Flavonoids 抑制 RAW 264.7 細胞因 LPS 刺激而產生的 NO 與其結構-活性關係

中文摘要
類黃鹼素 (flavonoids) 抑制小鼠巨噬細胞 RAW 264.7 因 LPS 刺激產生 NO 的能力，各方向有爭論，因此有必要重新檢討。我們用 12 well 而非 96 well 培養 RAW 264.7，以降低表面張力的影響。用 flavones、flavonols、flavanones 及 isoflavones 四大類之 flavonoids 共 13 種，去抑制因 LPS 刺激而產生的 NO，結果顯示 apigenin、luteolin、diosmetin、eriodictyol、quercetin、genistein 及 prunetin 有較強的抑制作用 (IC50<10 μM)，然後選擇一些藥物，研究是否抑制 iNOS 蛋白量的表現，Western blotting 分析結果 luteolin、eriodictyol 及 prunetin 呈現濃度依存性的抑制 LPS 誘發 iNOS protein 的表現，這些抑制作用並非因細胞毒性所引起，其 IC50 值均有意義地低於抑制 NO 產生之 IC50 值 (Table 2)。另外在 in vitro 的實驗，除 flavones 之 apigenin 與 diosmetin 及 isoflavones 之 genistein 與 prunetin 會隨著濃度的提高，而抑制 NO 生成的速率外，其他 flavonoids 均無抑制作用，但是抑制作用最大不超過 30%；然而所有的 flavonoids 都能有意義地捕捉 NO，但最大作用不及 25%。以上結果顯示 flavonoids 可能是經由抑制 iNOS 蛋白量表現而降低 NO 的產生。

英文摘要
The inhibitory effects of flavonoids on NO production in RAW 264.7 cells were still debated. Therefore, it needs further investigation. To attenuate the effect of surface tension of culture medium, we incubated RAW 264.7 cells in 12-well, but not 96-well plates. Thirteen flavonoids, divided into four classes, flavones, flavonols, flavanones and isoflavones, were used to examine their inhibitory effects on LPS-induced NO production. The results revealed that apigenin, luteolin, diosmetin, eriodictyol, quercetin, genistein and prunetin had more potent effects (IC50<10 μM). Some of them were selected for examining their suppressive effects on iNOS protein expression. The results demonstrated that luteolin, eriodictyol and prunetin attenuated LPS-induced iNOS protein expression in a dose-dependent manner using Western blot analysis. The attenuation was not due to cell cytotoxicity of these flavonoids. The IC50 values differ from those of NO production, respectively (Table 2). In addition, in a in vitro system, flavonoids did not attenuate SNP-induced NO production, with an exception that flavones (apigenin and diosmetin), and isoflavones (genistein and prunetin) concentration-dependently attenuated the NO production. This attenuating effects were not greater than 30%. However, all tested flavonoids significantly had
NO-scavenging effects, but the effects were not greater than 25%. The above results revealed flavonoids attenuate NO production maybe due to the inhibition of iNOS protein expression.