中国药理学与毒理学杂志 2010 24 (4): 291-297 ISSN: 1000-3002 CN: 11-1115/R

论著

短刺小克银汉霉AS 3.153菌株对安非他酮的代谢转化

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收稿日期 2009-9-3 修回日期 网络版发布日期 2010-7-23 接受日期 2010-2-17

摘要 目的 寻找适用体外转化安非他酮的微生物菌株及采用此菌株制备吗啉环羟基化安非他酮纯品的可能性。方法 首先采用液相色谱-质谱测定4种小克银汉霉对安非他酮的转化能力，确定菌株，再利用最佳菌株，采用高效液相色谱-多级质谱联用法检测转化液中安非他酮的代谢产物，并针对代谢产物2(M2)的转化进行了培养基初始pH值6水平(分别为6.0, 6.5, 7.0, 7.5, 8.0和8.5)，底物浓度4水平(分别为0.025, 0.05, 0.1和0.2 g·L^{-1})，转化时间5水平(分别为72, 96, 120, 144和168 h)等转化条件的单因素考察，以及采用四因素三水平的正交试验设计对安非他酮进一步优化转化条件。结果 根据液相色谱和质谱数据，经短刺小克银汉霉AS 3.153转化，安非他酮主要形成单羟基化安非他酮和单羟基化安非他酮的硫酸结合物等3种转化产物，对M2进行分离纯化，根据质谱和核磁共振数据，确证代谢产物M2为吗啉环羟基化安非他酮。M2的最优转化条件为采用短刺小克银汉霉AS 3.153培养基、初始pH 8.0、底物浓度0.1 g·L^{-1}和转化时间168 h时转化产率最高。结论 短刺小克银汉霉AS 3.153对安非他酮的转化与人体代谢结果相同，说明此菌株适宜作为研究人体药物代谢的体外模型，采用此模型及相应的优化转化条件可以制备M2纯品。

关键词 安非他酮 生物转化 短刺小克银汉霉

分类号 R969.1, R965

Microbial transformation of amfepramone by *Cunninghamella blakesleana* AS 3.153

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Abstract

OBJECTIVE To find a suitable microorganism that could metabolize amfepramone and yield morpholine-hydroxyamfepramone. **METHODS** The most suitable microorganism species was selected from among four species of *Cunnighamella* by high performance liquid chromatography-tandem mass spectrometry (HPLC-MS^n). The transformation conditions of initial medium pH 6.0, 6.5, 7.0, 7.5, 8.0 and 8.5, the substrate concentrations 0.025, 0.05, 0.1 and 0.2 g·L^{-1}, and the conversion time 72, 96, 120, 144 and 168 h were optimized. **RESULTS** Based on the data of HPLC-MS^n, it can be inferred that 3 metabolites, including mono-hydroxyamfepramone and sulfate conjugation of mono-hydroxyamfepramone, were transformed by *C. blakesleana* AS 3.153. M2 was defined as morpholine-hydroxyamfepramone by HPLC-MS^n. The yield of M2 was the highest when pH was 8.0, substrate concentration 0.1 g·L^{-1} and incubation time 168 h. After M2 was isolated and purified, M2 was confirmed to be morpholine-hydroxyamfepramone according to MS and NMR. **CONCLUSION** *C. blakesleana* AS 3.153 metabolizes amfepramone in a similar way to humans, so it can be used as an *in vitro* model for mammalian drug metabolism. M2 could be yielded by this microorganism under optimized conditions.

Key words amfepramone biotransformation Cunninghamella blakesleana

DOI: 10.3867/j.issn.1000-3002.2010.04.009

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