[PE1-32] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Drug releasing porous poly (L-lactide)-tricalcium phosphate-alginate membrane for bone regeneration therapy

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With an aim of obtaining effective bone regeneration, many studies using a guided tissue regeneration (GTR) technique have been attempted. Membrane-based barrier system is suitable for preventing connective tissue ingrowth and permeating nutritive elements to heal the bony defect and providing sufficient space for bone growth. In this study, porous poly (L-lactide)-Tricalcium phosphate(TCP)-alginate membrane was produced by solvent casting method using solvent mixture of methylene chloride and ethyl acetate. TCP was added to increase mechanical supportability and regulate porosity of the membrane. Sodium alginate was added to enhance hydrophilicity and moldability of the membrane. Scanning electron microscopic observation(SEM, JEOL, Ltd, Tokyo, Japan), drug release profile, biodegradation characterization, cellular attachment test and cytotoxicity test were investigated. Tetracycline improved bone regenerating efficacy after release from the membrane. This porous membrane system has proper drug releasing function and mechanical strength during therapeutic period, which can be suggested as an effective tool for guided bone regeneration.

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

A reliable and sensitive high performance liquid chromatographic assay of cisapride in human plasma and its pharmacokinetics

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In this study, a reliable and sensitive method for the quantitative determination of cisapride (CIS) in human plasma by reversed-phase liquid chromatography with fluorescence detection was developed and validated. CIS and internal standard, azelastin, in human plasma were extracted with the mixture of cyclohexane-isoamyl alcohol (98:2 v/v). The method was fully validated from 2 to 500 ng/ml linearity range with a recovery of 93.3 %. The lower limit of quantitation of the method was 0.1 ng/ml. The intra- and inter-day reproducibility was less than 10 %. This method was successfully applied to determine the pharmacokinetic parameters of Propulsid in 16 human subjects receiving a single peroral dose (10 mg). The mean maximum concentration (C_{max}) was 51.9 ng/ml, and the mean area under the concentration-time curve (AUC_{0-48}) was 494.4 ng.hr ml^{-1}. The time to reach the peak level (T_{max}) was 1.6 hr.

[PE2-2] [04/21/2000 (Fri) 10:30 - 11:30 / [1st Fl, Bldg 3]]

Rapid microbore liquid chromatographic analysis of Tofisofam in human plasma with column-switching

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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.