NON-TARGETED SCREENING OF EXTRACTABLES AND LEACHABLES IN E-CIGARETTES USING A SINGLE PLATFORM UPLC-APGC-QTOF-MS

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INTRODUCTION

Characterization of extractables and leachables is essential for ensuring the safety, quality and efficacy of inhalation tobacco products such as e-cigarettes. The characterization of extractables from e-cigarettes, e-liquids, refill cartridges and e-cigarette aerosol involves both targeted screening (i.e. testing the extracts for known impurities) and non-targeted screening to look for unknown impurities that may potentially migrate from the starting materials and other packaging and device components.

FDA Deeming Regulation (May 2016) and EU Tobacco Product Directive (2014/40/EU) require manufacturers and importers to conduct full scientific evaluation of e-cigarette products including disclosure of ingredient listing, harmful and potentially harmful constituents, labeling requirements, demonstration of good manufacturing practices, product registration and premarket approval required in the US. Regulatory submissions must demonstrate that products meet the product safety and quality requirements and are appropriate for the protection of public health.

Disposable E-cigarette
Closed System

Refillable E-cigarette
Tank Model, Open System

E-liquid
Refill Bottles

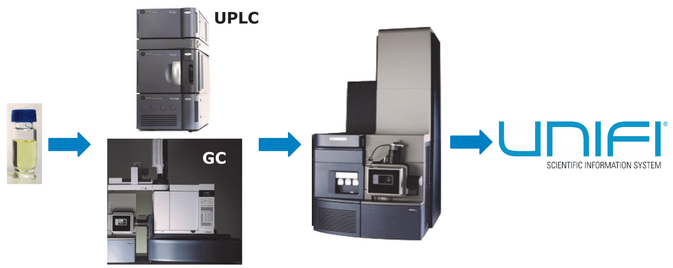
EXPERIMENTAL

In this study, the various components of an e-cigarette cartridge (end caps, mouth piece, gauze, heating element, metal shell and flavor formulation) were extracted separately and subjected to non-targeted high resolution screening using both UPLC and GC analysis on a single QTOF-MS platform. Data was acquired using alternating high and low collision energy states (MS^E) across the full analytical mass range, to generate accurate mass precursor and fragment ion spectra. The data from sample extracts was compared to isopropanol reagent blank extracts to determine the differences and potential extractables.

Packaging End Cap | Outer End Cap | Inner End Cap | Gauze W/ Flavor | Paper Wrap | Metal Shell

METHODS

Full System Solution for Chemical Profiling



SEPARATION
LIQUID/GAS CHROMATOGRAPHY
ACQUITY UPLC®
I-Class Or GC

DETECTION
MASS SPECTROMETRY
Xevo®
G2-XS QTof

DATA ANALYSIS
ADVANCED INFORMATICS
UNIFI
Software

LC Conditions:

LC System:	Waters ACQUITY I-Class
Column:	ACQUITY UPLC BEH C18 2.1 x 100 mm, 1.7 µm
Column Temp:	45 °C
Sample Temp:	4 °C
Flow Rate:	0.450 mL/min.
Mobile Phase A:	10mM ammonium acetate (pH5.0) in Water
Mobile Phase B:	10mM ammonium acetate (pH 5.0) in MeOH
Flow rate:	0.45 ml/min
Needle wash:	50:50 water: methanol (v/v)
Syringe purge:	10:90 Methanol: water (v/v)
Total run time:	17 min
Injection volume:	10 µL
Gradient:	

Time	% A	% B
0.00	98	2
0.25	98	2
12.25	1	99
13.00	1	99
13.01	98	2
17.00	98	2

GC Conditions:

GC System:	A7890 (w/APGC Interface)
Column:	DB-5MS 30m
Carrier Gas:	Nitrogen
Flow Rate:	1.2 mL/min
Initial Temperature:	35 °C (1.6 min)
Ramp:	25 °C /min
Final Temperature:	320 °C (7min)
Runtime:	20 min
Inlet Mode:	Splitless
Inlet Type:	Multimode
Temperature:	280 °C
Injection volume:	1 µL
Make-up Gas:	Nitrogen
Make-up Gas Flow:	250 mL/min
Transfer Line Temperature:	310 °C

LC-MS Ionization (ESI+):

Capillary (kV)	0.8
Sampling Cone	20.0
Source Temperature	120° C
Source Offset	80
Desolvation Temperature	550° C
Cone Gas Flow	50 L/Hr
Desolvation Gas Flow	1000 L/Hr
Acquisition range	50-1200 m/z
Scan time	0.25 sec
Lockmass	LeuEnk (556.2771m/z)

GC-MS Ionization:

Corona current (µA)	3.0
Sampling Cone	20.0
Source Temperature	120° C
Source Offset	80
Cone Gas Flow	175 L/Hr
Auxiliary Gas Flow	50 L/Hr
Acquisition range	50-1200 m/z
Scan time	0.25 sec
Lockmass	Siloxane (281.0517m/z)

RESULTS AND DISCUSSION

Both the LC and GC data were processed using UNIFI data analysis platform. The potential candidate markers were screened against a known library of extractables and leachables which automatically identifies compounds using several criteria including accurate mass precursor and fragment ion matching, peak response, retention time, isotopic fit to simplify data review and facilitate decision-making.

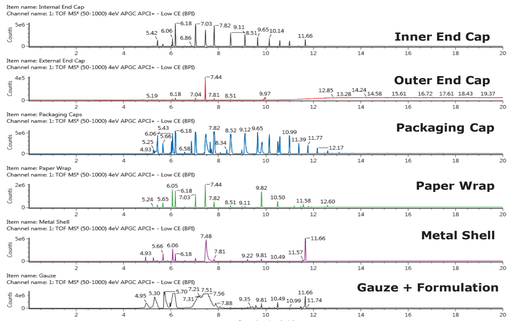


Fig 1. GC-QTOF-MS profiles for E-cigarette components

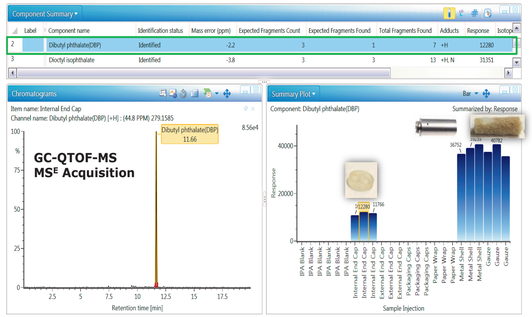


Fig 2. Identification of Dibutyl Phthalate using GC-QTOF-MS

Analysis	Extractables ID	Function	Inner End Cap	Outer End Cap	Packaging Cap	Paper Wrap	Metal Shell	Gauze
GC-QTOF-MS	Dibutyl Phthalate (DBP)	Plasticizer	✓				✓	✓
	Octadecanoic Acid	Surfactant/softening agent			✓	✓		✓
	Dioctyl Sebacate	Plasticizer			✓	✓		
	4-Methyl Benzophenone (4-MBP)	Stabilizing agent			✓	✓	✓	✓
	Sorbic acid	Food preservative					✓	✓
	N,N-Dimethyl-p-phenylenediamine	Polymer additive				✓	✓	
LC-QTOF-MS	HMBTAD	Light stabilizer	✓				✓	✓
	Disperse Red 11	Dye			✓			
	Uvinull 120	Anti-oxidant			✓			
	Irgafos 168	Light Stabilizer			✓			

Table 1. Tentative identifications using APGC-UPLC-QTOF-MS

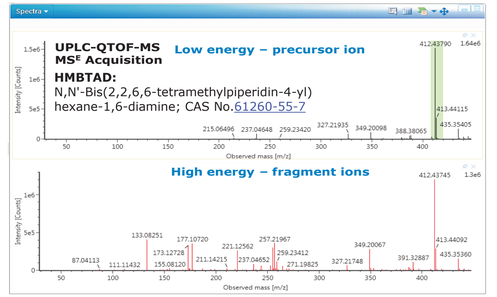


Fig 3. Identification of HMBTAD using UPLC-QTOF-MS

CONCLUSIONS

- Comprehensive characterization of extractables and leachables requires evaluation using multiple chromatographic techniques (LC/GC), multiple ionization modes and integrated software (UNIFI)
- Accurate mass screening using MS^E data acquisition combined with scientific libraries can be used to automatically identify target components
- Sample comparison and elucidation toolsets are useful in characterizing unknown compounds using accurate mass data, retention time, isotopic patterns and searchable databases

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