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# 液相色谱-串联质谱法测定人血浆中布南色林及其代谢物的浓度

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摘要 目的 建立液相色谱-串联质谱法(LC-MS/MS)测定人血浆中布南色林及其代谢产物N-去乙基物的药物浓度方法。方法 血浆样品经饱和碳酸氢钠水溶液0.2 mL碱化后用醋酸乙酯-二氯甲烷(4∶1)萃取,布南色林与其代谢物N-去乙基物分别以布南色林B和布南色林D为内标,采用LC-MS/MS测定。色谱柱为Agilent Eclipse plus $C_{18}$(4.6 mm×150 mm,3.5 μm),以乙腈-水(87∶13,*V*/*V*,含0.005 mol·$L^{-1}$甲酸铵和0.1%甲酸)为流动相,流速为0.5 mL·$min^{-1}$,柱温为40 ℃;质谱条件采用ESI离子源,检测方式为正离子电离,选择性离子监测(SRM),用于定量分析的离子反应分别为*m/z* 368.2→297.2(布南色林),*m/z* 396.3→297.2(布南色林B),*m/z* 340.2→297.1(N-去乙基物),*m/z* 356.2→313.3(布南色林D)。结果 布南色林和N-去乙基物在10~2 000 ng·$L^{-1}$($r^2$=0.997)内线性良好,其平均回收率分别为93.5%和74.5%以上,批内、批间精密度分别小于9.0%与16.4%。结论 本试验建立的布南色林及N-去乙基物血药浓度的测定方法简便、快速、准确、灵敏,可用于临床研究中布南色林及其代谢物的药动学研究与治疗药物监测。

关键词: 液相色谱-串联质谱法 血药浓度 布南色林 药动学 N-去乙基物

Abstract: OBJECTIVE To establish an LC-MS/MS method for simultaneous determination of blonanserin and its metabolite blonanserin C in the plasma of healthy volunteers. METHODS After adding saturated aqueous solution of sodium bicarbonate as the basification reagent, blonanserin and blonanserin C were extracted from plasma by ethyl acetate-dichloromethane (4;1). Then blonanserin and blonanserin C were determined by LC-MS/MS using blonanserin B and blonanserin D as internal standards respectively. Separation was carried on an Agilent Eclipse plus $C_{18}$ column(4.6 mm×150 mm,5 μm)with a mobie phase of acetonitrile-0.005 mol·$L^{-1}$ ammonium formate aqueous solution containing 0.1% formic acid (87;13) at the flow rate of 0.5 mL·$min^{-1}$. The column temperature was set at 40 ℃. ESI source was applied and operated in positive ion mode. Quantitative determination was performed using selective reaction monitoring (SRM) at *m/z* 368.2→297.2 for blonanserin, *m/z* 396.3→297.2 for blonanserin B, *m/z* 340.2→297.1 for blonanserin C and *m/z* 356.2→313.3 for blonanserin D. RESULTS Blonanserin and blonanserin C showed good linearity in the range of 10-2 000 ng·$L^{-1}$ ($r^2$=0.997). The extraction recoveries for blonanserin and blonanserin C were more than 93.5% and 74.5% respectively,while the intra-day and inter-day RSDs were lower than 9.0% and 16.4% respectively. CONCLUSION The method is simple,rapid,accurate and sensitivie for simultaneous determination of blonanserin and blonanserin C in human plasma, which can be applied to the clinical pharmacokinetic study and therapeutic drug monitoring of blonanserin.

Keywords: LC-MS/MS, plasma concentration, blonanserin, pharmacokinetics, 2-(1-piperazinyl)-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta-pyridine]

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