十字花科蔬菜衍生物對於血管內皮 **E.A. hy 926** 細胞株增生及類血管生成抑制之影響

Inhibition of proliferation and tube formation by cruciferous vegetable derivatives in endothelial E.A. hy 926 cells

中文摘要

本研究主要以血管內皮 E.A. hy 926 細胞株爲實驗模式，探討十字花科蔬菜衍生物 indole-3-carbinol (I3C), benzyl isothiocyanate (BITC)及 phenylethyl isothiocyanate (PEITC)對於血管內皮細胞生長、增殖以及類血管生成的影響，並進一步了解其參與血管新生作用之可能機制。結果顯示，以 phorbol myristate acetate (PMA)誘導體外血管新生作用模式之細胞計數結果得知，I3C (100~250 μM), BITC (10~25 μM)與 PEITC (25 μM)添加於含 PMA 處理之細胞中 2、4、6 天後，隨著劑量及天數的增加，細胞生長抑制作用越顯著；MTS 分析結果亦顯示其可抑制細胞增殖速率；且 I3C 可顯著抑制 PMA 所誘導之類血管生成。此外，由 ELISA 分析結果指出 I3C (100~250 μM), BITC(5~25 μM)與 PEITC (10~25 μM)可抑制細胞因 PMA 所誘導之血管內皮細胞生長因子(vascular endothelial growth factor, VEGF)分泌，且呈劑量效應，其中又以 I3C 抑制作用最爲顯著。以 gelatin zymography 結果觀察發現 I3C 亦可抑制因 PMA 所誘導之基質金屬蛋白酶(matrix metalloproteinase, MMP)之 MMP-2、MMP-9 分泌，而 PEITC 和 BITC 對 MMP-2 及 MMP-9 則不具有抑制作用。西方墨點法分析結果顯示，I3C 不影響 vascular endothelial growth factor receptor-2 (VEGFR-2)蛋白質表現。綜合以上結果得知，在 PMA 存在下，十字花科蔬菜衍生物 I3C，可以抑制血管內皮細胞的增生及類血管生成，且此作用伴隨著 VEGF 及 MMP-2、MMP-9 分泌的降低；而 BITC 及 PEITC 僅在高濃度才可顯著抑制血管內皮細胞增生，其抑制類血管生成，僅部份與抑制 VEGF 分泌有關。

英文摘要

The purpose of this study was to investigate the inhibition of cell growth and angiogenesis by cruciferous vegetable derivatives, indole-3-carbinol (I3C), benzyl isothiocyanate (BITC), and phenylethyl isothiocyanate (PEITC) in phorbol myristate acetate (PMA)-stimulated endothelial E.A. hy 926 cells. Furthermore, possible mechanisms were also examined. The results showed that I3C significantly suppressed growth and PMA-induced tube formation, and this inhibition was associated with decreased vascular endothelial growth factor (VEGF) secretion. On the other hand, BITC and PEITC inhibited growth and PMA-induced tube formation at high concentration and this inhibition was only slighty associated with VEGF secretion . In addition, I3C suppressed the secretion of metalloproteinases-2 (MMP-2) and MMP-9 induced by PMA, but did not affect VEGFR-2 expression, and neither, BITC nor PEITC showed such effect. In conclusion, cruciferous vegetable derivative, I3C, suppressed PMA-induced cell growth and tube formation in E.A. hy 926 cells, and this inhibition was associated with decreased secretion of VEGF, MMP-2, and MMP-9 . On the other hand, BITC and PEITC inhibited cell growth and PMA stimulated tube formation only at high concentration, and this inhibition was only partially associated with VEGF secretion.