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*S*型与*R*型人参皂苷**Rh$_2$**对人肺腺癌**A549**细胞增殖和凋亡的影响

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中文摘要：目的: 探讨人参皂苷Rh$_2$(*S*型与*R*型)对人肺腺癌A549细胞增殖和凋亡的影响,以阐述人参活性成分抗肿瘤活性的构效关系及可能机制。 方法 :采用MTT实验测定细胞增殖;碘化丙啶(PI)单染流式细胞仪分析细胞周期中各时期的细胞百分数,观察人参皂苷Rh$_2$对人肺腺癌A549细胞增殖周期的影响。Annexin V -PI双染流式细胞术检测细胞凋亡,采用免疫荧光实验对作为细胞凋亡标志的Caspase-3活性进行测定。 结果 :人参皂苷Rh$_2$对人肺腺癌A549细胞毒活性明显存在构效关系,其中25 mg·L^{-1}的20(*R*)-人参皂苷Rh$_2$和20(*S*)-人参皂苷Rh$_2$作用48 h对肿瘤细胞株A549的增殖抑制率分别为28.5%,33.6%,IC$_{50}$值分别为33.4,28.5 mg·L^{-1}。20 mg·L^{-1}的20(*S*)-人参皂苷Rh$_2$作用A549细胞24 h后G$_0$/G$_1$期细胞比例显著高于对照组(*P*<0.01),S期细胞比例显著低于对照组(*P*<0.01),G$_2$/M期细胞比例与对照组比较无显著性差异,说明20(*S*)-人参皂苷Rh$_2$能阻滞细胞周期于G$_1$期。30 mg·L^{-1}的S型和R型人参皂苷Rh$_2$作用A549细胞24 h后,无论是早期还是晚期凋亡率均明显高于正常组细胞(*P*<0.05),并且20(*S*)-人参皂苷Rh$_2$组早期凋亡率明显高于20(*R*)-人参皂苷Rh$_2$组,表现出明显的构效效应(*P*<0.05)。20(*R*)-人参皂苷Rh$_2$和20(*S*)-人参皂苷Rh$_2$作用6 h的A549细胞中标记Caspase-3活性的荧光亮度明显增强,说明Caspase-3的激活参与了人参皂苷Rh$_2$诱导的A549细胞凋亡。 结论 :S型和R型人参皂苷Rh$_2$均可剂量依赖性地抑制A549细胞增殖,并且20(*S*)-人参皂苷Rh$_2$的抗肿瘤活性明显强于20(*R*)-人参皂苷Rh$_2$,阻滞细胞周期于G$_1$期,具有构效效应;S型和R型人参皂苷Rh$_2$均具有促进A549细胞凋亡作用,并且20(*S*)-人参皂苷Rh$_2$组早期凋亡率明显高于20(*R*)-人参皂苷Rh$_2$组,具有构效效应。

中文关键词：人参皂苷Rh$_2$ 人肺腺癌A549细胞 细胞周期 凋亡

Effects of 20(*S*)-ginsenoside Rh$_2$ and 20(*R*)-ginsenoside Rh$_2$ on proliferation and apoptosis of human lung adenocarcinoma A549 cells

Abstract: Objective : To evaluate and explore the effects of 20(*S*)-ginsenoside Rh$_2$ and 20(*R*)-ginsenoside Rh$_2$ on the cytotoxicity, proliferation and the apoptosis of human lung adenocarcinoma A549 cells, and to illustrate the structure-activity relationship and possible mechanisms of anti-tumor active ingredients of ginseng. Method : A549 cells were treated with different concentration gradient of ginsenoside Rh$_2$(*S* and *R* structure)and incubated for different time. Cell proliferation and cytotoxicity studies were detected by methyl thiazolyl tetrazolium (MTT) colorimetric assay, cell cycle and apoptotic was analyzed by PI stains and combination of Annexin V/Prop idium iodide double staining with flow cytometric analysis. The influences of activation on Caspase-3 were also detected by the immunofluorescence staining with fluorescence microscope. Result : MTT test indicated that ginsenoside Rh$_2$ had a strong cytotoxicity activity to A549 cells. Ginsenoside Rh$_2$ could obviously inhibit the cell proliferation in human lung adenocarcinoma cell line A549 at the effective doses of 25 mg·L^{-1} treated with 48 h. The inhibition ratio and the value of IC$_{50}$ for 48 h of 20(*R*)-Rh$_2$ and 20(*S*)-Rh$_2$ were respectively 28.5%, 33.6% and 33.4,28.5 mg·L^{-1}. The inhibition of ginsenoside Rh$_2$ to A549 showed structure relationship significantly, time-dependent and concentration-dependent. Flow cytometric analysis (FACS) with PI stains analysis results showed that the proportion of A549 cells in G$_1$ phase increased, while the number of cells in S phase decreased significantly and those in G$_2$ phase reduced slightly. This result indicated structure relationship significantly, especially in the 20(*S*) -ginsenoside Rh$_2$ inhibited the proliferation of A549 cell dramatically and retarded A549 cell cycle at G$_0$/G$_1$ phase. The immunofluorescent of combination with Annexin VFITC/PI by flow cytometric suggested ginsenoside Rh$_2$ can induce inchoate apoptosis rate and late apoptosis rate of A549 cell significantly. All the results showed structure relationship significantly, especially in the 20(*S*)-ginsenoside Rh$_2$. The immunofluorescent with fluorescence microscope suggested the activity of Caspase-3 were enhanced after ginsenoside Rh$_2$ treated. Conclusion : 20(*R*) and 20(*S*)-ginsenoside Rh$_2$ had a significant inhibitory effect on the proliferation. Compared with 20(*S*)-ginsenoside Rh$_2$, 20(*S*)-ginsenoside Rh$_2$ has been shown to have significant anticancer effects and to be capable of blocking cell proliferation and causing G$_1$ phase arrest in human lung adenocarcinoma A549 cells. 20(*R*) and 20(*S*)-ginsenoside Rh$_2$ have been shown to have anticancer effects and to be capable of increasing inchoate apoptotic rate, reducing apoptotic rate significantly, enhancing the activity of Caspase-3 and inducing apoptosis in human lung adenocarcinoma A549 cells.

keywords:ginsenoside Rh$_2$ human lung adenocarcinoma cell line A549 cell cycle apoptosis

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