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论文

银杏内酯B对慢性炎症血管生成的抑制作用

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摘要：

目的研究银杏内酯B对慢性炎症血管生成的作用及部分作用机制。方法比色法测定小鼠慢性肉芽肿气囊模型血管生成指数，组织形态学方法检测气囊病理变化；放射免疫方法测定白介素-1β(IL-1β)含量；L929生物测定法测定肿瘤坏死因子(TNF-α)含量；RT-PCR法检测IL-1β和TNF-α mRNA的表达。结果银杏内酯B可显著抑制模型小鼠的血管指数，与病理观察结果相符；银杏内酯B可显著抑制模型小鼠血清中IL-1和TNF-α的分泌；能显著抑制PMA诱导的U937细胞IL-1β和TNF-α的分泌及其mRNA的表达。结论银杏内酯B能抑制小鼠慢性炎症性血管生成模型的血管生成，能抑制促血管生成细胞因子IL-1β和TNF-α的转录及表达，这可能是其抑制慢性炎症血管生成的机制之一。

关键词： 银杏内酯B 血管生成 白介素-1β 肿瘤坏死因子

Inhibitory effect of ginkgolide B on angiogenesis in chronic inflammation

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Abstract:

AimTo investigate the inhibitory effect of ginkgolide B on angiogenesis in chronic inflammation and the possible mechanisms. MethodsThe murine chronic granulomatous air pouch model was used to observe the anti-angiogenesis effect of ginkgolide B. The vascular index was determined by colorimetry of carminic acid, and angiogenesis was observed by histology method. The interleukin-1β (IL-1β) levels in mice serum and in supernatants of U937 cell culture stimulated by phorbol 12-myristate 13-acetate (PMA) were detected by radioimmunoassay (RIA). The tumor necrosis factor-α (TNF-α) levels in mice serum and in supernatant of U937 cell culture were measured by cytotoxicity bioassay. The mRNA expression of IL-1β and TNF-α of U937 cell culture was investigated by RT-PCR. ResultsOral administration of ginkgolide B 25 and 100 mg·kg^{-1} was shown to significantly inhibit the vascular index of murine chronic granulomatous air pouch model with the inhibitory rate of 22.52% and 25.29%, respectively. This result was supported by histological observation. Concomitantly, the IL-1β levels in mice serums were also significantly decreased with the inhibitory rate of 50.61% and 58.66%; so were the TNF-α levels with the inhibitory rate of 28.91% and 52.41%. Ginkgolide B at concentration of 1×10^{-5} to 1×10^{-8} mol·L^{-1} could also reduce both the IL-1β and TNF-α contents in the supernatants of U937 cell culture stimulated by PMA, but the scopes of changes were much different. For IL-1β the IC50 was 1.93×10^{-8} mol·L^{-1}, while ginkgolide B at concentration of 1×10^{-5} mol·L^{-1} only decreased the release of TNF-α by 25.99%. Furthermore, ginkgolide B at concentrations of 1×10^{-5} to 1×10^{-7} mol·L^{-1} was shown to significantly inhibit TNF-α mRNA expression of U937 cells; and at concentrations of 1×10^{-5} and 1×10^{-6} mol·L^{-1} could inhibit IL-1β mRNA expression. ConclusionGinkgolide B was shown to significantly inhibit angiogenesis of the murine chronic granulomatous air pouch model, reduce the IL-1β and TNF-α levels in mice serums, and significantly inhibit IL-1β and TNF-α mRNA expression and protein secretion in supernatants of U937 cell culture. It was suggested that reduction of proangiogenic cytokines IL-1β and TNF-α secretion may contribute to the anti-angiogenesis effect of ginkgolide B in the murine chronic granulomatous air pouch model.

Keywords: angiogenesis interleukin-1β tumor necrosis factor-α ginkgolide B

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