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ECOLOGY

Tolerance and sequestration of macroalgal chemical defenses by an Antarctic amphipod: a 'cheater' among mutualists

Margaret O. Amsler, Charles D. Amsler, Jacqueline L. von Salm, Craig F. Aumack, James B. McClintock, Ryan M. Young, Bill J. Baker
Marine Ecology Progress Series, Volume 490, Pages 79-90, 2013

Shallow-water communities along the western Antarctic Peninsula support forests of large, mostly chemically defended macroalgae and dense assemblages of macroalgal-associated amphipods, which are thought to exist together in a community-wide mutualism. The amphipods benefit the chemically defended macrophytes by consuming epiphytic algae and in turn benefit from an associational refuge from fish predation. In the present study, we document an exception to this pattern. The amphipod *Paradexamine fissicauda* is able to consume *Plocamium cartilagineum* and *Picconia plumosa*, 2 species of sympatric, chemically defended red macroalgae. In previous studies, *Plocamium cartilagineum* was one of the most strongly deterrent algae in the community to multiple consumers, and was found here to be unpalatable to 5 other amphipod species which utilize it as a host in nature. *Paradexamine fissicauda* maintained on a diet of *Plocamium cartilagineum* for 2 mo were much less likely to be eaten by fish than *Paradexamine fissicauda* maintained on a red alga which does not elaborate chemical defenses, or than a different but morphologically similar sympatric amphipod species. Halogenated secondary metabolites produced by *Plocamium cartilagineum* were identified from tissues of the *Paradexamine fissicauda* that had eaten it but not those which had eaten the undefended red alga. This indicates that *P. fissicauda* is sequestering the potent chemical defenses of *Plocamium cartilagineum* for its own use.

ENERGY, CHEMICALS & MATERIALS

Deoxygenation of decanoic acid and its main intermediates over unpromoted and promoted sulfided catalysts

Soizic Brillouet, Elena Baltag, Sylvette Brunet, Frédéric Richard
Applied Catalysis B: Environmental, Volumes 148-149, 27 April 2014, Pages 201-211

The transformation of decanoic acid, used as a model oxygenated compound, was first studied over Mo/Al₂O₃ at 340 °C under 4 MPa of total pressure (H₂ pressure equal to 2.72 MPa) in a fixed-bed reactor. The deoxygenation of decanoic acid is considered to proceed through two main routes: (i) the HDO pathway yielding decenes and decane as ultimate hydrocarbons, oxygen being removed as water; (ii) the DEC pathway involving a decarbonylation reaction and mainly leading to nonene isomers, oxygen being discarded as water and carbon monoxide. Other products such as oxygenates (mainly decanal and 1-decanol) and sulfur-containing products (mainly 1-decanethiol) appeared as intermediates of the HDO way. A significant inhibiting effect of carboxylic acid on the deoxygenation of decanal was highlighted. A general reaction scheme of deoxygenation of decanoic acid over sulfided catalysts was established. Considering a sulfur vacancy as an active site, deoxygenation reaction mechanisms were proposed involving a cationic species as a common intermediate between the HDO and the DEC pathways. The effect of Co and Ni on the deoxygenation rate of decanoic acid was measured by using both CoMo/Al₂O₃ and NiMo/Al₂O₃. The DEC route was strongly promoted by Co and Ni, whereas an inhibiting effect of Co and Ni was observed on the HDO route. It was assumed that the promoter effect on the DEC route may result from an increase of the basicity of sulfur anions neighboring of Co or Ni present in the sulfided promoted phase.

Identification of unknown organosulfur compounds with GC/QTOF-MS in the water-soluble portion from mildly oxidized Jincheng No. 15 anthracite

Yu-Gao Wang, Xian-Yong Wei, Hong-Lei Yan, Zhan-Ku Li, Sheng-Kang Wang, Fang-Jing Liu, Peng Li, Xing Fan, Zhi-Min Zong
Fuel, Volume 135, 1 November 2014, Pages 188-190

The products in the water-soluble portion from mild oxidation of Jincheng No. 15 anthracite in aqueous hydrogen peroxide were analyzed with a gas chromatograph/quadrupole time-of-flight-mass spectrometer (GC/QTOF-MS) along with theoretical calculation for the first time. A series of heteroatom(s)-containing components were identified by comparing their mass spectra with NIST11 library data. Moreover, two organosulfur compounds without matched library mass spectra were inferred according to their tandem mass spectra and the formation of their fragmental ions was convincingly explained by energy calculation based on density functional theory. The investigation suggests that GC/QTOF-MS analysis combined with theoretical calculation would be a powerful tool for identifying unknown compounds in complicated mixtures from coals or their derivatives.

Synthetic Phenolic Antioxidants in Middle Distillate Fuels Analyzed by Gas Chromatography with Triple Quadrupole and Quadrupole Time-of-Flight Mass Spectrometry

Renée L. Webster, Paul M. Rawson, David J. Evans, and Philip J. Marriott
Energy Fuels, 2014, 28 (2), Pages 1097-1102

Methods for the selective determination and quantification of 10 synthetic phenolic antioxidants (SPA) in jet and diesel fuels have been developed. The analytical procedure involves no sample preparation and uses direct injection of the diluted parent fuel into the GC column. Gas chromatography with both triple quadrupole and quadrupole time-of-flight mass spectrometry was used to quantify synthetic phenolic antioxidants in the range of 0.1-20 mg/L. Precision was in the range of 3-9%. The method is demonstrated to be rugged and robust and, since no extraction is required, does not require estimation of extraction efficiencies. It is generally suited to volatile SPA compounds included in jet and diesel fuel specifications. The method is appropriate for the estimation of SPA in fresh and in-service middle distillate fuels stored on military bases and tankers or in use on aviation or naval platforms.

Formation of chlorobenzenes by oxidative thermal decomposition of 1, 3-dichloropropene

Nwakamma Ahubelem, Kalpit Shah, Behdad Moghtaderi, Mohammednoor Altarawneh, Bogdan Z. Dlugogorski, Alister J. Page
Combustion and Flame, Volume 162, Issue 6, June 2015, Pages 2414-2421

We combine combustion experiments and density functional theory (DFT) calculations to investigate the formation of chlorobenzenes from oxidative thermal decomposition of 1,3-dichloropropene. Mono- to hexa-chlorobenzenes are observed between 800 and 1150 K, and the extent of chlorination was proportional to the combustion temperature. Higher chlorinated congeners of chlorobenzene (tetra-, penta-, hexa-chlorobenzene) are only observed in trace amounts between 950 and 1050 K. DFT calculations indicate that cyclization of chlorinated hexatrienes proceeds via open-shell radical pathways. These species represent key components in the formation mechanism of chlorinated polyaromatic hydrocarbons. Results presented herein should provide better understanding of the evolution of soot from combustion/pyrolysis of short chlorinated alkenes.

Enrichment and identification of cyclized hopanoids from Shengli lignite

Xing-Shun Cong, Zhi-Min Zong, Min Li, Li Gao, Zhe-Hao Wei, Yan Li, Xing Fan, Yin Zhou, Xian-Yong Wei
Fuel Processing Technology, Volume 134, June 2015, Pages 399-403

Fourteen cyclized hopanoids, including hydrobenzohopanes, benzohopanes, and rearranged benzohopanes, were enriched from Shengli lignite via fractional extraction and preparative medium-pressure liquid chromatography. Their structures were tentatively identified by gas chromatography/mass spectrometry. Rearranged benzohopanes, which were unreported before, are probably produced from the corresponding benzohopanes via methyl rearrangement reaction.

Mechanism of low-molecular alkenes interaction with sulfur-containing spatially hindered phenols under conditions of thermal modification of polymer materials

A. P. Krysin, L. M. Pokrovskii, A. A. Nefedov, I. K. Shundrina, B. A. Selivanov
Russian Journal of General Chemistry, March 2015, Volume 85, Issue 3, Pages 659-666

Transformations in the course of high-temperature modification of polyolefins under action of sulfur-containing modifiers have been studied using hexene-1 and hexane as model compounds. Composition of products of thermolysis of bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propyl] disulfide and bis[3-(3,5-di-tert-butyl-4-hydroxyphenyl)propyl] sulfide at 200-270 °C has been elucidated by means of thermogravimetry and gas chromatography-mass spectrometry. Mechanism of olefins modification with sulfides and disulfides involving the formation of biradical intermediates is discussed.

Poly (oxypropylene)-amidoamine modified bentonite as potential shale inhibitor in water-based drilling fluids

Hanyi Zhong, Zhengsong Qiu, Weian Huang, Jie Cao
Applied Clay Science, Volumes 67-68, October 2012, Pages 36-43

A series of poly(oxypropylene)-amidoamine (POAA) compounds as potential shale inhibitors were synthesized by condensation of low molar mass polyoxypropylene diamine POP230 with diacids. The synthesized polymer was characterized by Fourier transform infrared spectroscopy (FT-IR) and mass spectrum (MS) analysis.

Chemical analysis of bleach and hydroxide-based solutions after decontamination of the chemical warfare agent O-ethyl S-2-diisopropylaminoethyl methylphosphonothiolate (VX)

F. B. Hopkins, M. R. Gravett, A. J. Self, M. Wang, C. Hoe-Chee, N. Lee Hoi Sim, J. T. A. Jones, C. M. Timperley, J. R. Riches
Analytical and Bioanalytical Chemistry, August 2014, Volume 406, Issue 21, Pages 5111-5119

This paper describes the application of modern analytical techniques to the analysis of decontamination solutions following decontamination of the chemical warfare agent O-ethyl S-2-diisopropylaminoethyl methylphosphonothiolate (VX). It employed Agilent GC/SQ, GC/QTOF, LC/QTOF.

ENVIRONMENTAL

Advanced Techniques in Gas Chromatography-Mass Spectrometry (GC-MS-MS and GC-TOF-MS) for Environmental Chemistry

Imma Ferrer, E. Thurman
October 2013, ELSEVIER, ISBN: 978-0-444-62623-3

GC/MS in environmental chemistry

Analysis of Trace-Level Volatile Compounds in Fresh Turf Crop (*Lolium perenne L.*) by Gas Chromatography Quadrupole Time-of-Flight Mass Spectrometry

Saisai Hong, Wenyu Kang, Yue Su, Yinlong Guo
Chinese Journal of Chemistry, Volume 31, Issue 10, October, 2013, Pages 1329-1335

In the traditional research of volatile compounds, some trace-level compounds could not be identified by gas chromatography-mass spectrometry. Target and post-targeted methods were applied in the investigation of trace-level volatile compounds in fresh turf crop (*Lolium perenne L.*) based on gas chromatography in combination with hybrid quadrupole time-of-flight mass spectrometry. According to literatures published, a target analysis was performed by using retention index, accurate masses of characteristic ions and second-stage mass spectra (MS_2 spectra). And a series of experiments showed that low electron impact energy was beneficial to the improvement of the abundances of low abundance molecular ion peak. Enhancing the abundances of low abundance molecular ion peak was beneficial to qualitative analysis. Totally, 60 volatile compounds were identified, the great majority compounds of which were benzeneacetaldehyde (14.8%), 2,5-dimethyl-pyrazine (9.6%), and hexanal (9.3%). Identification was complied by mass spectral search, retention index and accurate masses of characteristic ions.

Gas chromatography quadrupole time-of-flight mass spectrometry determination of benzotriazole ultraviolet stabilizers in sludge samples

J. Casado, I. Rodríguez, I. Carpinteiro, M. Ramil, R. Cela
Journal of Chromatography A, Volume 1293, 7 June 2013, Pages 126-132

In this research, a simplified procedure for the selective determination of nine benzotriazole UV stabilizers (BUVSs) in sludge from urban sewage treatment plants is presented. Analytes were extracted from the sample using the matrix solid-phase dispersion (MSPD) technique and further determined by gas chromatography (GC) with quadrupole time-of-flight mass spectrometry (QTOF-MS). Highly selective chromatographic records were attained considering a mass window of 0.005 Da, centred in the quantification product ion corresponding to each compound. Moreover, the availability of accurate ion product scan MS/MS spectra permitted to confirm the identities of peaks observed in extracted ion MS/MS chromatograms. As a result, a straightforward sample preparation procedure combining extraction and clean-up in the same step, and consuming just 10 mL of ethyl acetate, sufficed to deal with complex sludge samples. The developed method attained limits of quantification (LOQs) between 2 ng g^{-1} and 10 ng g^{-1} , referred to freeze-dried sludge, and recoveries from 70% to 111%, with standard deviations from 2% to 13%. Analysis of sludge samples and certified reference materials confirmed the existence of residues of eight out of nine BUVSs. UV-326, UV-328 and UV-234 displayed the highest occurrence frequencies and individual concentrations above 100 ng g^{-1} in several samples.

Profiling of soil fatty acids using comprehensive two-dimensional gas chromatography with mass spectrometry detection

Annie Xu Zeng, Sung-Tong Chin, Antonio Patti, Philip J. Marriott
Journal of Chromatography A, Volume 1317, 22 November 2013, Pages 239-245

Soil bacterial fatty acids esters were studied by using GC \times GC methods. A series of different column sets showed a non-polar \times polar set to be most suitable. Forest soil comprised saturated, unsaturated, branched, hydroxyl and oxygenated FAME. Accurate mass Q-TOF/MS analysis with GC \times GC permitted interpretation of all FAME.

Reliable screening of pesticide residues in maternal and umbilical cord sera by gas chromatography-quadrupole time of flight mass spectrometry

RuoJing Fan, Fang Zhang, HaoYang Wang, Li Zhang, Jing Zhang, Ying Zhang, ChongTian Yu, YinLong Guo
Science China Chemistry, May 2014, Volume 57, Issue 5, Pages 669-677

The widespread use of pesticides induces heavy adverse effects on human health, especially for the pregnant women and the newborns. In this study, a screening method has been developed for the determination of multi-pesticides in maternal and umbilical cord sera. All pesticides in sera were collected using solid phase extraction (SPE), and analyzed by gas chromatography-quadrupole time of flight mass spectrometry (GC-QTOF MS). To set up the quality criteria, a database of 50 pesticides was created and the accurate masses of 3 up to 5 representative ions with their intensity ratios were included for each pesticide. In addition, a novel "identification points" (IPs) system relying on the accurate MS_1 and MS_2 spectra was used to interpret the data for each suspected pesticide. The methodology was then applied to a pair of maternal and umbilical cord sera. A total of six pesticide residues were screened out successfully. In conclusion, GC-QTOF MS combined with an accurate mass database seemed to be one of the most efficient tools for systematic pesticide analysis.

Determination of benzotriazoles in water samples by concurrent derivatization-dispersive liquid-liquid microextraction followed by gas chromatography-mass spectrometry

J. Casado, R. Nescatelli, I. Rodriguez, M. Ramil, F. Marini, R. Cela
Journal of Chromatography A, Volume 1336, 4 April 2014, Pages 1-9

Concurrent acetylation-dispersive liquid-liquid microextraction (DLLME) combined with gas chromatography-mass spectrometry (GC/MS) has been proposed for the sensitive determination of five polar benzotriazolic compounds (1H-benzotriazole, BTri; 4 and 5-methyl-1H-benzotriazole, 4-TTri and 5-TTri; 5,6-dimethyl-1H-benzotriazole, XTri; and 5-chloro-1H-benzotriazole, 5-ClBTri) in water samples. Under optimized conditions, samples (10 mL volume) were combined with 1 mL of Na_2HPO_4 (8%, w/v) and mixed with the ternary acetylation-microextraction mixture, consisting of 100 μ L of acetic anhydride, 1.5 mL of acetonitrile and 60 μ L of toluene. Thus, analytes were simultaneously acetylated and transferred to the dispersed droplets of toluene. The proposed methodology achieved limits of quantification (LOQs) between 0.007 ng mL⁻¹ and 0.080 ng mL⁻¹, enrichment factors between 93 and 172 times, good reproducibility, with relative standard deviations lower than 10%, and linearity with determination coefficients above 0.9991 for all compounds in the range between LOQs and 20 ng mL⁻¹. Pseudo-external calibration, with fortified ultrapure water samples submitted to the acetylation-DLLME procedure, proved to be adequate for the accurate quantification of complex aqueous matrices such as surface or wastewater, providing recoveries comprised between 86% and 112%. BTri, 4-TTri and 5-TTri were measured in environmental samples up to a concentration of 1.9 ng mL⁻¹ for BTri in raw wastewater.

Multidimensional gas chromatography in combination with accurate mass, tandem mass spectrometry, and element-specific detection for identification of sulfur compounds in tobacco smoke

Nobuo Ochiai, Kazuhisa Mitsui, Kikuo Sasamoto, Yuta Yoshimura, Frank David, Pat Sandra
Journal of Chromatography A, Volume 1358, 5 September 2014, Pages 240-251

A method is developed for identification of sulfur compounds in tobacco smoke extract. The method is based on large volume injection (LVI) of 10 μ L of tobacco smoke extract followed by selectable one-dimensional (1D) or two-dimensional (2D) gas chromatography (GC) coupled to a hybrid quadrupole time-of-flight mass spectrometer (Q-TOF MS) using electron ionization (EI) and positive chemical ionization (PCI), with parallel sulfur chemiluminescence detection (SCD). In order to identify each individual sulfur compound, sequential heart-cuts of 28 sulfur fractions from 1D GC to 2D GC were performed with the three MS detection modes (SCD/EI-TOF-MS, SCD/PCI-TOF-MS, and SCD/PCI-Q-TOF-MS). Thirty sulfur compounds were positively identified by MS library search, linear retention indices (LRI), molecular mass determination using PCI accurate mass spectra, formula calculation using EI and PCI accurate mass spectra, and structure elucidation using collision activated dissociation (CAD) of the protonated molecule. Additionally, 11 molecular formulas were obtained for unknown sulfur compounds. The determined values of the identified and unknown sulfur compounds were in the range of 10-740 ng mg total particulate matter (TPM) (RSD: 1.2–12%, n = 3).

FOOD

Rapid simultaneous screening and identification of multiple pesticide residues in vegetables

Fang Zhang, Chongtian Yu, Wenwen Wang, Ruoqing Fan, Zhixu Zhang, Yinlong Guo
Volume 757, 13 December 2012, Pages 39-47

A method for the rapid simultaneous screening and identification of multiple pesticide residues in vegetables was established using a novel database and gas chromatography in combination with hybrid quadrupole time-of-flight mass spectrometry (GC/QTOF MS). A total of 187 pesticides with different chemical species were measured by GC/QTOF MS to create the database, which collected the retention time and exact masses of ions from the first-stage mass spectrum (MS1 spectrum) and second-stage mass spectrum (MS2 spectrum) for each pesticide.

Fast comprehensive two-dimensional gas chromatography method for fatty acid methyl ester separation and quantification using dual ionic liquid columns

Asia Nocheen, Blagoj Mitrevski, Asghari Bano, Philip J. Marriott
Journal of Chromatography A, Volume 1312, 18 October 2013, Pages 118-123

Safflower oil is a complex mixture of C18 saturated and unsaturated fatty acids among other fatty acids, and achieving separation between these similar structure components using one dimensional gas chromatography (GC) may be difficult. This investigation aims to obtain improved separation of fatty acid methyl esters in safflower oil, and their quantification using comprehensive two-dimensional GC (GC×GC). Here, GC×GC separation is accomplished by the coupling of two ionic liquid (IL) column phases: the combination of SLB-IL111 with IL59 column phases was finally selected since it provided excellent separation of a FAME standard mixture, as well as fatty acids in safflower and linseed oil, compared to other tested column sets. Safflower oil FAME were well separated in a short run of 16 minutes. FAME validation was demonstrated by method reproducibility, linearity over a range up to 500 mgL⁻¹, and limits of detection which ranged from 1.9 mgL⁻¹ to 5.2 mgL⁻¹ at a split ratio of 20:1. Quantification was carried out using two dilution levels of 200-fold for major components and 20-fold for trace components. The fatty acids C15:0 and C17:0 were not reported previously in safflower oil. The SLB-IL111/IL59 column set proved to be an effective and novel configuration for separation and quantification of vegetable and animal oil fatty acids.

Analysis of Volatile Compounds from *Siraitia grosvenorii* by Headspace Solid-Phase Microextraction and Gas Chromatography-Quadrupole Time-of-Flight Mass Spectrometry

Yi Xia, Fang Zhang, Weiyun Wang, Yinlong Guo
Journal of Chromatographic Science, (2014) doi: 10.1093/chromsci/bmu012

Headspace solid-phase microextraction (HS-SPME) coupled with gas chromatography-quadrupole time-of-flight mass spectrometry (GC/QTOF MS) has been used in the present study to isolate and identify volatile components from *Siraitia grosvenorii*, a herbaceous perennial vine used as a natural sweetener and medicine. Compared with the static HS extraction and the different SPME fiber coatings, HS-SPME with divinylbenzene/carboxen/polydimethylsiloxane fiber was preferred to extract the target analytes including aldehyde, alcohol, acid, ester and other compounds. In the identification, a multi-dimensional qualitative analysis approach containing library searching, retention index comparison, accurate mass measurement, the second-stage mass spectrum (MS² spectrum) and area normalization was utilized. Finally, a total of 46 compounds were identified from *S. grosvenorii*. Among them, *n*-hexadecanoic acid, 5-hydroxymethylfurfural, 2,3-dihydro-3,5-dihydroxy-6-methyl-4H-pyran-4-one, (Z, Z)-9,12-octadecadienoic acid and (*E, E*)-2,4-nonadienal were the main volatile components. The results showed that HS-SPME coupled with GC-QTOF MS is efficient for the extraction of polar volatiles from *S. grosvenorii* and accurate for the identification of volatile compounds in the complicated matrix.

Assessment of dispersive liquid-liquid microextraction conditions for gas chromatography time-of-flight mass spectrometry identification of organic compounds in honey

M Moniruzzaman, I Rodríguez, T. Rodríguez-Cabo, R. Cela, S.A. Sulaiman, S.H. Gan
Journal of Chromatography A, Volume 1368, 14 November 2014, Pages 26-36

The suitability of the dispersive liquid-liquid microextraction (DLLME) technique for gas chromatography (GC) characterization of minor organic compounds in honey samples is evaluated. Under optimized conditions, samples were pre-treated by liquid-liquid extraction with acetonitrile followed by DLLME using carbon tetrachloride (CCl₄, 0.075 mL) as extractant. The yielded settled phase was analyzed by GC using high resolution time-of-flight (TOF) mass spectrometry (MS). The whole sample preparation process is completed in approximately 10 min, with a total consumption of organic solvents below 4 mL, relative standard deviations lower than 12% and with more than 70 organic compounds, displaying linear retention index in the range from 990 to 2900, identified in the obtained extracts. In comparison with HS SPME extraction, higher peak intensities were attained for most volatile and semi-volatile compounds amenable to both extraction techniques. Furthermore, other species such as highly polar and water soluble benzene acids, long chain fatty acids, esters and flavonoids, which are difficult to concentrate by HS SPME, could be identified in DLLME extracts. Some of the compounds identified in DLLME extracts have been proposed as useful for samples classification and/or they are recognized as markers of honeys from certain geographic areas.

Assessment of gas chromatography time-of-flight accurate mass spectrometry for identification of volatile and semi-volatile compounds in honey

M. Moniruzzaman, I. Rodríguez, M. Ramil, R. Cela, S.A. Sulaiman, S.H. Gan
Talanta, Volume 129, 1 November 2014, Pages 505-515

The performance of gas chromatography (GC) combined with a hybrid quadrupole time-of-flight (QTOF) mass spectrometry (MS) system for the determination of volatile and semi-volatile compounds in honey samples is evaluated. After headspace (HS) solid-phase microextraction (SPME) of samples, the accurate mass capabilities of the above system were evaluated for compounds identification. Accurate scan electron impact (EI) MS spectra allowed discriminating compounds displaying the same nominal masses, but having different empirical formulae. Moreover, the use of a mass window with a width of 0.005 Da provided highly specific chromatograms for selected ions, avoiding the contribution of interferences to their peak areas. Additional information derived from positive chemical ionization (PCI) MS spectra and ion product scan MS/MS spectra permitted confirming the identity of novel compounds. The above possibilities are illustrated with examples of honey aroma compounds, belonging to different chemical classes and containing different elements in their molecules. Examples of compounds whose structures could not be described are also provided. Overall, 84 compounds, from a total of 89 species, could be identified in 19 honey samples from 3 different geographic areas in the world. The suitability of responses measured for selected ions, corresponding to above species, for authentication purposes is assessed through principal components analysis.

Enantiomeric Separation in Comprehensive Two-dimensional Gas Chromatography with Accurate Mass Analysis

Sung-Tong Chin, Yada Nolvachai, Philip J. Marriott
Chirality in Australia, Volume 26, Issue 11, Pages 747-753, November 2014

Chiral comprehensive two-dimensional gas chromatography (eGC×GC) coupled to quadrupole-accurate mass time-of-flight mass spectrometry (Q-TOF MS) was evaluated for its capability to report the chiral composition of several monoterpenes, namely, α -pinene, β -pinene, and limonene in cardamom oil. Enantiomers in a standard mixture were fully resolved by direct enantiomeric-GC analysis with a 2,3-di-*O*-methyl-6-*t*-butylsilyl derivatized β -cyclodextrin phase; however, the (+)-(*R*)-limonene enantiomer in cardamom oil was overlapped with other background components including cymene and cineole. Verification of (+)-(*R*)-limonene components based on characteristic ions at m/z 136, 121, and 107 acquired by chiral single-dimension GC/Q-TOF MS in the alternate MS/MSMS mode of operation was unsuccessful due to similar parent/daughter ions generated by interfering or co-eluting cymene and cineole. Column phases SUPELCOWAX, SLB-IL111, HP-88, and SLB-IL59, were incorporated as the second dimension column (²D) in chiral GC×GC analysis; the SLB-IL59 offered the best resolution for the tested monoterpene enantiomers from the matrix background. Enantiomeric ratios for α -pinene, β -pinene, and limonene were determined to be 1.325, 2.703, and 1.040, respectively, in the cardamom oil sample based on relative peak area data.

Suspected-target pesticide screening using gas chromatography quadrupole time-of-flight mass spectrometry with high resolution deconvolution and retention index/mass spectrum library

Fang Zhang, Haoyang Wang, Li Zhang, Jing Zhang, Ruoqing Fan, Chongtian Yu, Wenwen Wang, Yinlong Guo
Talanta, Volume 128, 1 October 2014, Pages 156-163

A strategy for suspected-target screening of pesticide residues in complicated matrices was exploited using gas chromatography in combination with hybrid quadrupole time-of-flight mass spectrometry (GC/QTOF MS). The screening workflow followed three key steps of, initial detection, preliminary identification, and final confirmation. The initial detection of components in a matrix was done by a high resolution mass spectrum deconvolution; the preliminary identification of suspected pesticides was based on a special retention index/mass spectrum (RI/MS) library that contained both the first-stage mass spectra (MS¹ spectra) and retention indices; and the final confirmation was accomplished by accurate mass measurements of representative ions with their response ratios from the MS¹ spectra or representative product ions from the second-stage mass spectra (MS² spectra). To evaluate the applicability of the workflow in real samples, three matrices of apple, spinach, and scallion, each spiked with 165 test pesticides in a set of concentrations, were selected as the models. The results showed that the use of high-resolution TOF enabled effective extractions of spectra from noisy chromatograms, which was based on a narrow mass window (5 mDa) and suspected-target compounds identified by the similarity match of deconvoluted full mass spectra and filtering of linear RIs. On average, over 74% of pesticides at 50 ng/mL could be identified using deconvolution and the RI/MS library. Over 80% of pesticides at 5 ng/mL or lower concentrations could be confirmed in each matrix using at least two representative ions with their response ratios from the MS¹ spectra. In addition, the application of product ion spectra was capable of confirming suspected pesticides with specificity for some pesticides in complicated matrices. In conclusion, GC/QTOF MS combined with the RI/MS library seems to be one of the most efficient tools for the analysis of suspected-target pesticide residues in complicated matrices.

Negative chemical ionization gas chromatography coupled to hybrid quadrupole time-of-flight mass spectrometry and automated accurate mass data processing for determination of pesticides in fruit and vegetables

Natalia Besil, Samanta Uclés, Milagros Mezcúa, Horacio Heinzen, Amadeo R. Fernández-Alba
Analytical and Bioanalytical Chemistry, August 2015, Volume 407, Issue 21, Pages 6327-6343

Gas chromatography coupled to high resolution hybrid quadrupole time-of-flight mass spectrometry (GC/Q-TOF MS), operating in negative chemical ionization (NCI) mode and combining full scan with MSMS experiments using accurate mass analysis, has been explored for the automated determination of pesticide residues in fruit and vegetables. Seventy compounds were included in this approach where 50 % of them are not approved by the EU legislation. A global 76 % of the analytes could be identified at $1 \mu\text{g kg}^{-1}$. Recovery studies were developed at three concentration levels (1, 5, and $10 \mu\text{g kg}^{-1}$). Seventy-seven percent of the detected pesticides at the lowest level yielded recoveries within the 70%-120% range, whereas 94% could be quantified at $5 \mu\text{g kg}^{-1}$, and the 100% were determined at $10 \mu\text{g kg}^{-1}$. Good repeatability, expressed as relative standard deviation (RSD <20%), was obtained for all compounds. The main drawback of the method was the limited dynamic range that was observed for some analytes that can be overcome either diluting the sample or lowering the injection volume. A home-made database was developed and applied to an automatic accurate mass data processing. Measured mass accuracies of the generated ions were mainly less than 5 ppm for at least one diagnostic ion. When only one ion was obtained in the single-stage NCI-MS, a representative product ion from MSMS experiments was used as identification criterion. A total of 30 real samples were analyzed and 67% of the samples were positive for 12 different pesticides in the range $1.0\text{-}1321.3 \mu\text{g kg}^{-1}$.

Tracing the origin of Lambrusco sparkling wines by a metabolomics approach using a HS-SPME-GC-CI-QTOF-MS method

Georg Weingart, Fulvio Mattivi
3rd MS Food Day 2013, oral presentation

Developing tools to protect consumers from food fraudulent practices is one of the main challenges nowadays. In the Ager Enologia 2009 project, about 100 samples of Lambrusco sparkling wine were collected from four different PDO areas. The volatile fraction of the wines was extracted by SPME and the new Agilent 7200 GC/Q-TOF MS instrument was used to measure the wine volatiles in CI mode. After compound extraction by mass spectra deconvolution, a PLS model was calculated with Mass Profiler Professional software, showing an overall accuracy of 97% for correct classification of the samples.

Analyses and profiling of extract and fractions of neglected weed *Mimosa pudica* Linn. traditionally used in Southeast Asia to treat diabetes

T. S. Tunna, I.S.M. Zaidul, Q.U Ahmed, K. Ghafoor, F.Y. Al-Juhaimi, M.S. Uddin, M. Hasan, S. Ferdous
South African Journal of Botany, Volume 99, July 2015, Pages 144-152

Mimosa pudica Linn. var. *hispida* Bren. (Family: Fabaceae) a neglected weed has been studied for its antidiabetic potential to propose alternative medicinal source against the global threat of diabetes mellitus. This study aimed to investigate *in vitro* inhibitory activity against diabetic enzymes (i.e. α -amylase & α -glucosidase) and three anti-oxidant assays were conducted to evaluate anti-diabetic potential of *M. pudica*'s methanol extract (MeOH_i) and its sub-fractions (Hexane_r, EtOAc_r, Acetone_r, and MeOH_r). In depth chemical profiling using GC/Q-TOF MS was also performed for the first time for this weed, to assess the probable compounds present in the extract and sub fractions that could be linked to anti-diabetic activity. Results showed the lowest (7.18 ± 0.0005) and highest (158.4 ± 0.0004) IC₅₀ for DPPH assay by MeOH_i and MeOH_r, respectively. Acetone_r and MeOH_r showed the highest TPC (60.07 ± 1.066) and TFC (16.97 ± 1.472), respectively. Three and two fold higher inhibitory activity than the standard acarbose at 1 mg/ mL was manifested by MeOH_i (95.65 ± 0.911) & EtOAc_r (51.87 ± 3.106), respectively. Hexane_r did not show inhibitory activity against both the enzymes. α -glucosidase results for the extract and sub fractions were found to be significant ($p < 0.05$). GC/Q-TOF MS analysis identified organic acids, quinolones, quinone, phenolic compounds and dodecaborane as major constituents. Presence of highly radical scavenging dodecaborane is being reported for the first time in *M. pudica*. High TPC and TFC values could be attributed to exert enzyme inhibitory action by *M. pudica* that can help in the regulation of glucose absorption and consequently glucose homeostasis. Results show that *M. pudica* can be proposed as an excellent alternative for future anti-diabetic implications.

Low-temperature headspace-trap gas chromatography with mass spectrometry for the determination of trace volatile compounds from the fruit of *Lycium barbarum L*

Fangjiao Chen, Yue Su, Fang Zhang, Yinlong Guo
Journal of Separation Science, Volume 38, Issue 4, Pages 670-676, February 2015

The total saccharides content of *Lycium barbarum L.* is very high, and a high temperature would result in saccharide decomposition and the emergence of a large amount of water. Moreover, the volatile compounds from the fruit of *L. barbarum L.* are rather low in concentration. Hence, it is difficult for a conventional headspace method to study the volatile compounds from the fruit of *L. barbarum L.* Since headspace-trap gas chromatography with mass spectrometry is an excellent method for trace analysis, a headspace-trap gas chromatography with mass spectrometry method based on low-temperature (30 °C) enrichment and multiple headspace extraction was developed to explore the volatile compounds from the fruit of *L. barbarum L.* The headspace of the sample was extracted in 17 cycles at 30 °C. Each time, the compounds extracted were concentrated in the trap (Tenax TA and Tenax GR, 1:1). Finally, all the volatile compounds were delivered into the gas chromatograph after thermal desorption. With the method described above, a total of 57 compounds were identified. The identification was completed by mass spectral search, retention index, and accurate mass measurement.

Analysis of pesticide residues in fruits and vegetables using gas chromatography–high resolution time-of-flight mass spectrometry

Noelia Belmonte Valles, Samanta Uclés, Natalia Besil, Milagros Mezcuca, Amadeo R. Fernández-Alba
Analytical Methods, Issue 5, 2015

This work reports a study on the operational parameters and development of a rapid automatic method for determining pesticide residues in fruit and vegetables using gas chromatography full spectra mass acquisition time-of-flight accurate mass spectrometry (GC/TOF-MS) in electron ionization mode (EI) based on the use of an “in-house” accurate-mass database. The database contains 110 GC amenable compounds, with their main fragment ions obtained under electron ionization at 70 eV. In addition, it includes the retention times of each pesticide working at constant flow. This customized database was linked to commercial software, which extracted all the potential compounds of interest from the GC/TOF MS raw data for each sample and matched them against the database to search for the targeted compounds in the sample. Ethyl acetate extracts spiked at 10, 20, 50 and 100 µg kg⁻¹ levels in tomato, orange and spring onion were tested using the automatic detection of the target pesticides; at 10 µg kg⁻¹, 100% of pesticides in tomato, 97.8% of pesticides in spring onion and 95.6% in orange were detected. These results were obtained under an acquisition rate of 4 GHz (12 000 FWHM) and a mass error tolerance of 5 ppm. The retention time window for detection and identification was ±0.2 min. Adequate linear responses in the 10-100 µg kg⁻¹ range were obtained for all the compounds in all the matrices, although saturation effects were observed in some cases. The developed method was applied to real samples with the qualitative and quantitative results comparable to those obtained using GC/QqQ-MS/MS.

Two-Dimensional Retention Indices Improve Component Identification in Comprehensive Two-Dimensional Gas Chromatography of Saffron

Ming Jiang, Chadin Kulsing, Yada Nolvachai, Philip J. Marriott
Analytical Chemistry, 2015, 87 (11), Pages 5753-5761

Comprehensive two-dimensional gas chromatography hyphenated with accurate mass time-of-flight mass spectrometry (GC × GC-accTOFMS) was applied for improved analytical accuracy of saffron analysis by using retention indices in the two-dimensional separation. This constitutes 3 dimensions of identification. In addition to accTOFMS specificity, and first dimension retention indices (¹/), a simple method involving direct multiple injections with stepwise isothermal temperature programming is described for construction of isovolatility curves for reference alkane series in GC × GC. This gives access to calculated second dimension retention indices (²/). Reliability of the calculated ²/ was evaluated by using a Grob test mixture, and saturated alkanes, revealing good correlation between previously reported / values from the literature, with R² correlation being 0.9997. This essentially recognizes the retention property of peaks in the GC × GC 2D space as being reducible to a retention index in each dimension, which should be a valuable tool supporting identification. The benefit of ²/ data, in supplementing ¹/ and MS library matching, was clearly demonstrated by the progressive reduction of the number of possible compound matches for peaks observed in saffron. 114 analytes were assessed according to ¹/ and ²/ values within ±20 index unit of reference values, and by MS spectrum matching above a match statistic of 750 (including mass accuracy of the molecular ion <20 ppm) and their possible identities derived. The described method provides a new avenue to utilize the full capability of the two-dimensional separation (GC × GC), in combination with MS library matching in complex sample analysis, to provide improved component identification.

FORENSIC TOXICOLOGY

Determination of $^{13}\text{C}/^{12}\text{C}$ ratios of endogenous urinary 5-amino-imidazole-4-carboxamide 1 β -D-ribofuranoside (AICAR)

Thomas Piper, Andreas Thomas, Norbert Baume, Timothy Sobolevsky, Martial Saugy, Grigory Rodchenkov, Wilhelm Schänzer, Mario Thevis
Rapid Communications in Mass Spectrometry, Volume 28, Issue 11, 15 June 2014, Pages 1194-1202

AICAR (5-aminoimidazole-4-carboxamide 1 β -D-ribofuranoside) is prohibited in sport according to rules established by the World Anti-Doping Agency. Doping control laboratories identify samples where AICAR abuse is suspected by measuring its urinary concentration and comparing the observed level with naturally occurring concentrations. As the inter-individual variance of urinary AICAR concentrations is large, this approach requires a complementary method to unambiguously prove the exogenous origin of AICAR. Therefore, a method for the determination of carbon isotope ratios (CIRs) of urinary AICAR has been developed and validated.

Measuring xenon in human plasma and blood by gas chromatography/mass spectrometry

Mario Thevis*, Thomas Piper, Hans Geyer, Andreas Thomas, Maximilian S. Schaefer, Peter Kienbaum, Wilhelm Schänzer
Rapid Communication in Mass Spectrometry, 2014 July 15, 28(13), Pages 1501-1506

Due to the favorable pharmacokinetic properties and minimal side effects of xenon, its use in modern anesthesia has been well accepted, and recent studies further demonstrated the intra- and postoperative neuro-, cardio-, and reno-protective action of the noble gas. Since the production of the hypoxia-inducible factor 1 α (HIF-1 α) and its downstream effect or erythropoietin as well as noradrenalin reuptake inhibition have been found to play key roles in this context, the question arose as to whether the use of xenon is a matter for doping controls and preventive doping research. The aim of the present study was hence to evaluate whether the (ab) use of xenon can be detected from doping control samples with the instrumentation commonly available in sports drug testing laboratories.

New Synthetic Cannabinoid – Methyl 2-{{1-(5-Fluoro-Pentyl)-3-Methyl-1H-Indol-3-Ylcarbonyl}-Amino}Butyrate– as a Designer Drug

V.A. Shevyrin, Yu. Yu. Morzherin, V.P. Melkozerov, A.S. Nevero
Chemistry of Heterocyclic Compounds, July 2014, Volume 50, Issue 4, Pages 583-586

Synthetic cannabinoids, which are being studied for the purpose of producing new pharmaceutical preparations [1, 2], have changed in recent years into a new form of designer drugs that are being actively circulated illegally throughout the world [3-11]. Whereas until recent times the chemical structures and data from pharmaceutical trials for the distributed compounds had been published in the scientific and patent literature, the distribution of compounds that have not been described in the literature and were synthesized by analogy with narcotic agents that are known and are already prohibited in a number of countries has now become the rule. Here not only compounds of already known groups of synthetic cannabinoids are being synthesized, but new groups are appearing [10, 11]. This fact bears witness to the illegal realization of significant and systematic work on the synthesis of new types of cannabinoids and their testing on the planet's population. For this reason, control over the distribution of designer drugs is an important international problem, the first stage in the solution of which is to establish the chemical structure of the newly appearing compounds.

Synthetic cannabinoids as designer drugs: New representatives of indol-3-carboxylates series and indazole-3-carboxylates as novel group of cannabinoids. Identification and analytical data

Vadim Shevyrin, Vladimir Melkozerov, Alexander Nevero, Oleg Eltsov, Alexander Baranovsky, Yuri Shafran
Forensic Science International, November 2014, Volume 244, Pages 263-275

By means of gas chromatography with mass spectrometry detection (GC/MS), including high resolution mass spectrometry (GC-HRMS) together with ultra-high performance liquid chromatography in combination with high resolution tandem mass spectrometry (UHPLC-HRMS), nuclear magnetic resonance spectroscopy (NMR) and Fourier transform infrared spectroscopy (FT-IR), structure of new synthetic cannabinoids, representatives of indol- and indazole-3-carboxylates groups, used in smoke mixtures, was determined. Obtained analytical data make reliable identification of these compounds in a course of analysis of criminal seizures possible.

Identification and analytical characteristics of synthetic cannabinoids with an indazole-3-carboxamide structure bearing a *N*-1-methoxycarbonylalkyl group

Vadim Shevyrin, Vladimir Melkozerov, Alexander Nevero, Oleg Eltsov, Yuri Shafran, Yuri Morzherin, Albert T. Labedev
Analytical and Bioanalytical Chemistry, August 2015, Volume 407, Issue 21, Pages 6301-6315

Illicit new psychoactive substances (NPS) are a serious threat to health throughout the world. Such NPS do not usually pass preliminary pharmacological trials. In 2014, we identified a series of five new synthetic cannabinoids with an indazole-3-carboxamide structure bearing an *N*-1-methoxycarbonylalkyl group. The compounds have very high cannabimimetic activity which has caused mass severe intoxication and deaths. The compounds were identified by means of gas chromatography-mass spectrometry (GC-MS), including high-resolution mass spectrometry (GC/HRMS), ultra-high-performance liquid chromatography-high-resolution tandem mass spectrometry (UHPLC-HRMS²), and ¹H and ¹³C nuclear magnetic resonance spectroscopy (NMR). The peculiarities of mass-spectral fragmentation of the compounds after electron ionization (EI) ionization and collision-induced dissociation (CID) were studied. The analytical characteristics reported for the compounds will enable their identification in a variety of materials seized from criminals.

Analytical characterization of some synthetic cannabinoids, derivatives of indole-3-carboxylic acid

Vadim Shevyrin, Vladimir Melkozerov, Alexander Nevero, Oleg Eltsov, Yuri Shafran
Forensic Science International, Volume 232, Issues 1-3, 10 October 2013, Pages 1-10

By means of gas chromatography with high resolution mass spectrometry (GC-HRMS), ultra-high performance liquid chromatography in combination with high resolution tandem mass spectrometry (UHPLC-HRMS), nuclear magnetic resonance spectroscopy (NMR) and Fourier transform infrared spectroscopy (FT-IR), structure of a series from a novel synthetic cannabinoids, derivatives of indole-3-carboxylic acid, was established. Methods for determination of the compounds in mixtures, involving chromatographic separation with mass-spectroscopic determination, were elaborated. Analytical data obtained in the paper will make reliable identification of synthetic cannabinoids of the new type during forensic examination possible.

Expanding sports drug testing assays: Mass spectrometric characterization of the selective androgen receptor modulator drug candidates RAD140 and ACP-105

Mario Thevis, Thomas Piper, Simon Beuck, Hans Geyer, Wilhelm Schänzer
Rapid Communications in Mass Spectrometry, Volume 27, Issue 11, Pages 1173-1182

The analytical characterization of substances with misuse potential is of great importance. In the present study, the SARM drug candidates RAD140 (comprising a 5-phenyloxadiazole nucleus) and ACP-105 (bearing an N-substituted tropanol pharmacophore) were studied regarding their mass spectrometric behavior under ESI-MS(/MS) and EI-MS(/MS) conditions. Reference material was synthesized according to established protocols and dissociation pathways of RAD140 and ACP-105 were elucidated with liquid chromatography/electrospray ionization quadrupole/time-of-flight or iontrap/orbitrap and gas chromatography/electron ionization quadrupole/time-of-flight high resolution/high accuracy mass spectrometry.

Hydrogen isotope ratio mass spectrometry and high-resolution/high-accuracy mass spectrometry in metabolite identification studies: Detecting target compounds for sports drug testing

Mario Thevis, Thomas Piper, Stevan Horning, Dieter Juchelka, Wilhelm Schänzer
Rapid Communications in Mass Spectrometry, Volume 27, Issue 17, pages 1904-1912, 15 September 2013

Combining IRMS with high-resolution mass spectrometry considerably facilitates and accelerates metabolite identification of deuterium-labeled compounds in urine. Of particular relevance in doping control, the principle is applicable also to other arenas of drug research, allowing the preparation and administration of e.g. radioactively labeled substances to be omitted.

3-Naphthoylindazoles and 2-naphthoylbenzimidazoles as novel chemical groups of synthetic cannabinoids: Chemical structure elucidation, analytical characteristics and identification of the first representatives in smoke mixtures

Vadim Shevyrin, Vladimir Melkozerov, Alexander Nevero, Oleg Eltsov, Yuri Morzherin, Yuri Shafran
Forensic Science International, Volume 242, September 2014, Pages 72-80

By means of gas chromatography with mass spectrometry detection (GC/MS), including high resolution mass spectrometry (GC-HRMS) together with ultra-high performance liquid chromatography in combination with high resolution tandem mass spectrometry (UHPLC-HRMS), nuclear magnetic resonance spectroscopy (NMR) and Fourier transform infrared spectroscopy (FT-IR), structure of novel synthetic cannabinoids, namely, 1-(5-fluoropentyl)-1*H*-indazol-3-yl(naphthalen-1-yl)methanone, naphthalen-1-yl(1-pentyl-1*H*-benzo[d]imidazol-2-yl)methanone and 1-(5-fluoropentyl)-1*H*-benzo[d]imidazol-2-yl(naphthalen-1-yl)methanone was established. Analytical data obtained in the paper enable reliable identification of these compounds during qualitative analysis of seizures, including smoke mixtures.

GENERAL

Mass Spectrometric Study of the Gas-Phase Difluorocarbene Expulsion of Polyfluorophenyl Cations via F-Atom Migration

Hao-Yang Wang, Ying Gao, Fang Zhang, Chong-Tian Yu, Chu Xu, Yin-Long Guo
Journal of the American Society for Mass Spectrometry, December 2013, Volume 24, Issue 12, Pages 1919-1926

An increasing number of fluorinated drugs, pesticides, and fine chemicals are now produced and applied, especially those containing polyfluorinated aromatic moieties. However, at present, the extent of literature covering the special mass spectrometric behaviors of these compounds remains limited. Herein, we report an unexpected but also general gas-phase dissociation mode of polyfluorinated aromatics in mass spectrometry: expulsion of difluorocarbene (50-Da neutral loss). Results from accurate mass measurements, tandem mass spectrometric experiments, and density functional theory (DFT) calculations support an intramolecular F-atom "ring-walk" migration mechanism for gas-phase CF_2 loss. Based on an assessment of the electron ionization-mass spectrometry (EI-MS) data of more than 40 polyfluorinated aromatic compounds from the National Institute of Standards and Technology data bank, we generalized on the substitution group effects on the difluorocarbene dissociation process of polyfluorinated aromatic compounds in EI-MS. These studies have enriched our knowledge of the special gas-phase reactivity of polyfluorinated aromatics and will provide valuable information in further analytical research of these compounds by mass spectrometry.

Comprehensive two-dimensional gas chromatography-mass spectrometry: Recent evolution and current trends

Peter Q. Tranchida, Flavio A. Franchina, Paola Dugo, Luigi Mondello
Mass Spectrometry Reviews, 30 September 2014 doi: 10.1002/mas.21443

The present contribution is focused on the evolution and current trends of comprehensive two-dimensional gas chromatography-mass spectrometry (GC \times GC-MS), with respect to a review that described this specific methodology published at the beginning of 2008 (Mondello et al., 2008). In fact, since then there has been considerable evolution in the MS field, certainly exceeding that observed in GC \times GC. In particular, the present paper will cover the combination of novel MS machines [single quadrupole (Q) and triple quadrupole, isotope ratio, low- and high-resolution time-of-flight (ToF), hybrid (Q-ToF)] to GC \times GC systems, and will position comprehensive two-dimensional gas chromatography within the wider context of separation science.

Gas-phase fluorine migration reactions in the radical cations of pentafluorosulfanylbenzene (Aryl-SF₅) and benzenesulfonyl fluoride (Aryl-SO₂F) derivatives and in the 2,5-xylylfluoroiodonium ion

Ying Gao, Hao-Yang Wang, Xiang Zhang, Jia-Shun Cheng, Fang Zhang, Yin-Long Guo
Journal of Mass Spectrometry, June 2014, Volume 49, Issue 6, Pages 481-489

The gas-phase reactions of Aryl-SF_5^+ and $\text{Aryl-SO}_2\text{F}^+$ have been studied with the electron ionization tandem mass spectrometry. Such reactions involve F-atom migration from the S-atom to the aryl group affording the product ion Aryl-F^+ by subsequent expulsion of SF_4 or SO_2 , respectively. Especially, the 4-pentafluorosulfanylphenyl cation $4\text{-SF}_5\text{C}_6\text{H}_4^+$ (m/z 203) from $4\text{-NO}_2\text{C}_6\text{H}_4\text{SF}_5^+$ by loss of $\cdot\text{NO}_2$ could occur multiple F-atom migration reactions to the product ion $\text{C}_6\text{H}_4\text{F}_3^+$ (m/z 133) by loss of SF_2 in the MS/MS process. The gas-phase reactions of 2,5-xylylfluoroiodonium ($p\text{Xyl-I}^+$, m/z 251) have also been studied using the electrospray tandem mass spectrometry, which involve a similar F-atom migration process from the I-atom to the aryl group giving the radical cation of 2-fluoro-*p*-xylene (or its isomer 4-fluoro-*m*-xylene, m/z 124) by reductive elimination of an iodine atom. All these gas-phase F-atom migration reactions from the heteroatom to the aryl group led to the aryl-F coupling product ions with a new formed $\text{C}_{\text{Aryl}}\text{-F}$ bond. Density functional theory calculations were performed to shed light on the mechanisms of these reactions.

Determination of Chlorophenoxy Acid Methyl Esters and Other Chlorinated Herbicides by GC High-resolution QTOF-MS and Soft Ionization

Viorica Lopez-Avila, Patrick Roach, Randall Urdahl
Analytical Chemistry Insights, 2015, Volume 10, Pages 1-9

Gas chromatography with quadrupole time-of-flight mass spectrometry (GC/QTOF-MS) and soft ionization generated by a rare-gas plasma is described here for the determination of various chlorophenoxy acid methyl esters and a few chlorinated herbicides. This plasma-based, wavelength-selectable ionization source, which can use Xe, Kr, Ar, Ne, or He as the plasma gas, enables ionization of GC-amenable compounds with ionization energies below 8.4, 10, 11.6, 16.5, or 22.4 eV, respectively. The advantages of soft ionization include enhanced molecular ions, reduced fragmentation, and reduced background noise as compared to electron ionization. In the study presented here for two plasma gases, we demonstrate that Kr plasma, which is softer than Ar plasma, yields molecular ions with a relative intensity >60% for 11 of the 16 test compounds. When using this "tunable" plasma to ionize the analytes, there is the possibility for selective ionization and less fragmentation, which may lead to increased sensitivity and may help structure elucidation, especially when using high-resolution mass spectrometry that generates accurate masses within a few parts per million (ppm)

mass errors. Data generated with the Ar plasma and real matrices such as a peppermint extract, a plum extract, and an orange peel extract, spiked with 16 test compounds, indicate that the test compounds can be detected at 1-10 pg/μL of extract, and compounds such as menthone, limonene, eucalyptol, pinene, caryophyllene, and other C₁₅H₂₄ isomers, which are present in the peppermint and the orange peel extracts at ppm to percent levels, do not appear to interfere with the determination of the chlorophenoxy acid methyl esters or the chlorinated herbicides, although there were matrix effects when the test compounds were spiked at 1-10 pg/μL of extract.

METABOLOMICS & PROTEOMICS

Identification of drug targets by chemogenomic and metabolomic profiling in yeast

M Wu, M Zheng, W Zhang, S Suresh, U Schlecht, WL Fitch, S Aronov, S Baumann, R Davis, R St Onge, DL Dill, G Peltz
Pharmacogenet Genomics, 22 December 2012, (12):877-86

OBJECTIVE: To advance our understanding of disease biology, the characterization of the molecular target for clinically proven or new drugs is very important. Because of its simplicity and the availability of strains with individual deletions in all of its genes, chemogenomic profiling in yeast has been used to identify drug targets. As measurement of drug-induced changes in cellular metabolites can yield considerable information about the effects of a drug, we investigated whether combining chemogenomic and metabolomic profiling in yeast could improve the characterization of drug targets. **BASIC METHODS:** We used chemogenomic and metabolomic profiling in yeast to characterize the target for five drugs acting on two biologically important pathways. A novel computational method that uses a curated metabolic network was also developed, and it was used to identify the genes that are likely to be responsible for the metabolomic differences found. **RESULTS AND CONCLUSION:** The combination of metabolomic and chemogenomic profiling, along with data analyses carried out using a novel computational method, could robustly identify the enzymes targeted by five drugs. Moreover, this novel computational method has the potential to identify genes that are causative of metabolomic differences or drug targets.

Opiate-induced changes in brain adenosine levels and narcotic drug responses

M Wu, P Sahbaie, M Zheng, R Lobato, D Boison, JD Clark, G Peltz
Neuroscience, 2013 January 3, 228: 235-42

We have very little information about the metabolomic changes that mediate neurobehavioral responses, including addiction. It was possible that opioid-induced metabolomic changes in brain could mediate some of the pharmacodynamic effects of opioids. To investigate this, opiate-induced brain metabolomic responses were profiled using a semi-targeted method in C57BL/6 and 129Sv1 mice, which exhibit extreme differences in their tendency to become opiate dependent. Escalating morphine doses (10-40 mg/kg) administered over a 4-day period selectively induced a twofold decrease ($p < 0.00005$) in adenosine abundance in the brainstem of C57BL/6 mice, which exhibited symptoms of narcotic drug dependence; but did not decrease adenosine abundance in 129Sv1 mice, which do not exhibit symptoms of dependence. Based on this finding, the effect of adenosine on dependence was investigated in genetically engineered mice with alterations in adenosine tone in the brain and in pharmacologic experiments. Morphine withdrawal behaviors were significantly diminished ($p < 0.0004$) in genetically engineered mice with reduced adenosine tone in the brainstem, and by treatment with an adenosine receptor(1) (A(1)) agonist (2-chloro-N⁶-cyclopentyladenosine, 0.5mg/kg) or an A(2a) receptor (A(2a)) antagonist (SCH 58261, 1mg/kg). These results indicate that adenosine homeostasis plays a crucial role in narcotic drug responses. Opiate-induced changes in brain adenosine levels may explain many important neurobehavioral features associated with opiate addiction and withdrawal.

Geranylinalool Synthases in Solanaceae and Other Angiosperms Constitute an Ancient Branch of Diterpene Synthases Involved in the Synthesis of Defensive Compounds

Vasiliki Falara, Juan M. Alba, Merijn R. Kant, Robert C. Schuurink, Eran Pichersky
Plant Physiology, September 2014 Volume 166, No. 1, Pages 428-441

Many angiosperm plants, including basal dicots, eudicots, and monocots, emit (*E,E*)-4,8,12-trimethyltrideca-1,3,7,11-tetraene, which is derived from geranylinalool, in response to biotic challenge. An *Arabidopsis* (*Arabidopsis thaliana*) geranylinalool synthase (GLS) belonging to the *e/f* clade of the terpene synthase (TPS) family and two Fabaceae GLSs that belong to the TPS-*g* clade have been reported, making it unclear which is the main route to geranylinalool in plants. We characterized a tomato (*Solanum lycopersicum*) TPS-*e/f* gene, TPS46, encoding GLS (*SIGLS*) and its homolog (*NaGLS*) from *Nicotiana attenuata*. The K_m value of *SIGLS* for geranylgeranyl diphosphate was 18.7 μM, with a turnover rate value of 6.85 s⁻¹. In leaves and flowers of *N. attenuata*, which constitutively synthesize 17-hydroxygeranylinalool glycosides, *NaGLS* is expressed constitutively, but the gene can be induced in leaves with methyl jasmonate. In tomato, *SIGLS* is not expressed in any tissue under normal growth but is induced in leaves by alamethicin and methyl jasmonate treatments. *SIGLS*, *NaGLS*, *AtGLSs*, and several other GLSs characterized only in vitro come from four different eudicot families and constitute a separate branch of the TPS-*e/f* clade that diverged from kaurene synthases, also in the TPS-*e/f* clade, before the gymnosperm-angiosperm split. The early divergence of this branch and the GLS activity of genes in this branch in diverse eudicot families suggest that GLS activity encoded by these genes predates the angiosperm-gymnosperm split. However, although a TPS sequence belonging to this GLS lineage was recently reported from a basal dicot, no representative sequences have yet been found in monocot or nonangiospermous plants.

Mapping of the circulating metabolome reveals α -ketoglutarate as a predictor of morbid obesity-associated non-alcoholic fatty liver disease

E Rodríguez-Gallego, M Guirro, M Riera-Borrull, A Hernández-Aguilera, R Mariné-Casadó, S Fernández-Arroyo, R Beltrán-Debón, F Sabench, M Hernández, D del Castillo, J A Menendez, J Camps, R Ras, L Arola, J Joven
International Journal of Obesity, (28 March 2014) | doi:10.1038/ijo.2014.53

We used liquid and gas chromatography quadruple time-of-flight mass spectrometry (LC/GC-QTOF-MS) analysis in a non-targeted metabolomics approach on the plasma from morbidly obese patients undergoing bariatric surgery to gain a comprehensive measure of metabolite levels. On the basis of these findings, we developed a method (GC/QTOF-MS) for the accurate quantification of plasma α -ketoglutarate to explore its potential as a novel biomarker for the detection of NAFLD.

Mass Spectrometry Combinations for Structural Characterization of Sulfated-Steroid Metabolites

Yuetian Yan, Don L. Rempel, Timothy E. Holy, Michael L. Gross
Journal of The American Society for Mass Spectrometry, May 2014, Volume 25, Issue 5, Pages 869-879

Steroid conjugates, which often occur as metabolites, are challenging to characterize. One application is female-mouse urine, where steroid conjugates serve as important ligands for the pheromone-sensing neurons. Although the two with the highest abundance in mouse urine were previously characterized with mass spectrometry (MS) and NMR to be sulfated steroids, many more exist but remain structurally unresolved. Given that their physical and chemical properties are similar, they are likely to have a sulfated steroid ring structure. Because these compounds occur in trace amounts in mouse urine and elsewhere, their characterization by NMR will be difficult. Thus, MS methods become the primary approach for determining structure. Here, we show that a combination of MS tools is effective for determining the structures of sulfated steroids. Using 4-pregnene analogs, we explored high-resolving power MS (HR-MS) to determine chemical formulae; HD exchange MS (HDX-MS) to determine number of active, exchangeable hydrogens (e.g., OH groups); methoxyamine hydrochloride (MOX) derivatization MS, or reactive desorption electrospray ionization with hydroxylamine to determine the number of carbonyl groups; and tandem MS (MS^n), high-resolution tandem MS (HRMS/MS), and GC/MS to obtain structural details of the steroid ring. From the fragmentation studies, we deduced three major fragmentation rules for this class of sulfated steroids. We also show that a combined MS approach is effective for determining structure of steroid metabolites, with important implications for targeted metabolomics in general and for the study of mouse social communication in particular.

Dosimetry Determines the Initial OH Radical Concentration in Fast Photochemical Oxidation of Proteins (FPOP)

Ben Niu, Hao Zhang, Daryl Giblin, Don L. Rempel, Michael L. Gross
Journal of The American Society for Mass Spectrometry, May 2015, Volume 26, Issue 5, Pages 843-846

Fast photochemical oxidation of proteins (FPOP) employs laser photolysis of hydrogen peroxide to give OH radicals that label amino acid side-chains of proteins on the microsecond time scale. A method for quantitation of hydroxyl radicals after laser photolysis is of importance to FPOP because it establishes a means to adjust the yield of $\cdot OH$, offers the opportunity of tunable modifications, and provides a basis for kinetic measurements. The initial concentration of OH radicals has yet to be measured experimentally. We report here an approach using isotope dilution gas chromatography/mass spectrometry (GC/MS) to determine quantitatively the initial $\cdot OH$ concentration (we found ~ 0.95 mM from 15mM H_2O_2) from laser photolysis and to investigate the quenching efficiencies for various $\cdot OH$ scavengers.

LC-MS-Based Metabolomics Study of Marine Bacterial Secondary Metabolite and Antibiotic Production in *Salinispora arenicola*

Utpal Bose, Amitha K. Hewavitharana, Yi Kai Ng, Paul Nicholas Shaw, John A. Fuerst, Mark P. Hodson
Marine Drugs, 2015, Volume 13, Issue 1, Pages 249-266

An LC/MS-based metabolomics approach was used to characterise the variation in secondary metabolite production due to changes in the salt content of the growth media as well as across different growth periods (incubation times). We used metabolomics as a tool to investigate the production of rifamycins (antibiotics) and other secondary metabolites in the obligate marine actinobacterial species *Salinispora arenicola*, isolated from Great Barrier Reef (GBR) sponges, at two defined salt concentrations and over three different incubation periods. The results indicated that a 14 day incubation period is optimal for the maximum production of rifamycin B, whereas rifamycin S and W achieve their maximum concentration at 29 days. A "chemical profile" link between the days of incubation and the salt concentration of the growth medium was shown to exist and reliably represents a critical point for selection of growth medium and harvest time.

Identification of serum biomarkers associated with hepatitis B virus-related hepatocellular carcinoma and liver cirrhosis using mass-spectrometry-based metabolomics

Yonghai Lu, Chong Huang, Liang Gao, Yong-Jiang Xu, Sin Eng Chia, Shengsen Chen, Ning Li, Kangkang Yu, Qingxia Ling
Metabolomics, 16 May 2015, Pages 1-13

Hepatitis B virus (HBV) infection is a major risk factor for deaths from liver cirrhosis and hepatocellular carcinoma (HCC). With a long-term goal of improving early diagnosis, we aimed to identify specific biomarkers associated with the development of HCC and liver cirrhosis in patients with HBV infection. Serum samples from 46 HBV infected patients with HCC and liver cirrhosis and 24 age-gender matched healthy subjects were profiled by liquid chromatography-mass spectrometry and gas chromatography-mass spectrometry. It was found that fatty acids and long-chain acylcarnitines were significantly elevated in HBV-related HCC patients, whereas most of the carbohydrates, amino acids, short- and medium-chain acylcarnitines, and glycerophospholipids were decreased, when compared to healthy subjects. The up-regulation of fatty acids and long-chain acylcarnitines in HCC was positively correlated with liver cirrhosis state. Logistic regression analysis indicated that palmitoylcarnitine together with arginine was an effective "combined marker" for diagnosing HBV-related HCC with 97.3% sensitivity and 100% specificity. Linoleic acid plus glucose was useful for discrimination of liver cirrhosis in HCC patients with 79.2% sensitivity and 75% specificity. These findings demonstrate that mass-spectrometry-based metabolomics is a promising tool that could provide special insights into tumor metabolism and identify novel biomarkers for detection of HCC and liver cirrhosis from HBV infected patients.

Evaluation of comprehensive two-dimensional gas chromatography with accurate mass time-of-flight mass spectrometry for the metabolic profiling of plant–fungus interaction in *Aquilaria malaccensis*

Yong Foo Wong, Sung-Tong Chin, Patrick Perimutter, Philip J. Marriott
Journal of Chromatography A, Volume 1387, 27 March 2015, Pages 104-115

To explore the possible obligate interactions between the phytopathogenic fungus and *Aquilaria malaccensis* which result in generation of a complex array of secondary metabolites, we describe a comprehensive two-dimensional gas chromatography (GC × GC) method, coupled to accurate mass time-of-flight mass spectrometry (TOF-MS) for the untargeted and comprehensive metabolic profiling of essential oils from naturally infected *A. malaccensis* trees. A polar/non-polar column configuration was employed, offering an improved separation pattern of components when compared to other column sets. Four different grades of the oils displayed quite different metabolic patterns, suggesting the evolution of a signalling relationship between the host tree (emergence of various phytoalexins) and fungi (activation of biotransformation). In total, ca. 550 peaks/metabolites were detected, of which tentative identification of 155 of these compounds was reported, representing between 20.1% and 53.0% of the total ion count. These are distributed over the chemical families of monoterpene and sesquiterpene hydrocarbons, oxygenated monoterpenes and sesquiterpenes (comprised of ketone, aldehyde, oxide, alcohol, lactone, keto-alcohol and diol), norterpene, diterpenoids, short chain glycols, carboxylic acids and others. The large number of metabolites detected, combined with the ease with which they are located in the 2D separation space, emphasises the importance of a comprehensive analytical approach for the phytochemical analysis of plant metabolomes. Furthermore, the potential of this methodology in grading agarwood oils by comparing the obtained metabolic profiles (pattern recognition for unique metabolite chemical families) is discussed. The phytocomplexity of the agarwood oils signified the production of a multitude of plant-fungus mediated secondary metabolites as chemical signals for natural ecological communication. To the best of our knowledge, this is the most complete information available so far about essential oils of *A. malaccensis*, which represents a valuable extension to available data for advanced studies on microbial-mediated biotransformation of terpenes, and offers promise for potential discovery of unanticipated phytochemicals, and biotechnological exploitation.

PHARMACEUTICAL

Convenient syntheses of halo-dibenz[*b,f*]azepines and carbamazepine analogues via *N*-arylindoles

Emma-Claire Elliott, James L. Maggs, B. Kevin Park, Paul M. O'Neill, Andrew V. Stachulski
Organic & Biomolecular Chemistry, 2013, 11, 8426-8434

The dibenz[*b,f*]azepine heterocyclic system and related molecules with a single 10,11-bond are important templates for well-prescribed drug molecules, notably carbamazepine (anticonvulsant), clomipramine and imipramine (antidepressants). We synthesised a range of halogenated carbamazepine analogues, in connection with metabolic and immunological studies, as probes for structure-metabolism and hypersensitive effects and have published on their metabolic behavior. While a number of synthetic routes to such analogues are possible, we naturally sought short and efficient methods for our target compounds. In the following report we present an effective two-step synthesis of a range of dibenz[*b,f*]azepines from appropriate indoles via *N*-arylation, then acid-catalysed rearrangement, with a critical analysis of other approaches. We showed earlier that this route was effective for fluoro analogues and here present a broader review of its scope. The 5-(carboxamido) side chain of carbamazepine may be added in various ways, affording overall a convenient access to drug molecules.

Identification of Human Semiochemicals Attractive to the Major Vectors of Onchocerciasis

Ryan M. Young, Nathan D. Burkett-Cadena, Tommy W. McGaha Jr, Mario A. Rodriguez-Perez, Laurent D. Toé, Monsuru A. Adeleke, Moussa Sanfo, Traore Soungalo, Charles R. Katholi, Raymond Noblet, Henry Fadamiro, Jose L. Torres-Estrada, Mario C. Salinas-Carmona, Bill Baker, Thomas R. Unnasch, Eddie W. Cupp
PLOS Neglected Tropical Diseases, 8 January 2015, DOI: 10.1371/journal.pntd.0003450

Human landing collections, which are the current standard for collecting the black fly vectors of *Onchocerca volvulus*, the causative agent of river blindness, are inefficient and pose certain ethical issues. As entomological methods are among the primary techniques recommended by the international community for verifying the elimination of onchocerciasis, there is a need to develop alternative methods to collect these vectors. Recent studies have demonstrated that traps baited with CO₂ and dirty clothing have the potential to replace human landing collections for this purpose. However, for these traps to be widely applied, it will be necessary to develop a consistent bait formulation. To this end, volatile compounds from human sweat that attract the principal black fly vectors of *O. volvulus* in Africa and the Americas have been identified and used to optimize traps that specifically collect these insects. To achieve this milestone, we report the use of electroantennography and behavioral assays to identify human compounds that are neurostimulatory to these vectors, and demonstrate that these compounds are attractive to the vectors in field studies using previously developed trap platforms. The development of such a defined bait formulation will permit the widespread use of these traps by onchocerciasis elimination programs in Africa and the Americas.

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