herb *Ligusticum wallichii* Franchat. It is well documented that TMP exerts a cardiovascular protective effect. The aims of the present study were to examine whether TMP alters angiotensin (Ang) II-induced endothelin (ET)-1 gene expression and to identify the putative underlying signalling pathways in vascular endothelial cells. 2. Cultured vascular endothelial cells were pre-incubated with TMP, stimulated with AngII and ET-1 gene expression was then examined. The effects of TMP pretreatment on AngII-induced extracellular signal-regulated kinase (ERK) phosphorylation were investigated to elucidate the intracellular mechanism responsible for the effects of TMP on ET-1 gene expression. 3. Tetramethylpyrazine inhibited AngII-induced ET-1 gene expression, as revealed by northern blotting and a promoter activity assay. Tetramethylpyrazine also inhibited the AngII-induced increase in intracellular reactive oxygen species (ROS), as measured by the redox sensitive fluorescent dye 2',7'-dichlorofluorescein diacetate and ERK phosphorylation. 4. In summary, we have demonstrated, for the first time, that TMP inhibits AngII-induced ROS generation, ERK phosphorylation and ET-1 gene expression in vascular endothelial cells. Thus, the present study delivers important new insights into the molecular pathways that may contribute to the proposed beneficial effects of TMP in the cardiovascular system