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论著

地非三唑在鼠肝微粒体中的体外代谢

姚彤炜*, 胡云珍

（浙江大学药学院药物代谢研究室, 浙江 杭州 310031）

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摘要 目的 为了解地非三唑(Dip)在不同预处理的鼠肝微粒体中主要受何种酶代谢影响，为其临床合理应用和进一步开发利用提供科学依据。方法 将Dip与6种不同诱导剂〔苯巴比妥(PB)、地塞米松(Dex)、β-萘黄酮(BNF)、Dip、吡啶和空白对照〕诱导的鼠肝微粒体进行体外共孵育，用氯仿终止反应，以地西泮为内标，采用反相高效液相色谱(RP-HPLC)法测定孵育后剩余的Dip的含量。结果 BNF诱导的鼠肝微粒体对Dip代谢具有强烈的催化活性，Dip诱导的微粒体的催化能力次之，PB诱导组也有一定的催化能力，其他几种诱导剂诱导的微粒体对Dip代谢能力与对照组无明显差别。测得Dip在BNF诱导的鼠肝微粒体中的K_m为（60.5±1.3）μmol·L^{-1}， v_m为（5.6±0.4）mmol·g^{-1}·min^{-1}。结论 由BNF诱导的鼠肝微粒体（主要为细胞色素P450 1A）和PB诱导的鼠肝微粒体（主要为细胞色素P450 2B）在Dip的体外代谢中可能起主导作用；Dip诱导的鼠肝微粒体对其自身的代谢也起了重要作用。

关键词 地非三唑 高效液相色谱 肝；微粒体 药物代谢

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Metabolism of diphenytriazol by rat liver microsomes *in vitro*

YAO Tong-Wei*, HU Yun-Zhen

(Department of Drug Metabolism, College of Pharmacy, Zhejiang University, Hangzhou 310031, China)

Abstract

AIM The metabolism of diphenytriazol in rat hepatic microsomal incubates *in vitro* was investigated in order to obtain the information about metabolic mechanism of diphenytriazol by liver drug enzymes. **METHODS** 〗The metabolism of diphenytriazol was investigated with six kinds of hepatic microsomal incubates of rats pretreated by phenobarbital(PB), dexamethasone(Dex), β-nphthoflavone(BNF), diphenytriazol(Dip), pyridine and control. The Dip in rat hepatic microsomal incubates was extracted by chloroform, and diazepam was used as internal standard. The determination was performed on a Lichrospher ODS-C_{18} reversed column (250 mm×46 mm, id) with a mobile phase of methanol- pH 7.5 phosphate buffer (70∶30, *V/V*) at a flow-rate of 1.0 mL·min^{-1}. A UV- VIS detector was operated at 235 nm. **RESULTS** The assay was linear from 7.23－358 μmol·L^{-1} for Dip in rat hepatic microsomal incubates. The limit of detection was 0.54 μmol·L^{-1} (signal-to-noise ratio 3). The method afforded average recoveries of (98.5±3.7)%（n=6）, intra day and inter-day variation coefficients were less than ＜4.0%（n=5）. The method allowed study of the metabolism of Dip in rat liver microsomal incubates *in vitro*. The microsome induced by BNF showed a major role in the metabolism of Dip, the microsome induced by Dip catalyzed the metabolism at 60% of the rate seen in BNF group, and the microsome induced by PB catalyzed the metabolism at 40% of the rate seen in BNF group. The others showed a lower enzymatic activity. The K_m is (60.5±1.3)μmol·L^{-1} and v_m is (5.7±0.44)mmol·g^{-1}·min^{-1} for Dip with the microsome induced by BNF.

CONCLUSION Cytochrome P450 1A and 2B may play the major role in metabolism of Dip.

Key words diphenytriazol high performance liquid chromatography liver microsomes drug metabolism

DOI:

通讯作者 姚彤炜 Yaotw@zju.edu.cn