Lycopene 與 inosine 的活體抗血栓活性及保護暫時性局部腦梗塞傷害的作用

Protective effect of lycopene and inosine in thrombosis and transient focal cerebral infarction in vivo

中文摘要

血栓性疾病會引起許多急性的血管徵候群 (acute vascular syndromes)，包括心肌梗塞 (myocardial infarction)、不穩定性心絞痛(unstable angina pectoris) 以及中風 (stroke)，其中腦血管疾病 (中風) 一直爲近十年來台灣地區國人十大死因之第二殺手，在全球死因也排名第三，並且約 80 %的人屬於缺血性中風 (ischemic stroke)。腦神經的缺血雖然能因腦血流的及時恢復而挽救神經細胞，但也因此產生再灌流傷害 (reperfusion injury)，在過去的研究推測可能與大量自由基 (free radicals) 的產生、白血球的浸潤 (leukocyte infiltration) 和一些能影響血管的成分 (vasoactive compounds) 有關。

本論文所要探討的兩種藥物：(1) lycopene (茄紅素)，不僅是色素而已，它還是很強的抗氧化劑，不但可以保護植物不受陽光、空氣污染的傷害，在人體也可以對抗許多種退化 (老化) 性疾病 (degeneration diseases)；(2) inosine，在發炎反應裡扮演著重要的角色。因此本論文利用兩種活體動物模式，分別爲 fluorescein sodium 誘導腸繫膜形成血栓以及阻塞/再灌流型動物中風實驗模式，評估兩種藥物在活體內的抗血栓活性，以及是否具有保護暫時性局部腦梗塞傷害的作用，其中包括評估藥物對於腦梗塞體積是否改善、脂質過氧化 (lipid peroxidation) 的測量、神經缺陷分級與抓力測試 (Grip test)。

由結果顯示 lycopene 和 inosine 在活體動物以 fluorescein sodium 誘導腸繫膜微血管形成血栓的實驗裡，皆能延長血栓時間 (occlusion time)，推測這兩種藥物能預防血栓的形成。在大腦中動脈血管阻塞/再灌流型中風模式中，結果發現 lycopene 在 4 mg/kg 的劑量下能有意義地減低腦梗塞體積，但對於神經缺陷與抓力測試並未有意義地改善。Inosine 的初步結果顯示在投與兩次劑量 (100 mg/kg) 以及在缺血前投與單一劑量 (150 mg/kg)，能有意義地減低腦梗塞體積，雖然對神經缺陷並未有意義地改善，但能有意義地提升運動行爲 (抓力測試)。

英文摘要

Arterial thrombosis after plaque disruption is the critical event leading to acute vascular syndromes, including myocardial infarction, unstable angina pectoris, and stroke. Stroke is the third largest cause of mortality in the world, and about 80 % of strokes are ischemic events due to the occlusion of a vessel. Although restoration of

blood flow to an ischemic area is crucial to tissue survival, these harmful aspects of this returning blood flow have been termed reperfusion injury, and were presumed to be mediated by massive free radicals, leukocyte infiltration, and vasoactive compounds.

In our study, we used two compounds, lycopene and inosine. (1) Lycopene is not only a pigment, but a very potent antioxidant. It could protect plants from damage of sun or air pollution, and also help us to fight against several degeneration diseases. (2) Inosine plays an important role in inflammation. In our experiments, we have established two animal models: (1) irradiation of the mesenteric microvessels in fluorescein sodium-pretreated mice, and (2) middle cerebral artery occlusion in the rat by intraluminal suture. We would use these models to evaluate whether lycopene or inosine had protective effect in thrombosis and transient focal cerebral infarction. These test included quantification of brain infarct volume, measurement of lipid peroxidation, neurological deficit and grip test.

Our results showed that both lycopene and inosine could prolong the occlusion time of inducing platelet plug formation in mesenteric venules. These suggested that these two compounds could have antithrombotic activity. In middle cerebral occlusion model, lycopene could significantly reduce the infarct size at the dosage of 4 mg/kg twice, but not significantly change score in neurological deficit and grip test. Another, our data showed that inosine (100 mg/kg ip twice or 150 mg/kg ip once) could significantly reduce the infarct size. Although inosine did not change the neurological deficit, it could increase score in grip test.