

三羟异黄酮对人乳腺癌MCF-7/ADM细胞体外抑瘤效应、细胞周期及凋亡的影响

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Genistein Plays Antitumor Role through Cell Cycle and Apoptosis Pathways in Human Breast Cancer Cell Line MCF-7/ADM in vitro

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摘要 目的探讨三羟异黄酮(Genistein GEN)对体外培养人乳腺癌耐药细胞MCF-7/ADM抑瘤作用、细胞周期及细胞凋亡的影响。方法采用MTT法检测GEN单独及联合阿霉素对体外培养人乳腺癌MCF-7/ADM细胞的抑制作用; 荧光分光光度法检测GEN对阿霉素在MCF-7/ADM细胞的蓄积作用; 用流式细胞仪(FCM)检测细胞周期及凋亡率的变化。结果GEN单独及联合阿霉素对体外培养MCF-7/ADM细胞均有明显生长抑制作用, GEN单独作用48 h后表现为随时间的延长抑制作用明显增强, 当GEN浓度达到60 $\mu\text{g}/\text{ml}$ 时, 其抑制作用急剧上升($P<0.01$)。联合阿霉素后与对照组相比抑制率明显上升($P<0.01$), 并随GEN浓度的加大其抑制作用增强, 细胞内阿霉素的浓度也随之升高。与对照组相比, 细胞周期均有G₂/M期阻滞作用, 细胞凋亡百分比以联合组最高($P<0.01$), G₁期前出现典型的亚二倍体凋亡峰。结论GEN单独及联合阿霉素对体外培养人乳腺癌MCF-7/ADM细胞具有抑瘤增效作用, 可以提高阿霉素在MCF-7/ADM细胞内的蓄积、对细胞周期具有G₂/M期阻滞作用, 显著诱导MCF-7/ADM细胞凋亡, 可能是其发挥逆转多药耐药分子生物学机制之一。

关键词: 三羟异黄酮 MCF-7/ADM 多药耐药 细胞周期 细胞凋亡

Abstract: ObjectiveTo study the antitumor effect of genistein (Genistein GEN) in cultured drug-resistant breast cancer cell line of MCF-7/ADM in vitro, and influences of genistein to cell cycle and apoptosis.

MethodsInhibitory effect of GEN alone or combined with doxorubicin on the cultured MCF-7/ADM was detected by MTT assay; the accumulative effect of GEN on doxorubicin in MCF-7/ADM was detected by fluorescence spectrophotometry; and cell cycle and apoptosis rate was detected by flow cytometry (FCM). ResultsSignificant inhibitory effect on cultured MCF-7/ADM in vitro was not observed under GEN alone or combined with Doxorubicin 48 h later GEN treated alone, the inhibition increased gradually in time-dependent model. When the concentration of GEN reached 60 $\mu\text{g}/\text{ml}$, inhibition effect was markedly increased ($P<0.01$). When Doxorubicin was added, the inhibition rate was significant increased compared with the control group ($P<0.01$), and the inhibition strengthened with the increasing concentration of GEN, concentration of intracellular doxorubicin was also increased. Compared with the control group, the cell cycle were both blocked at G₂/M phase, apoptosis was found to be the highest percentage in the combination group ($P<0.01$), typical hypodiploid apoptotic peak was detected before the G₁ phase. ConclusionGEN alone and combined with Doxorubicin had an inhibitory and additive effect on cultured human breast cancer cell line MCF-7/ADM in vitro, it could increase the intracellular accumulation of Doxorubicin and arrest cell cycle at phase G₂/M, as well as in inducing significant apoptosis of MCF-7/ADM cells, which may be one of its molecular mechanisms of the reversal of multidrug resistance.

Key words: Genistein (GEN) MCF-7/ADM MDR Cell cycle Cell apoptosis

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