

论文

18 $\alpha$ -甘草酸二铵对大鼠肝脏细胞色素P450和II相酶的影响

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摘要:

目的研究18 $\alpha$ -甘草酸二铵(18 $\alpha$ -GL)对肝脏药物代谢酶的影响。方法♂Wistar大鼠ig18 $\alpha$ -GL12.5和50mg·kg<sup>-1</sup>,分别给药3, 6和12d, 对照组给等容量的溶媒。酶学测定肝微粒体细胞色素P450(CYP), 尿苷二磷酸葡萄糖醛酸转移酶(GT)和谷胱甘肽巯基转移酶(GST)活性。结果18 $\alpha$ -GL抑制苯胺羟化酶,乙氧异唑脱乙酰酶和红霉素脱甲基酶活性,抑制率分别可达53.2%, 47.3%和34.3%; 增加GT<sub>1</sub>(底物为7-甲基-4-羟基-香豆素), GT<sub>2</sub>(底物为4-羟基联苯)和GST活性,分别可达29.9%, 70.3%和48.3%。结论18 $\alpha$ -GL对大鼠肝微粒体I相酶(CYP2E1,CYP1A1和CYP3A)主要是抑制作用,对II相酶(GT<sub>1</sub>, GT<sub>2</sub>和GST)是诱导。

关键词: 18 $\alpha$ -甘草酸二铵; 细胞色素P450 II相酶

EFFECTS OF 18 $\alpha$ -GLYCYRRHIZIC ACID ON RAT LIVER CYTOCHROME P450 ISOENZYMES AND PHASE II TRANSFERASE

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Abstract:

AIM To study the effect of 18 $\alpha$ -glycyrrhizic acid (18 $\alpha$ -GL) on hepatic microsomal drug metabolizing enzymes in rats. METHODS 18 $\alpha$ -GL (12.5, 50.0 mg·kg<sup>-1</sup>·d<sup>-1</sup>) were given ip to male Wistar rats for 3, 6 or 12 consecutive days. The rats were sacrificed 24 h after the last dose and the liver microsomes were prepared for analysis of cytochrome P450 (CYP) isozymes and phase II transferase activities. RESULTS Aniline hydroxylase (CYP2E1) activities in the rats treated with 18 $\alpha$ -GL (12.5, 50.0 mg·kg<sup>-1</sup>) for 6 days decreased dose-dependently by up to 53.2%; For 3, 6 or 12 days 7-ethoxyresorufin O-deethylase (CYP1A1) activities in the rats of 50 mg·kg<sup>-1</sup> dose group decreased time-dependently by 17.6%, 38.3% and 47.3%, respectively; Erythromycin N-demethylase (CYP3A) activities was significantly inhibited from 23.1% to 34.3%. UDP-glucuronosyltransferase activities toward 7-hydroxy-4-methylcoumarin significantly increased ranging from 19.3% to 29.9%. UDP-glucuronosyltransferase activities toward 4-phenylphenol in the rats treated with 18 $\alpha$ -GL (12.5, 50.0 mg·kg<sup>-1</sup>) for 6 days increased by 45.9% and 70.3%. Glutathione S-transferase (GST) activities in the rats treated with 18 $\alpha$ -GL (12.5, 50.0 mg·kg<sup>-1</sup>) for 6 days increased by 13.7% and 48.3% in dose-dependent manner. CONCLUSION 18 $\alpha$ -GL inhibited rat liver microsomal cytochrome P450 while induced phase II transferase.

Keywords: cytochrome P450 phase II transferase 18 $\alpha$ -glycyrrhizic acid

收稿日期 2000-07-17 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者:

作者简介:

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