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We recently reported that a new HPLC chiral stationary phase prepared by bonding (+)-(18-crown-6)-2,3,11,12-tetracarboxylic acid (18-C-6-TA) has been successfully employed in resolving various racemic compounds containing a primary amino functional group. Related to these results, in this study it is shown that the chiral selector 18-C-6-TA could be used as a chiral solvating agent for resolution of amino acids and their methyl esters by NMR spectroscopy. It was observed that the chemical shift changes of the alpha protons of these analytes were sufficiently large enough to determine the ratio of the enantiomers (0.2-0.3ppm).

[PD4-5] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Determination of Silibinin in human plasma by high performance liquid chromatography: validation and application in pharmacokinetic study

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A reversed phase high performance liquid chromatographic method for the determination of silibinin diastereomers in human plasma is described. The method was applied to the assay of total (free and conjugated) silibinin levels in healthy volunteers after oral administration. Total silibinin diastereomers were hydrolysed enzymatically using b-glucuronidase/sulfatase at pH 5.0 followed by extraction with diethyl ether of the pH 8.5 alkalinized solution. The diastereomers and the internal standard naringenin were seperated on a Lichrospher 100 C18 column (250mm´4mm I.D.) with ultraviolet detection at 288 nm. As the mobile phase, 40~60% acetonitrile in 2% formic acid by gradient elution was employed for the separation. Inter-day and intra-day precision were less than 6% and 4%(CV), respectively. The accuracy were 96~112% and the recovery were 60~70% for silibinin The calibration curve was linear over a concentration range of 20~2000 ng/ml. The method is relatively simple, sensitive, and satisfactory for the analysis of silibinin in plasma samples from pharmacokinetic study in humans.

[PD4-6] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Analysis of Furathiocarb and its Main Metabolite Carbofuran of Postmortem Specimens in a Fatal Case

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A fatal poisoning(suicide) by the insecticide furathiocarb is described. A 35-year-old man was found dead lying flat on the floor of the boiler room in a deserted house. A farmer found him dead and reported to the police. The public prosecutor ordered to examine the cause of death closely. The corpse was sended to Western District Office, National Institute of Scientific Investigation and the autopsy was performed. Besides the color of the gastric contents was milk-white, the autopsy findings were unremarkable. The following postmortem samples were taken for toxicological investigations: blood, gastric contents, spleen, kidney etc. The analytes in postmortem specimens obtained at autopsy were extracted by liquid-liquid extraction with ethyl acetate. After the ethyl acetate layer was evaporated, the residue was partitioned into hexane and acetonitrile, and the hexane layer was discarded to remove lipophyllic impurities. The acetonitrile layer was analyzed. Tissue specimens were homogenized with distilled water, deproteined with 10% trichloroacetic acid and applied for liquid-liquid extraction. After

extraction, the extracts were reconstituted in methanol for GC and GC/MS. Furathiocarb and its main metabolite carbofuran was detected in the gastric contents by TLC, GC and GC/MS, and quantitated in the blood and postmortem tissues (kidney, spleen etc) using GC/NPD.

[PD4-7] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Identification of Gamma-Hydroxybutyrate(GHB) in Seized materials and Urine samples.

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Gamma Hydroxybutyrate (GHB), known as liquid ecstasy, liquid x or Georgia home boy, is a central nervous system depressant abused for its ability to produce euphoric and hallucinatory states and its alleged ability to release a growth hormone and stimulate muscle growth. GHB can produce drowsiness, dizziness, nausea, unconsciousness, seizures, severe respiratory depression, and coma. It is taken orally and is frequently combined with alcohol and often used as "Date-Rape" drug. In recent days, liquid form of GHB solution and abuser's urine was received to our laboratory for analysis of the drug. The solution was acidified with 10%-HCl and extracted with ethyl acetate and evaporate to dryness at 48℃ under the nitrogen. The residue was derivatized with BSTFA and injected into GC/MSD. For the analysis and quantitation of urine sample, GHB-d6 was used for internal standard. Urine sample was solid phase extracted using CLEAN SCREEN ZSGHB020 column and also derivatized and injected into GC/MSD. The full scan mass spectrum of GHB-TMS identifies the following ions in order of abundance m/z 147, 233, 117, 158, 148 and 149. For detection of GHB in urine samples, the mass selective detector was run in selected ion monitoring mode (SIM) and GHB was not detected in urine samples.

[PD4-8] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

High Performance Liquid Chromatography / Electrospray Tandem Mass Spectrometric Method for Quantitation of Lovastatin Acid in Human Plasma

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Lovastatin acid, the major active metabolite of lovastatin in human blood, was analysed by high performance liquid chromatography /electrospray tandem mass spectrometry(LC/MS/MS). This method utilized a solid phase extraction(SPE) procedure for purifying and concentrating the lovastatin acid and internal standard, simvastatin acid. Reversed-phase mocrobore(15cm X 2.1 mm) column was used for chromatography and the flow rate was 0.2 ml/min. Tandem mass spectrometry was operated in multiple-reaction-monitoring(MRM) mode with a unit mass resolution on both mass analyzers. For quantitation in the MRM mode, the precursor → product ions monitored in the negative-ion mode were m/z 421.3 → 101 (lovastatin acid) and m/z 435.3 → 115 (simvastatin acid). The assay was linear in the concentration range 0.5-50 ng/ml for lovastatin acid when 1 ml aliquots of plasma was extracted. Detection and quantitation limits were 100pg/ml and 500pg/ml in human plasma respectively. The accuracy, intra-day and inter-day precision as determined from QC samples were less than 10%, 4% and 15% respectively. This method was applied to the analysis of clinical samples from a bioequivalence study of lovastatin preparation.

[PD4-9] [10/19/2001 (Fri) 09:00 - 12:00 / Hall D]

Determination of Acidic Drugs with Metal-Complex based Ion Selective Electrodes.