

[OD4-1] [2004-10-22 14:30 - 14:45 / Room 205]

Enantioseparation of Profens in Tablets and Patches as Diastereomeric (R)-(+)-1-phenylethylamide derivative by Achiral Gas Chromatography

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The antiinflammatory activities of nonsteroidal antiinflammatory drugs of 2-arylpropionic acid type are mainly ascribed to (S)-enantiomers. However, they are mostly marketed as racemic mixtures. In this study, the optical purity tests on (S)-ibuprofen in tablets and the enantiomeric composition tests on flurbiprofen and ketoprofen in patches and urine excretions following each topical application were performed indirectly by achiral gas chromatography as diastereomeric (R)-(+)-1-phenylethylamide derivatives. When applied to seven different commercial (S)-ibuprofen products after method validation, their optical purities (98.7 ~ 99.1%) were measured with good precision (% RSD \leq 4.0). And when applied to flurbiprofen patch of one brand and ketoprofen patches of five different brands after method validation, their enantiomeric compositions were found to be racemic, and % (R)-(+)-enantiomers of flurbiprofen (65.6 ± 0.9) and ketoprofen (53.5 ± 0.9) in urine were present at higher levels as compared to those antipodes (49.75 ~ 50.17%) in patches, while % (S)-(+)-enantiomer of flurbiprofen (34.4 ± 0.9) and ketoprofen (46.5 ± 0.9) in urine were lowered when compared with those (49.83 ~ 50.25%) in patches. The present enantioseparation method is expected to be useful for quality assurance of active profen developments and their stereospecific metabolism study.

[OD4-2] [2004-10-22 14:45 - 15:00 / Room 205]

Method Development for Simultaneous Profiling Analysis of Amines and Phenols as Ethoxycarbonylated Pentafluoropropionyl Derivatives by Gas Chromatography and its Clinical Applications

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An efficient method for simultaneous profiling of amines and phenols was developed. The 20 phenolic compounds in acidic solution (pH 2) were first ethoxycarbonylated with subsequent alkalization (pH 12) for ethoxycarbonylation (EOC) of 30 amines. The resulting EOC derivatives were recovered by solid-phase

extraction employing Chromosorb P column. And then the remaining active hydrogen atoms of amines were converted to pentafluoropropionyl derivatives for the direct analysis by gas chromatography (GC) on dual-columns with different polarities. The dual GC system provided complete separation of amines and phenols with characteristic I sets. Under the optimized conditions, the present method was well-validated for the simultaneous assay of 30 amines and 20 phenols from aqueous samples. When applied to urine specimens from patients with various metabolic disorders and cancer, amines and phenols for each disorder were simultaneously screened. The present method is expected to be useful for the simultaneous screening for phenols and amines in urine from patients with metabolic disorders including cancer.

[OE1-1] [2004-10-22 15:00 - 15:15 / Room 205]

^{99m}Tc-MAG₃-2-nitroimidazole accumulates in hypoxic tumor in mouse model

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^{99m}Tc-2-nitroimidazole derivatives have been reported to accumulate in hypoxic tissue. We prepared a novel ^{99m}Tc-MAG₃-2-nitroimidazole and evaluated the feasibility for hypoxia imaging agent. Bz-MAG₃-2-nitroimidazole was synthesized by direct coupling of Bz-MAG₃ and 2-nitroimidazole using dicyclohexylcarbodiimide. Bz-MAG₃-2-nitroimidazole was labeled with ^{99m}Tc in the presence of tartaric acid and SnCl₂ at 100°C for 30 min. And the reaction mixture was purified by C18 Sep-pak cartridge. The labeling efficiency and the radiochemical purity were checked by ITLC-SG/acetonitrile. The tumor was grown in balb/c mice for 8~13 days after the subcutaneous injection of tumor cells, CT-26 (1'10⁷ cell/0.1 ml). Biodistribution study and tumor autoradiography were performed in the xenografted mice after i.v injection of 74 kBq/0.1 ml and 19 MBq/0.1 ml of ^{99m}Tc-MAG₃-2-nitroimidazole, respectively. The labeling efficiency was 45±20%. Paper electrophoresis confirmed negative charge of ^{99m}Tc-MAG₃-2-nitroimidazole. The stability of ^{99m}Tc-MAG₃-2-nitroimidazole was 98% at room temperature for 6 hr, and its protein binding was 53%. The ^{99m}Tc-MAG₃-2-nitroimidazole exhibited high uptake in the liver, stomach and intestine. The uptake (% ID/g) in the tumor were 0.5±0.1, 0.4±0.0, 0.2±0.1 and 0.1±0.1 at 5, 15, 30 min and 4 hrs, Tumor/muscle ratio were 1.4±0.1, 2.2±0.83, 3.0±0.9, and 3.7 (n=2) for 5, 15, 30 min and 4 hrs. The uptake in hypoxic area was found higher than in non-hypoxic area of tumor tissue by autoradiography. ^{99m}Tc-MAG₃-2-nitroimidazole was successfully synthesized and found feasible for imaging hypoxia.