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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]