药学学报 2008, 43(11) 1099-1105 DOI: ISSN: CN:

论文

赖氨大黄酸通过抑制HER-2信号通路诱导乳腺癌SK-Br-3细胞凋亡

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摘要：

为研究赖氨大黄酸(rhein lysinate，RHL)对人乳腺癌细胞株SK-Br-3细胞增殖、凋亡的影响及HER-2信号通路在其中的作用。应用MTT法检测赖氨大黄酸对SK-Br-3细胞增殖的影响；应用流式细胞仪检测细胞周期变化及细胞凋亡；应用Western blotting检测HER-2信号通路蛋白表达水平及蛋白磷酸化水平；应用RT-PCR和免疫化学方法分别检测HER-2 mRNA和蛋白表达水平。结果显示， 赖氨大黄酸能有效抑制乳腺癌SK-Br-3细胞增殖， 作用48 h的IC_{50}值为85 μmol·L^{-1}，并能诱导其凋亡，随药物浓度的增加，细胞凋亡率也逐渐升高；Western blotting结果显示，赖氨大黄酸抑制HER-2蛋白表达和蛋白磷酸化，抑制NF-κB蛋白表达，升高p53和p21蛋白表达；RT-PCR和免疫化学结果表明，赖氨大黄酸能抑制HER-2 mRNA的转录水平，从而抑制其蛋白表达。因此，赖氨大黄酸能有效抑制SK-Br-3细胞增殖，并诱导其凋亡，HER-2/NF-κB/p53/p21参与了赖氨大黄酸诱导SK-Br-3细胞凋亡的过程。赖氨大黄酸解决了大黄酸不溶于水的难题，并且能够通过HER-2信号通路诱导细胞凋亡，有望成为临床肿瘤辅助化疗药物。

关键词： 赖氨大黄酸 细胞凋亡 HER-2信号通路 乳腺肿瘤

Rhein lysinate induces apoptosis in breast cancer SK-Br-3 cells by inhibiting HER-2 signal pathway

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Abstract:

This study is to investigate the effect of rhein lysinate on inducing human breast cancer cell line SK-Br-3 apoptosis and the role of HER-2 signal pathway in the apoptosis. MTT assay was used to detect SK-Br-3 cell proliferation. Cell cycle and apoptosis were analyzed by flow cytometry. The protein expression and the protein phosphorylation of HER-2 signal pathway were detected by Western blotting. The level of HER-2 mRNA was detected by RT-PCR and the level of HER-2 expression was also detected by immunofluorescence cytochemical methods. The results showed that rhein lysinate remarkably inhibited breast cancer SK-Br-3 cell proliferation. The IC_{50} value for 48 h treatment was 85 μmol·L^{-1}. Apoptosis in SK-Br-3 cells was induced by rhein lysinate in a dose dependent manner. The protein expressions of HER-2, NF-κB, and the protein phosphorylation of HER-2 were downregulated, however the protein expression of p53 and p21 was upregulated after rhein lysinate treatment. The level of HER-2 mRNA decreased by using RT-PCR assay and the level of HER-2 expression was also decreased by using immunofluorescence cytochemical assay after rhein lysinate treatment. It can be concluded that rhein lysinate could inhibit SK-Br-3 cell proliferation and induce apoptosis. HER-2/NF-κB/p53/p21 signal pathway might be involved in this process. Rhein lysinate has a good prospect to be an adjuvant chemotherapeutic drug.

Keywords: apoptosis HER-2 signal pathway breast neoplasm rhein lysinate

收稿日期 2008-07-10 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 甄永苏

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