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A fully automated method including microbore liquid chromatography and column-switching was developed for the analysis of tofisofam. After direct injection of plasma samples (100 ml) into the system, deproteinization and analyte fractionation occurred on a Capcell Pak MF Ph-1 column (20 x 4 mm I.D.) and tofisofam fraction was transferred from MF Ph-1 column to an intermediate column (35 x 2 mm I.D.) using 13 % acetonitrile in 50 mM phosphate buffer (pH 7.0) containing 5 mM octanesulfonic acid. The main separation was performed on a microbore C18 column (250 x 1.5 mm I.D.) using 43 % acetonitrile in 0.1% phosphoric acid containing octanesulfonic acid. The method showed excellent sensitivity (detection limit of 2 ng/ml) and good precision (C.V. ?3.0 %), and shortened total analysis time (20 min). In the concentration range of 5-200 ng/ml, the response was linear (r2 ?0.999). The suitability of the present method was proved in the pharmacokinetic study of tofisofam in human.

[PE2-3] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Simultaneous determination of loxoprofen and its diastereomeric alcohol metabolites in human plasma and urine by a simple HPLC-UV detection method

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The present method was developed for the simple HPLC analysis with an adequate sensitivity and convenience for the routine assay of loxoprofen and its alcohol metabolites in plasma and urine samples following oral administration of loxoprofen to human subjects. The samples were extracted with acetonitrile. The mobile phase system was acetonitrile : water = 35 : 65 v/v, pH 3.0. Separations were performed on octadecylsilica column (250 ´ 4.5 mm, 5㎛) with a guard column (3.2 ´ 1.5 cm, 7㎛) and loxoprofen and metabolites in the eluent were monitored at 220 nm. Coefficients of variations (CV %) for loxoprofen and its metabolites were below 10 % in the 0.2 ~ 15 ㎍/ml range for the plasma and 0.5 ~ 50 ㎍/ml range for the urine. Calibration curves for all the compounds in the plasma and urine were linear over the above-mentioned concentration ranges with a common correlation coefficient of 0.999. And there were no practical sensitivity problems by the present method in determining these compounds in plasma and urine samples from human bioavailability studies of loxoprofen

[PE2-4] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Pharmacokinetics and metabolism of the new anti-ulcer drug KR60436

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The metabolism of the new antiulcer drug KR60436, 1-(2-methyl-4-methoxyphenyl)-4-[(2-hydroxyethyl)amino]-6-trifluoromethoxy-2,3-dihydropyrrolo-[3,2c]-quinoline in the rat was identified using LC/MS/MS. Five metabolites were observed from in vitro and in vivo metabolism of KR60436 and four major metabolic pathways were O-demethylation, loss of hydroxyethyl from amino group, hydroxylation and glucuronidation. Pharmacokinetics of KR-60436 and its active metabolite O-desmethyl-KR60436 were studied in the rat after single intravenous and oral doses of KR60436. Oral bioavailability was 23 % and pharmacokinetic parameters at three different dose levels show approximately linear increases. KR-60436 is cleared almost exclusively by metabolism, in keeping with its lipophilic nature and very low renal clearance and excretion. KR60436 exhibits a large volume of distribution in keeping with high affinity to rat tissues.