

论著

洛贝林逆转人乳腺癌细胞MCF-7/ADM耐药作用及其机制

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摘要

目的: 探讨哌啶生物碱洛贝林对人乳腺癌多药耐药细胞株MCF-7/ADM耐药的逆转作用及其分子机制。方法: 利用MTT比色法测定不同浓度洛贝林对人乳腺癌细胞株MCF-7/ADM的阿霉素(ADM)和氟尿嘧啶(Fu)的耐药逆转指数。多功能酶标仪测定洛贝林干预对细胞内罗丹明123荧光强度以反映其对细胞多药耐药蛋白P-gp活性的影响。同时用流式细胞术检测洛贝林对MCF-7/ADM细胞内罗丹明123积聚浓度的影响, 从功能学的角度观察洛贝林的耐药逆转作用及其机制。结果: 洛贝林(10 μmol/L)干预下, 多药耐药细胞株MCF-7/ADM对化疗药的敏感性增加, ADM对耐药细胞株的IC50由(44.81±0.43)mg/L降至(16.72±0.75)mg/L, 逆转指数为2.68; Fu对耐药细胞株的IC50由(53.12±1.60)mg/L降至(38.90±1.43)mg/L, 逆转指数为1.37。洛贝林对细胞的罗丹明123外排有显著的浓度依赖性抑制作用。洛贝林(20 μmol/L)的多药耐药逆转有效率为经典耐药逆转剂维拉帕米(20 μmol/L)的71.6%, 但毒副作用显著降低。结论: 洛贝林对乳腺癌多药耐药细胞株MCF-7/ADM的耐药性具有逆转作用, 其机制主要为抑制细胞多药耐药蛋白P-gp的活性

关键词 [洛贝林](#); [乳腺癌](#); [多药耐药](#); [P-糖蛋白](#)

分类号

Reversal effect and mechanism of lobeline on the multidrug-resistance of human breast cancer cells MCF-7/ADM

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Abstract

Objective To explore the reversal effect and mechanism of lobeline on the multidrug-resistance (MDR) of human breast cancer cells MCF-7/ADM. Methods In human breast cancer cell line MCF-7/ADM, MTT assay was used to determine the cell growth inhibiting ratio of MCF-7/ADM by ADM and Fu. Fluorospectrophotometer was employed to investigate the intracellular concentration of rhodamine123 to reflect the effect of lobeline on the activity of MDR-related protein P-glycoprotein (P-gp). Taking untreated MCF-7/ADM cells as controls, flow cytometry was applied to detect the intracellular concentration of rhodamine123 in MCF-7/ADM cell intervened with lobeline of 20 μmol/L. Results The sensitivity of MCF-7/ADM to ADM and Fu was significantly increased by lobeline in a dose-dependent manner. The inhibitive concentration 50 (IC50) of ADM declined from (44.81±0.43) mg/L to (16.72±0.75) mg/L with a reversion index of 2.68. The IC50 of Fu declined from (53.12±1.60) mg/L to (38.90±1.43) mg/L with a reversion index of 1.37. The fluorescence intensity of lobeline-treated cells was significantly higher than that of the controls, when the concentration of lobeline was more than 10 μmol/L. With fewer side effects, the reversal efficacy of 20 μmol/L lobeline was 71.6% of the classical MDR reversal agent of verapamil at the same concentration. Conclusion Lobeline can reverse the MDR of MCF-7/ADM cells by inhibiting the activity of P-glycoprotein.

Key words [lobeline](#) [breast cancer](#) [multidrug-resistance \(MDR\)](#) [P-glycoprotein \(P-gp\)](#)

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