Sustainability in Extractables and Leachables: Implementing Green Chemistry Principles to a LC-HRAMS Screening Method

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Introduction

At Resolian Analytical Sciences, Extractables and Leachables (E&L) testing profiles potential impurities from primary packaging or device materials and target leachables in the final product for pharmaceutical, biopharmaceuticals, medical devices, nicotine delivery products and consumer healthcare products. Our extensive capability in bespoke E&L assessments is in accordance with the latest regulatory guidance and utilises organic and inorganic screening methods (HS-GCMS, GCMS, LC-HRAMS, ICP-MS) alongside diverse sample preparation techniques.

The objective of the presented work was to implement and evaluate green chemistry principles in a liquid chromatography-high-resolution accurate mass spectrometry (LC-HRAMS) screening method for the analysis of low volatility extractables and leachables, aiming to reduce environmental impact and improve sustainability.

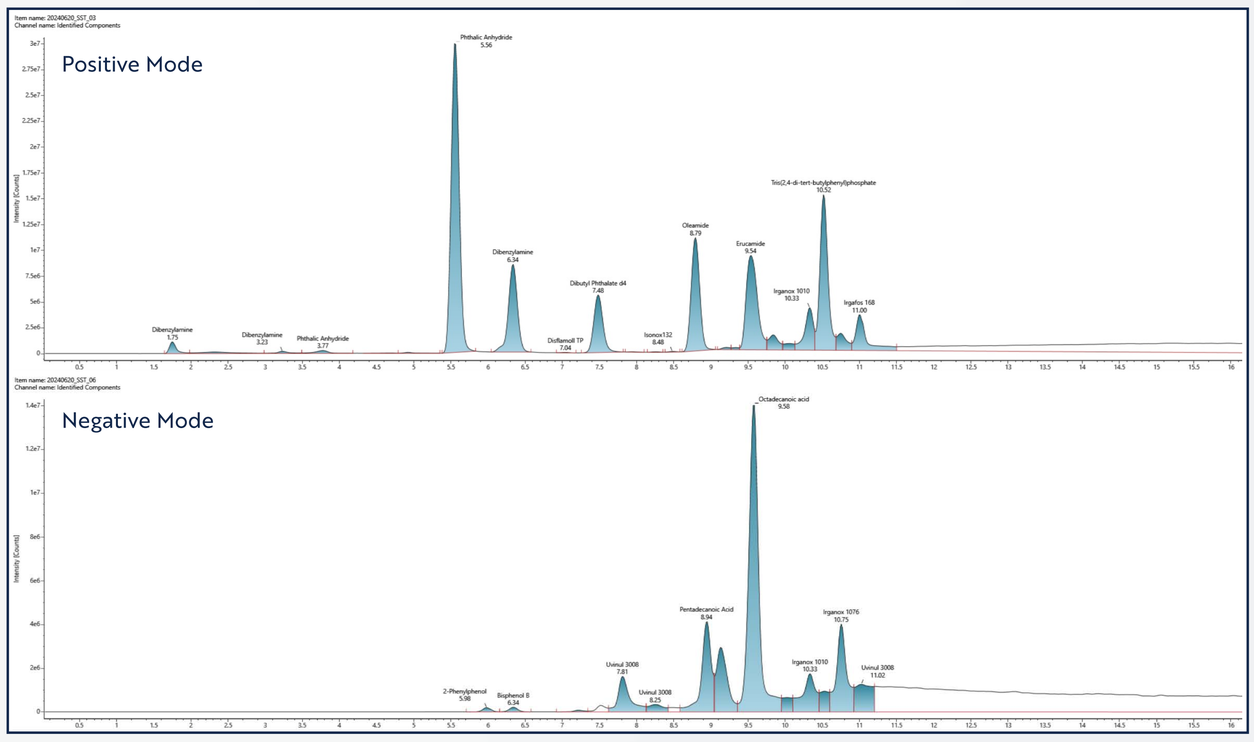
Ethanol VS Acetonitrile

Ethanol		Acetonitrile
2	Number of Associated Health Hazards (Lowest number of codes is best)	5
50.1	Solvent Production CED* (per kg solvent/MJ-eq.) (Smallest number is best)	88.5
-31.2	Solvent Distillation CED* (per kg solvent/MJ-eq.) (Smallest number is best)	-79.6
-31.7	Solvent Incineration CED* (per kg solvent/MJ-eq.) (Smallest number is best)	-29.7
1.08	CO2 emissions (kg) for the production of 1 kg solvent (Smallest number is best)	1.95
1.11	Total mass of waste emissions released to air, water and soil (kg/kg solvent produced) (Smallest number is best)	2.12
100	Cost per Litre (Smallest number is best)	172
TOTAL SCORE		
117	Normalised Green Chemistry Rating (Smallest number is best)	207

*CED = Cumulative Energy Demand

Materials and Method

- The LC-HRAMS screening method was redeveloped, acetonitrile was substituted with ethanol as organic mobile phase.
- The reversed phase method was applied with both ESI and APCI ionization techniques on a Waters Acquity I-class UPLC paired with a Synapt G2 time-of-flight mass spectrometer.
- Performance was evaluated using 21 typical leachable components purchased from Merck and Waters.
- Comparative analyses of solvent production energy input, environmental impact, health and safety (EHS) scores[1,2] and chromatographic performance were conducted.



Results

The updated method conditions led to:

- ✓ Enhanced separation of a model mixed standard.
- ✓ Reduced run time: from 30 minutes to 19 minutes.
- ✓ Reduced the total use of organic solvent per injection by 17%.
- ✓ Decreased instrumental energy and gas consumption per injection.
- ✓ Reduced laboratory running costs, due to ethanol being 42% cheaper.
- ✓ Reduced exposure risk for laboratory staff.

The method met all previous acceptance criteria with a suitable limit of detection (LOD) and has been applied for routine analysis in E&L screening studies.

Conclusions

Our E&L LC-HRAMS screening method was successfully redeveloped to use ethanol instead of acetonitrile as organic mobile phase. Analytical performance was maintained whilst gaining:

- ✓ Significant reduction in environmental impact
- ✓ Laboratory costs reduced
- ✓ The ability to incorporate bioethanol in the future

References
1. Capello, C., Fischer, U., & Hungerbühler, K. (2007). A comprehensive framework for the environmental assessment of solvents. Green Chemistry, 9(9), 927–934.
2. Raymond, M., Slater, S. and Savelski, M. (2010). LCA approach to the analysis of solvent waste issues in the pharmaceutical industry Green Chemistry, 12, 1826 - 1834.