Current Awareness

Drug Testing
and Analysis

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Current awareness in drug testing and analysis

1 Reviews

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Clin Chem 2009 **55** (11) 1910
Oral fluid testing for drugs of abuse
Oral fluid (OF) is an interesting optional source for monitoring drugs of abuse in workplace, clinical toxicology, criminal justice, and driving under the influence of drugs (DUID) programs. Over the last 5 years, scientific and technological advances in OF collection, point-of-collection testing devices, and screening and confirmation methods have been accomplished. Criteria have been specified for workplace OF testing by the Substance Abuse and Mental Health Services Administration, DUID testing by the European Union's Driving under the Influence of Drugs, Alcohol and Medicines (DRUID) program, and standardization of DUID research. Whereas OF testing is now routine in many monitoring programs, currently, the major shortcoming is the dearth of controlled drug administration studies published to guide interpretation. This review presents an overview of OF testing benefits and limits. Progress in OF that has occurred during the last 5 years in respect of collection, screening, confirmation, and interpretation of cannabinoids, opioids, amphetamines, cocaine, and benzodiazepines is reviewed. Methodology examined includes controlled drug administration studies, immunoassay and chromatographic methods, collection devices, point-of-collection testing device performance, and recent applications of OF testing. Substance Abuse and Mental Health Services Administration approval of OF testing has been delayed because questions about drug OF disposition had not yet been resolved, and performance of collection device and testing assays necessitated advancement. Documented here are the many advances accomplished in the use of OF. Additional research is required to identify new biomarkers, determine drug detection windows, characterize OF adulteration methods and evaluate stability of analytes. However,it is apparent that OF provides multiple advantages as an alternative matrix for drug monitoring. It will have an important role in DUID, treatment, workplace, and criminal justice programs

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Trends Anal Chem 2009 **28** (10) 1164
Sorptive microextraction for liquid-chromatographic determination of drugs in urine
Biological fluids are prevalent specimens in clinical and toxicological laboratories with urine being most frequent due to its ready availability. However, the inherent complexity of urine with the presence of many substances and the low concentration of target analytes, means that, in many instances, direct analysis is not practical. Consequently, sample pre-treatment, focusing mainly on enhancement of selectivity and sensitivity, is usually necessary prior to quantification. In this review, focus is placed upon on the sorptive microextraction of urine samples before the determination of analytes of interest by liquid chromatography. The most important developments such as fiber and in-tube solid-phase microextraction, stir-bar sorptive extraction and microextraction in packed syringe are examined. The most relevant examples reported in the literature are discussed to clearly illustrate how beneficial this method is for the analysis of endogenous and exogenous compounds in urine samples

Pohanka M, Skladal P// Univ Def, Ctr Advanced Studies, CZ-50001 Hradec Kralove, Czech Republic
Folia Microbiol (Praha) 2009 **54** (4) 263
***Bacillus anthracis*, *Francisella tularensis* and *Yersinia pestis*. The most important bacterial warfare agents - Review**
Bacillus anthracis (the causative agent of anthrax) is the most usually mentioned agent of biological warfare. However, *Fracisella tularensis* (the causative agent of tularemia) and *Yersinia pestis* (the causative agent of plague) are additional bacterial agents enlisted by Centers for Disease Control and Prevention into the category A of potential biological weapons. These are three most important bacterial causative agents of serious infections that could be misused for warfare purposes. This review designed to summarize basic information about these bacterial agents. Military aspects of their pathogenesis and the detection techniques suitable for field use are also discussed

2 Sports Doping - General

Beuck S, Schwabe T, Grimme S, Schlorer N, Kamber M, Schanzer W, Thevis M*// *German Sport Univ Cologne, Inst Biochem, Ctr Preventive Doping Res, Am Sportpark Mungersdorf 6, DE-50933 Cologne, Germany
J Am Soc Mass Spectrom 2009 **20** (11) 2034
Unusual mass spectrometric dissociation pathway of protonated isoquinoline-3-carboxamides due to multiple reversible water adduct formation in the gas phase
Collision-induced dissociation behavior of various substituted isoquinoline-3-carboxamides, which are amongst a group of drug candidates for the treatment of anemic disorders (e.g., FG-2216), was studied and facilitated the formulation of the general mechanisms underlying the unusual fragmentation behavior

In order to keep subscribers up-to-date with the latest developments in their field, John Wiley & Sons are providing a current awareness service in each issue of the journal. The bibliography contains newly published material in the field of drug testing and analysis. Each bibliography is divided into 18 sections: 1 Reviews; 2 Sports Doping - General; 3 Steroids; 4 Peptides; 5 Diuretics; 6 CNS Agents; 7 Equine; 8 Recreational Drugs - General; 9 Stimulants; 10 Hallucinogens; 11 Narcotics; 12 Forensics; 13 Alcohol; 14 Tobacco; 15 Homeland Security; 16 Workplace; 17 Product Authenticity; 18 Techniques. Within each section, articles are listed in alphabetical order with respect to author. If, in the preceding period, no publications are located relevant to any one of these headings, that section will be omitted.

of this class of compounds. Characterization was accomplished with high-resolution/high accuracy LTQ-Orbitrap tandem mass spectrometry of the protonated precursor ions. Data were validated by the synthesis and analysis of proposed gas-phase intermediate structures and stable isotope labeled analogues in addition to density functional theory calculations. Typically, CID of protonated *N*-[(1-chloro-4-hydroxy-7-isopropoxy-isoquinolin-3-yl)carbonyl] glycine produces the isoquinoline-3-carboxy-methyleneamide product ion which nominally eliminates a fragment of 11 u. This was ascribed to the loss of methyleneamine (-29 u) and a concomitant spontaneous and reversible water addition (+18 u) to the resulting acylium ion to produce the protonated isoquinoline-3-carboxylic acid. The same water addition pattern was noted after loss of propylene (-42 u). A further nominal loss of 10 u is attributable to the elimination of carbon monoxide (-28 u) followed by another water adduct formation (+18 u) to yield the protonated 1-chloro-3,4,7-trihydroxy-isoquinoline. The source of the multiple gas-phase water addition remained unclear. The atypical fragmentation pattern proved to be highly characteristic of all studied and differentially substituted isoquinoline-3-carboxamides. This provides powerful analytical tools for the production of a LC/MS(/MS) based screening procedure for model HIF-stabilizers and their potential metabolites in clinical, forensic and sports drug testing

Lippi G, Banfi G, Franchini M// Univ Verona, Ospedale Policlin GB Rossi, Dipt Sci Morfol-Biomed, Sezione Chim Clin, IT-37134 Verona, Italy
Clin Chim Acta 2009 **408** (1-2) 141
The International Anti-Doping System: Why it might not work (Letter)
No abstract available

Scarano S, Spiriti MM, Tigli G, Bogani P, Buiatti M, Mascini M, Minunni M*// *Univ Florence, Dipt Chim, IT-50019 Sesto Fiorentino, Italy
Anal Chem 2009 **81** (23) 9571
Affinity sensing for transgenes detection in antidoping control
A new form of sports abuse termed gene doping which is based on the misuse of gene therapy represents an emerging important problem to sports authorities. So far, there are no methods are available for detecting it. Since 2003, the World Anti-Doping Agency (WADA) has included gene doping methods in the "Prohibited List of Substances and Methods". Therefore, detection of this new form of doping presents a challenge for analytical chemists. In this study, affinity-based biosensors (ABBs), in particular DNA piezoelectric sensing is applied for detection of target DNA sequences selected as transgenosis markers. Two sequences widely employed in transgenosis experiments were identified as markers.These were the enhanced green fluorescence protein (EGFP) gene and the promoter of cytomegalovirus (CMV). The analytical performances of the biosensors were established with their use of synthetic oligonucleotides and amplified DNA obtained from purified plasmid employed as a template. They were applied to transgenic human cell cultures (human embryonic kidney HEK-EGFP), transformed with the same plasmid and carrying the target markers. This represents the nearest real human matrix available for the transgenes

3 Steroids

Fragkaki AG, Tsantili-Kakoulidou A, Angelis YS, Koupparis M, Georgakopoulos C*// *Olympic Athlete Ctr Athens Spiros Louis, Doping Control Lab Athens, Kifisias 37, GR-15123 Maroussi, Greece
J Chromatogr A 2009 **1216** (47) 8404
Gas chromatographic quantitative structure-retention relationships of trimethylsilylated anabolic androgenic steroids by multiple linear regression and partial least squares
A quantitative structure-retention relationship (QSRR) study has been achieved to equate relative retention times (RRTs) of trimethylsilylated (TMS) anabolic androgenic steroids (AAS) with their molecular characteristics, encoded by the respective descriptors, for the prediction of RRTs of unfamiliar molecules, using gas chromatography time-of-flight mass spectrometry (GC-TOF-MS). The elucidation of similarities and dissimilarities among the data structures was accomplished by employing principal component analysis (PCA). Models were successfully established using multiple linear regression (MLR) and partial least squares (PLS) protocols as a function of topological, three-dimensional (3D) and physicochemical descriptors. The models may assist the estimation of RRTs of designer steroids where no analytical data are available

4 Peptides

Boateng J, Kay R, Lancashire L, Brown P, Velloso C, Bouloux P, Teale P, Roberts J, Rees R, Ball G, Harridge S, Goldspink G, Creaser C*// *Univ Loughborough, Dept Chem, Ctr Anal Sci, Loughborough LE11 3TU, England
Proteomics Clin Appl 2009 **3** (8) 912
A proteomic approach combining MS and bioinformatic analysis for the detection and identification of biomarkers of administration of exogenous human growth hormone in humans
An integrated MS-based proteomic approach is described that combines MALDI-MS and LC-MS with artificial neural networks for the identification of protein and peptide biomarkers associated with recombinant human growth hormone (rhGH) administration. Serum from exercised males administered with rhGH or placebo was analysed using ELISA to determine insulin-like growth factor-I concentrations. Diluted serum from rhGH- and placebo-treated subjects was analysed for protein biomarkers by MALDI-MS, whereas LC-MS was used to analyse tryptically digested ACN-depleted serum extracts for peptide biomarkers. Ion intensities and *m/z* values were used as inputs to artificial neural networks to classify samples into rhGH- and placebo-treated groups. Six protein ions (MALDI-MS) correctly classified 96% of samples into their respective groups, with a sensitivity of 91% (20 of 22 rhGH treated) and specificity of 100% (24 of 24 controls). Six peptide ions (LC-MS) were also identified and correctly classified 93% of samples with a sensitivity of 90% (19 of 21 rhGH treated) and a specificity of 95% (20 of 21 controls). The peptide biomarker ion with the highest significance was sequenced using LC-MS/MS and database searching and found to be associated with leucine-rich α-2-glycoprotein

Lamon S, Giraud S, Egli L, Smolander J, Jarsch M, Stubenrauch KG, Hellwig A, Saugy M, Robinson N*// *CHU Vaudois, Lab Suisse Anal Dopage, Ctr Univ Romand Med Legale, Croisettes 22, CH-1066 Epalinges, Switzerland
J Pharm Biomed Anal 2009 **50** (5) 954
A high-throughput test to detect CERA doping in blood
A new third-generation erythropoiesis-stimulating agent (ESA) namely C.E.R.A., a continuous erythropoietin receptor activator, has recently been linked with abuse in endurance sports. An enzyme-linked immunosorbent assay (ELISA) designed to identify the presence of C.E.R.A. in serum samples was developed. The performance of the assay was dtermined using a pilot excretion study that involved six subjects receiving C.E.R.A. Validation data confirmed excellent reproducibility and verified the applicability of the assay for anti-doping purposes. To optimize the possibility of detecting the drug in serum samples, it is suggested the use of this specific ELISA test as a high-throughput screening method, combined with a classic isoelectric focusing test as a confirmatory assay. This protocol should make C.E.R.A. abuse relatively easy to detect, thereby deterring the future use of this drug as a doping agent

Mallorqui J, Gutierrez-Gallego R, Segura J, De Bolos C, Pascual JA*// *Hosp del Mar, IMIM, Neuropsychopharmacol Res Program, Bioanal Grp, Dr Aiguader 88, ES-08003 Barcelona, Spain
J Pharm Biomed Anal 2009 **51** (1) 255
New screening protocol for recombinant human erythropoietins based on differential elution after immunoaffinity purification
A screening technique capable of differentiating recombinant human erythropoietins (rhEPOs) and analogues like CERA from human urinary erythropoietin (uhEPO) is described. The technique employs discrimination between isoforms observed when the protein is eluted under acidic followed by basic conditions from immunoaffinity microtiter wells. By comparison with the complex IEF protocol currently applied in anti-doping analysis, the newly developed assay protocol is amenable to wide screening application and provides good resolving power between rhEPOs and uhEPO

6 CNS Agents

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J Chromatogr B 2009 **877** (29) 3767
Detection in urine of 4-methyl-2-hexaneamine, a doping agent
The World Anti-Doping Agency prohibits the use of stimulants in-competition for all categories of sports. Urinalysis of 4-methyl-2-hexaneamine, a primary amine exhibiting sympathomimetic properties was investigated by employing a simple liquid chromatography-tandem mass spectrometry (LC-MS/MS) assay with electrospray ionisation in positive mode. After a simple pretreatment procedure, the analyte was separated using a gradient mobile phase on reverse phase C8 column. Selected reaction monitoring *m/z* 116.2→57.3 was specific for detection of 4-methyl-2-hexaneamine and the assay showed a linear

dynamic range of 50-700 ng/ml. The validated technique was successfully applied to analyze the target compound in both food supplements and in urine specimens. Following administration of the drug (40 mg), it was detectable at the level of 350 ng/ml in the urine for up to 4 days

Ventura R, Ramirez R, Monfort N, Segura J// IMIM-Hospital del Mar, Bioanal Res Grp, Doctor Aiguader 88, ES-08003 Barcelona, Spain
J Pharm Biomed Anal 2009 **50** (5) 886
Ultraperformance liquid chromatography tandem mass spectrometric method for direct quantification of salbutamol in urine samples in doping control
Direct, fast and reliable quantitative urinanalysis for salbutamol by ultraperformance liquid chromatography tandem mass spectrometry (UPLC/MS/MS) is described. Urine samples were spiked with salbutamol-d_6 (internal standard), and, then, they were diluted with ultrapure water (1:1, v/v). Aliquots of 1 µl of the mixture were directly analyzed by UPLC/MS/MS. Chromatographic separation was achieved with a UPLC BEH C18 (100 mm x 2.1 mm, 1.7 µm) column with a mobile phase contained 0.01% formic acid in ultrapure water (v/v) and 0.01% formic acid in acetonitrile (v/v), using gradient elution at 0.6 ml/min. The temperature of the column was set to 45 °C. Total run time was 3.2 min. Electrospray ionization in positive ion mode was employed under multiple reaction monitoring (MRM) at different collision energies. Nitrogen and argon were used as desolvation and collision gas, respectively. The method was demonstrated to be linear from 200 to 5000 ng/ml (r^2>0.99). The limit of quantitation was estimated in 200 ng/ml. Intra-assay precision and accuracies, evaluated by using quality control samples containing 550 and 1100 ng/ml salbutamol, were always better than 8.4%.The intermediate precision was determined to be in the range of 5.6-8.9%. The technique was demonstrated to be reliable when applied to routine samples.The short analysis time resulting from a simple sample preparation and a fast instrumental analysis illustrates its potential for antidoping control purposes

7 Equine

Vonaparti A, Lyris E, Panderi I, Koupparis M, Georgakopoulos C*// *Olympic Athlete Ctr Athens Spiros Louis, Doping Control Lab Athens, 37 Kifissias Ave, GR-15123 Maroussi, Greece
Anal Bioanal Chem 2009 **395** (5) 1403
Direct injection horse urine analysis for the quantification and identification of threshold substances for doping control. III. Determination of salicylic acid by liquid chromatography/quadrupole time-of-flight mass spectrometry
In equine sport, salicylic acid is prohibited with a threshold level of 750 µg/ml in urine. Consequently, doping control laboratories nedd to develop quantitative and qualitative techniques for its determination. A simple and rapid liquid chromatographic/mass spectrometric method has been developed and validated for the quantification and identification of salicylic acid. Following 900-fold dilution and addition of the internal standard (4-methylsalicylic acid), urine samples were directly injected to a liquid chromatography/quadrupole time-of-flight mass spectrometry system. Electrospray ionization in negative mode with full scan acquisition mode and product ion scan mode were selected for the quantification and identification of salicylic acid, respectively. Run time was 2.0 min. The tested linear range was 2.5-50 µg/ml (after 100-fold sample dilution). The relative standard deviations of intra- and inter-assay analysis of salicylic acid in horse urine were lower than 2.5% and 2.8%, respectively. Overall accuracy (relative percentage error) was less than 3.3%. The procedure was employed with two real samples and found to be positive for salicylic acid, demonstrating simplicity, accuracy, and selectivity

8 Recreational Drugs - General

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Chromatographia 2009 **70** (7-8) 1295
Simultaneous determination of benzodiazepines and ketamine from alcoholic and nonalcoholic beverages by GC-MS in drug facilitated crimes
The simultaneous analysis of underivatized flunitrazepam, clonazepam, alprazolam, diazepam and ketamine from drinks by extraction with chloroform: isopropanol 1:1 (v/v) followed by GC-MS with HP-5MS capillary column is described. All linearity ranges were between 50 and 1,000 µg/ml for all compounds both in beer and in peach juice. Limit of detection was between 1.3 and 34.2 µg/ml, limit of quantification was between 3.9 and 103.8 µg/ml, the range of recoveries was 73.0 and 112.6% for all drugs in both beverages. The described protocol proved to be sensitive, rapid, and suitable for the analysis of the spiked drinks as evidence of sexual assault and robbery

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Clin Chem 2009 **55** (11) 2004
Simultaneous screening and quantification of 29 drugs of abuse in oral fluid by solid-phase extraction and ultraperformance LC-MS/MS
The European DRUID (Driving under the Influence of Drugs, Alcohol And Medicines) project calls for analysis of oral fluid (OF) samples, collected randomly and anonymously at the roadside from drivers in Denmark throughout 2008-2009. An ultra performance liquid chromatography-tandem mass spectrometry (UPLC-MS/MS) technique was developed for detection of 29 drugs and illicit compounds in OF. Solid-phase extraction was achieved with a Gilson ASPEC XL4 system equipped with Bond Elut Certify sample cartridges. OF samples (200 mg) diluted with 5 ml of ammonium acetate/methanol (vol/vol 90:10) buffer were applied to the columns and eluted with 3 ml of acetonitrile with aqueous ammonium hydroxide. Target drugs were quantified with a Waters ACQUITY UPLC system coupled to a Waters Quattro Premier XE triple quadrupole (positive electrospray ionization mode, multiple reaction monitoring mode). Extraction recoveries were 36%-114% for all analytes, including Δ^9-tetrahydrocannabinol and benzoylecgonine. The lower limit of quantification was 0.5 µg/kg for all analytes. Total imprecision (CV) was 5.9%-19.4%. By employing deuterated internal standards for most substances, the performance of the technique noted to not be influenced by matrix effects. Drugs detected included opioids, amphetamines, cocaine, benzodiazepines, and Δ^9-tetrahydrocannabinol. A preliminary account of OF samples collected at the roadside showed the presence of amphetamine, cocaine, codeine, Δ^9-tetrahydrocannabinol, tramadol, and zopiclone. UPLC-MS/MS facilitates detection of all 29 analytes in 1 chromatographic run (15 min), including Δ^9-tetrahydrocannabinol and benzoylecgonine, which previously have been difficult to incorporate into multicomponent methods

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Anal Bioanal Chem 2009 **395** (8) 2499
Determination of basic drugs of abuse in human serum by online extraction and LC-MS/MS
The analysis of drugs of abuse (opiates, amphetamine and derivatives, cocaine, methadone and metabolites) in serum has been achieved by application of a new quantitation technique employing online extraction coupled to liquid chromatography (LC)-mass spectrometry (MS)/MS. The online extraction was performed using two extraction columns simultaneously and one analytical column. One extraction column is loaded, while the other one is eluted by a gradient. The elution gradient also separates the analytes in the analytical column. In sample preparation, serum is spiked with a mixture of deuterated analogues of the drugs. Following protein precipitation with methanol/zinc sulphate, centrifugation, evaporation and reconstitution, the sample is injected into the LC system. Quantitation is calculted on the analysis of two multiple reaction monitoring transitions per drug. Recovery of the protein precipitation step is over 80% for all analytes. Intra- and interday precision, as relative standard deviation, is lower than 6%, and in the case of accuracy, RE is lower than 15%. Only the most polar analytes exhibited matrix effects. Limits of quantitation for the analysed compounds varied between 0.5 and 2.8 ng/ml. The technique was employed to quantify basic drugs in samples obtained "from driving under the influence of drugs" cases. Results were compared with those produced by using solid-phase extraction-GC-MS

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J Chromatogr B 2009 **877** (27) 3065
Development and validation of a liquid chromatography mass spectrometry assay for the simultaneous quantification of methadone, cocaine, opiates and metabolites in human umbilical cord
Methadone, 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), cocaine, benzoylecgonine (BE), 6-acetylmorphine, morphine and codeine quantification in human umbilical cord was achieved with a liquid chromatography mass spectrometric selected reaction monitoring mode (SRM) method. The procedure was developed and fully validated. Analytes were extracted from homogenized tissue (1g) by solid phase extraction. Linearity was 2.5-500ng/g, except for methadone (10-2000ng/g). Method imprecision was <12.7%CV with analytical recovery 85.9-112.7%, extraction efficiency >59.2%, matrix effect 4.5-39.5%, process efficiency 48.6-92.6% and stability >84.6%. Analysis of an umbilical cord following controlled methadone administration and illicit drug use contained 40.3 ng/g morphine, 3.6 ng/g codeine, 442 ng/g BE, 186 ng/g

methadone and 45.9 ng/g EDDP

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Chromatographia 2009 **70** (9-10) 1373

High-throughput screening of drugs of abuse in urine by supported liquid-liquid extraction and UHPLC coupled to tandem MS

A protocol for the rapid tentative identification of various drugs of abuse in urine was developed involving supported liquid-liquid extraction (SLE) and ultra high pressure liquid chromatography coupled to tandem mass spectrometry (UHPLC-MS-MS). In this work, 28 drugs and metabolites were covered by the screening procedure. Before analysis, urine samples were extracted by SLE and good recoveries were produced for most compounds under investigation. UHPLC was employed for the rapid separation of amphetamines, cocaine, opiates and related compounds in urine. Using columns packed with sub-2 µm particles, analysis time was reduced down to 2 min, while maintaining acceptable performance. Detection was by tandem MS operating in the single reaction monitoring (SRM) mode. The most intense transition was selected for the different drugs and SRM dwell times set at 5 ms, to maintain sufficient data points across the narrow UHPLC peaks. Tentative identification of the drugs of interest, including amphetamines, opiates and cocaine was based on both retention times and mass spectrometry information. Limits of detection were estimated at about 1 ng/ml. Applicability was assessed by successfully analyzing several samples of drug abusers. This work demonstrates the potential of UHPLC coupled to tandem MS for the rapid screening of drugs of abuse in urine

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Anal Bioanal Chem 2009 **395** (5) 1411

Rapid, sensitive and simultaneous determination of fluorescence-labeled designated substances controlled by the Pharmaceutical Affairs Law in Japan by ultra-performance liquid chromatography coupled with electrospray-ionization time-of-flight mass spectrometry

For 16 "designated substances" (Shitei-Yakubutsu) controlled by the Pharmaceutical Affairs Law in Japan, a simultaneous analytical technique based on ultra-performance liquid chromatography (UPLC) with fluorescence (FL) detection and electrospray-ionization time-of-flight mass spectrometry (ESI-TOF-MS) has been developed. Firstly, the compounds were labeled with 4-(*N*,*N*-dimethylaminosulfonyl)-7-fluoro-2,1,3-benzoxadiazole at 60 °C for 2 h in 0.1 M borax (pH 9.3). Subsequently, the resulting fluorophores were well separated by reversed-phase chromatography using an Acquity UPLC BEH C_{18} column (1.7 mum, 100 mm x 2.1 mm i.d.) by isocratic elution with a mixture of water and acetonitrile-methanol (20:80) containing 0.1% formic acid. The separated derivatives were sensitively detected by both FL and TOF-MS. However, the analysis of several designated substances by FL detection demonstrated interference from endogenous substances in biological samples. Consequently, the analysis in real samples was achieved with a combination of UPLC separation and ESI-TOF-MS detection. The structures of the designated substances were identified from the protonated-molecular ions $[M+H]^+$ obtained from the TOF-MS measurement. The calibration curves derived from the peak area ratios of the internal standard (I.S.), i.e., 3-phenyl-1-propylamine, and the designated substances *versus* the injection amounts demonstrated good linearity. The limits of detection and the limits of quantification in 0.1 ml of human plasma and urine for the present method were 0.30-150 pmol and 1.0-500 pmol, respectively. Good accuracy and precision (according to intraday and interday assays) were also derived from the present procedure. The procedure was applied to analyses of human plasma, urine and real products

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Int J Legal Med 2009 **123** (5) 363

Cocaine and opiate concentrations in hair from subjects in a heroin maintenance program in comparison to a methadone substituted group

Controlled i.v. heroin-HCl (10-100 mg/day) was employed in the context of a heroin maintenance program (HMP). One month before (T-1) and 12 months after (T12) administration, concentrations of opiates, cocaine and metabolites were determined in head hair (*n* = 46) using a validated gas chromatographic-mass spectrometric method. Furthermore, patients treated with a methadone maintenance program (MMP, daily doses 15-260 mg) were investigated (*n* = 35). In both groups, the incidence of additional cocaine consumption decreased during the study period (T-1 to T12): in HMP from 64.6% to 45.8% and in MMP from 71.4% to 60.0%. A significant reduction of cocaine consumption was defined as an at least 30% reduction of analyte concentrations in hair (Δc > 30%). Accordingly, in HMP, a decrease in 45.8% of initially (T-1) cocaine-positive patients was noted; in MMP, the reduction was 48.6%. In 22.9% of HMP and 37.1% of MMP, an increase of cocaine concentrations was determined. Codeine and acetylcodeine were found in 50.0% and 43.5% (T-1) and 13.0% and 10.9% (T12) of the samples of the HMP, as well as in 45.7% and 25.7% (T-1) and 17.1% and 5.7% (T12) in MMP, respectively. The absence of acetylcodeine, especially at T-1, questions its usefulness as a signature of a preceding consumption of illicit heroin in hair analysis

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Anal Bioanal Chem 2009 **395** (8) 2547

Determination of ketamine and amphetamines in hair by LC/MS/MS

The determination of ketamine (with its metabolite norketamine) and some amphetamines (amphetamine, methamphetamine, methylenedioxyamphetamine, and 3,4-methylenedioxymethamphetamine) has been achieved by the development of a liquid chromatography-tandem mass spectrometry technique. The technique was produced to determine the compounds in hair and is capable of simultaneously quantifying all of them. Hair samples (20 mg) were washed and pulverized, and an extraction with formic acid (0.01%) and ultrasonication for 4 h was utilised. Deuterated analogs of the analytes were employed as internal standards for quantification. Linearity from 0.5 to 25 ng/mg was produced for both ketamine (and norketamine) and amphetamines with correlation coefficients exceeding 0.99. The limit of detection and the limit of quantification were 0.1 and 0.5 ng/mg, respectively, for ketamine and amphetamines. A total of 25 hair samples from known drug abusers (relating to designer drug consumption or consumption of amphetamines) were investigated by this validated technique. This study show that the proposed method is applicable to testing these drugs in a single sample of hair. Furthermore, it is simpler and faster than analysis with conventional methods, for example gas chromatography-mass spectrometry. These usually require a more laborious extraction procedure and often an additional derivatization process

9 Stimulants

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J Anal Toxicol 2009 **33** (8) 550

Cocaine detection in postmortem samples following therapeutic administration

One of the most widely abused drugs and one that is frequently encountered in forensic toxicology laboratories is cocaine. Frequently, the detection of cocaine would lead toxicologists and forensic pathologists to believe that the drug had been used illicitly. However, cocaine is an effective local anesthetic and vasoconstrictor and is clinically employed in eye, ear, nose and throat surgery. Consequently, it is should be noted that the presence of cocaine and its metabolites in forensic samples cannot always be attributed to abuse. A thorough investigation and review of medical records is necessary before an informed conclusion may be made. A 54-year-old male died three days after an altercation in which he suffered multiple injuries. In addition to natural disease and injuries documented at autopsy, cocaine and its metabolites were detected in the decedent's urine. A review of surgical records demonstrated that earlier on the day of death, he was administered cocaine during a procedure to repair nasal bone fractures. Were it not for this comprehensive investigation and review of surgical records, an assumption of cocaine abuse might have otherwise been made and the cause and manner of death incorrectly determined

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Anal Chem 2009 **81** (22) 9291

Electrochemical, photoelectrochemical, and surface plasmon resonance detection of cocaine using supramolecular aptamer complexes and metallic or semiconductor nanoparticles

Metallic or semiconductor nanoparticles (NPs) may be employed as labels for the electrochemical, photoelectrochemical, or surface plasmon resonance (SPR) analysis of cocaine using a common aptasensor configuration. The aptasensors rely upon the use of two anticocaine aptamer subunits, where one subunit is assembled on a Au support, acting as an electrode or a SPR-active surface, and the second aptamer subunit is labeled with Pt-NPs, CdS-NPs, or Au-NPs. In the different aptasensor configurations, the addition of cocaine produces supramolecular complexes between the NPs-labeled aptamer subunits and cocaine on the metallic surface, facilitating the quantitative analysis of cocaine. The supramolecular Pt-NPs-aptamer subunits-cocaine complex allows the detection of cocaine by the electrocatalyzed reduction of H_2O_2. The photocurrents generated by the CdS-NPs-labeled aptamer subunits-cocaine complex, in the presence of triethanol amine as a hole scavenger, facilitates the photoelectrochemical detection of cocaine. The supramolecular Au- NPs-aptamer subunits-cocaine complex formed on the Au support allows the SPR detection of cocaine through the reflectance changes stimulated by the electronic coupling between the localized plasmon of the Au-NPs and the surface plasmon wave. All aptasensor configurations permit the analysis of cocaine with a detection limit in the range of 10^{-6} to 10^{-5} M. The primary benefit of the sensing platform is the absence of background interfering signals

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J Chromatogr A 2009 **1216** (48) 8435

Comparison of molecularly imprinted, mixed-mode and hydrophilic balance sorbents performance in the solid-phase extraction of amphetamine drugs from wastewater samples for liquid chromatography-tandem mass spectrometry determination

Amphetamines and other drugs of abuse residues have previously discovered in wastewater. Several techniques have been produced for their analysis by solid-phase extraction (SPE) and liquid chromatography-tandem mass spectrometry (LC-MS/MS). However, a prominent shortcoming of these techniques is the absence of selectivity during SPE which causes reduced sensitivity, due to matrix effects, and in some cases in low precision and poor accuracy. In order to address this issue, three different SPE alternatives (common hydrophilic balance (Oasis HLB), mixed-mode (Oasis MCX) and molecularly imprinted polymers (MIPs) sorbents) have been evaluated for the determination of five amphetamines. Of the three, Oasis HLB showed the poorest performance because three amphetamines (MDA, MDMA and MDEA) could not be determined because of interfering signals in the LC-MS/MS chromatogram. In addition, amphetamine recoveries could not be corrected by employing the deuterated analogue as internal standard. Oasis MCX facilitated the analysis of all target analytes but with still strong signal suppression of approximately 70% signal drop with wastewater samples. This could be corrected by the internal standards providing acceptable trueness (overall recoveries: 101-137%), precision (RSD: 2.0-12%) and limits of detection (LOD: 1.5-4.4 ng/l). On-the-other-hand, MIPs produced cleaner extracts with less matrix effects (ca. 30% signal drop), and thereby lower LODs (0.5-2.7 ng/l) and even greater trueness (91-114% overall recovery) and precision (1.5-4.4%RSD). MIP cartridges demonstrated the presence of MDA and MDMA in the seven wastewater samples at the 4-20 ng/l level

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J Anal Toxicol 2009 **33** (8) 447

Sensitive method for detection of cocaine and associated analytes by liquid chromatography-tandem mass spectrometry in urine

Cocaine (COC) is a potent CNS stimulant. Is metabolized to benzoylecgonine (BE) and subsequently to minor metabolites such as *m*-hydroxybenzoylecgonine (*m*-HOBE). COC is also metabolized to norcocaine (NC). Cocaethylene (CE) is formed when cocaine and ethanol are taken simultaneously. Anhydroecgonine methyl ester (AEME) is a unique marker following smoked cocaine, and anhydroecgonine ethyl ester (AEEE) is found in cocaine smokers who also take ethanol. A liquid chromatography-tandem mass spectrometry (LC-MS-MS) procedure for the identification and quantitation of COC, BE, NC, CE, *m*-HOBE, AEME, and AEEE in urine is described. Two hundred samples previously analyzed by gas chromatography (GC) coupled with MS were extracted using solid-phase extraction. Chromatographic separation was accomplished using a gradient consisting of mobile phase A [20 mM ammonium formate (pH 2.7)] and mobile phase B (methanol/acetonitrile, 50:50), an XDB-C_8 (50 x 2.1 mm, 1.8 µm) column and a flow rate of 270 µl/min. Concentrations were derived by comparing the peak-area with the internal standard and plotted against a standard curve. The assay displayed linearity from 1.0 to 100 ng/ml. Within- and between-run coefficients of variation were < 10% throughout the linear range. A method comparison between GC-MS and LC-MS-MS showed good correlation for COC ($r^2 = 0.982$) and BE ($r^2 = 0.955$). The technique described here is a sensitive one which may be employed to identify clinically and forensically relevant cocaine and associated analytes at concentrations as low as 1.0 ng/ml

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J Therm Anal Calorim 2009 **97** (1) 337

Development of forensic analytical chemistry method for examination of Merla by thermal analysis and high resolution gas chromatography

The aim of this research was the TG and DSC analysis of "Merla" samples as well as the separation and identification of organic compounds by Ultra Fast GC method. The data demonstrated the grouping and the establishment of the degree of the sample's similarity based in the Euclidean Distance. The cluster was a useful technique with which to determine if the samples, confiscated from different users by police, were produced in one or many different laboratories. Therefore, it would be possible to conclude whether any city has one or more illegal drug manufacturing laboratories

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Forensic Sci Int 2009 **192** (1-3) 94

Voltammetric determination of cocaine in confiscated samples using a cobalt hexacyanoferrate film-modified electrode

A fast, non destructive voltammetric procedure for the the detection of cocaine in acetonitrile medium using a platinum disk electrode chemically modified with cobalt-hexacyanoferrate (CoHCFe) film is described. The deposition of CoHCFe film at platinum disk (working electrode) was achieved in aqueous solution containing $NaClO_4$ at 0.1 mol/l as supporting electrolite. Studies on the stability of the film and subsequent voltammetric analysis of cocaine were made in acetonitrile medium with $NaClO_4$ at 0.1 mol/l as supporting electrolite. A reversible interaction between cocaine and CoHCFe at the film produces a proportional decrease of original peak current, due to the production of a complex between cocaine and cobalt íons. Subsequent partial passivation of the film surface resulting in the intensity of current decrease is employed as an analytical signal for cocaine. A linear dependence of cocaine detection was accomplished in the range from 2.4 x 10^{-4} to 1.5 x 10^{-3}mol/l, with a linear correlation coefficient of 0.994 and a detection limit of 1.4 x 10^{-4}mol/l. Analysis of seized samples by the proposed technique demonstrated cocaine levels from 37% to 95% (m/m). These results were validated by comparison to HPLC techniqueand showed good correlation between both methods

10 Hallucinogens

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J Anal Toxicol 2009 **33** (8) 439

Urinary MDMA, MDA, HMMA, and HMA excretion following controlled MDMA administration to humans

The aim of this paper was to analyse the pattern and timeframe for the excretion of 3,4-methylenedioxymethamphetamine (MDMA, Ecstasy) and its metabolites in urine. MDMA is excreted as unchanged drug, 3,4-methylenedioxyamphetamine (MDA), and free and glucuronidated/sulfated 4-hydroxy-3-methoxymethamphetamine (HMMA), and 4-hydroxy-3-methoxyamphetamine (HMA) metabolites. Placebo, 1.0 mg/kg, and 1.6 mg/kg oral MDMA doses were administered double-blind to healthy adult MDMA users on a monitored research unit. Urine was collected, aliquots hydrolyzed and analytes quantified by gas chromatography-mass spectrometry. Median C_{max}, T_{max}, ratios, first and last detection times, and detection rates were determined. Sixteen participants provided 916 urine specimens. After 1.6 mg/kg, median C_{max} were 21,470 (MDMA), 2229 (MDA), 20,793 (HMMA), and 876 ng/ml (HMA) at median T_{max} of 13.9, 23.0, 9.2 and 23.3 h. In the first 24 h, 30.2-34.3% total urinary excretion occurred. The final detection of HMMA exceeded MDMA by more than 33 h after both doses. Identification of HMMA as well as MDMA increased the ability to identify positive specimens but required hydrolysis. These pharmacokinetic data on MDMA, MDA, HMMA, and HMA may be helpful for interpreting workplace, drug treatment, criminal justice and military urine drug tests. Measurement of urinary HMMA provides the longest detection of MDMA exposure. However, it is not included in routine monitoring procedures

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Forensic Sci Int 2009 **192** (1-3) 98

The analytical profile of some 4-methylthioamphetamine (4-MTA) homologues

4-Methylthioamphetamine (4-MTA) is a sulphur-containing amphetamine-type stimulant (ATS) which appeared on the illicit drug market in Europe at the end of the 1990s. To facilitate this study, several *N*-alkyl homologues of 4-MTA, including 4-methylthiomethamphetamine (4-MTMA), 4-methylthioethylamphetamine (4-MTEA), 4-methylthiodimethamphetamine (4-MTDMA), 4-methylthiopropylamphetamine (4-MTPA) and 4-methylthiobutylamphetamine (4-MTBA) were synthesized. These were characterized by means of gas chromatography/mass spectrometry (GC-MS), infrared (IR) spectroscopy and the magnetic resonance spectroscopy (^{1}H and ^{13}C NMR). The gas chromatography and mass spectrometry properties of their acetyl, trifluoroacyl (TFA), pentafluoropropionyl (PFP) and heptafluorobutyryl (HFB) derivatives were also determined and are discussed

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Forensic Sci Int 2009 **191** (1-3) 42

Different likelihood ratio approaches to evaluate the strength of evidence of MDMA tablet comparisons

Two likelihood ratio (LR) approaches are described to analyse the strength of evidence of MDMA tablet comparisons. Firstly, a more 'traditional' comparison of MDMA tablets is employed using distance measures (e.g., Pearson correlation distance or a Euclidean distance). In this instance, LRs are derived from the distribution of distances between tablets of the same-batch and that of different-batches. Secondly, a protocol based on methods used in some other fields of forensic comparison. Accordingly, LRs are derived from the distribution of values of MDMA tablet characteristics within a specific batch and from all batches. Data employed in this paper should be seen as examples to illustrate both methods. In future studies, the protocols may be applied to other and more complex data. Herein, the procedures and their results are discussed in respect of their performance in evidence evaluation and several practical aspects. With respect to evidence supporting of the correct hypothesis, the second technique was shown to be better than the first. It is demonstrated that the LRs in same-batch comparisons are generally higher compared to the first method and the LRs in different-batch comparisons are usually lower. However, for practical purposes (where rapid data are required), the first method may be preferable because it is less time consuming. Here, a model has to be developed occasionally, thus few measurements are necessary. With the second method more measurements are necessary because each time a new model has to be produced

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J Anal Toxicol 2009 **33** (8) 461

Solid-phase extraction and analysis of THC and carboxy-THC from whole blood using a novel fluorinated solid-phase extraction sorbent and fast liquid chromatography-tandem mass spectrometry

A solid-phase extraction (SPE) procedure is described employing a novel fluorinated [heptadecafluorotetrahydrodecyl ($C_{10}H_4F_{17}$)] phase to isolate THC and its primary metabolite carboxy-THC from whole blood samples. Following samples of whole blood precipitated with acetonitrile, SPE was performed in hydrophobic mode. Subsequent to application of the sample to the SPE column in aqueous phosphate buffer (pH 7), the sorbent was washed with deionized water and phosphate buffer (pH 7) and dried. The SPE column was eluted with a solvent consisting of ethyl acetate/hexanes (50:50) containing 2% acetic acid. The eluate was collected, evaporated to dryness and dissolved in mobile phase (50 μl) for analysis by fast liquid chromatography-tandem mass spectrometry in positive/negative multiple reaction monitoring mode. Chromatography was achieved in gradient mode employing a C_{18} column and a mobile phase consisting of acetontitrile (containing 0.1% formic acid) and 0.1% aqueous formic acid. The total run time for each analysis was less than 5 min. The limits of detection/quantification for this method were determined to be 0.1 and 0.25 ng/ml, respectively. The method was found to be linear from 0.25 to 50 ng/ml (r^2 >or= 0.995). Recoveries of the individual cannabinoids were found to be greater than 85%. In this paper, analysis of authentic samples analyzed for THC and carboxy-THC are described employing this new procedure

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J Chromatogr B 2009 **877** (22) 2153

On-line solid-phase extraction combined with liquid chromatography-tandem mass spectrometry for high throughput analysis of 11-nor- ^{9}-tetrahydrocannabinol-9-carboxylic acid in urine

An automated on-line solid-phase extraction (SPE) combined with liquid chromatography (LC)-mass spectrometry (MS/MS) technique for the analysis of THC-COOH in urine has been developed and fully validated according to international guidelines which combines simplicity, expediency ana sensitivity. Chromatographic separation was accomplished with an Atlantis dC_{18} column employing an isocratical gradient, providing an elution of THC-COOH within 4.1 min. Total run time was 6 min. 500 μl of sample was required. SPE using C_8 cartridges was highly efficient, reproducible and resulted in significant decreases of the interferences present in the matrix. The protocol exhibited excellent intra- and inter-assay precision (relative standard deviation (RSD) <7% and bias <13%) for four external quality control (QC) samples and three 'in house' QCs. Responses were linear over the investigated range (r^2>0.99, 5-200 μg/l). Limits of quantification (LOQ) and detection (LOD) were ascertained to be 5 μg/l and 0.25 μg/l, respectively. In addition, the analyte and the processed samples were shown to be stable. Furthermore, no carryover was noted following the analysis of highly concentrated urine samples (5000 μg/l THC-COOH)). Subsequently, the procedure applied to authentic samples previously screened by a routine immunoassay method

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J Chromatogr B 2009 **877** (29) 3701

Determination of amphetamine and methamphetamine in umbilical cord using liquid chromatography-tandem mass spectrometry

The gold standard of care of newborns for the past two decades has been the use of meconium as a drug-screening matrix. A recent study employing matched pairs of meconium and umbilical cord demonstrated a high degree of agreement. Herein, for the first time, the use of liquid chromatography-tandem mass spectrometry as a procedure to confirm amphetamines presumed positive umbilical cord specimens for amphetamine and methamphetamine is described. The limit of detection for both compounds was 0.2 ng/g. The limit of quantitation for both compounds was 0.6 ng/g. The assay was linear for both compounds up to 100 ng/g

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J Anal Toxicol 2009 **33** (8) 469

Implications of plasma ^{9}-tetrahydrocannabinol, 11-hydroxy-THC, and 11-nor-9-carboxy-THC concentrations in chronic cannabis smokers

Forensic specimens from driving under the influence and accident investigations frequently feature Δ^9-tetrahydrocannabinol (THC). In 18 long-term heavy cannabis smokers residing on an in-patient research unit for seven days of monitored abstinence, plasma cannabinoid concentrations were analysed. THC, 11-hydroxy-THC, and 11-nor-9-carboxy-THC (THCCOOH) were measured with two-dimensional gas chromatography-mass spectrometry with cryo-focusing. THC concentrations were > 1 ng/ml in nine (50.0%) participants (1.2-5.5 ng/ml) on abstinence day 7. THCCOOH was detected (2.8-45.6 ng/ml) in all participants on study day 7. THC and THCCOOH median percent concentration decreases (n = 18) were 39.5% and 72.9% from day 1 to 7, respectively. Many (88.9%) of the participants produced at least one specimen with greater THC compared with the previous day. Duration of cannabis use and plasma THCCOOH concentrations were positively correlated on days 1-3 (R = 0.584-0.610; p = 0.007-0.011). There were no significant correlations between THC concentrations > 0.25 ng/ml and body mass index on days 1-7 (R = -0.234-0.092; p = 0.350-0.766). THC concentrations determined after seven days of abstinence suggest a potential mechanism for residual neurocognitive impairment observed in chronic cannabis users. The presence of THC in plasma for seven days of abstinence indicates that its detection may not prove evidence of recent daily cannabis use

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J Anal Toxicol 2009 **33** (8) 557

A fatality from an oral ingestion of methamphetamine

A case presented is of a 49-year-old white male who admitted to oral ingestion of methamphetamine and subsequenltly died. He believed he was being followed by the police while walking his daughter to school in the morning and swallowed the "8-ball of meth," which is known to be one-eighth of an ounce or the equivalent of about 3 g. Autopsy specimens including femoral blood, urine, bile, vitreous fluid, brain, liver, and gastric contents were analyzed for the presence of methamphetamine and amphetamine by gas chromatography-mass spectrometry. Blood taken at the hospital approximately 12 h after ingestion was also analyzed. The methamphetamine concentration in the hospital blood was 3.0 mg/l, and the concentration in the femoral blood from autopsy was 30 mg/l. Other drugs detected included tramadol, lorazepam, and 11-carboxy-Δ^9-tetrahydrocannabinol. The cause of death determined by the coroner was cardiac dysrhythmia due to excited delirium as a consequence of methamphetamine drug effects. Discussion of the period from ingestion to death and the clinical presentation are included

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Anal Lett 2009 **42** (16) 2556

Determination of 3,4-methylenedioxymethamphetamine (MDMA) and 3,4-methylenedioxyamphetamine (MDA) in urine by high performance liquid chromatograpy

A simple, inexpensive method for the identification and quantification of 3,4-methylenedioxymethamphetamine (MDMA) and its principal metabolite 3,4-methylenedioxyamphetamine (MDA) for urinalysis is described utilizing high performance liquid chromatography with a UV detector. The optimized technique demonstrated adequate linearity, sensitivity, precision, selectivity, and robustness. Its feasibility for adoption as a laboratorial option for the confirmation of the presence of the drug in urine samples from users was demonstrated

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Forensic Sci Int 2009 **191** (1-3) 58

Spice: A never ending story?

Several non-traditional cannabinoids which proved to be the active components in popular "bio-designer-drugs" such as "Spice" and analogous products were banned by the German Health Authorities on January 22nd 2009. Recent detection of CP 47,497-C8 in Europe and Japan suggests that these products have already spread worldwide. Several potentially interesting alkylaminoindoles (alkylchain C_3 to C_7) were synthesized and CP 47,497-C8 was isolated from "Spice Gold". Compounds were purified and characterized by NMR and mass spectrometry methods. By employing these authentic references, it was possible to detect and quantify added psychoactive compounds in different herbal blends. All samples that were acquired before the prohibition in December 2008 contained either CP 47,497-C8 (5.4-11.0mg/g) or JWH-018 (2.3mg/g). Some samples acquired in March 2009, 4 weeks after the prohibition took place, still contained CP 47,497-C8 (3.0-3.3mg/g) but JWH-018 was no longer detectable. Instead it was replaced by its non-regulated C_4-homolog JWH-073 (5.8-22.9 mg/g). In addiition, some of the new products did not contain any non-traditional cannabinoids. This paper may be the first report of the appearance JWH-073 as a new designer drug. The data and protocol described here should facilitate and accelerate the identification of these compounds in complex matrices

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Drug Alcohol Depend 2009 **105** (1-2) 24

Extended urinary ^{9}-tetrahydrocannabinol excretion in chronic cannabis users precludes use as a biomarker of new drug exposure

Even when last use of cannabis may have been weeks prior to urinalysis, 11-nor-9-carboxy-Δ^9-tetrahydrocannabinol (THCCOOH) after alkaline hydrolysis is employed to detect abuse. Δ^9-Tetrahydrocannabinol (THC) and 11-hydroxy-THC (11-OH-THC) concentrations in urine following *Escherichia coli* β-glucuronidase hydrolysis have been suggested as biomarkers of recent (within 8h) cannabis use. The aim of this paper was to examine the validity of THC and 11-OH-THC in urine as indicators of recent cannabis use. The subjects were 33 chronic cannabis smokers who resided on a secure research unit under 24h continuous medical surveillance. Urine specimens were collected individually *ad libidum* for up to 30 days, were hydrolyzed with a tandem *E. coli* β-glucuronidase/base procedure, and analyzed for THC, 11-OH-THC and THCCOOH by one- and two-dimensional-cryotrap gas chromatography mass spectrometry (2D-GCMS) with limits of quantification of 2.5 ng/ml. Prolonged THC and 11-OH-THC excretion in chronic cannabis users' urine was noted during monitored abstinence; 14 of 33 participants had measurable THC in specimens collected at least 24h after abstinence initiation. Seven subjects had quantifiable THC in urine for 3, 3, 4, 7, 7, 12, and 24 days after cannabis cessation. 11-OH-THC and THCCOOH were detected in urine specimens from one heavy, chronic cannabis user for at least 24 days. For the first time, extended urinary excretion of THC and 11-OH-THC is documented for at least 24 days. Consequently, their effectiveness as biomarkers of recent cannabis exposure is negated. The data also substantiate long terminal elimination times for urinary cannabinoids following chronic cannabis smoking

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Forensic Sci Int 2009 **192** (1-3) 115

GC-MS and GC-IRD studies on dimethoxyamphetamines (DMA): Regioisomers related to 2,5-DMA

Mass spectra of the drug of abuse, 2,5-dimethoxyamphetamine (2,5-DMA) are characterized by an imine fragment base peak at *m/z* 44 and additional fragments at *m/z* 151/152 for the dimethoxybenzyl cation and radical cation, respectively. Five positional ring isomers of imethoxyamphetamines (DMA) have an isomeric relationship to 2,5-DMA. All six compounds have the same molecular weight and produce similar EI mass spectra. The lack of specific mass spectra for the isomers and the possibility of chromatographic coelution could result in misidentification. The absence of reference materials for the potential confounding molecules presents a significant analytical challenge. Perfluoroacylation of the amine group reduced the nitrogen basicity and facilitated individual fragmentation pathways for discrimination between these compounds based on some unique fragment ions and the relative abundance of common ions. GC-IRD studies produced additional structure-IR spectra relationships and yielded confirmation level identification for each of the six regioisomeric dimethoxyamphetamines. The amines and their perfluoroacylated derivatives were resolved by capillary gas chromatography and the amines demonstrated excellent resolution on the more polar stationary phase, Rtx-200

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J Anal Toxicol 2009 **33** (8) 456

Automated solid-phase extraction-liquid chromatography-tandem mass spectrometry analysis of 11-nor- ^{9}-tetrahydrocannabinol-9-carboxylic acid in human urine specimens: Application to a high-throughput urine analysis laboratory

A procedure for the analysis of 11-nor-Δ^9-tetrahydrocannabinol-9-carboxylic acid (THC-COOH) in human urine specimens employing automated solid-phase extraction coupled with liquid chromatography and tandem mass spectrometry (SPE-LC-MS-MS) is described. The method was linear (r^2 = 0.9986) to 1000 ng/ml with no carryover evidenced at 2000 ng/ml. Limits of quantification and detection were found to be 2 ng/ml. Interrun precision was evaluated at the 15 ng/ml level over nine batches spanning 15 days (n = 45). The coefficient of variation (%CV) was found to be 5.5% over the course of the validation. Intrarun precision of a 15 ng/ml control (n = 5) ranged from 0.58% CV to 7.4% CV for the same set of analytical batches. Interference was examined by employing (+/-)-11-hydroxy-Δ^9-tetrahydrocannabinol, cannabidiol, (-)-Δ^8-tetrahydrocannabinol, and cannabinol. One hundred and nineteen specimens previously found to contain THC-COOH by a previously validated gas chromatographic mass spectrometry (GC-MS) technique were compared by employing the SPE-LC-MS-MS method. Excellent agreement was found (r^2 = 0.9925) for the parallel comparison study. The automated SPE procedure precludes human factors of specimen handling, extraction and derivatization, thus reduces labor costs and rework resulting from human error or technique issues. Furthermore, technique runtime is substantially reduced (e.g., during parallel studies the SPE-LC-MS-MS instrument was often finished with analysis by the time the technician finished the offline SPE and derivatization procedure prior to the GC-MS analysis)

11 Narcotics

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J Anal Toxicol 2009 **33** (8) 423

Oxycodone-related fatalities in the west of Scotland

A liquid chromatography-electrospray ionization-tandem mass spectrometry technique is described for the determination of oxycodone and *N*- and *O*-demethylated metabolites in unhydrolyzed postmortem specimens. Fatalities involving oxycodone in the west of Scotland are reviewed. Ten oxycodone positive postmortem cases were detected, and nine were drug-related fatalities. Five cases were attributed solely to oxycodone intoxication and four to polydrug intoxication. Notwithstanding that there was overlap between blood oxycodone levels in deaths attributed to oxycodone only and those due to polydrug intoxication, lower oxycodone levels (< 1 mg/l) were discovered in polydrug intoxication in comparison with cases due to oxycodone alone (> 1 mg/l). The role of oxycodone in fatalities has been fully studied. However, the role of metabolites (noroxycodone and oxymorphone) was examined in this report for the first time. Oxycodone was more usually detected in blood, urine, and vitreous humor followed by noroxycodone. The ratio between oxycodone and its *N*-demethylated metabolite was investigated and found to be helpful in ascertaining whether death occurred shortly after drug administration or if there was a significant delay. High oxycodone/metabolite ratios were correlated with short survival times after ingestion. The median ratio of oxycodone/noroxycodone was 2.4 but ranged from 0.7 to 49. Prescriptions for oxycodone have increased sharply in Scotland in recent years. Furthermore, the identification of 10 oxycodone-related deaths in the past 18 months demonstrates the importance of including this drug in routine laboratory screening and confirmation procedures

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J Anal Toxicol 2009 **33** (8) 409

Determination of naloxone and nornaloxone (noroxymorphone) by high-performance liquid chromatography-electrospray ionization-tandem mass spectrometry

Naloxone and its metabolite nornaloxone were analysed in human plasma, urine, and human liver microsomes (HLM) by highly sensitive method. Naltrexone-d_3 and oxymorphone-d_3 were employed as respective internal standards. Solid-phase extraction, utilising mixed mode extraction columns and 0.1 M phosphate buffer (pH 5.9), was combined with high-performance liquid chromatography interfaced by electrospray ionization to tandem mass spectrometry. The calibration range in plasma was 0.025 to 2 ng/ml for naloxone and 0.5 to 20 ng/ml for nornaloxone. It was 10 to 2000 ng/ml in urine and 0.5 to 20 ng/ml in HLM for both. Enzymatic hydrolysis of urine was optimized for 4 h at 40 °C. Intra- and interrun accuracy was within 15% of target; precision within 13.4% for all matrices. The mean recoveries were 69.2% for naloxone and 32.0% for nornaloxone. Analytes were stable in plasma and urine for up to 24 h at room temperature and in plasma after three freeze-thaw cycles. In human subjects receiving 16 mg buprenorphine and 4 mg naloxone, naloxone was detectable for up to 2 h in all three subjects and up to 4 h in one subject. Mean AUC(0-24) was 0.303 +/- 0.145 ng/ml.h; mean C_{max} was 0.139 +/- 0.062 ng/ml; and T_{max} was 0.5 h. In 24-h urine samples, about 55% of the daily dose was excreted in either conjugated or unconjugated forms of naloxone and nornaloxone in urine. When cDNA-expressed P450s were incubated with 20 ng of naloxone, nornaloxone formation was detected for P450s 2C18, 2C19, and 3A4. Products other than nornaloxone are possible because naloxone utilization exceeded nornaloxone formation for 2C19 and 3A4. The data demonstrate a new procedure appicable for both *in vivo* and *in vitro* metabolism and pharmacokinetic studies of naloxone

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J Chromatogr A 2009 **1216** (44) 7570

On-line stacking and sweeping capillary electrophoresis for detecting heroin metabolites in human urine

Cation-selective exhaustive injection and sweeping micellar electrokinetic chromatography (CSEI-sweep-MEKC) was employed to determine heroin metabolites including morphine, codeine, and 6-acetylmorphine. Liquid-liquid extraction was employed for urine pretreatment. An uncoated fused silica capillary (Ld=30 cm, 50 µm ID) was filled with phosphate buffer (50 mM, pH 2.5) containing 30% methanol, then high conductivity buffer (100 mM phosphate, 41.3 kPa for 18 s) followed. Specimens were injected electrokinetically (20 kV, 300 s). The sweeping and separation were performed at -25 kV using phosphate buffer (20 mM, pH 2.5) and 80 mM sodium dodecyl sulfate. The baseline separation was done within 10 min. During method validation, the calibration curves were linear over a range of 50-500 ng/ml (*r* > or = 0.994). The RSD and RE values in intra-day and inter-day assays were all below 20%, which indicated good precision and accuracy. Their detection limits were 10 ng/ml (S/N = 3). The optimized method was applied to analyse authentic urine samples from addicts. Samples were verified by liquid chromatography/mass spectrometry

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J Anal Toxicol 2009 **33** (8) 433

Comparison of oxycodone in vitreous humor and blood using EMIT screening and gas chromatographic-mass spectrometric quantitation

In instances where blood samples are not available or are of poor/limited quantity, vitreous humor may serve as a useful alternative specimen for oxycodone analysis in death investigations. The aim of this research was to examine the relationship between immunoassay results and gas chromatography-mass spectrometry (GC-MS) quantitation of oxycodone in postmortem vitreous humor and blood. When used with vitreous humor calibrators, the Microgenics DRI Oxycodone (EMIT) Assay was found to be linear from 25 to 500 ng/ml with an limit of detection of 25 ng/ml. Vitreous humor and postmortem blood precipitate immunoassay responses in 57 oxycodone-positive cases were noted to be correlated (r^2 = 0.69, p < 0.01). Confirmation and quantitation of oxycodone in vitreous humor by GC-MS was linear from 50 to 1000 ng/ml with a limit of detection of 10 ng/ml and a limit of quantitation of 50 ng/ml. In 30 cases, oxycodone vitreous humor concentrations ranged from less than 50 to 945 ng/ml, and blood concentrations ranged from 103 to 768 ng/ml. The average vitreous humor/blood ratio was 1.16 and ranged from 0.12 to 3.26. Disparities between vitreous fluid and blood oxycodone concentrations were noted in several instances

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J Anal Toxicol 2009 **33** (8) 418

Potential biomarkers of smoked fentanyl utilizing pyrolysis gas chromatography-mass spectrometry

Fentanyl is a potent opioid clinically employed as an anesthetic/analgesic. However, it is increasingly becoming a choice drug of abuse. Fentanyl transdermal patches (FTPs) may be easily obtained and administered by smoking the reservoir gel and/or the whole patch. This facilitates increased bioavailability when inhaled. A procedure employing analytical pyrolysis is described to identify possible biomarkers associated with smoked fentanyl and FTPs. Pyrolysis was achieved under anaerobic and aerobic conditions using helium and air coupled to a gas chromatograph-mass spectrometer. The presence of a trap enhanced recovery and afforded a positive identification of pyrolytic products. Anaerobic and aerobic pyrolysis of fentanyl and FTPs routinely produced propionanilide as the major pyrolytic product together with pyridine and previously reported metabolites (norfentanyl and despropionyl fentanyl). Analysis of fentanyl demonstrated chlorine-containing compounds, presumably formed from the HCl salt of fentanyl. Analysis of FTPs indicated significant polymeric and hydrocarbon compounds and products likely derived from the gel matrix. Fentanyl in the FTPs was in the citrate salt form. Therefore, the chlorine-containing pyrolytic products obtained with the neat drug were not observed. By employing this protocol, it may be possible to identify what salt form of the drug was smoked based on pyrolytic products and to target distinguishing metabolic products for future research

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J Anal Toxicol 2009 **33** (8) 398

A comparison of the validity of gas chromatography-mass spectrometry and liquid chromatography-tandem mass spectrometry analysis of urine samples for morphine, codeine, 6-acetylmorphine, and benzoylecgonine

The U.S. Department of Health and Human Services posted a final notice in the Federal Register on November 25, 2008 authorizing the use of liquid chromatography-tandem mass spectrometry (LC-MS-MS) and other technologies in federally regulated workplace drug testing (WPDT) programs. This is expected to become effective in May 2010. To endorse this change, it is essential to fully substantiate that LC-MS-MS as a technology produces results at least as valid as gas chromatography-mass spectrometry (GC-MS), the long-accepted standard in confirmatory analytical technologies for drugs of abuse and currently the only confirmatory technique allowed for use in support of federally regulated WPDT programs. A series of manufactured control urine samples (*n* = 10 for each analyte) containing benzoylecgonine, morphine, codeine, and 6-acetylmorphine at concentrations ranging from 10% to 2000% of federal cutoffs were analyzed with replication by five federally regulated laboratories using GC-MS (five replicate analyses per lab) and at RTI International using LC-MS-MS (10 replicate analyses). In addition, interference samples as described in the National Laboratory Certification Program 2009 Manual were analyzed by both GC-MS and LC-MS-MS. Furthermore, matrix effects were investigated for LC-MS-MS, and both analytical technologies were employed to analyze previously confirmed urine specimens of WPDT origin. Data suggest that LC-MS-MS analysis was at least as precise, accurate, and specific as GC-MS for the analytes examined in this study. Whilst apparent, matrix effects could be controlled by the use of matrix-matched controls and calibrators with deuterated internal standards. LC-MS-MS data parameters, such as retention time and product ion ratios, were highly reproducible

12 Forensics

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J Anal Toxicol 2009 **33** (8) 478

Determination of specific absorbance (A|:) for zaleplon (Sonata) by spectrophotometry

Specific absorbance (A|) is the maximum absorbance of a 1% solution over a 1-cm path length when measured with a spectrophotometer. Where a reliable A| determination is available for a drug, it imparts an extremely useful reference for the quantitative evaluation of a stock drug solution. Whereas zaleplon was introduced into the market in 1999, the A| has not been published in the literature. The A| of zaleplon was measured with a spectrophotometer at 229 nm in aqueous acid and confirmed with three independent external sources to be 1186 (1042-1262; *n* = 18). The experimentally measured AI of zaleplon isuseful to a toxicology laboratory in order to verify the quantitative accuracy of a drug solution before its use in casework

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J Anal Toxicol 2009 **33** (8) 481

Zaleplon (Sonata) analysis in postmortem specimens by gas chromatography-electron capture detection

Zaleplon (Sonata) is a sedative hypnotic available on prescription and employed for the short-term treatment of insomnia. Whereas zaleplon was approved by the FDA in 1999, there has been limited postmortem data regarding the drug cited in the toxicology literature. Zaleplon was separated from postmortem biological specimens by employing a liquid-liquid extraction technique coupled with a solid-phase extraction. Detection was achieved with a gas chromatography-electron capture detector. The method was linear from 5.0 to 150 ng/ml with the limit of quantitation and detection determined to be 3.0 and 0.50 ng/ml, respectively. Analysis of the postmortem tissue distribution of zaleplon in seven cases was as follows: 6.1-1490 ng/ml central blood (seven cases), < 3.0-503 ng/ml femoral blood (five cases), 108 ng/ml harvest blood (one case), 343-679 ng/g liver (four cases), 950 ng/g spleen (one case), < 3.0-85 ng/ml bile (three cases), 3.8-106 ng/ml urine (four cases), < 3.0-486 ng/ml vitreous humor (five cases), and 0.005-3.4 mg total gastric contents (four cases). A validated technique for the determination of zaleplon and postmortem concentrations of autopsy specimens is reported to assist the forensic toxicologist with interpretation of future casework

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Chromatographia 2009 **70** (7-8) 1201

Analysis and confirmation of rodenticide pindone in human plasma by IC-ESI-IT-MS

An improved assay for the analysis and confirmation of pindone (a highly effective anticoagulant rodenticide) in human plasma is described. Following protein precipitation with 10% (v/v) methanol in acetonitrile and cleaning with solid-phase extraction, separation was carried out on an IonPac AS11-HC analytical column (250 mm × 2 mm) using 20 mmol/l KOH containing 10% (v/v) methanol as organic modifier by eluent generator reagent free ion chromatography. Quantification was achieved with negative electrospray ionization ion trap mass spectrometry employing diphacinone as an internal standard. The transition for quantitative analysis was *m/z* 229 → 172, and for qualitative analysis were *m/z* 229 → 145 and *m/z* 229 → 214 for pindone. The transition for quantitative analysis was *m/z* 339 → 167 for IS. The limit of detection, the limit of quantification, recovery, linearity, precision, and stability were all authenticated. The cracking approach of characteristic fragments for pindone and IS is proposed. It was ascertained that this procedure might be useful in clinical diagnosis and forensic toxicology analysis

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Anal Bioanal Chem 2009 **395** (8) 2521

ESI-MS/MS library of 1,253 compounds for application in forensic and clinical toxicology

By use of a hybrid tandem mass spectrometer with a linear ion trap, an electrospray ionization tandem mass spectrometry (ESI-MS/MS) library containing over 5,600 spectra of 1,253 compounds relevant in clinical and forensic toxicology has been produced. Pure compound solutions (in some cases solutions made of tablets) were prepared and 1 to 2,000 ng of each were injected into the system utilising standard reversed-phase analytical columns with gradient elution. To produce optimum mass spectral information, enhanced product ion spectra were gained with positive and/or negative ionization at low, medium, and high collision energies and additionally applying collision energy spread. In this mode, all product ions produced by the different collision energies were trapped in the linear ion trap prior to detection. The feasibility of the library to other types of hybrid tandem mass spectrometers with a linear ion trap from the same manufacturer as well as a standard triple-quadrupole tandem mass spectrometer has been examined with a selection of compounds. The spectra in the library may be employed to create methods for target analysis, either screening methods or quantitative procedures by generating transitions for multiple reaction monitoring. In those instances, suitable transitions and convenient collision energies are selected from the library. The library has been employed to identify compounds with a multi target screening approach for clinical and forensic toxicology with a standardized and automated system. The newer aspects of the library compared the former in-house library produced with a standard triple-quadrupole mass spectrometer are the enlargement of the ESI-MS/MS library and the additional acquisition of spectra with collision energy spread

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J Anal Toxicol 2009 **33** (8) 491

Urinary detection times and excretion patterns of flunitrazepam and its metabolites after a single oral dose

The excretion profiles of flunitrazepam metabolites in urine following a single dose were investigated. Sixteen volunteers received either 0.5 or 2.0 mg flunitrazepam. Urine samples were collected after 2, 4, 6, 8, 12, 24, 48, 72, 96, 120, 240, and 336 h. Specimens were screened using CEDIA (300 µg/l cutoff) and quantified by liquid chromatography-tandem mass spectrometry. The cutoff was 0.5 µg/l for flunitrazepam, *N*-desmethylflunitrazepam, 7-aminoflunitrazepam, 7-aminodesmethylflunitrazepam, 7-acetamidoflunitrazepam, and 7-acetamidodesmethylflunitrazepam. None of the subjects receiving 0.5 mg screened as positive. Only 23 of 102 samples from the subjects given 2.0 mg were positive with CEDIA. The principal metabolites were 7-aminoflunitrazepam and 7-aminodesmethylflunitrazepam. For all subjects provided with the low dose, 7-aminoflunitrazepam was detectable up to 120 h, and for two subjects for more than 240 h. Seven subjects administered the high dose were positive up to 240 h for 7-aminoflunitrazepam. It is concluded that the ratio 7-aminodesmethylflunitrazepam to 7-aminoflunitrazepam increased with time, independent of dose, and may be used to estimate the time of intake. However, in some low-dose subjects, the metabolite concentrations in the early specimens were low and a chromatographic method may not detect intake. This should be taken into consideration when advising police and hospitals about sampling in addition to when they set up protocols for analysis

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J Anal Toxicol 2009 **33** (8) 564

A fatality due to cyproheptadine and citalopram

A first-generation antihistamine available in over-the-counter cold medications and used to treat allergic-type symptoms is cyproheptadine (Periactin). Whereas antihistamines in general have long been known to cause serious adverse drug reactions, particularly when taken in overdose, few reports that specifically concern cyproheptadine-related fatalities exist. The body of a 42-year-old healthy female was discovered at her home with no anatomic cause of death and a recent history of suicidal ideations. Toxicology determined cyproheptadine and citalopram in the femoral postmortem blood at concentrations of 0.49 and 2.3 mg/l, respectively. Concentrations of < 0.04 and 0.80 mg/l in the vitreous for cyproheptadine and citalopram, respectively; 0.23 and 8.2 mg/l in the urine; and 30.7 and 9.0 mg/l in the bile were noted. The cause of death was attributed to suicide by cyproheptadine and citalopram intoxication. Whereas cyproheptadine is widely available in the United States and Europe, there are only two published fatalities as a result of this antihistamine and only one that specifically cites blood and tissue concentrations. Consequently, thes results should be beneficial in forensic toxicology by providing additional information regarding postmortem interpretation

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J Anal Toxicol 2009 **33** (8) 486

Development of a homogeneous immunoassay for the detection of zolpidem in urine

About 40 million people in the U.S every year are affected by sleep disorders of which insomnia is the most frequent cause. Zolpidem (Ambien) is a non-benzodiazepine drug available on prescription which is employed to treat insomnia. Is often preferred over more commonly used benzodiazepines because of its smaller adverse drug reaction profile. This results from the non-benzodiazepine binding more selectively to GABA-A receptors *versus* the non-selective binding of benzodiazepines. Since non-benzodiazepines have increased in popularity, drug abuse and driving-while-impaired cases involving sleep-inducing drugs have risen concomitantly. Consequently, a highly sensitive and rapid homogeneous immunoassay (EMIT-type assay) has necessarily been developed for the detection of zolpidem in urine. The antibody to zolpidem is highly specific and does not cross-react with other newer sleep medications such as zopiclone and zaleplon. The assay has a detection limit of 5 ng/ml for zolpidem in urine. Further validation of this assay by employing liquid chromatography-tandem mass spectrometry (LC-MS-MS) analysis of authentic urine samples demonstrated that the accuracy of the assay is greater than 90%. This assay is designed to measure the non-conjugated drug in urine. Consequently, it provided simplification of gas chromatography-MS or LC-MS-MS confirmation methods which do not require urine hydrolysis before solid-phase extraction or liquid-liquid extraction

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J Anal Toxicol 2009 **33** (8) 553

Hair analysis to demonstrate administration of sildenafil to a woman in a case of drug-facilitated sexual assault

In recent years, the drugs sildenafil (Viagra, Pfizer) and, subsequently, tadalafil (Cialis, Lilly-Icos) and vardenafil (Levitra, Bayer), have drawn public attention to the possibility of aphrodisiacs. Adverse drug reactions attributed to these drugs include hypotension, tachycardia, headache, flushing, blurred vision, dyspepsia, and musculoskeletal pain. Whereas sildenafil has been marketed for male impotence, recent attention has been paid to its application for women, including enhancement of success of *in vitro* fertilization but also better responses in cases of sexual disorders (increased desire, satisfaction, and orgasm). Currently, there is a debate on internet forums regarding the potential properties of sildenafil to promote women's sexual pleasure. A 12-cm length of light brown hair was submitted by a British police force after an allegation that a young female (15-17 years of age at the time) had been subjected to sexual assaults over a two-year period. Her stepfather was the alleged perpetrator and there was some suspicion that drugs may have been employed to facilitate the attacks. Following decontamination and segmentation (6 x 2-cm section), the specimen was analyzed by liquid chromatography coupled with tandem mass spectrometry after alkaline (pH 9.5) extraction using dichloromethane/isopropanol/*n*-heptane (25:10:65, v/v/v). The limit of quantitation was 5 pg/mg. The proximal segment of the hair tested positive for sildenafil at 38 pg/mg, and all others segments proved negative. This was in accordance with the victim's claim. However, in the absence of any controlled studies, it was not possible to attribute any quantitative interpretation on the measured concentration

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Rapid Commun Mass Spectrom 2010 **24** (1) 75

Rapid screening and confirmation of drugs and toxic compounds in biological specimens using liquid chromatography/ion trap tandem mass spectrometry and automated library search

Recent advances in liquid chromatography/tandem mass spectrometry (LC/MS/MS) technology have provided an opportunity for the development of more specific approaches to achieve the screen and confirmation goals in a single analytical step. For this purpose, this study adapts the electrospray ionization ion trap LC/MS/MS instrumentation (LC/ESI-MS/MS) for the screening and confirmation of over 800 drugs and toxic compounds in biological specimens. Liquid-liquid and solid-phase extraction protocols were coupled to LC/ESI-MS/MS using a 1.8-μm particle size analytical column operated at 50°C. Gradient elution of the analytes was conducted using a solvent system composed of methanol and water containing 0.1% formic acid. Positive-ion ESI-MS/MS spectra and retention times for each of the 800 drugs and toxic compounds were first established using 1-10 μg/ml standard solutions. This spectra and retention time information was then transferred to the library and searched by the identification algorithm for the confirmation of compounds found in test specimens - based on retention time matches and scores of fit, reverse fit, and purity resulting from the searching process. The established method was found highly effective when applied to the analyses of postmortem specimens (blood, urine, and hair) and external proficiency test samples provided by the College of American Pathology (CAP). The development of this approach has significantly improved the efficiency of our routine laboratory operation that was based on a two-step (immunoassay and GC/MS) approach in the past.

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J Anal Toxicol 2009 **33** (8) 525

Convenient headspace gas chromatographic determination of azide in blood and plasma

Azide occasionally accounts for poisonings. A technique was employed whereby azide in human blood and plasma samples was derivatized with propionic anhydride in a headspace vial without prior sample preparation. The reaction proceeds rapidly at room temperature to form propionyl azide. A portion of the headspace was analysed by gas chromatography with a nitrogen-phosphorus detector. In the heated injector of the gas chromatograph, the propionyl azide undergoes thermal rearrangement, forming ethyl isocyanate, which is subsequently chromatographed and detected. Propionitrile was employed as the internal standard. The method is linear to at least 20 μg/ml. Limit of quantitation was 0.04 μg/ml, and the within-run coefficient of variation was 5.6% at 1 μg/ml. There was no interference from cyanide. A fatality report following the ingestion of an unknown amount of sodium azide is presented. The patient became critically ill following his self-inflicted sodium azide ingestion. He was intubated and treated with vasopressors and aggressive supportive care, including extracorporeal membrane oxygenation therapy, in the intensive care facility but died from neurological brain damage secondary to anoxia. Blood and plasma azide concentrations from a 59-year-old man were monitored for 24 h. Upon admission, 1.4 h after ingestion, his azide level was 5.6 μg/ml (blood); shortly thereafter, it had risen to 13.7 μg/ml (plasma) and, subsequently, was projected to have been eliminated by 16.7 h. Significantly, no azide was detected in the postmortem blood and vitreous humor

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J Anal Toxicol 2009 **33** (8) 545

Prevalence of gabapentin in impaired driving cases in Washington State in 2003-2007

Gabapentin (Neurontin) is an antiepileptic/anticonvulsant drug. It is also commonly prescribed for (neuropathic) pain treatment. Whereas the complete mechanism of action is unknown, during the past 15 years, indications for gabapentin have been increasing. Adverse drug reactions include somnolence, dizziness, ataxia, nystagmus, and fatigue. Herein are reviewed all cases positive for gabapentin submitted to the Washington State Toxicology Laboratory between January 2003 and December 2007. For impaired driving cases (n = 137) the concentrations of gabapentin in blood ranged from < 2.0 to 24.7 mg/l with a mean of 8.4 +/- 5.4 mg/l and a median of 7.0 mg/l. The cases were 50% male with a mean age of 43.0 +/- 10.9 years (range 23-73). Of those studied, only 7% were positive for gabapentin alone with the remaining 93% indicative of polydrug use. Drug Recognition Expert reports of four cases where the only drug detected and likely to be causing impairment was gabapentin were examined. The reports suggested that subjects may exhibit psychophysical indicators of a central nervous system depressant (e.g., horizontal gaze nystagmus, poor performance on standardized field sobriety tests) with clinical indicators (e.g., dilated pupils, low body temperature, and elevated pulse and blood pressure) which are not consistent with a depressant

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J Anal Toxicol 2009 **33** (8) 508

Ethylene glycol and glycolic acid in a postmortem blood from fatal poisonings

An analytical challenge for forensic confirmation in postmortem toxicology is the use of ethylene glycol (EG), a relatively infrequent cause of fatal intoxication. Using a modification of a previously reported clinical method, EG and glycolic acid (GA) quantification in postmortem blood by gas chromatography coupled with ion trap mass spectrometry (GC-MS) has been achieved. The method is linear from 50 to 4000 mg/l with a limit of detection of 25 mg/l for both EG and GA. Interassay coefficient of variation (2.1-8.6%, 4.3-6.0%) and accuracy (96-101%, 92-105%) were determined for EG and GA, respectively. EG concentration by ion trap GC-MS correlated closely (r^2 = 0.995) with EG quantified by GC-flame-ionization detection. For 20 autopsies where there was no evidence of EG exposure, analysis of blood did not reveal detectable EG or GA. In 12 medical examiner cases with EG poisoning as cause of death, EG concentrations ranged widely from 58 to 7790 mg/l with a mean of 1830 mg/l, and the GA concentration averaged 1360 mg/l with a narrower range of 810-1770 mg/l. EG and GA levels correlated poorly (r^2 = 0.15) in postmortem blood with discordantly low EG concentrations in two cases. In addition, birefringent oxylate crystals in renal tissue was a consistent finding. A sensitive and specific GC-MS method for detection and quantification of EG and GA has been validated and a study of fatal EG poisonings demonstrated the forensic utility of the technique

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Chromatographia 2009 **70** (9-10) 1381

Simultaneous determination of anabolic androgenic steroids and their esters in hair by LC-MS-MS

The simultaneous determination of anabolic androgenic steroids and their esters in hair has been developed employing a liquid chromatographic-tandem mass spectrometric technique. The hair sample was treated with methanol to extract the esters, followed by alkaline digestion for optimum recovery of the anabolic androgenic steroids. Following liquid-liquid extractions, the extract was dried, redissolved and analyzed by multiple reaction monitoring with a quadrupole mass spectrometer. The lower limits of detection ranged from 0.001 to 0.020 ng/mg for the 21 analytes. The applicability of the technique was demonstrated using guinea pig hair samples gained from controlled experiments

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Anal Sci 2009 **25** (11) 1301
Simple isotope dilution headspace-GC-MS analysis of naphthalene and *p*-dichlorobenzene in whole blood and urine
A very simple, sensitive and simultaneous analytical technique employing headspace capillary gas chromatography-mass spectrometry (GC-MS) for naphthalene and *p*-dichlorobenzene in human whole blood and urine is described. The benefits of this technique were that as much as 1 ml of headspace vapor could be injected into a GC port in the splitless mode. In addition, the addition of deuterated naphthalene and *p*-dichlorobenzene as internal standards achieved much better headspace extraction efficiencies, which resulted in high sensitivity. The detection limits for both naphthalene and *p*-dichlorobenzene were 1 ng/ml for whole blood and 0.5 ng/ml for urine. Validation data, including linearity of calibration curves, reproducibility and recovery rates, were all adequate. Both compounds were detected with this technique in whole blood samples of a male volunteer following inhalation of gaseous forms of the compounds

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Int J Legal Med 2009 **123** (6) 451
Determination of antidepressants in human postmortem blood, brain tissue, and hair using gas chromatography-mass spectrometry
Analysis of a new-generation antidepressants and their metabolites in postmortem blood, brain tissue, and hair was achieved with an optimized gas chromatographic-mass spectrometric (GC-MS) method in positive ion chemical ionization mode in combination with a solid phase extraction. Twelve antidepressants and their active metabolites (i.e., mirtazapine, viloxazine, venlafaxine, citalopram, mianserin, reboxetine, fluoxetine, fluvoxamine, sertraline, maprotiline, melitracen, paroxetine, desmethylfluoxetine, desmethylmianserin, desmethylmirtazapine, desmethylsertraline, desmethylmaprotiline, desmethylcitalopram, and didesmethylcitalopram) were quantifiable. In addition to the validation of the GC-MS method, it was applied to four postmortem cases in order to demonstrate the usefulness of the described technique in forensic toxicology. In these cases, sertraline, fluoxetine, citalopram, and trazodone in combination with their active metabolites were determined. Blood concentrations ranged from subtherapeutic to toxic concentrations, while brain to plasma ratios ranged from 0.8 to 17. Hair concentrations ranged from 0.4 to 2.5 ng/mg depending on the substance and hair segment

13 Alcohol

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Traffic Inj Prev 2009 **10** (6) 519
Alcohol biomarkers as tools to guide and support decisions about intoxicated driver risk
Herein is described a pilot study that employed alcohol biomarkers to direct decisions about driving under the influence (DUI) driver risk in the United States by replicating a European best practices model. The study examined whether biomarkers may assist the assessor to identify high-risk drivers who persist to drink heavily following their arrest and detect relapses in drivers enrolled in rehabilitation. Carbohydrate-deficient transferrin (CDT) and the Early Detection of Alcohol Consumption (EDAC) test were employed to assess the drinking behavior of repeat offenders during the assessment interview (baseline) and at 3, 6, 9, and 12 months' follow-up. The cutoff used to determine heavy drinking at baseline was 2.2% CDT and 40% P-positive for EDAC. A 30% point increase in biomarker value from an abstinent baseline indictated a relapse and a 30% point decrease in biomarker value from a previous positive measure suggested reduced drinking/abstinence. The study demonstrated that the EDAC when employed alone identified 18% of drivers as heavy drinkers at baseline compared to 5% for CDT and 8% for GGT. The best detection rate resulted from an EDAC-CDT combination which identified heavy drinking in 20% of the repeat offenders at baseline, most of whom (68%) denied drinking at the assessment interview. At follow-up, 52% of drivers abstained/reduced their drinking, almost 20% experienced a relapse, and 30% remained noncompliant with testing. Drivers who relapsed were less likely to be in full-time employment (67 *versus* 84%) or married (17 *versus* 30%) compared to those who abstained. Of the drivers who relapsed, 80% returned to abstinence or reduced their drinking after biomarker information was employed as brief intervention by the counselors. Biomarker testing improved the assessment and monitoring of repeat offenders in this pilot study. It provided an objective tool with which to identify high-risk drivers allowing for better treatment recommendations. In addition, it assisted identified drivers who relapsed during follow-up and facilitated a brief intervention by the counselor which resulted in reduced alcohol consumption. The data contribute to institute evidence-based practices in highway safety and the setting up of new bench marks in the United States to reduce drunk driving

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J Anal Toxicol 2009 **33** (8) 521
Manual *versus* automatic sampling variations of a preliminary alcohol screening device
With the Alco-Sensor IV Black Dot Model, the manufacturer has recognized the potential to underestimate an individual's true breath alcohol content (BrAC) if manual sampling function is employed as an alternative to automatic sampling function. Consequently, a controlled human subject investigation was undertaken to analyze the possible breath-sampling differences between the standard automatic technique and three manual techniques. Subjects were administered vodka and orange juice and then tested during the descending limb of their BrAC curve. Statistically significant differences were noted between the two types of technique with the three manual ones underestimating the BrAC. The average maximum difference between the automatic BrAC level, when compared with the lowest manual level in each data set, was 27.9% (median 27.7%) with underestimations from 20.8% to 40.0%. The manual techniques never produced higher BrACs than the automatic technique

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J Mass Spectrom 2010 **45** (1) 121
No-discharge atmospheric pressure chemical ionization mass spectrometry of ethyl glucuronide and ethyl sulfate (Letter)
No abstract available

Hassan HMA, Cooper GAA// Univ Glasgow, Forensic Med & Sci, Glasgow G12 8QQ, Scotland
J Anal Toxicol 2009 **33** (8) 502
Determination of -hydroxybutyrate in blood and urine using gas chromatography-mass spectrometry
β-Hydroxybutyrate (BHB) is regarded a potential biomarker for alcoholic ketoacidosis (AKA). A robust and sensitive technique has been developed and validated for the quantification of BHB in postmortem blood and urine by employing deuterated γ-hydroxybutyrate as an internal standard. Specimens were analyzed by gas chromatography-mass spectrometry following liquid-liquid extraction and silyl derivatization. The limits of detection and lower limits of quantification in blood and urine were 2 and 7 mg/l and 2 and 6 mg/l, respectively. The interday and intraday precision was determined by coefficients of variation for blood and urine and ranged from 1.0 to 12.4% for quality control samples spiked at 50 and 300 mg/l. The linear range of 50-500 mg/l resulted in an average correlation of $r^2 > 0.99$, and the average extraction recoveries in blood and urine were >or= 82% and >or= 59%, respectively. BHB remains stable in blood spiked at a concentration of 300 mg/l for 15 days when stored within a refrigerator (2-5 °C). Postmortem blood and urine samples were investigated with the validated method for cases where the deceased had a history of chronic alcohol abuse in order to demonstrate the use of BHB as a potential marker of AKA

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J Anal Toxicol 2009 **33** (8) 561
Evaluation of potential lactate/lactate dehydrogenase interference with an enzymatic alcohol analysis
A legal challenge to a hospital alcohol dehydrogenase (ADH)-based serum ethanol determination based on the suggestion of interference by lactate dehydrogenase (LDH)-catalyzed oxidation of lactate was addressed by the Connecticut Department of Public Safety laboratory. Both ADH- and LDH-oxidations require NAD^+ (present in excess in the assay). NADH produced by LDH-catalyzed lactate oxidation in the assay is taken as derived from ethanol. However, hepatic trauma was suggested as the cause of elevated levels of lactate and LDH. Clinical laboratory results were analysed, particularly serum hepatic enzymes, ions, and anion gap. Aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT) were 229 and 144 U/l, respectively (approximately 8x and 4x reference range midpoint values). Na^+, K^+, Cl-, and CO_2 levels were 143, 3.0, 112, and 20 meq/l, respectively, yielding an anion gap of 8 meq/l (ref. range 8-15). Serum lactate contributes to "unmeasured anions"; hence, the anion gap was inconsistent with a significant lactate elevation. On the basis of the slight elevation of ASAT and ALAT, LDH levels were

estimated to be elevated to no more than 10-fold. Determination of the amount of LDH and ADH present in the ethanol assay suggest an ADH/LDH ratio of 200:1. Consequently, contribution by lactate oxidation to the serum ethanol concentration in this case would have been negligible

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J Anal Toxicol 2009 **33** (8) 514
Examination of some performance characteristics of breath alcohol measurements obtained with the Intoxilyzer 8000C following social drinking conditions
For 10 healthy subjects under social drinking conditions, the Intoxilyzer 8000C was used to measure breath alcohol concentration (BrAC). Measurements ranged from 5 min of commencement to the end of drinking (EOD). For 14 blood-breath pairs, measured BrACs were compared with corresponding venous blood alcohol concentrations (vBAC) of specimens drawn at least 30 min after EOD and within 5 min of the corresponding breath test. BAC was determined with an enzymatic method. Concentration differences between breath and blood (BrAC - vBAC) ranged from -32 to +3 mg/dl (untruncated BrAC) and from -32 to -4 mg/dl (truncated BrAC). The "Invalid Sample" message was activated in five out of 23 BrAC profiles. Of the remaining 18 samples, residual mouth alcohol was determined by comparing the maximum difference between successive (5 min apart) measurements (MID5) over 20-30 min after EOD with the precision of replicate BrAC values taken 30-40 min after EOD (5 mg/dl or less; precision unaffected by breath sample volume over the range of 2-3 l). MID5 values were noted within the first three measurements in 16/18 cases, suggesting a significant mouth alcohol effect. Therefore, obligatory delays must be employed with the Intoxilyzer 8000C before testing to reduce the possibility of overestimation of BrAC due to mouth alcohol

14 Tobacco

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J Chromatogr B 2009 **877** (29) 3537
Simultaneous and sensitive measurement of nicotine, cotinine, *trans*-3'-hydroxycotinine and norcotinine in human plasma by liquid chromatography-tandem mass spectrometry
The simultaneous quantification of nicotine, cotinine, *trans*-3'-hydroxycotinine and norcotinine in human plasma was developed and fully validated by employing an LC-MS/MS technique. Possible internal and external interferences were comprehensively assessed and limits of quantification were calculated by decreasing the analyte concentration. Analytical ranges were 1-500 ng/ml for nicotine and cotinine, 5-500 ng/ml for *trans*-3'-hydroxycotinine and norcotinine. Mean intra- and inter-assay analytical recoveries ranged 101.9 from 116.8%, and intra- and inter-assay imprecision were less than 11% RSD for all analytes (parameters were evaluated at three different concentrations across the linear range of the assay). Extraction efficiency was > or = 70% for all analytes. This validated technique may benefit the determination of nicotine and metabolites in human plasma to support research on the role of nicotine biomarkers on neuronal systems mediating cognitive and affective processes. In addition, it may be employed to differentiate active, passive and environmental exposure

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Anal Bioanal Chem 2009 **395** (7) 2349
Optimization and validation of a liquid chromatography-tandem mass spectrometry method for the simultaneous quantification of nicotine, cotinine, *trans*-3'-hydroxycotinine and norcotinine in human oral fluid
An analytical method was developed and validated for the simultaneous identification and quantification of nicotine, cotinine, *trans*-3'-hydroxycotinine, and norcotinine in 0.5 ml of human oral fluid collected with the Quantisal oral fluid collection device. Solid phase extraction and liquid chromatography-tandem mass spectrometry with multiple reaction monitoring was employed. Internal and external interferences were comprehensively assessed. Limits of quantification were empirically identified by decreasing analyte concentrations. Linearity was from 1 to 2,000 ng/ml for nicotine and norcotinine, 0.5 to 2,000 ng/ml for *trans*-3'-hydroxycotinine, and 0.2 to 2,000 ng/ml for cotinine. Correlation coefficients for calibration curves were >0.99 and analytes quantified within +/-13% of target at all calibrator concentrations. Suitable analytical recovery (>91%) was accomplished with extraction efficiencies >56% and matrix effects <29%. The procedure will be applied to quantify nicotine and metabolites in oral fluid in a clinical study to determe the most appropriate nicotine biomarker concentrations to differentiate active, passive, and environmental nicotine exposure

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J Chromatogr A 2009 **1216** (45) 7899
Rapid and sensitive gas chromatography-ion-trap tandem mass spectrometry method for the determination of tobacco-specific *N*-nitrosamines in secondhand smoke
Some of the most potent carcinogens in tobacco and cigarette smoke are tobacco-specific nitrosamines (TSNAs). Accurate quantification of these chemicals is required to aid assessment of public health risks. A specific and sensitive technique to measure four TSNAs adsorbed to model surfaces and secondhand smoke (SHS) particles using gas chromatography-ion-trap tandem mass spectrometry was developed and validated. In an 18-m^3 room-sized chamber, a smoking machine generated realistic concentrations of SHS that were actively sampled on Teflon-coated fiber glass (TCFG) filters, and passively sampled on cellulose substrates. A simple solid-liquid extraction technique using methanol as solvent was successfully applied to both substrates with recoveries ranging from 85 to 115%. For each TSNA, tandem MS parameters were optimized and the major fragmentation pathways were determined. The protocol showed excellent performance with a linear dynamic range from 2 to 1000ng/ml, low detection limits (S/N > 3) of 30-300pg/ml and precision with experimental errors below 10% for all compounds. In addition, no interfering peaks were noted, suggesting a high selectivity of MS/MS without the need for a sample clean-up step. The technique provides a suitable analytical tool to detect and quantify traces of TSNA in indoor environments polluted with SHS

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J Chromatogr Sci 2009 **47** (10) 902
Rapid and chemically selective nicotine quantification in smokeless tobacco products using GC-MS
Smokeless products with a variety of nicotine content and flavoring formulations that may appeal to new users and existing cigarette smokers have proliferated recently. The CDC nicotine method, which utilises gas chromatography-flame ionization detection (GC-FID), provides a robust technique for determining nicotine in smokeless tobacco. However, several compounds, identified in a several flavored smokeless products, interfere with nicotine quantification using GC-FID. To mitigate this effect, the standard nicotine technique (26.7 min run time) was modified to use faster GC ramping (3.7 min run time) and detection with mass spectrometry (GC-MS) in selected ion-monitoring mode to diminish signal interferences that might introduce bias in nicotine values. Seven conventional smokeless samples (n = 12) and blank tobacco samples spiked at three nicotine concentration levels (n = 5) were analyzed using the GC-FID and GC-MS methods and found to be in excellent agreement. However, only the GC-MS technique provided confirmation of chromatographic peak purity in certain highly flavored products. The GC-MS method is not intended to replace GC-FID but to facilitate analysis of a wide range of nicotine values in domestic and international samples of varying complexity. Accurate nicotine quantification is essential for determining total nicotine content in tobacco and in subsequent calculations of un-protonated nicotine content

15 Homeland Security

Anandakathir R, Ojha U, Ada ET, Faust R, Kumar J*// *Univ Massachusetts, Ctr Advanced Materials, Lowell, Ma 01854, USA
J Macromol Sci Pure Appl Chem 2009 **46** (12) 1217
Stilbene-based fluorescent sensor for detection of organophosphorus warfare nerve agents
The synthesis of stilbene-based fluorophore, 3,4-dihydroxy-4'-aminostilbene (DHAS) for the detection of chemical warfare agents such as organophosphorus nerve gases is described. DHAS was characterized by various spectroscopic techniques and grafted on to electrospun nanofibers. The interaction of DHAS with the nerve agent simulant, diethyl chlorophosphate (DCP) was investigated in solution and vapor phase by fluorescence spectroscopy

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Anal Chem 2009 **81** (22) 9314
Biomonitoring of organophosphorus agent exposure by reactivation of

cholinesterase enzyme based on carbon nanotube-enhanced flow-injection amperometric detection

A portable, rapid, and sensitive prorocol for subclinical organophosphorus (OP) agent exposure employing the reactivation of cholinesterase (ChE) from OP-inhibited ChE using rat saliva (*in vitro*) was produced utilising an electrochemical sensor coupled with a microflow-injection system. The sensor employed a carbon nanotube (CNT)-modified screen printed carbon electrode (SPE), which was integrated into a flow cell. The extent of interindividual ChE activity is variable. Therefore, ChE biomonitoring necessitates an initial baseline determination (noninhibited) of enzyme activity which is then directly compared with activity following OP exposure. Herein is described an alternative strategy whereby reactivation of the phosphorylated enzyme is utilised to enable measurement of both inhibited and baseline ChE activity (after reactivation by an oxime, i.e., pralidoxime iodide) in the same sample. CNTs facilitate the electrochemical detection of the products from enzymatic reactions more feasible with extremely high sensitivity (5% ChE inhibition) and selectivity. Paraoxon was employed as a model OP compound for *in vitro* inhibition studies. Some experimental parameters, e.g., inhibition and reactivation time, have been optimized such that 92-95% of ChE reactivation maybe achieved over a broad range of ChE inhibition (5-94%) with paraoxon. The extent of enzyme inhibition employing this electrochemical sensor compares well with conventional enzyme activity measurements. By employing the double determinations of enzyme activity, the flow-injection device was successfully used to detect paraoxon inhibition efficiency in saliva samples (95% of ChE activity is due to butyrylcholinesterase), which illustrates its promise as a sensitive monitor of OP exposure in biological fluids. The technique precludes inter- or intra-individual variation in the normal levels of ChE. Therefore, this new CNT-based electrochemical sensor is a sensitive and quantitative tool for point-of-care assessment and noninvasive biomonitoring of the exposure to OP pesticides and chemical nerve agents

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J Chromatogr A 2009 **1216** (45) 7906

Enhanced detectability of fluorinated derivatives of *N,N*-dialkylamino alcohols and precursors of nitrogen mustards by gas chromatography coupled to Fourier transform infrared spectroscopy analysis for verification of chemical weapons convention

N,N-Dialkylamino alcohols, *N*-methyldiethanolamine, *N*-ethyldiethanolamine and triethanolamine are the precursors of VX type nerve agents and three different nitrogen mustards respectively. The detection and identification of these compounds is of fundamental importance for confirmatory analysis under the Chemical Weapons Convention. GC-FTIR was employed as a complimentary method to GC-MS analysis for identification of these analytes. One limit of GC-FTIR, its low sensitivity, was circumvented by converting the analytes to their fluorinated derivatives. Due to their high absorptivity in IR region, these derivatives facilitated their detection by GC-FTIR analysis. Derivatizing reagents bearing trimethylsilyl, trifluoroacyl and heptafluorobutyryl groups on imidazole moiety were screened. Derivatives were analyzed by GC-FTIR quantitatively. Of the reagents investigated, heptafluorobutyrylimidazole (HFBI) produced the greatest increase in sensitivity by GC-FTIR detection. 60-125 folds of sensitivity enhancement were noted for the analytes by HFBI derivatization. Absorbance derived from various functional groups responsible for enhanced sensitivity were compared by determination of their corresponding relative molar extinction coefficients considering uniform optical path length. The RSDs for intraday repeatability and interday reproducibility for various derivatives were 0.2-1.1% and 0.3-1.8%. Limit of detection (LOD) was achieved up to 10-15ng. Applicability of the technique was examined with unknown samples employed in international proficiency tests

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Talanta 2009 **80** (1) 231

Simple, rapid and highly sensitive detection of diphosgene and triphosgene by spectrophotometric methods

Procedures for the identification and quantification of diphosgene and triphosgene are described. These compounds are routinely used phosgene precursors and produce an intensely colored purple pentamethine oxonol dye when reacted with 1,3-dimethylbarbituric acid (DBA) and pyridine (or a pyridine derivative). Two quantitative techniques are described employing either UV absorbance or fluorescence of the oxonol dye. Limits of detection are approximately ~4 µmol/l by UV and <0.4 µmol/l by fluorescence. The third procedure is a test strip for the simple and rapid detection and semi-quantitative estimation of diphosgene and triphosgene, using a filter paper embedded with dimethylbarbituric acid and poly(4-vinylpyridine). Addition of a test solution to the paper causes a color change from white to light blue at low concentrations and to pink at higher concentrations of triphosgene. The test strip is useful for rapid field detection of triphosgene and diphosgene in reaction mixtures. The test is easy to perform and produces clear signal readouts indicative of the presence of phosgene precursors

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Appl Environ Microbiol 2009 **75** (22) 7229

Identification of *Bacillus anthracis* by using matrix-assisted laser desorption ionization-time of flight mass spectrometry and artificial neural networks

The applicability of a combination of matrix-assisted laser desorption ionization-time of flight (MALDI-TOF) mass spectrometry (MS) and chemometrics for rapid and reliable identification of vegetative cells of the causative agent of anthrax, *Bacillus anthracis* is demonstrated. Bacilli were cultured under standardized conditions and inactivated in accordance with a recently developed MS-compatible inactivation protocol for highly pathogenic microorganisms. MALDI-TOF MS then used to collect spectra from the microbial samples and compile a database of bacterial reference spectra. The database comprised mass peak profiles of 374 strains from *Bacillus* and related genera, among them 102 strains of *B. anthracis* and 121 strains of *B. cereus*. The information in the database was examined by means of visual inspection of gel view representations, univariate *t* tests for biomarker identification, unsupervised hierarchical clustering, and artificial neural networks (ANNs). Analysis of gel views and independent *t* tests indicated *B. anthracis* and *B. cereus* group-specific signals. For example, mass spectra of *B. anthracis* provided discriminating biomarkers at 4,606, 5,413, and 6,679 Da. A systematic search in proteomic databases allowed tentative assignment of some of the biomarkers to ribosomal protein or small acid-soluble proteins. Multivariate pattern analysis by unsupervised hierarchical cluster analysis further demonstrated a subproteome-based taxonomy of the genus *Bacillus*. Superior classification accuracy was achieved when supervised ANNs were utilised. For the identification of *B. anthracis*, independent validation of optimized ANN models yielded a diagnostic sensitivity of 100% and a specificity of 100%

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Epidemiol Infect 2009 **137** (11) 1623

Evaluation of Gram-positive rod surveillance for early anthrax detection

Since 2003, Connecticut laboratories have been able to report Gram-positive rod (GPR) isolates detected within 32 h of inoculation from blood or cerebrospinal fluid. The aim of this study was to rapidly identify inhalational anthrax and unusual *Clostridium* spp. infections, and to establish round-the-clock laboratory reporting of potential indicators of bioterrorism. Between 2003 to 2006, Connecticut's GPR surveillance system identified 1134 isolates, including 657 *Bacillus* spp. (none *B. anthracis*) and 241 *Clostridium* spp. Reporting completeness and timeliness improved to 93% and 92%, respectively. Baseline rates of *Bacillus* spp., *Clostridium* spp. and other GPR findings were established and are stable. To date, no cases of anthrax and no unusual clusters of *Clostridium* spp. have been detected by the GPR surveillance system. This system may have confirmed the inhalational anthrax case in Pennsylvania in 2006, three days earlier than traditional reporting. Using audits and ongoing evaluation, the system has evolved into a highly functional 24/7 laboratory telephone reporting system with almost complete reporting

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J Am Soc Mass Spectrom 2009 **20** (11) 2093

Ionization mechanism of the ambient pressure pyroelectric ion source (APPIS) and its applications to chemical nerve agent detection

The ionization mechanism operative in the ambient pressure pyroelectric ionization source (APPIS) was studied in addition to applications that include the detection of simulants of chemical nerve agents. It was discovered that ionization by APPIS occurs in the gas-phase. As the crystal is thermally cycled over a narrow temperature range, electrical discharges near the surface of the crystal produce energetic species which, through reactions with atmospheric molecules, produce reactant ions such as protonated water clusters or clusters of hydroxide and water. Reactant ions may be observed directly in the mass spectrometer. Subsequently, they react with trace neutrals *via* proton transfer reactions to generate the ions observed in mass spectra, which are usually singly protonated or deprotonated species. Further implicating gas-phase ionization, observed product distributions are highly dependent on the composition of ambient gases, especially the concentration of water vapor and oxygen surrounding the source. Basic species such as triethylamine are observed as singly protonated cations at a water partial pressure of 10 torr. At a water pressure of

4 torr, reactive oxygen species are generated and lead to observation of protonated amine oxides. The ability of the APPIS source to detect basic molecules with high proton affinities makes it highly applicable to the detection of chemical nerve agents. This application was tested using simulants corresponding to VX and GA (Tabun). By employing the present source configuration, pyridine was detected readily at a concentration of 4 ppm, indicating ultimate sensitivity in the high ppb range

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Biosens Bioelectron 2009 **25** (3) 592

Molecularly imprinted nanopatterns for the recognition of biological warfare agent ricin

In order to avoid harsh environments during the synthesis of MIP, a molecularly imprinted polymer (MIP) for biological warfare agent (BWA) ricin was synthesized using silanes. The synthesized MIP was employed for the recognition of ricin. Complete removal of ricin from the polymer was confirmed by fluorescence spectrometry and SEM–EDAX. SEM and EDAX studies verified the attachment of the silane polymer on the surface of silica gel matrix. The SEM image of ricin-MIP showed nanopatterns and it was completely different from the SEM image of non-imprinted polymer (NIP). BET surface area analysis indicated more surface area (227 m^2/g) for ricin-MIP than that of NIP (143 m^2/g). Furthermore, surface area study demonstrated more pore volume (0.5010 cm^3/g) for ricin-MIP than that of NIP (0.2828 cm^3/g) at 12 nm pore diameter verifying the presence of imprinted sites for ricin as the reported diameter of ricin is 12 nm. The recognition and rebinding ability of the ricin-MIP was tested in aqueous solution. Ricin-MIP rebound more ricin when compared to the NIP. The chromatogram produced with ricin-MIP demonstrated two peaks due to imprinting. However, the chromatogram of NIP exhibited only one peak for free ricin. The SDS-PAGE result confirmed the second peak noted in the chromatogram of ricin-MIP as the ricin peak. Ricin-MIP displayed an imprinting efficiency of 1.76 and also revealed 10% interference from the structurally similar protein abrin

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J Chromatogr A 2009 **1216** (48) 8452

Combination of solid phase extraction and *in vial* solid phase derivatization using a strong anion exchange disk for the determination of nerve agent markers

Organophosphorous (OP) nerve agents are employed in chemical warfare. Alkylphosphonic acids (APAs) are their degradation products and chemical markers. A technique employing anion exchange disk-based solid phase extraction (SPE) combined with in vial solid phase derivatization (SPD) and GC-MS has been devised for the analysis of APAs in aqueous samples. The optimization of critical method parameters, such as the SPD reaction, was accomplished by employing statistical experimental design and multivariate data analysis. The optimized technique produced quantitative recoveries in the range from 83% to 101% (n=13, RSD from 4% to 10%). The technique was sensitive, with LODs in SIM mode of 0.14 ppb, and demonstrated excellent linearity with an average r^2>or=0.99 over the concentration range of 0.07-1.4 ppm in full scan mode and from 0.14 ppb to 14 ppb in SIM mode. For forensic investigations, aqueous samples containing APAs at concentrations exceeding 14 ppb were concentrated and target analytes were successfully analysed by spectral library and retention index matching. Method robustness was assessed with aqueous samples from the official OPCW Proficiency Test (round 19) and all APAs present in the sample were definitively identified. The SPE disk retained underivatized APAs in a stable form for prolonged periods of time. Significant losses of APAs from the disk were not observed over a 36-day period. Overall, the technique is apprpriate to the qualitative and quantitative analysis of degradation markers of OP nerve agents in aqueous matrices. It demonstrates simplicity, a low risk of cross-contamination and trace level sensitivity

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Immunopharmacol Immunotoxicol 2009 **31** (3) 417

Simultaneous detection of five biothreat agents in powder samples by a multiplexed suspension array

A rapid, sensitive, specific, and simultaneous detection method for multiple biothreat-associated agents in powder samples has been produced employing suspension array-based multiplexed immunoassay. The 5-plexed immunoassays utilising sets of 9-plexed coupled fluorescent beads were applied to simultaneously detect five representative biothreat agents, including *B. anthracis* spore, *Y. pestis*, SARS-CoV, staphylococcal enterotoxin B (SEB) and ricin from a single powder sample. The feasibility for field samples was tested with both blinded and standard laboratory trials. The detection sensitivity and dynamic range of the five biothreat agents from different powders might vary dependent upon the nature of the powder and the feature of the contaminating agent. The limit of detection for *Y. pestis*, *B. anthracis* spores, SEB, ricin, SARS-CoV N protein in milk powder was 20 cfu, 111 cfu, 110pg, 5.4 ng and 2 ng per test respectively. When compared with conventional ELISA method, the suspension array has a higher sensitivity, and is able to detect five biothreat agents simultaneously with high reproducibility

16 Workplace

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Anal Bioanal Chem 2009 **395** (8) 2583

Sampling of benzene in environmental and exhaled air by solid-phase microextraction and analysis by gas chromatography-mass spectrometry

The International Agency for Research on Cancer (IARC) classifies benzene as a Group I carcinogen. Risk assessment for benzene may be performed by monitoring environmental and occupational air and through biological monitoring of biomarkers. A GC/MS using SPME technique for benzene analysis was developed and validated as the sampling technique for ambient air and breath. The results of the analysis of air in parks and avenues demonstrated a significant difference, with average values of 4.05 and 18.26 $\mu g/m^3$, respectively, for benzene. Sampling of air in the occupational environment indicated an average of 3.41 and 39.81 $\mu g/m^3$. Furthermore, the correlations between ambient air and expired air showed a significant tendency to linearity (r^2 = 0.850 and r^2 = 0.879). Results obtained for two groups of employees (31.91 and 72.62 $\mu g/m^3$) produced the same trend compared with that from the analysis of environmental air

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Ann Occup Hyg 2009 **53** (7) 713

Recombinant factor C (rFC) assay and gas chromatography/mass spectrometry (GC/MS) analysis of endotoxin variability in four agricultural dusts

Of significant concern in agricultural environments are endotoxins because of relatively high exposure levels. The aims of this work were to estimate patterns of 3-hydroxy fatty acid (3-OHFA) distribution in dusts from four types of agricultural environments (dairy, cattle feedlot, grain elevator, and corn farm) and to evaluate correlations between the results of gas chromatography/mass spectrometry (GC/MS) analysis (total endotoxin) and biological recombinant factor C (rFC) assay (free bioactive endotoxin). An existing GC/MS-MS technique (for house dust) was modified to reduce sample handling and optimized for small amount (<1 mg) of agricultural dusts using GC/EI-MS. A total of 134 breathing zone samples using Institute of Occupational Medicine (IOM) inhalable samplers were collected from agricultural workers in Colorado and Nebraska. Livestock dusts included approximately two times higher concentrations of 3-OHFAs than grain dusts. Patterns of 3-OHFA distribution and proportion of each individual 3-OHFA differed with dust type. The rank order of Pearson correlations between the biological rFC assay and the modified GC/EI-MS results was feedlot (0.72) > dairy (0.53) > corn farm (0.33) > grain elevator (0.11). In livestock environments, both odd- and even-numbered carbon chain length 3-OHFAs correlated with rFC assay response. The GC/EI-MS technique may be especially useful for identification of specific 3-OHFAs for endotoxins from various agricultural environments. In addition, it may provide useful information for evaluating the relationship between bacterial exposure and respiratory disease among agricultural workers

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J Chromatogr A 2009 **1216** (41) 6970

Separation and analysis of dimethylaniline isomers by supercritical fluid chromatography-electrospray ionization tandem mass spectrometry

Specific isomers of dimethylanilines (DMA's) are of interest as a result of their potential exposure-human health outcome relationships. Improved analytical procedures will assist in identifying the environmental sources of such exposures. Supercritical fluid chromatography (SFC), without derivatization was employed to separate of all six DMA isomers. In addition, when combined with electrospray ionization/tandem mass spectrometry, SFC provided selective detection in crude extracts of spiked (40 ppb of 3,5-dimethylaniline) raw materials. The raw materials chosen for analysis are routinely employed in the production of consumer hair-dye products

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J Chromatogr B 2009 **877** (29) 3743

Direct determination of *N*-methyl-2-pyrrolidone metabolites in urine by HPLC-electrospray ionization-MS/MS using deuterium-labeled compounds as internal standard

N-Methyl-2-pyrrolidone (NMP) has been used in many industries. Biological monitoring of NMP exposure is favoured to atmospheric monitoring in occupational health. An analytical method which excluded solid phase extraction (SPE) but employed deuterium-labeled compounds as internal standards for high-performance liquid chromatography-electrospray ionization-mass spectrometry using a C30 column has been developed. Urinary concentrations of NMP and its known metabolites 5-hydoxy-*N*-methyl-2-pyrrolidone (5-HNMP), *N*-methyl-succinimide (MSI), and 2-hydroxy-*N*-methylsuccinimide (2-HMSI) were achieved with a single run. The technique produced baseline separation of these compounds. The limits of detection in 10-fold diluted urine were 0.0001, 0.006, 0.008, and 0.03 mg/l, respectively. Linear calibration covered a biological exposure index (BEI) for urinary concentration. The within-run and total precisions (CV, %) were 5.6% and 9.2% for NMP, 3.4% and 4.2% for 5-HNMP, 3.7% and 6.0% for MSI, and 6.5% and 6.9% for 2-HMSI. The technique was assessed by employing international external quality assessment samples and urine samples from workers exposed to NMP in an occupational area

17 Product Authenticity

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J Pharm Biomed Anal 2009 **50** (5) 724

Isolation and structural elucidation of dapoxetine as an adulterant in a health supplement used for sexual performance enhancement

The Health Sciences Authority of Singapore received a health supplement employed for sexual performance enhancement. An unknown compound was detected. It was isolated and its structure determined using NMR, high-resolution MS, ESI-MS/MS, UV and IR. The compound was identified as dapoxetine. Dapoxetine is a selective serotonin reuptake inhibitor currently under investigation for the treatment of premature ejaculation

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J Chromatogr A 2009 **1216** (47) 8426

Identification of sildenafil, tadalafil and vardenafil by gas chromatography-mass spectrometry on short capillary column

Some dietary supplements, herbal preparations and food products are claimed to enhance male sexual function in cases of impotence but have been found to contain synthetic drugs. Sildenafil and its analogues (tadalafil and vardenafil) are synthetic phosphodiesterase type 5 inhibitors employed in the treatment of male erectile dysfunction. A gas chromatograph-mass spectrometer (GC-MS) assay has been developed for identification of these drugs. Chromatographic separation was achieved within 6 min by using a short 10 m capillary column. No prior sample clean-up before GC-MS analysis was required, therby making this assay a cost saving and rapid technique. In addition, the assay was specific because the identification of sildenafil, tadalafil and vardenafil was achieved by detection of molecular ions (*m/z* 474, 389 and 448, respectively) and several other characteristic ions resulted from the mass fragmentation of individual molecules. By employing the developed assay, sildenafil and its analogues were successfully identified in food and herbal matrices

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LC-MS-MS in MRM mode for detection and structural identification of synthetic hypoglycemic drugs added illegally to 'natural' anti-diabetic herbal products

Herbal products for the enhancement of anti-diabetic function are marketed. However, several have been analyzed and found to contain synthetic hypoglycemic drugs. The LC-MS analysis ten synthetic drugs [gliquidone (GLQ), glipizide (GLZ), gliclazide (GLC), glibenclamide (GLB), glimepiride (GLM), rosiglitazone (RGL), repaglinide (RPG), metformin (DMBG), phenformin (DBI), and tolbutamide (TOL)] has been improved. Quantification employed multiple reaction monitoring mode. The intra-day and inter-day precision of the method ranged from 2.13 to 5.55% and from 3.78 to 8.14%, respectively. LOQ was 1, 1, 1.2, 2, 3, 3, 5, 5, 2, and 1 µg/l for GLQ, GLZ, GLC, GLB, GLM, RGL, RPG, DMBG, DBI, and TOL, respectively. Structures were identified by collision-induced dissociation mass spectral analysis. The data indicate that a variety of synthetic drugs had been illegally added to anti-diabetic herbal products. However, a surprising result was that some of the adulterants were added into the capsule shell instead of capsule contents. LC-MS-MS is a powerful tool, and the method has wide applicability

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Use of a hydrolytic procedure and spectrometric methods in the structure elucidation of a thiocarbonyl analogue of sildenafil detected as an adulterant in an over-the-counter herbal aphrodisiac

An herbal dietary supplement marketed as an aphrodisiac was found to be supplemented with a sildenafil-related compound. It was identified as an analogue of sildenafil whereby the carbonyl group in the pyrimidine ring of sildenafil was substituted with a thiocarbonyl group, and the methyl group on the piperazine ring was substituted with a hydroxyethyl group. On the basis on this structure, the compound was designated thiohydroxyhomosildenafil. Its structure of the compound was established using HPLCIMS, UV spectrometry, electrospray ionization-MS/MS, NMR spectrometry, and a hydrolytic process. Hydrolysis resulted in a notable compound namely 1-(2-hydroxyethyl)-piperazine; the identification of this product defined the amine portion of the compound. An additional significant product of hydrolysis was hydroxyhomosildenafil, generated by hydrolysis of the thiocarbonyl group to a carbonyl group ($C = S \rightarrow C = O$). Hydroxyhomosildenafil was detected as a minor component in the dietary supplement

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Looking beyond the column: An investigation into method reproducibility for an active pharmaceutical ingredient

Lack of reproducibility during initial development of a high performance liquid chromatography technique is rarely examined in a thorough and rigourous manner in the context of an industrial setting. For a drug project in the early developmental stages, the LC method is frequently amended, sometimes drastically, if irreproducibility in the method is discovered. A frequent excuse for irreproducibility is justified by column lot variability, diluent effects, or pH effects with little or no investigations taking place for justification and little thought given to why lack of reproducibility may have occurred in the first case. In this study, a case study is presented whereby a systematic approach was undertaken in order to determine the exact cause of how method irreproducibility was taking place. The resultss of the research were then employed to amend a technique with poor reproducibility into one that was rugged without the necessity to start from the beginning and develop an entirely new method

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Development and validation of LC-MS/MS method for the determination of cyproheptadine in several pharmaceutical syrup formulations

The qualitative and quantitative assay of cyproheptadine (CP) in pharmaceutical samples was achieved by development and validation of a rapid and sensitive liquid chromatographic-tandem mass spectrometric (LC-MS/MS) technique. Diphenylpyraline hydrochloride (DPP) was used as an internal standard (IS). Two multiple reaction-monitoring (MRM) transitions for each analyte were observed: 288.1/96.1 and 288.1/191.2 for CP and 282.1/167.2 and 282.1/116.3 for DPP. The retention time of the drug was 7.29 min. The analytical technique was successfully validated for linearity (1-100 ng/ml), intra-day precision, inter-day precision, and accuracy. The limit of detection (LOD) and limit of quantification (LOQ) were 0.86 and 0.98 ng/ml, respectively. The proposed technique was applied in the analysis of the cyproheptadine content from seven different syrup formulations

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The uncertainty of reference standards - A guide to understanding factors implicating uncertainty, uncertainty calculations, and vendor certifications

Certified solution standards are routinely employed in forensic toxicological, clinical/diagnostic, and environmental testing. These standards are usually purchased as ampouled solutions with a certified concentration. However, vendors present concentration and uncertainty differently on their Certificates of Analysis. Understanding the factors that affect uncertainty and which parameters have been taken into consideration in the vendor's assignment of uncertainty are vital to understanding the accuracy of the standard and the impact on testing results. An understanding these variables is also required by laboratories seeking to comply with ISO/IEC 17025 requirements and for those preparing reference solutions from neat materials at the bench. The effect of uncertainty associated with the neat material purity (including residual water, residual solvent, and inorganic content), mass measurement (weighing techniques), and solvent addition (solution density) on the overall uncertainty of the certified concentration is described along with uncertainty calculations

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Identification of gentamicin impurities by liquid chromatography tandem mass spectrometry

Identification of impurities in gentamicin was achieved by development of an HPLC/MS/MS technique. HPLC was performed on a Synergy Hydro-RP column using 50 mM trifluoroacetic acid (TFA), pH 2 adjusted with ammonium solution and methanol as mobile phase. Impurities in gentamicin were separated from main gentamicin components. Atmospheric pressure chemical ionization (APCI) was employed and product mass spectra of protonated molecules were determined. Seventeen impurities were detected in gentamicin. Gentamicins (C2b, B, B1, G-418), sisomicin, garamine and gentamines (C1, C1a, C2, C2a) were used as references for interpretation of spectra and identification of impurities. All MS/MS spectra were interpreted and fragmentation transitions for gentamicins and in general for aminoglycoside antibiotics (AG) were proposed. All impurities were identified. In addition, more than one isomer were proposed for three impurities

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Use of single particle aerosol mass spectrometry for the automated nondestructive identification of drugs in multicomponent samples

Single particle aerosol mass spectrometry (SPAMS) has been employed to identify the active drug ingredients in samples of multicomponent over-the-counter (OTC) drug tablets with minimal damage to the tablets. OTC drug tablets of various formulations were analyzed including single active ingredient tablets and multi-ingredient tablets. By employing an in-house developed sampling apparatus, micrometer-sized particles were displaced from tablets and introduced to the SPAMS, where dual-polarity mass spectra were derived for individual particles. Active ingredients were identified on the basis of the parent ions and fragment ions formed from each sample. Alarm files were produced for each active ingredient therby facilitating successful automated identification of each compound in a mixture. The alarm algorithm produced for SPAMS correctly identified all drug substances in all single-ingredient and multi-ingredient tablets studied. Additional work demonstrated the ability of this method to identify the active ingredient in a single tablet analyzed in the presence of several other nonidentical tablets. *In situ* analysis was also made by sampling directly from a drug sample in its original bottle. The technique was able to identify a single tablet embedded in 11 identical tablets of different composition. Overall, this work demonstrates the ability of the SPAMS technique to detect a target drug compound both in complex tablets (multidrug ingredient tablets) and complex sampling environments (multitablet sampling sources). The method is virtually nondestructive, leaving the characteristic shape, color, and imprint of a tablet unchanged for further analysis. The technique may find application in both forensic and pharmaceutical analysis

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Application of ion-trap mass spectrometry for identification and structural determination of an unknown impurity in simvastatin

Simvastatin, a statin, is a hypolipidemic drug. During its production, the two main impurities in the fermentation broth are anhydro-simvastatin and simvastatin dimer. An unknown impurity with *m/z* 451 for $[(M + H)^+]$ was detected in the analysis of final simvastatin drug sample. The unknown impurity was detected and identified with the use of reverse phase high performance liquid chromatography (HPLC)-mass spectrometry (MS) and MS/MS spectra. Separation was achieved on ACE-5 C18 (150 x 4.6 mm, 3 µm column) at the flow rate of 1.2 ml/min applying gradient elution of mobile phase A consisting of Milli-Q water of pH 3.0 with formic acid and B consisting of acetonitrile. The MS/MS spectrum of the unknown impurity was obtained using HPLC-MS equipped with positive electrospray ionization (ESI). It has been identified as 7-[7-(2,2-dimethyl-butyryloxy)-2,6-dimethyl-1,2,6,7,8,8a-hexahydro-naphthalen -1 -yl]-3-hydroxy-5-hydroxymethyl-heptanoic acid.

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A high-throughput liquid chromatography tandem mass spectrometry method for the comparative determination of fluticasone propionate by reversed-phase liquid chromatography and capillary electrophoresis methods in pharmaceutical nasal sprays

The analysis of fluticasone propionate (FP) in pharmaceutical formulations with a simple, specific, rapid and sensitive liquid chromatography-tandem mass spectrometry (LC-MS/MS) technique has been developed and validated using deflazacort as internal standard (IS). LC-MS/MS was conducted out on a C8 column (50 mm) with a mobile phase consisted of methanol : water (95 : 5, v/v) 100 mM formic acid-50 mM ammonium acetate (90 : 5 : 5, v/v/v). Mass spectrometry method was achieved by employing positive atmospheric pressure chemical ionization operating in multiple reaction monitoring mode. Chromatographic separation was produced within 1.5 min and it was linear in the concentration range of 10-1000 ng/ml. In addition, method validation demonstrated acceptable results for the specificity, accuracy, precision and robustness. The proposed technique was successfully employed in the quantitative analysis of FP nasal sprays and the results were compared to validated liquid chromatography and capillary electrophoresis methods with photodiode array detectors showing non-significant difference ($P > 0.05$)

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Real-time trace detection of security-relevant compounds in complex sample matrices by thermal desorption-single photon ionization-ion trap mass spectrometry (TD-SPI-ITMS) spectrometry (TD-SPI-ITMS)

The coupling of thermal desorption-single photon ionization-ion trap mass spectrometry (TD-SPI-ITMS) for the detection of security-relevant substances at low concentrations in complex matrices was successfully examined. The main benefit of obtaining solid samples with a wipe pad followed by thermal desorption is the low detection limit by enhanced vapor pressure. Single photon ionization is a soft ionization technique which reduces the target ion fragmentation and shields bulk components with high ionization energies (IE) like nitrogen yielding to clearly arranged mass spectra with significant high mass peaks. To produce low false-positive and false-negative rates, particularly necessary for security-relevant substances, the ion trap mass spectrometer allows identification of signals with MS/MS studies. In respect of this concept, the soft ionization technique accords well with the MS/MS studies because peaks with high masses are generated yielding significant MS/MS fragments. For the ionization, photon energies between about 8 eV (155 nm) and 12 eV (103 nm) were generated with electron-beam-pumped rare gas excimer lamps (EBEL). Dependent upon the rare gas employed, light with different photon energy is generated, adapted to the substances of interest. Therefore, even most narcotics, having relatively low IEs, can be ionized with 8.4 eV photons without massive fragmentation. For most explosives, photons with higher energy must be employed because their IEs are higher. In this work, a mobile setup with a commercial ion trap mass spectrometer has been developed and tested. In addition, a first real-scenario measurement campaign was accomplished successfully proving the field-suitability of the system

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Rapid and simple methods for determination of medazepam in pharmaceutical preparations using GC-FID and GC-MS

Two rapid, sensitive, and specific methods employing gas chromatography (GC) with flame ionization (FID) and mass spectrometric (MS) detection have been employed for the determination of medazepam with internal standard (diazepam) in pharmaceutical preparations. Linearity was established over the concentration range of 0.25-5 µg/ml for GC-FID and 50-1000 ng/ml for GC-MS method. Intra- and inter-day relative standard deviation was less than 2.94 and 4.95%, respectively. The two techniques developed in this work are accurate, sensitive, and precise and maybe directly and easily applied to Tranko buskas as pharmaceutical preparation