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马鞭草C部位单体4′-甲醚-黄芩素对人绒毛膜癌细胞增殖的抑制作用 点此下载全文

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摘要：

摘 要 目的: 探讨马鞭草有效成分所提取的单体4′-甲醚-黄芩素(4′ methylether scutellarein，4 MS)对人绒毛膜癌JAR细胞的增殖抑制作用及其相关机制。方法：JAR细胞传代后加入不同浓度4 MS作用一定时间，应用MTT法检测对细胞增殖的抑制作用,流式细胞术测定细胞凋亡率及细胞周期变化, AO/EB双染法区分早、晚期凋亡细胞和坏死细胞，RT PCR技术分析4 MS对人绒毛膜癌JAR细胞凋亡相关基因Caspase 3、p38 MAPK及Survivin表达的影响, 并进一步用Western blotting测定Caspase 3、p38 MAPK及Survivin 在用药前后蛋白水平的表达差异。结果：不同质量浓度(10、20、40 mg/L)的4 MS对JAR细胞均有增殖抑制作用,并随药物浓度和作用时间的增加而不断增强(P <0.05, P<0.01)；流式细胞术显示,随着药物浓度的增加细胞凋亡率亦逐渐升高,G 2/M期细胞所占比例增大 (P<0.05)；AO/EB双染后发现，随着4 MS剂量的增加，晚期凋亡细胞逐渐增多；20和40 mg/L的4 MS作用48 h后, JAR细胞中p38 MAPK及Caspase 3 mRNA表达下降，Survivin mRNA表达上升，与对照组相比均有统计学意义(P <0.05)；Western blotting证实，20 mg/L和40 mg/L 4 MS作用48 h后Survivin蛋白表达量显著下降，p38磷酸化水平升高，Caspase 3被明显激活。 结论： 4 MS能抑制人绒毛膜癌JAR细胞的增殖并诱导凋亡，可能与其阻滞细胞生长于G 2/M期、抑制Survivin抗凋亡活性，直接激活p38 MAPK信号通路和Caspase 3 活化有关。

关键词：4′-甲醚-黄芩素(4 MS) 人绒毛膜癌JAR细胞 Caspase 3 Survivin p38 MAPK信号通路

Inhibitory effect of 4′ methylether scutellarein on human choriocarcinoma JAR cells and the possible mechanism Download Fulltext

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Abstract:

Abstract Objective: To investigate the inhibitory effect of 4′ methylether scutellarein (4 MS), an extract from Verbena officinalis , on human choriocarcinoma JAR cell line and the possible mechanism. Methods: JAR cells were exposed to 4′ methylether scutellarein of different concentrations for 48 h. MTT assay was used to examine the anti proliferative effect of 4′ methylether scutellarein. Flow cytometry was used to investigate the apoptosis and the changes of cell cycle. AO/EB double staining was applied to discriminate the apoptotic cells from dead ones. The changes of Survivin, p38 MAPK and Caspase 3 mRNA expressions were detected by RT PCR in JAR cells treated with 4 MS. Furthermore, Western blotting assay was used to determine Survivin protein expression, phosphorylation level of p38 and Caspase 3 in JAR cells before and after 4 MS treatment. Results: 4 MS inhibited the proliferation of JAR cells in a dose and time dependent manner (P<0.05,P<0.01). 4 MS treatment also induced apoptosis in JAR cells in a concentration dependent manner, and percentage of cell cycle progression in G 2/M phase increased dramatically compared with the control group (P<0.05). The result of AO/EB double staining showed that there were more viable apoptotic cells in 4 MS treated groups than in the control group and the number of non viable apoptotic cells and dead cells increased with dose. Phosphorylated p38 and Caspase 3 expressions in 4 MS treated cells were increased at both mRNA and protein levels according to RT PCR and Western blotting results, while Survivin expression was down regulated; there were significant differences between the 4 MS group and the control group (P<0.05). Conclusion: 4 MS can inhibit proliferation of JAR cells and induce their apoptosis, which might be related to cell arrest at G 2/M, down regulation of Survivin activity, and direct activation of p38 MAPK pathway and Caspase 3.

Keywords:4′-methylether scutellarein (4 MS) Choriocarcinoma JAR cell line Caspase 3 Survivin p38 MAPK signal pathway

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