

coefficient of variation of less than 20 %. Good linearity was observed in the concentration range of 5 to 150 ng/ml. The results suggest that this method could be used successfully to study levosulpiride pharmacokinetics in adult humans.

[PD4-20] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Potentiometric Characteristics of Metal(II)-Triethylene tetramine-Acidic Drug Membrane Electrodes

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Potentiometric sensors are important and viable devices for use in pharmaceutical analysis. Liquid polymeric membrane electrodes for many basic drugs and a few acidic drug were reported. The acidic drug-metal(II)-triethylene tetramine ion pair complexes were prepared and used in poly(vinyl chloride) membrane electrodes to analyze anionic drugs such as mefenamic acid and ibuprofen. Metal ion used were Fe²⁺, Co²⁺, Ni²⁺ and Cu²⁺. Plasticizer used was *o*-nitrophenyl octyl ether. The electrodes exhibited a fast stable and linear response for 10⁻⁵ - 10⁻³ mol/L mefenamic acid and ibuprofen with a response slope of almost 50 - 60 mV/dec. in borate buffer solution of pH 8.9. Potentiometric selectivity measurements revealed negligible interferences from aromatic and aliphatic carboxylic acid salts.

[PD4-21] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Determination of triflusal in human plasma by high performance liquid chromatography with automated column switching system

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To study the pharmacokinetics of triflusal, more reliable and sensitive analytical method of triflusal in plasma sample was developed. Analytical method of triflusal in human plasma was developed using semi-microbore HPLC equipped with automated column switching system. *p*-Toluic acid, which is structural analogue of triflusal, was used as an internal standard and 2 M HCl was employed as a stabilizer. The load phase and mobile phase were prepared using acetonitrile and 20 mM KH₂PO₄ with the volume ratios of 10:90 (pH 2.5) and 43:57 (pH 2.3), respectively. The signals were monitored by UV detector at 275 nm with flow-rate of load phase, 0.5 ml/min, and mobile phase, 0.1 ml/min, respectively. The retention time of triflusal and *p*-toluic acid was about 20.2 min and 16.4 min, respectively. The detection limit of triflusal in human plasma was 10 ng/ml and the limit of quantitative analysis was 50 ng/ml. The accuracy of the assay was from 97.76% to 116.51% while the intra-day and inter-day coefficient of variation of the same concentration range was less than 15%. This analytical method demonstrated excellent sensitivity, reproducibility, specificity, and speed using the plasma sample. This method could be successfully applied to evaluate the bioavailability of triflusal in human subjects without time-consuming sample clean-up after oral administration of low dose.

[PD4-22] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Simultaneous quantitation of enalapril and enalaprilat in human plasma by high-throughput solid phase extraction and liquid chromatography/tandem mass spectrometry

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Enalapril (ENP) maleate is effective drug for the treatment of renovascular hypertension and heart failure. ENP acts as inhibitor of the enzyme angiotensin-convertase (ACE-inhibitor) and metabolized to enalaprilat (ENPT), which is the active metabolite that is really responsible for the therapeutic action. In the present study, a sensitive and

rapid liquid chromatography/ electrospray ion trap tandem mass spectrometry (LC/MS/MS) method combined with high-throughput solid phase extraction (SPE) has been developed and validated for the simultaneous quantitative determination of ENP and ENPT in human plasma. After addition of internal standard, samples were simultaneously extracted by 96-well C18-SPE cartridge. The organic extract was evaporated to dryness, with subsequent analyzed by LC/MS/MS using the selective reaction monitoring (SRM) mode and time segment. The product ions of ENP and ENPT were characterized by m/z 234, m/z 303 and m/z 206, m/z 303, respectively. These product ions were monitored for the quantitation of ENP and ENPT. As a results, the present method for the simultaneous determination of ENP and ENPT was accurate and reproducible.

[PD4-23] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Simultaneous determination of sildenafil and its active metabolite in human plasma using LC/MS/MS

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The LC/MS/MS method for the simultaneous determination of sildenafil and its active metabolite N-demethylsildenafil in human plasma was developed. Sildenafil, its active metabolite and the internal standard, DA-8159 were extracted from human plasma by liquid-liquid partitioning. A reverse-phase HPLC separation was performed on Luna phenylhexyl column with the mixture of acetonitrile-5 mM ammonium formate (55:45, v/v) as mobile phase. The detection was conducted by electrospray ionization tandem mass spectrometry in the multiple reaction monitoring mode. The lower limits of quantification for sildenafil and N-demethylsildenafil were 2.0 ng/ml. The method showed a satisfactory sensitivity, precision, accuracy, recovery and selectivity.

[PD4-24] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Algorithm for finding the best regression models using NIR spectra

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An algorithm for finding the best regression models has been developed using NIR spectral data. In cases of regression analysis for quantitation with NIR spectral data, it is very critical to find essential features from the spectral data. This task was accessed in two ways. The first one was to use all-possible combinations of variables (wavelengths). Correlation coefficients at each spectral points were calculated to get initial set of variables and all of the possible combinations of variable sets were tested with SEC, SEP and/or R². The second one was to use principal component(PC) analysis with PC selection by all-possible combinations. The initial set of PCs was obtained using Malinowski's IND function or PRESS and all-possible combinations of the PCs were evaluated in terms of SEC and/or SEP. These algorithms were tested with NIR spectral data of synthetic biological fluid to find concentrations of minor component.

[PD4-25] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Chromatographic Analysis of Cilostazol in Human Plasma

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Cilostazol, a quinolinone derivative that inhibits phosphodiesterase, is used for the treatment of intermittent claudication resulting from peripheral arterial disease. In order to perform pharmacological and pharmacokinetic studies of cilostazol, specific, sensitive and reproducible analysis methods are demanded. Therefore, in the present study, an analytical method of cilostazol in human plasma was developed using semi-microbore HPLC equipped with automated column switching system. After direct injection of human plasma, deproteinization and fraction of analyte occurred on a Capcell Pak MF Ph-1 column (20 x 4 mm I.D.). The cilostazol fraction was transferred from the MF Ph-1 column to an intermediate C18 column (35 x 2 mm I.D.) using 10% acetonitrile in