measurement of lansoprazole in human plasma, and the application of pharmacokinetic study has been evaluated. Omeprazole was used as an internal standard. After adding methyl tert-butyl ether, samples were stored at -70°C. The extracts were easily obtained only with pouring the organic phase. The mobile phase was prepared using acetonitrile and water at the volume ratio of 38:62. The signals were monitored by UV detector at 285 nm with a flow-rate of 1 ml/min. The retention time of lansoprazole and omeprazole were 6.1 min and 10.2 min, respectively. The limits of lansoprazole in human plasma were 10 ng/ml for detection and 50 ng/ml for quantitation. As a result of the intra-day and inter-day validations, the accuracy of the assay was from 99.51% to 102.24% and the coefficient of variation was less than 9.4%. Moreover, this method was available for pharmacokinetic studies in humans. The maximum plasma concentrations (Cmax), time of maximum plasma concentration (Tmax), and area under the curve ($AUC_{0 \to 12hr}$) of lansoprazole were 1.08±0.11 μg/ml, 2.14±0.38 hr, and 2.89±0.36 μg·hr/ml, respectively. This method is suitable for the analysis and pharmacokinetic study of lansoprazole in human subjects.

[PD4-6] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Studies on the Analysis of Anti-impotent Drugs(II) - Rapid analysis of Sildenafil and modified Sildenafils using HPTLC

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Drug Evaluation in Korea Food & Drug Administration

HPTLC(High Performance Thin Layer Choromatography) method was developed for rapid and precise analysis of Sildenafil and modified Sildenafils(Vardenafil, Homosildenafil, Tadanafil). Chromatographic conditions were Optimized for simultaneous analysis of them and each specific UV spectra were obtained. The calibration curve of Sildenafil and modified Sildenafils had a linearity in the range of 1.0 ~ 56.5 μg/mL at 254nm. The Limit of Detection(LOD) and the Limit of Quantification(LOQ) of Sildenafil and modified Sildenafils were 0.8μg/mL and 1.0 μg/mL. The percentage of C.V was not more than 2.3% in precision test. Finally, We rapidly assayed Sildenafil and modified Sildenafils in health supplemental food by this method.

[PD4-7] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Proficiency Test for Pharmaceutical Companies in Analyzing Drug Products (II) - Analysis of Variance of Factors Influencing Test Results

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Analytical results during the proficiency test managed by Kyungin Regional Korea Food & Drug Administration were proposed to be influenced by several factors. Data of several factors were collected along with the test results with ibuprofen and sobrerol formulations. The collected data were the use of internal standard, academic background and career of analytical personnel, production size of the company and location of the participating laboratory. The analytical result itself and deviation from the median value were subject to one-way analysis of variance(ANOVA). The statistical test was performed in a double-blind manner. The use of internal standard gave a significantly different analytical accuracy in the cases of gas chromatographic analysis but not in the cases of liquid chromatographic analysis. The academic background of analytical personnel was influential to the analytical results, that is, analysts with chemistry-related major gave better results. Those with more than 5-year career of pharmaceutical analysis gave better results according to ANOVA. Analytical results from one out of 4 locations of participating laboratories were significantly different from others, which is believed to be an artifact in data. Finally, laboratories of major companies gave more accurate results compared to those of smaller companies.

[PD4-8] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Chiral Separation of Non-Steroidal Inflammatory Drugs and Metabolites by Achiral Gas Chromatography as O-Trifluoroacetylated (-)-Menthyl Esters

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Because of the differences in biological and pharmacological properties between enantiomers of chiral acidic non-steroidal antiinflammatory drugs (NSAIDs) in human body, accurate determinations of their optical purities have been in great need. Racemic ibuprofen, tiaprofen, suprofen, flubiprofen and napoxen were reacted with (1R, 2S, 5R)-(-)-menthol to convert them to corresponding diastereomeric (1R, 2S, 5R)-(-)-menthyl esters. The resulting derivatives were extracted with hexane after adjustment to pH>11, evaporated to dryness under gentle nitrogen stream and reconstituted in toluene for the direct analysis by achiral capillary column gas chromatography. Optimization of the present method and its application to chiral separation of ibuprofen and its metabolites in urine will be discussed.

[PD4-9] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Determination of Histamine in a Pharmaceutical Preparation after Clean-Up by Solid- Phase Extraction

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A human immune globulin preparation (histobulin?) are made to bind a small amount of histamine (0.15 ug) to the protein (12 mg) to increase the resistance of histamine susceptibility in the treatment of allergic diseases. Strict control of histamine content of the drug are required since intake of histamine might result in hypo- or hypertension, headache, or anaphylactic shock syndromes. HPLC analytical method with pre-column fluorescent derivatization after clean-up by solid-phase extraction (SPE) was developed. Sample was applied to a polystyren-divinylbenzene (PS-DVB) SPE cartridge followed by solvent washings and eluting histamine with 100 mM NaAc in 80% methanol successively. An aliquot of the extract was pre-labeled with o-phthaldehyde-mercaptoethanol (OPA-ME) for fluorescence detection (Ex 340- Em 450 nm) in HPLC. HPLC analysis was performed under the conditions: Eluent with 35% AcCN in 50 mM phosphate(pH 6.8) showed the retention time of the analyte and internal standard (3-methylhistamine) at 7.0- and 10.8 min., each respectively on a phenyl column. Histamine was recovered quantitatively afforded 80% in 0.1 ppm range with efficient removal of proteins and glycine by the SPE method. Good linerarity was obtained up to 10 ug/mL of histamine. Quantitation range was between 0.01 and 0.5 ug/mL for the sample. The method was successfully applied to determine micro-amount of histamine in the pharmaceutical

[PD4-10] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Studies on the Analysis of Anti-impotent Drugs

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Sildenafil citrate(SC, Viagra[R]) is the oral treatment for erectile dysfunction. Vardenafil hydrochloride, tadalafil and modified sildenafil have anti-impotent effect and have possibility to be used illegally. The aim of this study was to set up simultaneous determination method of anti-impotent drugs using TLC and HPLC. The anti-impotent drugs were extracted with 50% methanol and then diluted with mobile phase for HPLC and also extracted with developing solvents as sample solutions for TLC. The sample solutions for TLC was applied to Silica gel F_{254} plates with chloroform/ethanol(9:1) as developing solvents. Spots were located under UV radiation at 254nm and visualized with iodine vapor. The HPLC analysis was carried out reverse phase of CAPCELL PAK C_{18}(4.6× 250mm, 5μm) with 0.1% SHS in 0.1% phosphoric acid/acetonitrile(73:27) as mobile phase and the eluate was detected by a photo-diode array. This method can be used in detecting the fake Viagra[R] and other anti-impotent drugs illegally used in the products.