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

most frequently encountered in oligosaccharides. The results demonstrate that ELLA is a very useful tool for rapid estimation of the types and relative amounts of specific carbohydrate structures within intact glycoproteins. The microheterogeneity of some oligosaccharides was also studied by using lectins that bind to their terminal residues. These results are compared with the results from direct structural analysis of oligosaccharide using a liquid chromatography system.

[PE3-3] [04/19/2002 (Fri) 10:00 ~ 13:00 / Hall E]

Characterization and cytotoxicity of lectin from Maackia fauriei

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A lectin has been purified from the bark of the legume plant *Maackia fauriei*. *M. fauriei* agglutinin (MFA) demonstrated high homogeneity with the lectin from *M. amurensis* in its N-terminal amino acid sequence and amino acid composition, however, the carbohydrate-binding specificity was different. The hemagglutination activity of MFA with human erythrocytes was specifically inhibited by N-acetylneuraminic acid as well as by Neu5Aca2-3Galb1-4GlcNAc. The hemagglutination activity of MFA is stable at pH values from 4.04 to 7.34, and at temperatures below 45℃. MFA exerts cytotoxic effects on human breast cancer MCF-7 cells, human melanoma G-361 cells, and human liver cancer SNU-449 cells.

Poster Presentations - Field F1. Clinical Pharmacy

[PF1-1] [04/19/2002 (Fri) 10:00 ~ 13:00 / Hall E]

Urinary profiles of fatty acids and androgens in female patients with thyroid cancer

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In female thyroid cancer, the relationship and potential effect of 11 endogenous androgens and 8 polyunsaturated fatty acids (PUFAs) were quantitatively determined in the urine of patients with thyroid cancer and normal subjects using the gas chromatography-mass spectrometry with selected ion-monitoring (SIM) mode. The values of urinary PUFAs as the long chain fatty acid, the precursor of cholesterol, was not different between normal controls and patients with thyroid cancer. But, in female thyroid cancer, the level of docosahexaenoic acid (DHA) was increased significantly higher than those of normal subjects. The concentrations of adrenal androgens derived from the parent cholesterol were not different significantly in the two groups. However, urinary values of dihydrotestosterone (DHT, $P<0.2$), androsterone (An, $P<0.05$), and etiocholanolone (Et, $P<0.05$) are different to the values of the other androgens. Especially, concentrations of An and Et were incresed in patients with thyroid cancer than those of normal controls. These data indicate that fatty acids can be related to the 5a-reductase, which is one of the enzyme in androgen metabolism.

[PF1-2] [04/19/2002 (Fri) 10:00 ~ 13:00 / Hall E]

Determination of Practical Dosing of Warfarin in Korean Outpatients with Mechanical Heart Valves

Lee Byungkoo° Lee Ju Yeun, Jeoung Young Mi, Suh Ok Kyung, Shin Wan Gyoon, Lee Myung Koo