

Application News

High Performance Liquid Chromatograph Mass Spectrometer

Non-Targeted Identification of Extractables and Leachables from Medical Device Polymers Using ESI and SICRIT-LC/QTOF with LabSolutions Insight Profiler

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User Benefits

- ◆ Application of a single processing method with a novel software application LabSolutions Insight™ Profiler, to identify extractable and leachable (E&L) compounds in medical polymer materials extracted in water or isopropanol.
- ◆ The screening workflow enabled detection of E&L compounds in foam extracts that were not detected in representative blanks.
- ◆ Application of SICRIT ion source extended the chemical search space for the LC-DIA-MS/MS method, enabling detection of additional E&L compounds that were not detected using ESI.

Introduction

Extractables and leachables (E&L) from medical device polymers may present toxicological risks during clinical use. Regulatory frameworks such as ISO 10993 require chemical characterisation to ensure patient safety. ISO 10993-18, part of the ISO 10993 series for the biological evaluation of medical devices, provides a framework for the chemical characterisation of materials to identify substances that could leach from a device during clinical use. Within this regulatory framework, the objective is to assess biological risk and potential patient exposure by identifying E&L components in medical devices. This application presents a workflow for the non-targeted analysis of medical foam extracts to identify potential E&L compounds.

To highlight the non-targeted screening workflow for E&L, LC/QTOF was applied to the analysis of different polymer materials used in medical devices for sleep apnoea. LC/QTOF data were acquired using TOF MS and data independent acquisition (DIA)-MS/MS with Electrospray Ionization (ESI) and Soft Ionization by Chemical Reaction in Transfer (SICRIT™) in positive and negative ion modes. SICRIT was applied to increase chemical space in detecting potential E&L compounds by LC/QTOF through gas-phase ionization, where a stable dielectric barrier discharge ionization (DBDI) plasma promotes multiple concurrent ionization pathways, including proton transfer, radical cation formation, and charge-transfer/photoionization (Fig. 1).

Both ESI and SICRIT data were processed using LabSolutions Insight Profiler. The application software is designed to help automate feature detection, alignment and compound identification with suspect screening. In this work, compound screening lists included the ELSIE chemical list hosted within EPA's CompTox Chemicals Dashboard, FDA-CLAP, and NIST 2023. Following this workflow, E&L compounds were identified in the medical foam extracts including hindered amine light stabilisers (HALS), hindered phenolic antioxidants, flame retardants, slip and anti-blocking agents, common plasticisers and surface modifiers, as well as residual surfactant or processing aids.

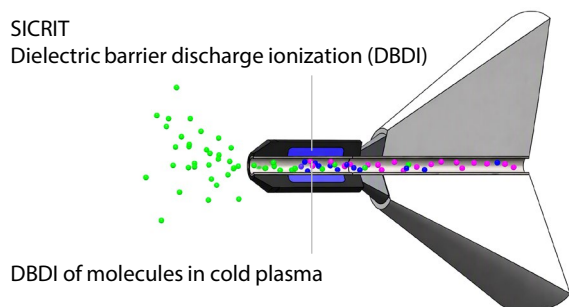


Fig. 1 SICRIT ion source schematic.

Sample Preparation

Samples were prepared in five technical replicates from four different medical polymers (mattress extract, silicone foam, polyesterurethane and polyetherurethane) extracted in water or isopropanol for analysis. Blank extraction samples were prepared using the same solvents for comparison to the foam extracts.

Data Acquisition

High resolution UHPLC-MS/MS data were acquired in both positive and negative ion mode using TOF MS and DIA-MS/MS and two different ion sources for the LCMS-9050 QTOF: ESI and SICRIT. Table 1 details the parameters used for data acquisition.

Table 1. Analytical conditions

[UHPLC conditions] (Nexera X2)	
Column	Shim-pack XR-ODS III (2.0 x 150 mm 2.2 µm)
Oven temp.	40 °C
Flow Rate	0.4 mL/min
Mobile Phase	A: Water + 0.1% formic acid B: Methanol
Rinse (R0, R1, R2)	IPA:MeOH:MeCN:H ₂ O (1:1:1:1) + 1% formic acid
Time program (%B)	20% B (0-0.1min) → 100% B (8-18.5 min) → 20% B (18.6-22 min)
Injection	0.5 µL; autosampler temperature 4 °C
[MS conditions] (LCMS-9050)	
Interface	ESI: 4.5 kV (+) / -3 kV (-) SICRIT: 1.8 kV, 4.5 kHz
Mode	Data Independent Acquisition (DIA)
Interface temp.	ESI: 300 °C SICRIT: 500 °C
Heat block temp.	400 °C
DL temp.	250 °C
Nebulizing gas flow	ESI: 2 L/min SICRIT: 1 L/min
Heating gas flow	10 L/min
Drying gas flow	10 L/min
CID gas pressure	210 kPa
MS	TOF-MS (m/z 70-1250)
MS/MS	m/z 40-1250, 41 events precursor isolation 35 Da collision energy spread 5-55 V
Total cycle time (MS and MS/MS)	1.125 seconds

■ Data Processing in LabSolutions Insight Profiler

To process the ESI and SICRIT LC/QTOF data acquired from foam extracts and corresponding blanks, all data files were imported into LabSolutions Insight Profiler and assigned to groups based on five technical replicates of each sample type and extraction solvent. The processing method considered feature detection, screening and MS/MS library identification for all data files. The software application method editor is designed to create a single workflow for feature detection of unknowns through to compound identification in a single batch process (Fig. 2).

Statistical comparisons between sample groups were made based on reproducible feature detection, with features required to be present in at least four of five technical replicates for inclusion in volcano plot analysis.

Compound identification within LabSolutions Insight Profiler includes automated MS/MS library searching against up to five libraries and screening of detected features against compound lists according to accurate m/z , retention time, or molecular formula. Where molecular formulae are available, the software automatically evaluates the specified adduct species to support precursor-ion assignment. In this application, suspect screening was performed against the ELSIE chemical list, FDA-CLAP, and NIST 2023. Experimental MS/MS spectra were searched against the NIST 2023 and MassBank libraries for orthogonal identification support.

After initial processing, the software application allows subsets of the dataset to be interrogated without reprocessing individual data files, enabling rapid and iterative evaluation of different sample comparisons, such as the identification of signals reproducibly detected in extracts but absent from the corresponding blanks, or comparison of ionization responses obtained using ESI and SICRIT for the same sample type.

Interactive and intuitive data review in LabSolutions Insight Profiler enabled analysis of E&L targets in the samples (Fig. 3). Chromatogram and library identification are linked with results tables and plots to help data interpretation.

Feature Detection and Alignment

Detects and aligns all ion signals that behave as a peak.

Statistics

Applied to identify significant ion signals and remove highly variable ions according to predefined filtering criteria.

Screening and Identification

Using large scale screening lists and multiple libraries to identify ion signals of interest.

Batch

A single, configurable workflow integrates feature detection, alignment, and compound identification, enabling automated batch processing for non-targeted analysis.

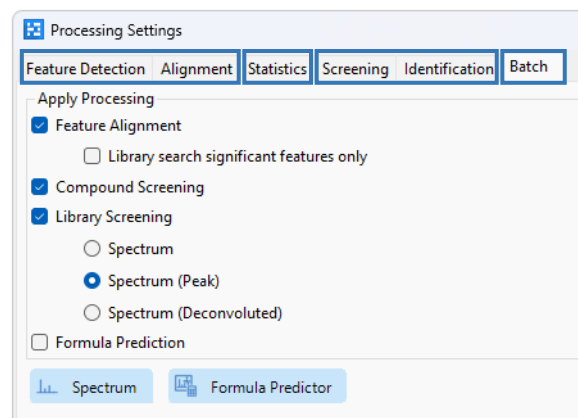


Fig. 2 LabSolutions Insight Profiler processing settings.

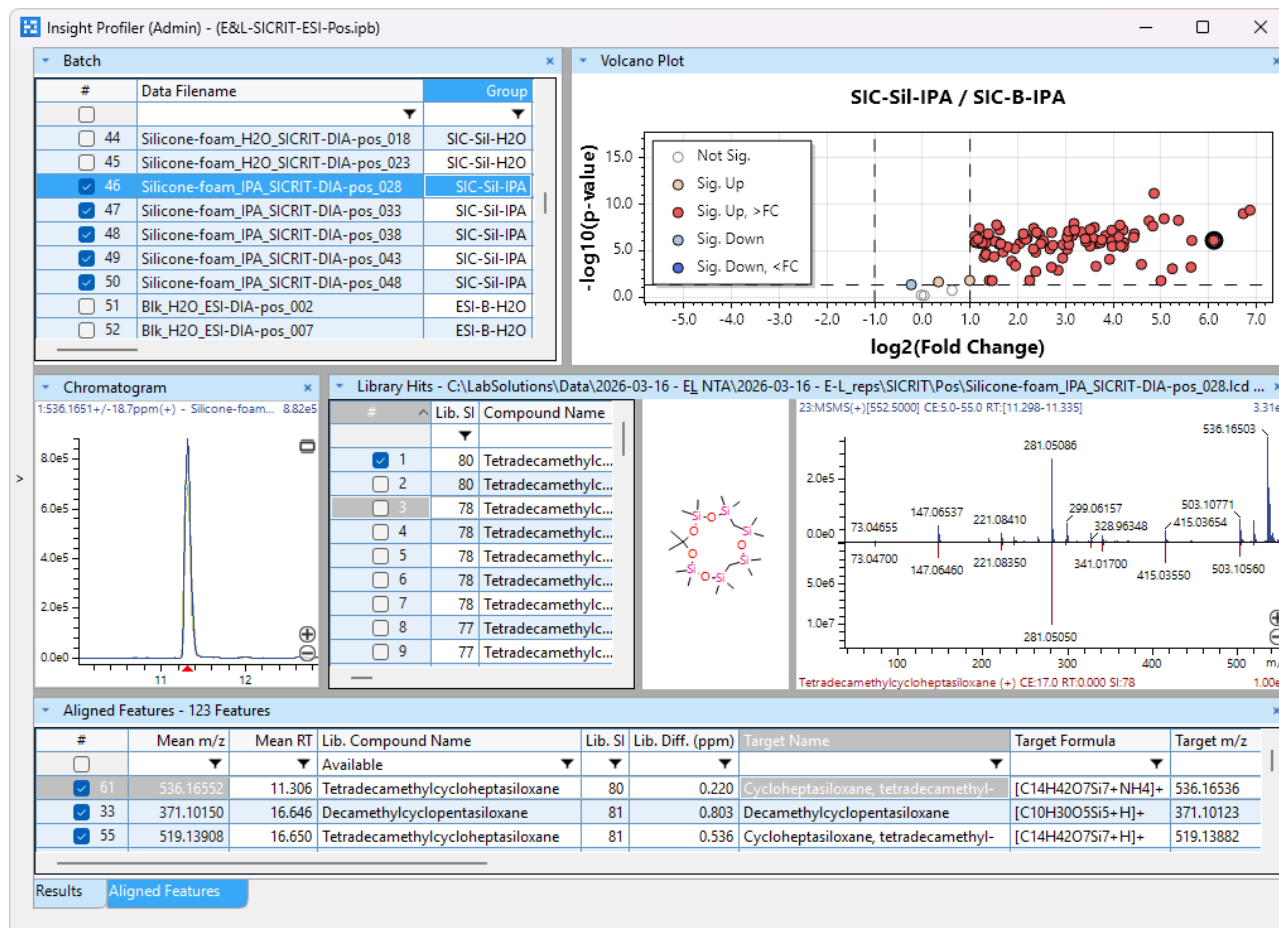


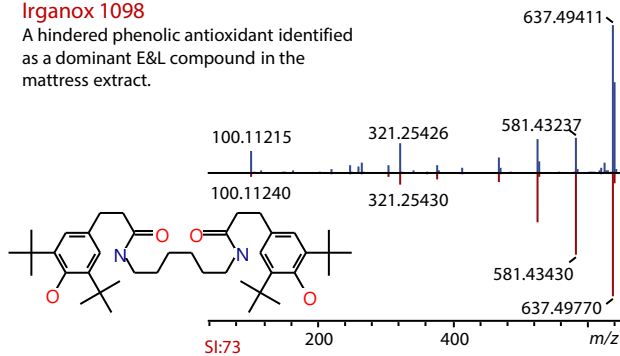
Fig. 3 LabSolutions Insight Profiler software used to analyse data from foam extracts compared to blanks following non-targeted analysis (LC-DIA-MS/MS). The example shows the identification of Tetradeamethylcycloheptasiloxane, which was best detected using SICRIT in the silicone foam extract and absent in the blanks.

Detection of E&Ls in Medical Foam Extracts by ESI

The mattress, polyesterurethane, polyetherurethane and silicone foam extracts each showed distinct E&L profiles. Diverse mixtures of antioxidants, fatty acid amides/slip agents, amines, plasticisers, cyclic and linear siloxanes, amines phosphate additives and other polymer additives were identified, reflecting typical processing additives for each type of foam (Table 2). To increase reporting confidence, results from E&L compound screening were verified by MS/MS library spectral matching to a high-resolution accurate mass library (NIST 2023 or MassBank). Fig. 4 highlights MS/MS identifications of dominant E&Ls detected in each of the medical foam extracts.

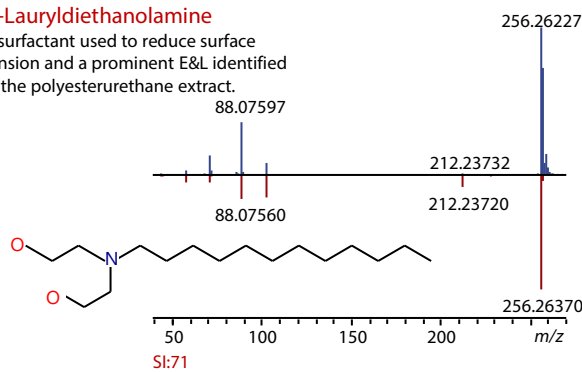
Irganox 1098

A hindered phenolic antioxidant identified as a dominant E&L compound in the mattress extract.



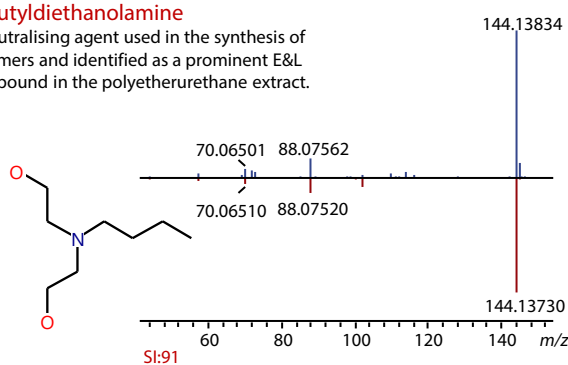
N-Lauryldiethanolamine

A surfactant used to reduce surface tension and a prominent E&L identified in the polyesterurethane extract.



N-Butyldiethanolamine

A neutralising agent used in the synthesis of polymers and identified as a prominent E&L compound in the polyetherurethane extract.



Decamethylcyclotrisiloxane

One of the dominant siloxane compounds identified in the silicone foam extract.

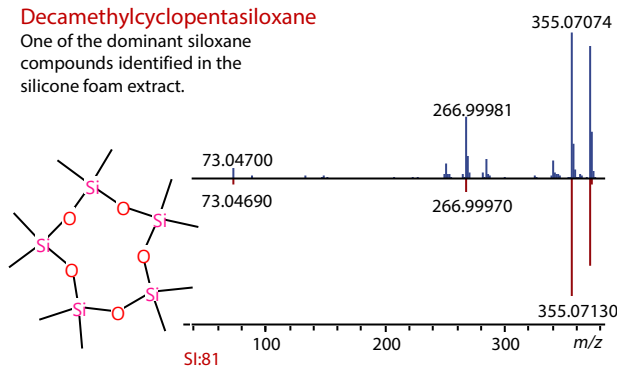


Fig. 4 E&L compounds identified by MS/MS library matching in the medical foam extracts by LC-DIA-MS/MS with ESI. Examples of MS/MS library match for dominant E&Ls identified in each extract are highlighted.

Table 2. E&L compounds identified in each of the medical foam extracts analysed using LC/QTOF with ESI.

Mattress Extract	
1,4,7-Trioxacyclotridecane-8,13-dione	[M+H] ⁺
1,6-Dioxacyclododecane-7,12-dione	[M+H] ⁺
2,2'-Methylene-bis(6-tert-butyl-4-methylphenol)	[M+H-C11H16O] ⁺
2,6-Di-tert-butyl-4-methoxyphenol	[M+H-CH4] ⁺
2-Hydroxyethyl benzoate	[M+H-H2O] ⁺
3,5-Di-tert-butyl-4-hydroxybenzaldehyde	[M+H] ⁺
7,9-Di-tert-butyl-1-oxaspiro[4.5]deca-6,9-diene-2,8-dione	[M+H] ⁺
Acetyl tributyl citrate	[M+Na] ⁺
Acridine	[M+H] ⁺
Benzaldehyde	[M+H] ⁺
Bis(1,2,2,6,6-pentamethyl-4-piperidyl) sebacate	[M+H] ⁺
Bis(2,2,6,6-tetramethyl-4-piperidyl) sebacate	[M+H] ⁺
Bis(2-ethylhexyl) adipate	[M+H] ⁺
Bis(p,p'-tert-octylphenyl)amine	[M+H] ⁺
Caprolactam	[M+H] ⁺
Dibutyl adipate	[M+H] ⁺
Dipropyl adipate	[M+H-C6H14O] ⁺
Erucamide	[M+H] ⁺
Irganox 1098	[M+H] ⁺
Irganox 565	[M+H] ⁺
N,N-Dimethylaniline	[M+H-CH4] ⁺
N-Benzyl-N,N-dimethyl-1-tetradecanaminium cation	[M+H] ⁺
N,N-Diacetylenediamine	[M+H] ⁺
N,N-Dibutylformamide	[M+H] ⁺
Oleamide	[M+H] ⁺
Poly THF n4-12	[M+H] ⁺
Tetradecamethylcyclotrisiloxane	[M+H] ⁺
Trans-1,2-Cyclohexanediol	[2M+H] ⁺
Polyesterurethane	
1,3-Bis(2-hydroxyethoxy)benzene	[M+H] ⁺
1,4,7-Trioxacyclotridecane-8,13-dione	[M+H] ⁺
1-Dodecyl-2-pyrrolidinone	[M+H] ⁺
3,5-Di-tert-butyl-4-hydroxybenzaldehyde	[M+H] ⁺
Docosanamide	[M+H] ⁺
Elaidic acid	[M+H] ⁺
Erucamide	[M+H] ⁺
N,N-Bis(2-hydroxyethyl)dodecanamide	[M+H-H2O] ⁺
N-Lauryldiethanolamine	[M+H-H2O] ⁺
Octadecanamine	[M+H] ⁺
Octyl decyl phthalate	[M+H] ⁺
Stearamide	[M+H] ⁺
Stearoyl ethanolamide	[M+NH4] ⁺
Tetradecyltrimethylammonium cation	[M+H] ⁺
Polyetherurethane	
3,5-Di-tert-butyl-4-hydroxybenzaldehyde	[M+H] ⁺
Benzaldehyde	[M+H] ⁺
Bis(p,p'-tert-octylphenyl)amine	[M+H] ⁺
Erucamide	[M+H] ⁺
N,N,N'-Trimethyl-N'-(2-hydroxyethyl)bis(2-aminoethyl) ether	[M+H-C3H9NO] ⁺
N,N-Dibutylaniline	[M+H] ⁺
N-Butyldiethanolamine	[M+H-H2O] ⁺
N-Lauryldiethanolamine	[M+H-H2O] ⁺
Tetradecamethylcyclotrisiloxane	[M+H] ⁺
Silicone foam	
1,4,7-Trioxacyclotridecane-8,13-dione	[M+H] ⁺
2,3-Dihydroxypropyl octadecanoate	[M+H-H2O] ⁺
Acetyl tributyl citrate	[M+Na] ⁺
Bis(2-ethylhexyl) adipate	[M+H] ⁺
Bis-(3,4-dimethyldibenzylidenesorbitol)	[M+H] ⁺
Bis(p,p'-tert-octylphenyl)amine	[M+H] ⁺
Decamethylcyclotrisiloxane	[M+H] ⁺
Diisodecyl phthalate	[M+Na] ⁺
Di-n-octyl phthalate	[M+H] ⁺
Erucamide	[M+H] ⁺
Hexamethylcyclotrisiloxane	[M+H] ⁺
N-Benzyl-N,N-dimethyl-1-tetradecanaminium cation	[M+H] ⁺
N-Lauryldiethanolamine	[M+H-H2O] ⁺
Octamethylcyclotetrasiloxane	[M+H-CH4] ⁺
Oleamide	[M+H] ⁺
Stearamide	[M+H] ⁺
Tetradecamethylcyclotrisiloxane	[M+H] ⁺
Tris-(2,4-di-tert-butylphenyl) phosphate	[M+H] ⁺

Application of SICRIT in E&L Analysis

Using SICRIT DBDI in addition to ESI, the analytical coverage can be expanded across lower-polarity and intermediate m/z ranges (Fig. 5). In this E&L application, the LC/QTOF analysis with SICRIT highlighted the enhanced detection of hydrophobic, non-polar E&L compounds such as the antioxidant Irganox 1135, the cyclic siloxane tetradecamethylcyclheptasiloxane, the phenolic stabiliser 2,6-di-tert-butyl-4-methoxyphenol, and the plasticiser dibutyl adipate, which typically exhibit poor response or pose analytical challenges under standard atmospheric pressure ionization conditions (Fig. 6).

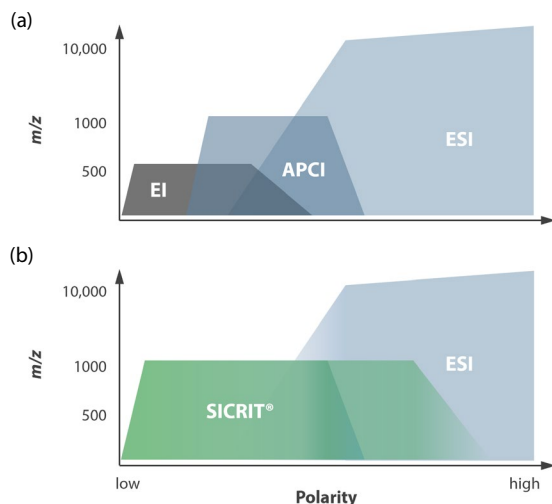


Fig. 5 Comparison of analyte coverage domains across compound polarity (low to high) and mass-to-charge ratio (m/z) for conventional ionization techniques (a) versus SICRIT DBDI integrated with ESI (b).

Conventional methods display distinct operational boundaries for Electron Ionization (EI), Atmospheric Pressure Chemical Ionization (APCI), and ESI, whereas SICRIT expands analytical coverage across lower-polarity and intermediate m/z ranges.

Conclusion

The inherent challenges in reporting E&L reflect both the complexity of the chemical space and the complexity of data analysis. In this work, the HRMS DIA-MS/MS method optimised the LC separation and applied two complementary ionization techniques for LC/QTOF (ESI and SICRIT) to the analysis of medical foam extracts.

LabSolutions Insight Profiler software was used to automatically process all data with a single method, including feature detection and alignment, MS/MS library identification using the NIST 2023 and MassBank repositories and compound screening using open-source databases including the ELSIE chemical list and the FDA-CLAP list.

The results of the analysis revealed that the medical mattress, polyesterurethane and polyetherurethane extracts showed diverse E&L profiles dominated by typical polymer additives, while the silicone foam extracts were characterised primarily by cyclic and linear siloxanes alongside other additives.

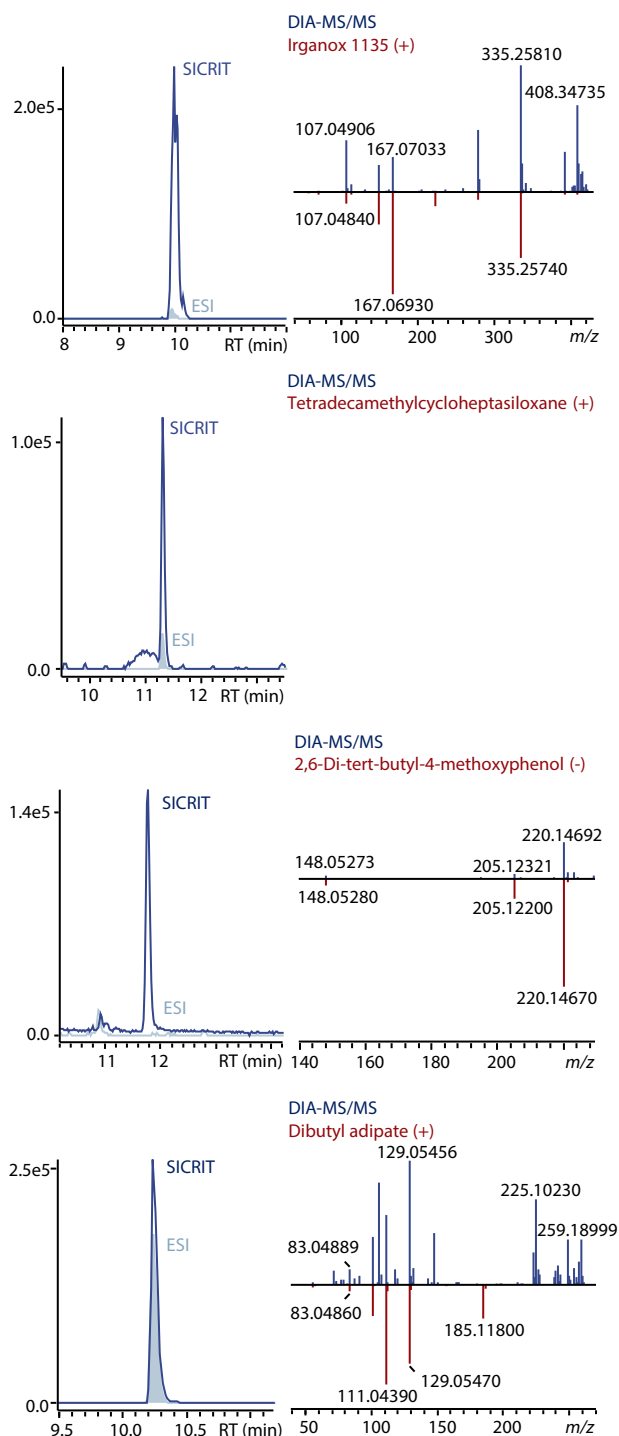


Fig. 6 Chromatograms and MS/MS spectra for E&L compounds identified in the medical mattress extract (IPA) that resulted in a higher response using SICRIT compared to ESI. The upper spectra show the acquired DIA-MS/MS spectra and the lower spectra are NIST library MS/MS spectra.

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