中国药理学与毒理学杂志 2001 15 (2): 155-158 ISSN: 1000-3002 CN: 11-1115/R

论著

18 α-甘草酸下调“胶原蛋白凝胶三明治”培养的大鼠肝细胞P450酶活性及mRNA表达

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收稿日期 2000-11-2 修回日期 网络版发布日期 2009-2-24 接受日期 2000-1-20

摘要 研究18 α-甘草酸（18 α-GA）对肝细胞主要细胞色素P450（CYP）药物代谢酶的影响，并初步探讨其分子机理. 采用“胶原蛋白凝胶三明治”培养的原代大鼠肝细胞，加18 α-GA孵育，酶学测定CYP1A1 （7-乙氧基异噁唑*O*-脱乙基酶，EROD）， CYP2E1（苯胺羟化酶，ANH）和CYP3A（红霉素*N*-脱甲基酶，ERD）活性，逆转录聚合酶链反应测定CYP1A1，CYP2E1和CYP3A1 mRNA表达水平. 结果可见，18 α-GA浓度依赖性（50～400 mg·L^{-1}）抑制大鼠肝细胞EROD， ANH和ERD活性，200 mg·L^{-1}作用最强，抑制率分别可达59.6%，69.7%和44.7%，且呈时间依赖性，于d 4达高峰；浓度依赖性（50～200 mg·L^{-1}）抑制CYP1A1， CYP2E1和CYP3A1 mRNA表达水平，分别可达44.5%，58.1%和37.0%. 上述结果表明18 α-GA在转录水平下调大鼠肝细胞CYP1A1，CY P2E1和CYP3A1表达.

关键词 18 α-草酸 细胞, 培养的 胶原蛋白凝胶三明治 细胞色素P450 逆转录聚合酶链反应

分类号 R963

18 α-Glycyrrhizic acid down-regulated the activities and mRNA expression of cytochrome P450 isoenzymes in rat hepatocyte sandwich cultures

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Abstract

To study the effect and mechanisms of 18α-glycyrrhizic acid (18 α-GA) on cytochrome P450 (CYP) enzymes, the expression of CYP1A1, CYP2E1 and CYP3A was determined in rat hepatocyte sandwich cultures by using enzyme assay and semi-quantitative reverse transcriptase polymerase chain reaction(RT-PCR). The results showed that the activities of CYP1A1 (7-ethoxyresorufin *O*- deethylase, EROD), CYP2E1(aniline hydroxylase, ANH) and CYP3A (erythromycin *N*-demethylase, ERD) were decreased in concentration-dependent manner after treatment with 18 α-GA(50－400 mg·L^{-1}), and at the concentration of 200 mg·L^{-1} inhibitory rate reached the maximum (the maximum inhibitory rate was 59.6%, 69.7% and 44.7%, respectively). The time course revealed that the inhibition reached plateau level at d 4 of culure. 18 α-GA Decreased CYP1A1, CYP2E1 and CYP3A1 mRNA expression in dose- dependent manner, the maximum inhibitory rate was 44.5% , 58.1% and 37.1%, respectively. The results suggest that 18 α-GA down-regulate CYP expression at the transcriptive levels.

Key words 18 α-glycyrrhizic acid cells cultured collagen gel sandwich cytochrome P450 reverse transcriptase-polymerase chain reaction

DOI:

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