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• 計畫英文名稱	Study of Antiplatelet Activity of Tmpz---An Alkaloid from Chung Chong		
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• 中文摘要	<p>Tetramethylpyrazine(TMPZ)是傳統中藥川芎的主要活性成份。在本實驗中，我們將評估 TMPZ 的抗血小板能力。在人類的血小板中，TMPZ(0.5-1.5 mM)可依劑量的相關性而抑制不同的血小板活化劑(如 ADP、Collagen 和 U46619)所引起的血小板凝集反應及 ATP 釋放反應。TMPZ(0.5 mM)不會影響血小板細胞膜的流通性，即使濃度高到 1.5mM 亦然。再者，TMPZ(0.5-1.5 mM)可依劑量的相關性而抑制 Collagen 所引起血小板(/sup 3/H) Inositol monophosphate 的形成；另外，TMPZ(0.5-1.5mM)亦可依劑量的相關性而抑制 Collagen 所引起血小板內鈣的釋放。再者，TMPZ(0.5-1.5mM)亦可抑制 Collagen 所引起的 Thromboxane A/sub 2/的合成。在較高的濃度(1.0 mM)，我們亦發現 TMPZ 可干擾 FITC-triflavin 結合到血小板細胞膜糖蛋白受體 Glycoprotein IIb/IIIa complex. Triflavin 是一種蛇毒蛋白 Trimeresurus flavoviridis 所純化出的 Glycoprotein IIb/IIIa complex 的專一性拮抗劑。另一方面，TMPZ 在較低的濃度下(50-200μM)，我們發現 TMPZ 隨著時間及劑量的增加而可明顯的促進 Nitrate 及 cyclic GMP 的產生。由本研究顯示 TMPZ 抗血小板凝集作用可能經由兩種作用機轉：(1)在較低的濃度下(50-200 μM)，TMPZ 可促進血小板 NO 的釋放，導致 cyclic GMP 增加而降低細胞內鈣離子濃度。(2)在較高的濃度下(0.5-1.5 mM)，TMPZ 可抑制血小板的 Phosphoinositide 的分解以及 Thromboxane A2 的合成，進而降低細胞內鈣離子而抑制血小板凝集反應。</p>		
• 英文摘要	<p>Tetramethylpyrazine (TMPZ) is the active ingredient of a Chinese herbal medicine. In this study, TMPZ was tested for its antiplatelet activities in human platelet suspensions. In human platelets, TMPZ (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). TMPZ (0.5 mM) did not significantly change the fluorescence of platelet</p>		

membranes labeled with dipheylhexatriene (DPH), even at the high concentration (1.5 mM). Furthermore, TMPZ (0.5-1.5 mM) dose-dependently inhibited (^3H) inositol monophosphate formation stimulated by collagen (5 $\mu\text{g}/\text{ml}$) in (^3H) myoinositol loaded platelets. In addition, TMPZ (0.5-1.5 mM) also dose-dependently inhibited the intracellular free Ca^{+2} rise of Fura 2-AM loaded platelets stimulated by collagen (5 $\mu\text{g}/\text{ml}$). Moreover, TMPZ (0.5-1.5 mM) inhibited thromboxane A_2 formation stimulated by collagen. At a higher concentration (1.0 mM), TMPZ 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. On the other hand, TMPZ (50-200 μM) significantly increased production of nitrate and cyclic GMP formation in human platelets within a 15-min incubation period. It is concluded that the antiplatelet activity of TMPZ may possibly involve two pathways: (1) at a lower concentration (50-200 μM), TMPZ may activate the nitric oxide and cyclic GMP formation. (2) at a higher concentration (1.0 mM), TMPZ is shown to inhibit phosphoinositide breakdown and thromboxane A_2 formation in human platelets.