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胶束液相色谱法同时测定血浆中的苯巴比妥、艾司唑仑和氯硝西泮

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Simultaneous determination of phenobarbital, estazolam and clonazepam in human plasma by micellar liquid chromatography

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摘要 采用胶束液相色谱法(MLC)分离测定血浆中苯巴比妥、艾司唑仑和氯硝西泮,运用三相平衡理论探讨了流动相中表面活性剂浓度(CM)、氢离子浓度(CH)、助表面活性剂浓度(Cφ)对溶质保留行为的影响,同时运用多元线性回归建立了保留因子的对数(log k)与溶质性质参数和流动相组成之间的相关模型。结果表明,溶质保留因子(k)随CM、Cφ和CH的增加而减小,与理论模型完全一致。而且log k与溶质的疏水性常数的对数(log P)和电离常数(Ka)以及CM、CH和Cφ之间呈现良好的多元线性关系。在确定的色谱条件下,血浆中的3种药物与其他组分之间有较好的分离效果。3种药物的血药浓度分别在2.5～50 mg/L、0.25～5.0 mg/L和0.05～5.0 mg/L间具有良好的线性关系。本方法简便、准确、重现性良好、灵敏度高。3种药物的最低检出限(S/N=3)分别为10.27、1.17、0.867 ng,平均加标回收率范围分别为99.80%～102.9%, 94.00%～98.20%和96.30%～98.70%。

关键词： 胶束液相色谱 苯巴比妥 艾司唑仑 氯硝西泮 血浆

Abstract： An analytical method based on micellar liquid chromatography has been developed for simultaneous determination of phenobarbital, estazolam and clonazepam in human plasma. The effects of the concentrations of surfactant, cosurfactant and hydrogen ion in mobile phase (hereafter abbreviated respectively as CM, Cφ and CH) on the retention behavior of the 3 compounds were investigated in terms of three-phase equilibrium theory. The quantitative relationships between the logarithm of retention factor (log k) and the parameters of solutes properties and the composition of mobile phase were set with multiple linear regression method. The experimental results showed that the retention factors (k) of solutes were decreased with the increase of the concentration of surfactant, cosurfactant and hydrogen ion in the mobile phase. The effects of changes of CM, CH and Cφ on retention factors were fully consistent with the theoretical modeling. And there is better multielement linear relationship between the log k of solutes and the logarithm of hydrophobic parameter (log P) and ionization constant (Ka) of solutes and CM, CH and Cφ in the mobile phase. The separation efficiency between phenobarbital, estazolam, clonazepam and other components in human plasma was better under the selected chromatographic conditions. The linearities were good in the ranges of 2.5~50 mg/L of phenobarbital, 0.25~5.0 mg/L of estazolam and 0.05~5.0 mg/L of clonazepam. The method is simple, accurate and reproducible for the determination of phenobarbital, estazolam and clonazepam. The limits of detection (LODs) for phenobarbital, estazolam and clonazepam were found to be 10.27, 1.17 and 0.867 ng (S/N=3), respectively. The recoveries of the method for the determination of phenobarbital, estazolam and clonazepam were 99.80%~102.9%, 94.00%~98.20% and 96.30%~98.70%, respectively.

Keywords： micellar liquid chromatography phenobarbital estazolam clonazepam human plasma

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