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论文

体液中29种中枢神经系统药物的高效毛细管电泳系统分析方法

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摘要:

建立了高效毛细管电泳系统分析法,分析体液样品中29种CNS药物,作为CNS药物中毒的快速的初筛方法。血、尿样品用有机溶剂萃取,胃液直接进样。用酸、弱碱和中性3组缓冲液体系进行电泳分离。以组分与电渗流迁移时间之比的相对迁移时间和紫外吸收光谱为定性指标。最低检测浓度0.5～5μg·mL^{-1}。在此法基础上可增加分析品种。通用的提取方法可避免漏检,广谱分离条件便于分类,专一分离条件便于定性。本法用于实际中毒样品分析,证实所建方法操作简便、分析时间短、杂质干扰小。

关键词: 高效毛细管电泳 中枢神经系统药物 系统分析 巴比妥类 苯二氮 类 吩噻嗪类

A SYSTEMATIC SCREENING AND IDENTIFICATION METHOD FOR 29 CENTRAL NERVOUS SYSTEM DRUGS IN BODY FLUID BY HIGH PERFORMANCE CAPILLARY ELECTROPHORESIS

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Abstract:

A systematic screening method has been developed for the detection of 29 central nervous system (CNS) drugs in human plasma, urine and gastric juice by high performance capillary electrophoresis (HPCE). The first step is sample preparation. The patient's or normal human plasma (0.5 ml) spiked with CNS drugs was extracted with 2×4 ml dichloromethane, while 2 ml of patient's or spiked urine was extracted with 2×6 ml chloroform. The combined extract from plasma or urine was evaporated to dryness in a rotation evaporator at 35℃. The residue was dissolved in 100 μl methanol and subsequently 400 μl of redistilled water was added. The patient gastric juice (3 ml) was centrifuged at 2 000 r·min^{-1} for 5min. The supernatant was filtered through 0.45 μm microporous membrane for injection onto capillary columns. The second step was to perform CZE separation in acidic buffer composed of 30 mmol·L^{-1} $(NH_4)_3PO_4$ (pH 2.50) and 10% acetonitrile (condition A). Most of the benzodiazepines (diazepam, nitrazepam, chlordiazepoxide, flurazepam, extazolam, alprazolam) and methaqualone were baseline separated and detected at 5～13 min, while thiodiphenylamines showed group peaks at 3～5 min and barbiturates migrate with electroosmotic fluid (EOF) together. The third step is to separate the drugs in basic buffer constituted of 70 mmol·L^{-1} Na_2HPO_4 (pH 8.60) and 30% acetonitrile (condition B). The thiodiphenylamines and some other basic drugs could be well separated, which include thihexyphenidyl, imipramine, amitriptyline, diphenhydramine, chlorpromazine, doxepin, chlorprothixene, promethazine and flurazepam, while the rest of the CNS drugs did not interfere with the separation. The last step was to separate the drugs by micellar electrokinetic chromatography (MEKC) in such a buffer as 70 mmol·L^{-1} SDS plus 15 mmol·L^{-1} Na_2HPO_4 (pH 7.55) and 5% methanol (condition C). Barbiturates (barbital, phenobarbital, methylphenobarbital, amobarbital, thiopental, pentobarbital, secobarbital) and some hydrophobic drugs (glutethimide, alprazolam, clonazepam, carbamazepine, trifluoperazine, oxazepam) could be well separated. These drugs might be identified by both the relative migration time ($rt_m=t_{drug}/t_{EOF}$) and the ratios of peak heights (rh) monitored at different wavelength, since the ratios are characteristic of the spectrum of a drug. This method has been used in several real clinical samples of intoxication. For example, perphenazine and doxepin were detected in the gastric juice and phenobarbital in blood and gastric juice of an intoxicated patient.

Keywords: Micellar electrokinetic chromatography (MEKC) Systematic drug screening Benzodiazepines Thiodiphenylamines Barbiturates High performance capillary electrophoresis (HPCE)

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