

论文

氟他胺在大鼠肝微粒体经细胞色素P450 1A2代谢的性别差异

王海学;李端;许长江;刘骁

复旦大学药学院药理学教研室, 上海 200032

摘要:

目的体外研究大鼠肝微粒体细胞色素P450 1A2(CYP1A2)对氟他胺(flutamide Flu)代谢的性别差异影响。方法制备正常♀♂大鼠肝微粒体,用CYP1A2抗体与氟他胺(2 mg·L<sup>-1</sup>)共同温孵,测定氟他胺主要代谢产物2-羟基氟他胺(2-hydroxyflutamide, HF)和原药的浓度比(HF/Flu),评价氟他胺在大鼠肝微粒体代谢的性别差异。结果在CYP1A2抗体浓度为1:400,孵育时间为30 min条件下,氟他胺在♂大鼠肝微粒体中的HF/Flu为(1.5±0.6),而♀动物为(0.9±0.4)。不同性别大鼠肝微粒体对氟他胺的代谢存在性别差异(P<0.01)。结论Flu在♂大鼠肝微粒体中代谢快,而在♀大鼠肝微粒体中代谢较慢。♂大鼠体内的CYP1A2酶活性高于♀大鼠。

关键词: 氟他胺 2-羟基氟他胺 细胞色素P450 1A2 肝微粒体

SEX-DIFFERENCE ON FLUTAMIDE METABOLISM IN RAT LIVER MICROSOMAL CYTOCHROME P450 1A2

WANG Hai-xue; LI Duan; XU Chang-jiang; LIU Xiao

Abstract:

AIMTo assess the sex-difference on flutamide metabolism in rat liver microsomes using rat cytochrome P450 1A2, inhibitory monoclonal antibody. METHODSLiver microsomes were prepared from male or female rats. Protein concentration and total cytochrome P450 content were determined. Incubation mixture included liver microsomes (1.0 nmol·L<sup>-1</sup>), reduced form of nicotinamide adenine dinucleotide phosphate (NADPH, 0.1 nmol·L<sup>-1</sup>), CYP1A2 (1:400) and flutamide (2 mg·L<sup>-1</sup>). The incubation time was 30 min. The concentration of flutamide and its major metabolite 2-hydroxyflutamide were analyzed by reverse high-performance liquid chromatography. The mobile phase was a mixture of methanol-acetonitrile-water-diethylether (40:20:35:1) with methyltestosterone as internal standard. The detection wavelength was 234 nm. The reaction mixture was extracted with acetic ether 4 mL. Sex-difference on flutamide metabolism was expressed as the difference between the concentration ratio of 2-hydroxyflutamide to flutamide in male and female rat liver microsomes. RESULTSThe recoveries of flutamide and 2-hydroxyflutamide for the proposed method were more than 75%. The formation of 2-hydroxyflutamide from flutamide was inhibited by CYP1A2 antibodies (1:400) in male and female rat liver microsome for 30 min of incubation time, but the inhibition of flutamide metabolism in female rat was stronger than that in male. The concentration ratios of 2-hydroxyflutamide to flutamide were (1.5±0.6) and (0.9±0.4) in male and female rat liver microsomes, respectively (P<0.01). CONCLUSIONThe results indicate that the activity of male rat CYP1A2 is higher than that of the female rat. There is difference in sex-related rate of flutamide metabolism in rat liver microsomes.

Keywords: 2-hydroxyflutamide cytochrome P450 1A2 liver microsomes flutamide

收稿日期 2001-10-08 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 王海学

作者简介:

参考文献:

本刊中的类似文章

扩展功能

本文信息

- ▶ Supporting info
- ▶ PDF(124KB)
- ▶ [HTML全文]
- ▶ 参考文献

服务与反馈

- ▶ 把本文推荐给朋友
- ▶ 加入我的书架
- ▶ 加入引用管理器
- ▶ 引用本文
- ▶ Email Alert
- ▶ 文章反馈
- ▶ 浏览反馈信息

本文关键词相关文章

- ▶ 氟他胺
- ▶ 2-羟基氟他胺
- ▶ 细胞色素P450 1A2
- ▶ 肝微粒体

本文作者相关文章

- ▶ 王海学
- ▶ 李端
- ▶ 许长江
- ▶ 刘骁

PubMed

- ▶ Article by
- ▶ Article by
- ▶ Article by
- ▶ Article by

反馈人	<input type="text"/>	邮箱地址	<input type="text"/>
反馈标题	<input type="text"/>	验证码	<input type="text"/> 9951