

论文

LC-MS/MS及离子簇技术分析鉴定盐酸戊乙奎醚外消旋体在大鼠体内的代谢产物

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摘要:

目的研究盐酸戊乙奎醚外消旋体在大鼠体内的代谢产物。方法健康大鼠同时等量im盐酸戊乙奎醚外消旋体及其氙标盐酸戊乙奎醚,收集尿样并处理。用LC/MS/MS,GC-MS,FAB-MS及氙标离子簇示踪技术分析鉴定盐酸戊乙奎醚在大鼠体内的代谢产物。结果共检测到8个代谢产物,分别为原形环戊基上的单氧化产物(M1与M1*)、原形环戊基上的单羟基化产物(M2与M2*)、原形环戊基间位上的氧化羟基化产物(M3与M3*)及原形环戊基与奎宁环上的羟基化产物(M4与M4*)。其中,M1与M1*,M2与M2*,M3与M3*及M4与M4*互为异构体。结论 此法为临床合理用药及新抗胆碱能手性药物研究提供有价值的信息。

关键词: 盐酸戊乙奎醚 外消旋体 代谢产物 LC-MS/MS

IDENTIFICATION OF THE METABOLITES OF PENEHYCLIDINE HYDROCHLORIDE RACEME IN RATS BY LC-MS/MS AND ION CLUSTER

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Abstract:

AIMTo study the metabolites of penehyclidine hydrochloride (PH) raceme, a new anti-cholinergic drug invented by the Institute of Pharmacology and Toxicology, Academy of Military Medical Sciences. METHODS Three healthy rat urine samples were collected within 24 h after a single im dose of PH raceme and PH-d₅ [(5+5) mg·kg⁻¹] simultaneously. The eight metabolites of PH raceme were identified by the methods of LC-MS/MS, GC-MS, FAB-MS and the stable isotope ion cluster. Mass spectrometry was operated in the positive mode for the method of LC-MS/MS. RESULTSM1 and M1* were identified as the oxygenated products of PH in the cyclopentyl group; M2 and M2* were as the hydroxylated products of PH in the cyclopentyl group; M3 and M3* were as the oxygented and hydroxylated products of PH at the meta-position of cyclopentyl group; M4 and M4* were identified as the dihydroxylated metabolites of PH, the hydroxylated position were at the cyclopentyl group and quinuclidinol ring of PH. Among them, M1 and M1*, M2 and M2*, M3 and M3*, M4 and M4* were the isomers of eath other. CONCLUSIONThese characteristics can be used for future structure elucidation in studies of the metabolites of PH optical isomers. The structure data of PH metabolites provide important information for the clinical use and for developing better anti-cholinergic drug.

Keywords: raceme metabolites LC-MS/MS penehyclidine hydrochloride

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