Quercetin 及其衍生物抑制 RAW 264.7 細胞因 LPS 刺激而產生的 NO 與其結構-活性關係

Inhibitory Effects of Quercetin and Its Derivatives on LPS-Induced NO Production in RAW 264.7 Cells and Their Structure-Activity Relationships

中文摘要

Quercetin 及其衍生物對 Phosphodiesterase（PDE）isozyme 分別有不同程度的抑制作用，特別 Quercetin 對 PDE 4/3 有選擇性及競爭性的抑制作用，並對氣喘治療具有潛力，因此它們應有抗發炎的作用，但很少有此報告，特別是它們抗發炎的構造－活性之關係更是缺如。我們擬將 RAW 264.7 細胞以 LPS（100 ng/ml）刺激 RAW 264.7 細胞使產生 NO，NO 含量的測定採用 Griess reaction。根據結果顯示 Quercetin 抑制 NO 產生的能力最強，這可能因 C3，C5，C7，C3’，C4’位上都有-OH group，因此很容易與其標的蛋白質形成氫鍵，因這些 OH group 若被-CH_3 取代越多，其抑制 NO 產生的能力就越弱，但以 4 個 OH group 被取代爲最，如 QTME 就完全沒有作用（IC50>100 μM）。此種抑制 NO 產生的 IC50 值與抑制 iNOS 蛋白質表現的 IC50 值非常吻合，顯示抑制 NO 產生主要來自於 iNOS 蛋白質受抑制，因以 cell－free system 研究 SNP 產生的 NO 或 SNP 產生 NO 後被捕抓的情形，顯示這些 Quercetin 及其衍生物並無作用。此構造－活性關係之探討，有助於合成有用的抗發炎藥物。

英文摘要

Quercetin and its derivatives have been reported to inhibit phosphodiesterase（PDE）isozyme in various extent. Especially, quercetin selectively and competitively inhibits PDE 4/3, and has potential in the treatment of asthma. Therefore, they have anti-inflammatory effect. However, there are few reports about that, especially the relationships between structure and activity is little known. We plan to determine NO production according to the method of Griess in LPS（100 ng/ml）—activated RAW 264.7 cells. In the present results, quercetin and its derivatives except QTME, concentration-dependently inhibited the NO production. It revealed quercetin the most potently inhibited the NO production with an IC50 value of 2.17 ± 0.06μM. The IC50 values of other derivatives are presented in Table 2, Quercetin had the most potency among these compounds, suggesting its C3-, C5-, C7-, C3’- and C4’-hydroxyl groups may bind to the binding sites of target proteins. It seems the more hydroxyl group are substituted by methoxy groups the more potency decreases. However the number of substitution maximally occurs at four. For example, QTME almost had no effect

（IC50 > 100 μM） on the NO production. The IC50 values of quercetin and its derivativeson NO production were similar to those of iNOS protein expression, suggesting the NO production is mainly due to iNOS protein expression, because in cell-free system, they had no effect on SNP-induced NO production and NO release. It may be helpful to syntheaize useful anti-inflammatory drugs, after the study of relationships between their structures and activities.