

论著

三氧化二砷对皮肤成纤维细胞、中性粒细胞MMPs活性,TIMP-1及TGF- β_1 表达的影响

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摘要 目的: 砒石是化腐生肌的常用中药, 其主要成分是三氧化二砷 (As_2O_3)。本研究通过观察 As_2O_3 对基质金属蛋白酶 (MMPs) 活性、基质金属蛋白酶组织抑制因子-1 (TIMP-1) 及转化生长因子 β_1 (TGF- β_1) 表达影响, 探讨化腐中药能否调节胶原代谢, 从而治疗慢性皮肤溃疡。方法: 明胶酶谱法检测大鼠中性粒细胞 (PMNs) 来源的MMP-9活性、人成纤维细胞 (hFb) 分泌的MMP-1、MMP-2的活性, 免疫细胞化学法检测hFb TIMP-1、TGF- β_1 的表达。结果: As_2O_3 浓度在50 mg/L时可以提高大鼠PMNs来源的MMP-9的活性 ($P<0.01$); 在0.8 mg/L可以提高hFb分泌的MMP-1、MMP-2的活性 (分别 $P<0.01$); 同时 As_2O_3 作用于hFb 6 h、12 h、18 h后, TIMP-1、TGF- β_1 表达持续降低 ($P<0.01$)。结论: As_2O_3 在一定范围内可提高PMNs来源的MMP-9的活性; 也可提高hFb分泌的MMP-1、MMP-2的活性, 同时抑制hFbTIMP-1、TGF- β_1 的表达。提示砒类制剂可通过提高多种MMPs的活性, 降低TIMP-1的表达从而发挥化腐作用。

关键词 [砒](#); [成纤维细胞](#); [中性白细胞](#); [胶原代谢](#)

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Effects of arsenic trioxide on activities of MMPs and expression of TIMP-1 and TGF- β_1 in skin fibroblasts and polymorphonuclear neutrophils

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Abstract

AIM: To observe the effects of arsenic trioxide (As_2O_3) on activities of matrix metalloproteinases (MMPs), expression of tissue inhibitor of metalloproteinase-1 (TIMP-1) and transforming growth factor beta1 (TGF- β_1) in human fibroblast (hFb), and to discuss whether As_2O_3 promotes the healing of chronic skin ulcer through regulating collagen metabolism. METHODS: Zymography was used for testing activity of MMP-9 deriving from rat polymorphonuclear neutrophils (PMNs) and activities of MMP-1, MMP-2 secreted by hFb. Immunocytochemical method was used to determine the expressions of TIMP-1 and TGF- β_1 . RESULTS: At the concentration of 50 mg/L, As_2O_3 elevated the activity of MMP-9 ($P<0.01$). At the concentration of 0.8 mg/L, As_2O_3 increased the activities of MMP-1 and MMP-2 ($P<0.01$, respectively). After hFb was cultured with As_2O_3 for 6 h, 12 h and 18 h, the expressions of TIMP-1 and TGF- β_1 decreased continuously ($P<0.01$). CONCLUSION: As_2O_3 elevates the activities of MMP-1, MMP-2 and MMP-9, also inhibits the expressions of TIMP-1 and TGF- β_1 , suggesting that arsenic preparation may exert positive effect on healing chronic skin ulcer through regulating collagen metabolism.

Key words [Arsenic](#) [Fibroblasts](#) [Neutrophils](#) [Collagen metabolism](#)

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