

# **Inhibitory mechanisms of tetramethylpyrazine in middle cerebral occlusion (MCAO)-induced focal cerebral ischemia in rats**

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## **Abstract**

Tetramethylpyrazine (TMPZ) is an active ingredient isolated from a commonly used Chinese herb, *Ligusticum wallichii* Franchat, which has long been used in China for the treatment of vascular diseases. In the present study, TMPZ significantly attenuated middle cerebral artery occlusion (MCAO)-induced focal cerebral ischemia in rats. Administration of TMPZ at 10 and 20 mg/kg produced concentration-dependent reductions in infarct size compared to that of control rats. MCAO-induced focal cerebral ischemia was associated with increases in both nitrotyrosine and inducible nitric oxide synthase (iNOS) expression in ischemic regions. The expressions of nitrotyrosine and iNOS were markedly inhibited by TMPZ (20 mg/kg) treatment. Furthermore, TMPZ (100-250 microM) concentration-dependently inhibited respiratory bursts in human neutrophils stimulated by fMLP (800 nM) and PMA (320 nM). TMPZ (100-250 microM) also significantly inhibited neutrophil migration stimulated by fMLP (800 nM) and LTB<sub>4</sub> (160 nM). An electron spin resonance (ESR) method was used to further study the scavenging activity of TMPZ on free radicals formed in human neutrophils. TMPZ (100 and 200 microM) greatly reduced the ESR signal intensity of hydroxyl radical formation. In conclusion, we demonstrate a neuroprotective effect of TMPZ in MCAO-induced focal cerebral ischemia in vivo. TMPZ mediates at least part of the free radical-scavenging activity and inhibits neutrophil activation, resulting in a reduction in the infarct volume in ischemia-reperfusion brain injury. Thus, TMPZ treatment may represent an ideal approach to lowering the risk of or improving function in ischemia-reperfusion brain injury-related disorders.