

# 阿帕替尼联合大剂量丹参酮IIA对肺腺癌A549细胞株凋亡及Bim异构体的影响

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**Title:** Effect of combination of apatinib and high-dose tanshinone IIA on apoptosis and Bim isomers of lung adenocarcinoma A549 cell line

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**关键词:** 肺腺癌; A549; 阿帕替尼; 丹参酮IIA

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**摘要:** 目的:观察阿帕替尼与丹参酮IIA单药及不同时序联合用药方案对人肺腺癌细胞A549凋亡的影响,并探究其作用机制。方法:培养肺癌A549细胞,用梯度浓度的阿帕替尼(0、5、10、20、40、80 μmol/L)及丹参酮IIA(0、5、10、20、40、80 μmol/L)分别处理A549细胞,应用CCK8法检测其对细胞增殖的抑制作用;流式细胞技术(Annexin V/PI双染法)检测不同用药组作用48 h后的细胞凋亡率;半定量RT-PCR检测凋亡相关基因Bim异构体的表达情况。结果:阿帕替尼及丹参酮IIA单药对A549细胞的增殖均有抑制作用,且呈现浓度依赖性。两种药物联合使用时,联合用药组增殖抑制和凋亡率优于单药组和改变药物顺序的序贯组。结论:阿帕替尼与丹参酮IIA单药以及联合用药均可抑制A549细胞的增殖并促进凋亡;最佳联合方案为阿帕替尼联合丹参酮IIA同时使用,细胞凋亡率最高;其作用机制之一可能是联合用药通过转录和mRNA选择性剪接来上调Bim L基因的表达,从而促进细胞凋亡。

**Abstract:** Objective:To observe the effect of apatinib and tanshinone IIA alone and sequential medication on the apoptosis of human lung adenocarcinoma cell line A549,and to explore its mechanism.Methods:Lung adenocarcinoma A549 cells were cultured and treated with gradient concentrations of apatinib (0,5,10,20,40,80 μmol/L) and tanshinone IIA (0,5,10,20,40,80 μmol/L).CCK8 was used to detect the inhibition of cell proliferation.Flow cytometry (Annexin V/PI) was used to detect the apoptosis rate of different drug groups after 48 hours.Semi-quantitative RT-PCR was used to detect apoptosis-related genes Bim isomers.Results:Apatinib and tanshinone IIA alone inhibited the proliferation of A549 cells in a concentration-dependent manner.When two drugs were used in combination,the proliferation inhibition rate and apoptosis rate of the group were superior to the single drug group and the sequential group changing the drug sequence.Conclusion:The combination of apatinib and tanshinone IIA can inhibit the proliferation and promote apoptosis of A549 cell line.The best combination regimen is combination of apatinib and tanshinone IIA with a higher apoptotic rate.One of the mechanism may be transcription and mRNA selective splicing to upregulate the expression of the Bim L gene,thereby promoting apoptosis.

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