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UPLC-MS/MS法同时测定人血浆中卡马西平、拉莫三嗪、氯硝西泮、地西泮及其代谢物奥沙西泮浓度

Simultaneous Determination of Carbamazepine, Lamotrigine, Clonazepam, Diazepam and Oxazepam in Human Plasma by UPLC-MS/MS

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中文摘要:

目的 建立同时测定人血浆中卡马西平、拉莫三嗪、氯硝西泮、地西泮及其代谢物奥沙西泮浓度的方法。方法 采用超高效液相色谱-质谱联用法(UPLC-MS/MS)，以磺胺甲噁唑(SMZ)为内标，血浆经甲醇直接沉淀后进样分析。色谱柱为Waters ACQUITY UPLC HSS PFP柱(2.1 mm×100 mm，1.8 μm)，流动相为0.1%甲酸的5 mmol·L^{-1}乙酸铵水溶液-0.1%甲酸的甲醇溶液(0~5 min，35∶65→10∶90)，流速为0.2 mL·min^{-1}。电喷雾离子源，正离子多反应监测扫描分析，卡马西平、拉莫三嗪、氯硝西泮、地西泮和奥沙西泮的离子对分别为*m/z* 237.0→194.06、*m/z* 255.98→144.95、*m/z* 316.01→270.0、*m/z* 285.04→193.07和*m/z* 287.02→241；内标磺胺甲噁唑的离子对为*m/z* 253.96→91.97。结果 卡马西平、拉莫三嗪、氯硝西泮、地西泮和奥沙西泮血药浓度分别在2.4~600 ng·mL^{-1}(*r*=0.999 7)，2.52~630 ng·mL^{-1}(*r*=0.992 0)，2.08~520 ng·mL^{-1} (*r*=0.997 9)，2.28~570 ng·mL^{-1}(*r*=0.998 2)，8.0~800 ng·mL^{-1}(*r*=0.999 2)线性关系良好；最低检出限分别为0.24，0.63，0.52，0.57，3.2 ng·mL^{-1}。日内、日间精密度均<15%；提取回收率均>70%，且RSD<15%。结论 该方法灵敏、快速、专属性强，可用于临床血药浓度测定及药动学研究。

英文摘要:

OBJECTIVE To develop the method for concentration determination of carbamazepine, lamotrigine, clonazepam, diazepam and oxazepam in human plasma. METHODS UPLC-MS/MS was adopted to analyze plasma with protein precipitated by methanol and sulfamethlazole(SMZ) was used as internal standard. Plasma samples were separated on Waters ACQUITY UPLC HSS PFP(2.1mm×100 mm,1.8 μm) column with aqueous solution(0.1% formic acid 5 mmol·L^{-1} ammonium acetate buffer)-0.1% formic acid method (0-5 min, 35∶65→10∶90) as mobile phase, and at a flow rate of 0.2 mL·min^{-1}. The protonated ion of samples was detected in positive ionization by multiple reaction monitoring(MRM) mode. The target compounds carbamazepine, lamotrigine, clonazepam, diazepam, oxazepam and SMZ were quantified with *m/z* 237.0→194.06, *m/z* 255.98→144.95, *m/z* 316.01→270.0, *m/z* 285.04→193.07, *m/z* 287.02→241 and *m/z* 253.96→91.97, respectively. RESULTS The liner calibration curve of carbamazepine, lamotrigine, clonazepam, diazepam and oxazepam were obtained in the concentration range of 2.4-600 ng·mL^{-1}(*r*=0.999 7), 2.52-630 ng·mL^{-1}(*r*=0.992 0), 2.08-520 ng·mL^{-1}(*r*=0.997 9), 2.28-570 ng·mL^{-1} (*r*=0.998 2) and 8.0-800 ng·mL^{-1}(*r*=0.999 2), respectively. The lowest detection limit were 0.24 ng·mL^{-1}, 0.63 ng·mL^{-1}, 0.52 ng·mL^{-1}, 0.57 ng·mL^{-1} and 3.2 ng·mL^{-1}, respectively. The RSD of inter-day and intra-day were less than 15%. The relative recovery was more than 70%, and the RSD was less than 15%. CONCLUSION The method is accurate, sensitive and suitable for blood concentration monitoring and pharmacokinetic study of carbamazepine, lamotrigine, clonazepam, diazepam and oxazepam.