Automated and Simultaneous Identification and Quantification in Extractables and Leachables Analysis

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Overview

- The safety impact of leachable chemicals found in medical devices, food packaging, or pharmaceuticals is determined by accurate qualitative and quantitative chemical analysis.
- Gas chromatography-mass spectrometry (GC/MS) and liquid chromatography-mass spectrometry (LC/MS) are the primary instruments used.

Methods

- A test solution of molecules commonly found in ELs at unknown concentrations was prepared for evaluating the method, as well as free five level calibration curves of several surrogate molecules. Calibrated mass spectra were obtained in free mode and analyzed with Cerno Multithrive to improve spectral accuracy. Calibration curves based on the MS results were used to quantify the unknowns as surrogate molecules. The Polyarc/FID results were obtained using a single internal standard concentration.

GC conditions
- Free GC: Injector Temp 300°C Column: 2.6mm SepPak purged splitter to 3mm Split ratio: 10:1
- Agilent 7890A/5975C Oven: 40°C (5 min), 1°C/5 to 275°C (12 min) Column ID: DB-5MS.
- Injection volume: 0.1 µL

Polyarc/FID:
- Oven: 70°C
- Scan range: 55-550 m/z
- Source Temp: 230°C
- Transfer line Temp: 350°C
- Transfer line length: 0.8 m
- Retention time: 0.1 mm ID

MS conditions
- Energetic: 70 eV
- Full scan range: 55-550 m/z
- Source temperature: 230°C
- Transfer line temperature: 350°C
- Transfer line length: 0.8 m
- Injection volume: 0.1 μL

FID conditions
- Temperature: 300°C
- H2 Flow rate: 1.5 scm
- Air Flow rate: 300 scm
- Air Make up: 5.0 scm
- Sampling rate: 50 Hz

Polyarc detector conditions
- Temperature: 203°C
- H2 Flow rate: 30 scm
- Air Flow rate: 2.5 scm

Quantification can be done with a single point calibration with any internal or external standard.

Calibration Curves

The use of surrogate or reference compounds for calibration can introduce significant error into the quantification of analytes because of the variability of detector response factors and sample stability. Five level calibration curves were prepared with compounds of varying functionalities and retention times. The resulting response factors were used to calibrate for various compounds in a test mixture based on similar functionality and/or retention time.

Results

Polyarc/FID results showed better linearity with a drastically more uniform response per mole of carbon. The plot below shows the response per mole of carbon for the Polyarc/FID in black and the MS in blue. Responses can differ by orders of magnitude in the MS, depending on the functionality, where the response is independent of molecule type with the Polyarc.

Enhanced Unknown Determination

Compound identification was improved through spectral calibration with PPTBA and subsequent software analysis with Cerno MassWorks. Fragmentation patterns of several compounds did not always result in accurate identification using standard NIST library search routines. Instead, calibrated mass and spectral accuracy were used to identify several potential molecular candidates and quantification errors were compared. The results suggest that unknowns present in library searches can be approximately identified and quantified with a single quadrupole Cerno-calibrated GC/MS-Polyarc-FID. The entire method for the identification and quantification has been automated through software to greatly increase the speed and accuracy of EL analysis.

Accurary

With standard GC/MS, average errors exceeded 40% and response factors did not correlate with functionality or retention time. With this novel setup, average errors were reduced, typically below 10%, and reproducibility improved to less than 2% standard deviation versus 8.7% with MS. Furthermore, all surrogate and reference molecules gave similar per compound response factors with the Polyarc, suggesting that the choice of calibration surrogate is arbitrary. A single surrogate calibration was sufficient for full quantification. The quantification results in the tables are based on surrogate molecules that matched chemical functionalities, and the chart below the table displays the variations in error that would be observed if different surrogate molecules were chosen for the MS.

Conclusions

- When calculating concentrations using GC/MS with surrogate molecule assignment, errors range from 2%-71% in an unknown sample.
- This calibration requires at least 15 different injections to create linearity plots.
- Using a single internal standard, Polyarc errors are under 10% in the same unknown sample for most compounds, requiring no calibration curves.
- Choosing the incorrect surrogate compound results in errors as high as 350%, as shown to the right.
- Limits of detection are roughly 30x lower for Eucamide and Tinunin 328 when using the Polyarc/FID.
- Splits the column effluent using a helium purged splitter allows for identification and quantification in a single injection when using the Polyarc.
- Cerno MassWorks allows for accurate mass measurements and can identify compounds not available in the NIST database.