[PD4-17] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Enantiomeric Profiling Analysis of NSAIDs by Capillary Electrophoresis Using TM β-Cyclodextrin as the Chiral Selector

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Because of the differences in 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. An efficient capillary electrophoretic (CE) profiling method was developed for the enantioseparation of NSAIDs. Capillary electrophoretic conditions were optimized using TMβ-cyclodextrin as the chiral selectors under MES buffer. The effects of chiral selector concentration, and pH of run buffer on the resolution and migration behavior of each enantiomeric pair will be discussed.

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

Qualification of various polymorphs by near-infrared(NIR) spectrophotometer.

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Near-infrared(NIR) reflectance spectroscopy was employed to qualify various ploymorphs. We collected 8 potential polymorphs forms of Medicine T for this study. Near-infared spectra of the powder samples contained in glass vials were obtained over the wavelength region of 1100-1750nm. There were the peak around 1560nm in the 6 spectra among 8 spectra. Principal component analysis(PCA) has been performed to examine the qualitative difference of 8 polymorphs PC space. Before performing PCA, all the sample spectra were preprocessed using a second derivatization algorithm to reduce baseline variations and enhance the spectral features. NIR spectral data for the 8 polymorphs were divided moderately into two groups using PCA. The separated patterns of the spectral data had similar trend with differential scanning calorimetry(DSC) These studies have indicated that NIR spectroscopy could be utilized to identify polymorphs based on the molecular structure using PCA.

[PD4-19] [10/18/2002 (Fri) 13:30 - 16:30 / Hall C]

Development of a high-performance liquid chromatographic method for the determintion of levosulpiride in plasma

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Levosulpiride is the levo-enantiomer from of racemic sulpride, abenzamide derivative selectively inhibition doparninergic D2 receptos at the trigger zone both in the central nervous system and in the gastrointestinal tract. We report a rapid and sensitive HPLC method using reverse phase C18 column with fluorescence detection for separation and quantitation of levosulpiride in plasma. Tiapride was used as an internal standard. After adding an internal standard, levosulpiride in 800 μl of plasma was extracted under basic conditions with ethyl acetate and methylene chloride. Then, the organic extract was evoporated to dry and the residue was reconstituded in 160 μl of mobile phase. This extraction method exhibited higher recovery (> 90 %) and shorter processing time (1 h). The mobile phase was prepared by mixing 20 mM phosphate buffer (pH 3.5) and methanol at the ratio of 84: 16 (v/v, %). The signal was monitored by fluorescence detector with maximum excitation at 300 nm and maximum emission at 365 nm at the flow rate of 0.6 ml/min. The limit of quantitation of levosulpiride was 5 ng/ml with a

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 KH_2PO_4 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 renivascular 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