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Two formulations of tiropramide {(±) α-(benzoylamino)-4-[2-(diethylamino)-ethoxy]-N,N-dipropyl-benzenepropanamide hydrochloride}, an antispasmodic agent, were orally administered to 16 healthy volunteers by the Latin crossover design with the purpose of evaluating bioeqivalence and pharmacokinetics of tiropramide. Tiropramide in human plasma was determined by a gas chromatography/nitrogen phosphorus detector. Detection limit of tiropramide was 5 ng/ml. C_{max} in test and reference formulations was 93.9 ±54.3 and 96.4 ±51.6 ng/ml, respectively. $AUC_{0\rightarrow last}$ and $AUC_{0\rightarrow inf}$ were, respectively, 330.7 ±193.9 and 349.5 ±205.3 ng.hr/ml for test formulation, 348.9 ±207.7 and 380.8 ±239.0 ng.hr/ml for reference formulation. Terminal half-life was 2.3-2.6 hr. Bioavailability differences for C_{max} and $AUC_{0\rightarrow last}$ were 2.48% and 5.22%, respectively. Minimum detection differences were less than 20 % in both C_{max} and AUC. Based on this results, two formulations of tiropramide were considered to be bioequivalent.

[PE2-4] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

pharmacokinetics of paclitaxel in rabbits with carbon tetrachloride-induced hepatic failure

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Pharmacokinetic of paclitaxel was investigated in rabbits with carbon tetrachloride-induced hepatic failure. The AUC of paclitaxel was significantly increased in severe hepatic failure rabbits(1364ng/ml.hr)compared to that of normal rabbits(567ng/ml.hr). The volume of distribution of paclitaxel in severe hepatic failure rabbits was significantly decreased compared to that of normal rabbits.Total body clearance of paclitaxel in severe hepatic failure rabbits(0.733) was significantly decreased compared to that of normal rabbits (1.762).This results could be due to inhition of paclitaxel metabolism in liver disorder rabbits since paclitaxe is essentially metabolized in liver. this findings suggest that the dosage regimen of paclitaxel should be adusted when the drug would be administered in patients with liver disorder in a clinical situation.

[PE2-5] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Tissue distribution study in CDF1 mice bearig solid lung tumor after administration of thermosensitive drug AspPt

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AspPt is a thermosensitive anti-tumor drug conjugate for local delivery of the drug to solid tumors. The platinum distribution of AspPt was compared with that of cisplatin in nude mice bearing solid lung tumor after single dose treatment. Various main organs such as liver, lung, heart, brain, tumor, kidney and whole blood were collected at 1, 5, 12, 24, 48 hours after intra-tumor administration. After digestion with HNO3 and then H202, Pt was measured with inductively coupled plasma-mass spectrometry(ICP-MS). Platinum concentration at tumor after AspPt was significantly higher, whereas this concentration at other organs was much less than those of cisplatin. Based on these results, this novel platinum(II) thermosensitive compound (AspPt) represents a valuable lead in the development of a new anticancer chemotherapeutic agent capable of improving antitumor activity and low nephrotoxicity.

[PE2-6] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Comparative bioavailability of novel antitumor platinum (IV) complexes, K101, K102, K103, and K104 in rats

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The pharmacokinetics and bioavailability of novel antitumor platinum (IV) complexes were investigated after intravenous and oral administration of the complexes to rats. I.V. doses of 5 mg/kg (k101 and K102) and 10 mg/kg (K103 and K104) and oral doses of 30 mg/kg (K101, K102, K104) and 150 mg/kg (K103) were given separately to male rats. Total platinum concentrations in plasma and urine were determined by flameless atomic absorption spectrometry. After i.v. administration, AUC values of K101, K102, K103, and K104 were 3023, 2861, 2530 and 1514 ug×min/ml, respectively. Renal clearances of K101, K102, K103, and K104 were 0.51, 0.75, 3.39, 4.52 ml/min/kg, respectively. K101 and K102 had 2.2- to 3.6-fold larger AUC and 4.5- to 9-fold slower renal clearances compared with K103 and K104. After oral administration, Cmax values of K101 and K104 were 6.7- to 10-fold higher than those of K102 and K103. The absolute bioavailability of K101, K102, K103, and K104 were 20.11%, 2.14%, 3.69%, and 16.43%, respectively. The oral bioavailability of K101 and K104 were 4.5- to 10-fold higher than those of K102 and K103.

Poster Presentations - Field E3. Physical Pharmacy

[PE3-1] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Oligosaccharide analyses on the glycoproteins using HPAE/PAD and HPLC/fluorescence detector

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The analysis of protein glycosylation is an important part of glycoprotein characterization, especially because the sialylation or desialylation in oligosaccharides often causes dramatic changes in the function of glycoproteins.In the present study, we used two methods to structurally analyze sialylated oligosaccharides: high-performance anion-exchange chromatography with pulsed amperometric detection, and fluorescence detection using a conventional high-performance liquid chromatography system. As a result, oligosaccharides with no derivatization and PA-oligosaccharides were successfully detected, and exhibited different retention times. We are currently using these methods to analyze the structure of sialylated oligosaccharides from glycoproteins such as fetuin and bovine submaxillary mucin, and from diseased glycoproteins.

[PE3-2] [04/19/2002 (Fri) 10:00 - 13:00 / Hall E]

Detection of carbohydrate on the glycoproteins using enzyme-linked lectin assay

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An enzyme-linked lectin assay(ELLA) was developed for the characterization of glycoproteins such as fetuin, asialofetuin, ribonuclease B, bovine submaxillary mucin, and thyroglobulin. Peroxidase-labeled lectins were obtained from wheat-germ agglutinin, *Bandeiraea simplicifolia* lectin, *Ricinus communis* agglutinin, concanavalin A, and soybean agglutinin, since they specifically bind to the saccharide residues