药学学报 2007, 42(2) 221-225 DOI: ISSN: CN:

论文

人肝脏微粒体在体外对丝裂霉素C的代谢

郝福荣;严敏芬;胡卓汉;金一尊

1. 潍坊市人民医院 放疗科, 山东 潍坊 261000; 2. 复旦大学 放射医学研究所, 上海 200032; 3. 瑞德肝脏疾病研究所, 上海 201203

摘要:

关键词: 丝裂霉素 药代动力学 微粒体, 肝 HPLC

Metabolism of mitomycin C by human liver microsomes *in vitro*

HAO Fu-rong; YAN Min-fen; HU Zhuo-han; JIN Yi-zun

Abstract:

To provide the profiles of metabolism of mitomycin C (MMC) by human liver microsomes *in vitro*, MMC was incubated with human liver microsomes, then the supernatant component was isolated and detected by HPLC. Types of metabolic enzymes were estimated by the effect of NADPH or dicumarol (DIC) on metabolism of MMC. Standard, reaction, background control (microsomes was inactivated), negative control (no NADPH), and inhibitor group (adding DIC) were assigned, the results were analyzed by Graphpad Prism 4.0 software. Reaction group compared with background control and negative control groups, 3 NADPH-dependent absorption peaks were additionally isolated by HPLC after MMC were incubated with human liver microsomes. Their retention times were 10.0, 14.0, 14.8 min (named as M1, M2, M3), respectively. Their formation was kept as Sigmoidal dose-response and their *Km* were 0.52 (95% CI, 0.40-0.67) mmol·L^{-1}, 0.81 (95% CI, 0.59-1.10) mmol·L^{-1}, 0.54 (95% CI, 0.41-0.71) mmol·L^{-1}, respectively. The data indicated that the three absorption peaks isolated by HPLC were metabolites of MMC. DIC can inhibit formation of M2, it's dose-effect fitted to Sigmoidal curve and it's IC_{50} was 59.68 (95% CI, 40.66-87.61) μmol·L^{-1}, which indicated DT-diaphorase could take part in the formation of M2. MMC can be metabolized by human liver microsomes *in vitro*, and at least three metabolites of MMC could be isolated by HPLC in the experiment, further study showed DT-diaphorase participated in the formation of M2.

Keywords: pharmacokinetics microsomes, liver HPLC mitomycin

收稿日期 2006-05-30 修回日期 网络版发布日期

DOI:

基金项目:

通讯作者: 严敏芬

作者简介:

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