homozygous mutant-type (T/T) was 10, 12 and 1, respectively. MDR1 C3435T genotyping revealed that homozygous wild-type (C/C), heterozygous (C/T) and homozygous mutant-type (T/T) was 9, 11 and 3, respectively. A correlation between the risperidone pharmacokinetics and genotype was observed. There were significant differences ($p<0.05$) in the disposition kinetics of risperidone and 9-hydroxyrisperidone between homozygous for *1 and homozygous for *10. A significant relationship was observed between MDR1 genetic polymorphisms in exon 21 (G2677T), 26 (C3435T) and risperidone pharmacokinetics ($p<0.05$). The ratio between risperidone and 9-hydroxyrisperidone was related to the CYP2D6*10 allele and the MDR1 (exon 21 and 26) gene significantly ($p<0.05$) affected risperidone disposition kinetics.

[PE2-2] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

Determination of lisinopril in human plasma by liquid chromatography tendem mass spectrometry and its application to human bioavailibility study

Shim Hee-OK°, Kim Dong-Chul
iBiopharm Co., Ltd. Research Laboratory, #307 Expotel, 381 Mannyon-dong, Suh-ku, Taejon, 302-834 Korea., Taejon, 302-834 Korea. Colleage of Pharmacy Chungnam National University, 220 Gung-dong, Yusung-ku, Taejon, South Korea

This study was to develop a quantification method of lisinopril using liquid chromatography tendem mass spectrometry in human plasma. Quntitation of lisinopril by MRM(multiple reaction monitoring) in the electrospray positive mode was validated according to FDA guideline. Extraction of lisinopril and enalapril as internal standard from plasma was perfomed by means solide phase extraction. The calibration curve of lisinopril showed a good linearity in the concentration range 2~ 200ng/ml. The coefficients of variations for the inter-day and intra-day precision was less than 15%, and the inter-day and intra-day accuracy was 97.6~101.0%. The recovery of lisinopril in the SPE was approximately 80%. This analytical method was applied to bioavailibility study. Following oral administration of lisinopril tablets (10mg dose) in 9 healthy volunteers, bioavailibility parameters were calculated by BAcal 2002 for windows(ver 1.1.1). Bioavailibility parameters(mean±S.D) were as follows : AUC_{last} =581.4 ± 236 ng hr/mL, C_{max} =36.2±15.7 ng/mL, T_{max}= 6.7±1.0 hr, $T_{1/2}$ =9.9±2.6 hr, K_e= 0.069±6.9 hr^{-1} .

[PE2-3] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]

High throughput approaches to predicting drug absorption potential using the immobilized artificial membrane phosphatidylcholine column and molar volume

Yoon Chi Ho°, Shin Beom Soo, Chang Hyun Sook, Yoo Sun Dong
College of pharmacy, Sungkyunkwan University

The purpose of this study was to evaluate the predictability of the fraction of drug absorbed in humans using the immobilized artificial membrane phosphatidylcholine column (IAMPC) under optimized conditions in comparison with a conventional IAMPC method. Twenty commercial drugs, both acidic and basic in nature, were used in the study, Drugs were dissolved in acetonitrile:water (50:50, v/v) at a concentration of 100 mg/ml, and were injected on HPLC/UVD at a mobile phase (acetonitrile:DPBS = 10:90,v/v) with a flow rate of 0.5 ml/min equilibrated at 37℃. The IAM capacity factor (K'_{IAM}) and the membrane permeability corrected for molecular size (K'_{IAM}/MW^n) were determined at different pHs (2.6, 5.5 and 7.0). A better correlation was found when the human fraction absorption Fa (%) was plotted as a function of K'_{IAM}/MW instead of K'_{IAM} (0.550 vs. 0.446). The predictability was further improved when plotted against the corrected molecular size ($K'_{IAM}/MW^{2.53}$) (r=0.873). The prediction of Fa was higher at the pH 5.5 than at pH 2.6 and pH 7.0. The pH dependence of membrane interaction for groups of acidic and basic drugs was in accordance with the pH partition theory. This optimized IAMPC method appears to provide a good prediction of the fraction of oral drug absorbed in humans.

[PE2-4] [2003-10-11 09:00 - 12:30 / Grand Ballroom Pre-function]