lycopene 抑制血小板凝集作用

Mechanisms involved in the antiplatelet activity of lycopene

中文摘要

茄紅素 (lycopene) 是一種屬於類胡蘿蔔素的天然色素，存於蕃茄、紅肉西瓜、紅心芭樂、紅葡萄柚等食物中。其分子式爲 C40H56，分子量爲 537，結構上屬直鏈碳氫化合物。

茄紅素爲很強的抗氧化物，能掃除自由基，不僅可延緩老化，近年來在癌症的預防相關研究上也逐漸獲得證實，對於攝護腺癌、乳癌、口腔癌、肺癌等罹患率上，都有降低的效果。在心血管疾病方面，茄紅素可避免低密度脂蛋白氧化，降低血脂。然而，在心血管系統中佔重要地位的血小板，在受刺激活化的過程，是否會受茄紅素的影響，至今未有一套完整研究證實。由於血小板的活化過程中，會有自由基的產生且進而加強血小板的活化作用，因此，本研究係針對茄紅素掃除自由基的特性，探討其是否對血小板會有抗凝集的作用，而對心血管疾病有所幫助。經此一系列實驗後，研究結果顯示： (1) 在 in vitro 實驗中已發現外加茄紅素確實具有抑制血小板凝集之能力。亦即在血小板凝集實驗中若外加茄紅素，則會隨著濃度之增加而有效地抑制由 collagen、ADP、與 arachidonic acid 等血小板活化劑所引起的凝集作用，隨著血小板活化劑使用種類的不同，茄紅素之 IC50 約爲 6 mM。 (2) 同時茄紅素可有效得抑制由 collagen 刺激之血小板活化所引起的細胞內鈣離子移動與 phosphoinositide breakdown。 (3) 茄紅素可促進 NO 與 cGMP 之增加，抑制 TxB2 之形成，降低細胞內 pH 值，但對 cAMP 的量沒有影響。 (4) 對於血小板中之 47 kDa 蛋白質磷酸化，這是一個標記 protein kinase C 活性的方法，在本實驗中我們使用 PDBu (0.06 mM) 促進血小板 47 kDa 的蛋白質磷酸化；由研究結果顯示茄紅素可抑制其活性。

由結果發現茄紅素抗血小板活性可能涉及以下路徑： (1) 茄紅素在一開始會抑制血小板 phospholipase C 的活性，接著進一步抑制 phosphinositide breakdown、 47 kDa 的 PKC 之磷酸化和 thromboxane A2 (TxA2) 的形成； (2) 另一方面，茄紅素可能經由活化血小板內 NO synthetase 產生 NO，活化 guanylate cyclase，使 cGMP 的含量增加。藉由上述 (1) 和 (2) 的作用最後導致細胞內鈣離子之濃度的減少，最後抑制血小板凝集反應。

英文摘要

Lycopene is a natural pigment that belongs to b-carotene, which is abundant in natural foods like tomatoes, watermelons, guavas, grapefruits, and so on. It’s molecular formula is C40H56; molecular weight is 537, and the structure is a kind of hydrocarbon compounds.

Lycopene plays an important role in the scavenging of free radicals. It not only can delay human ageing, but also has been convinced for it's effects on cancer prevention. Lycopene can decrease the risks of prostate cancer, breast cancer, lung cancer, and so on. During the process of platelet aggregation, there are free radicals produced which further strengthen the platelet activation. Therefore, the purpose of the study is to see if lycopene can inhibit platelet aggregation through it's effects on free radicals and further to find the mechanisms involved in. In this study, we found that (1) the activated lycopene could effectively inhibit the platelet aggregation. Lycopene dose-dependently inhibited the aggregation induced by collagen, ADP and AA , the IC50 concentration is about 6 mM. (2) Lycopene significantly inhibited the intracellular Ca2+ mobilization and PI breakdown stimulated by collagen. (3) Lycopene increased the cGMP and NO formation in human platelets. In addition, lycopene also decreased the formation of TxB2, and the intracellular pH values. (4) Lycopene also significantly inhibited platelet aggregation and decreased the 47 kDa protein phosphorylation induced by PDBu, an PKC activator.

Therefore, basing on the above observations, we suggest that the possible mechanisms maybe involved as follows : (1) Lycopene inhibited phospholipase C, and then inhibited the phosphoinositide breakdown, 47 kDa protein phosphorylation and formation of TxA2. (2) On the other hand, lycopene increased the amount of NO and c-GMP by activating guanylate cyclase. Through the effects of (1) and (2), the intracellular Ca2+ concentration was decreased finally and leading to the inhibition of platelet aggregation.