

# **Mechanisms involved in the antiplatelet activity of tetramethylpyrazine in human platelets.**

許準榕

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## **Abstract**

Tetramethylpyrazine is the active ingredient of a Chinese herbal medicine. In this study, tetramethylpyrazine was tested for its antiplatelet activities in human platelet suspensions. In human platelets, tetramethylpyrazine (0.5-1.5 mM) dose-dependently inhibited both platelet aggregation and ATP-release reaction induced by a variety of agonists (i.e., ADP, collagen, and U46619). Tetramethylpyrazine (0.5 mM) did not significantly change the fluorescence of platelet membranes labeled with diphenylhexatriene, even at the high concentration (1.5 mM). Furthermore, tetramethylpyrazine (0.5-1.5 mM) dose-dependently inhibited [<sup>3</sup>H]inositol monophosphate formation stimulated by collagen (5 microg/ml) in [<sup>3</sup>H]myoinositol loaded platelets. Tetramethylpyrazine (0.5-1.5 mM) also dose-dependently inhibited the intracellular free Ca<sup>2+</sup> rise of Fura 2-AM loaded platelets stimulated by collagen (5 microg/ml). Moreover, tetramethylpyrazine (0.5-1.5 mM) inhibited thromboxane B<sub>2</sub> formation stimulated by collagen. At a higher concentration (1.0 mM), tetramethylpyrazine has also been shown to influence the binding of FITC-triflavin to platelet glycoprotein IIb/IIIa complex. Triflavin, a specific glycoprotein IIb/IIIa complex antagonist purified from *Trimeresurus flavoviridis* venom. It is concluded that the antiplatelet activity of tetramethylpyrazine may possibly involve two pathways: 1) at a lower concentration (0.5 mM), tetramethylpyrazine is shown to inhibit phosphoinositide breakdown and thromboxane A<sub>2</sub> formation; and 2) at a higher concentration (1.0 mM), it leads to the inhibition of platelet aggregation through binding to the glycoprotein IIb/IIIa complex.