

Comprehensive Characterization of E-Cigarette Liquids

Identifying e-liquid sample constituents using GC/MS with Agilent MassHunter Unknowns Analysis and Target Deconvolution

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Abstract

Electronic-cigarette (e-cigarette) liquids contain carrier solvents, flavoring agents, and numerous minor constituents that require both untargeted screening and targeted confirmation. In this study, a commercially available e-cigarette liquid was diluted with dichloromethane and analyzed using an Agilent 5977C GC/MSD system in full-scan mode. Menthol and nicotine reference standards were added to the sample to demonstrate target compound confirmation capabilities. Data was processed using Agilent MassHunter Unknowns Analysis for automated component discovery and Target Deconvolution (a feature of Agilent MassHunter Quantitative Analysis software) for confirmation of selected analytes.

Unknowns Analysis enabled identification of major and minor sample constituents through spectral deconvolution and library searching, while Target Deconvolution successfully confirmed menthol and nicotine directly from the same full-scan dataset. The results demonstrate that comprehensive compound discovery and targeted confirmation can be achieved from a single GC/MS acquisition. These results demonstrate how a single GC/MS full-scan acquisition can support both broad chemical characterization and confident confirmation of target analytes in complex e-cigarette liquid matrices.

Introduction

E-cigarette and vaping products have gained widespread popularity over the past decade and are now available in a broad range of formulations and flavors. Unlike conventional cigarettes, these products generate an inhalable aerosol by heating a liquid formulation rather than combusting tobacco. As a result, the chemical composition of the e-liquid directly influences the composition of the generated aerosol and therefore plays an important role in product quality and consumer exposure.

E-liquid formulations are typically composed of carrier solvents such as propylene glycol (PG) and vegetable glycerin (VG), together with flavoring ingredients and other formulation additives. Although these major constituents are generally known, commercial products can contain dozens to hundreds of individual flavor-related compounds, manufacturing residues, impurities, reaction products, and degradation products. Consequently, characterization of e-liquid formulations presents a significant analytical challenge, particularly when unexpected or previously unrecognized compounds are present.

The Japanese market presents a unique analytical scenario compared to many international markets. In Japan, nicotine-containing e-liquids are subject to regulatory controls and therefore are not commonly distributed through conventional retail channels. As a result, many commercially available vaping liquids sold in Japan are marketed as nicotine-free formulations. Nevertheless, analytical laboratories may need to verify the absence of nicotine or investigate imported products where nicotine may be present.

Flavoring agents represent another important class of compounds within vaping products. Among these, menthol is one of the most frequently encountered flavor additives because of its characteristic cooling sensation and widespread consumer acceptance. Consequently, menthol serves as an excellent model target compound for evaluating targeted confirmation workflows in complex e-liquid matrices.

Gas chromatography/mass spectrometry (GC/MS) remains one of the most powerful analytical techniques for characterization of volatile and semivolatile compounds in vaping products. When operated in full-scan mode, GC/MS provides comprehensive mass spectral information for every detectable chromatographic peak, enabling both targeted and non-targeted investigations from a single acquisition. However, the complexity of e-liquid formulations frequently results in overlapping chromatographic peaks and coeluting components that can complicate traditional data review approaches based solely on the total ion chromatogram.

To address these challenges, advanced data-processing tools have become increasingly important. MassHunter Unknowns Analysis enables automated detection of chromatographic components, spectral deconvolution, and library searching, allowing for comprehensive non-target screening of complex samples. Target Deconvolution is a targeted screening capability available within Agilent MassHunter Quantitative Analysis software. The workflow is designed for compounds of known analytical interest and utilizes user-defined target libraries containing compound-specific mass spectral information. Unlike conventional extracted-ion chromatogram (EIC) approaches, Target Deconvolution evaluates the overall spectral pattern of the target compound and compares it against the reference library. By leveraging full-scan GC/MS data, the software can selectively recognize and confirm target analytes even in the presence of chromatographic overlap, matrix interference, or coeluting compounds. This approach enables targeted screening and compound confirmation without requiring dedicated SIM acquisition methods.

In this study, two commercially available e-cigarette liquids obtained in Japan were diluted with dichloromethane and analyzed using a 5977C GC/MS system operating in full-scan mode. To demonstrate both comprehensive screening and target confirmation capabilities, menthol and nicotine reference standards were added to the sample prior to analysis. The resulting full-scan data were processed using both Unknowns Analysis and Target Deconvolution.

Experimental

Sample preparation

Commercial e-cigarette liquids (Samples 1 and 2) were diluted 1:10 (v/v) with dichloromethane. Menthol and nicotine were spiked at approximately 10 µg/mL each prior to analysis.

Instrumentation

The final GC/MS analysis parameters are shown in Table 1.

Table 1. GC/MS analysis parameters.

Parameter	Condition
GC/MS	Agilent 8890 GC/Agilent 5977C GC/MSD
Column	Agilent J&W DB-624 UI, 30 m × 0.32 mm, 1.8 μm
Carrier Gas	Helium
Flow Rate	1.8 mL/min
Injection Volume	1 μL
Split Ratio	20:1
Inlet Temperature	250 °C
Oven Program	50 °C (2 min), 10 °C/min to 240 °C, Hold 10 min
Transfer Line Temperature	250 °C
Ion Source Temperature	250 °C
Quadrupole Temperature	150 °C
Scan Range	<i>m/z</i> 30–400

Results and discussion

Characterization of the e-cigarette liquid matrix

Commercially available e-cigarette liquids typically contain a wide variety of chemical components including carrier solvents, flavoring agents, and formulation additives. As a result, GC/MS analysis often reveals a complex chemical profile with peaks distributed throughout the chromatographic run.

Figure 1 shows the full-scan total ion chromatogram (TIC) of the e-cigarette liquid analyzed in this study after dilution with dichloromethane. Major peaks were identified as propylene glycol and glycerin, while additional peaks corresponding to menthol and synthetic cooling agents (peaks 4 and 5) were observed in vape sample 2. The broad distribution of chromatographic peaks indicates the chemical complexity of the sample and highlights the need for comprehensive characterization approaches capable of identifying both major and trace-level compounds.

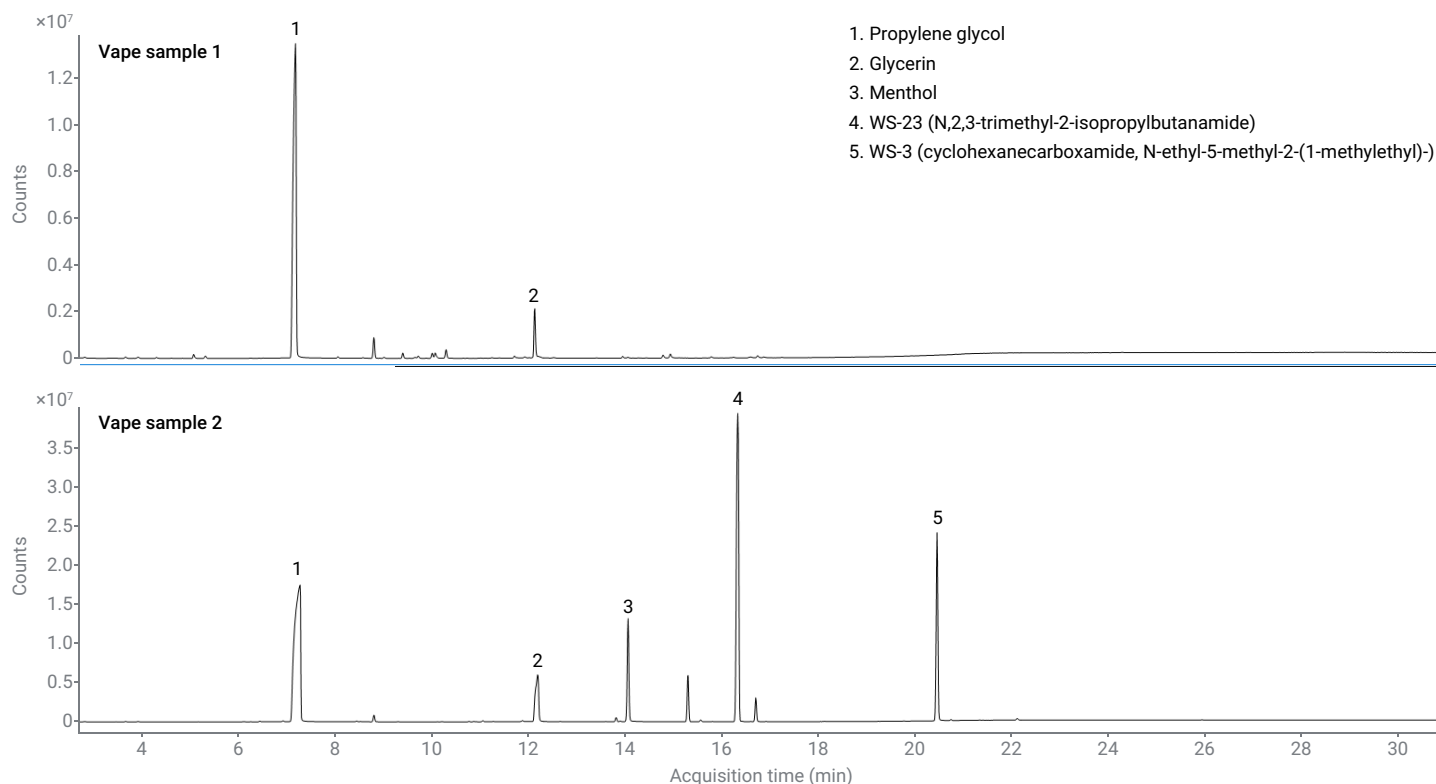


Figure 1. Full-scan total ion chromatograms (TICs) of two commercial e-cigarette liquids. Major peaks correspond to propylene glycol, glycerin, menthol, and synthetic cooling agents.

Although TIC review provides a useful overview of sample composition, interpretation becomes increasingly challenging when multiple compounds coelute or when trace-level components are masked by dominant matrix constituents. Consequently, additional data-processing approaches are required to maximize the information obtained from the full-scan dataset.

Comprehensive component discovery using Unknowns Analysis

The full-scan dataset was processed using MassHunter Unknowns Analysis to perform automated peak detection, spectral deconvolution, and library searching using the NIST23 Mass Spectral Library. Unknowns Analysis automatically extracted individual chromatographic components from the acquired dataset and generated

deconvoluted mass spectra suitable for library matching. This approach enables rapid and objective characterization of complex samples without requiring a predefined target list.

Figure 2 presents the Unknowns Analysis workflow applied to the e-cigarette liquid dataset. Automated component extraction identified many compounds throughout the chromatographic run, including both major formulation components and lower-abundance flavor-related constituents.

Library searching of the deconvoluted spectra provided tentative identification of multiple compounds associated with flavor formulations. Because the software processes deconvoluted spectra rather than raw TIC peak spectra, library matching performance can be significantly improved in chromatographically crowded regions.

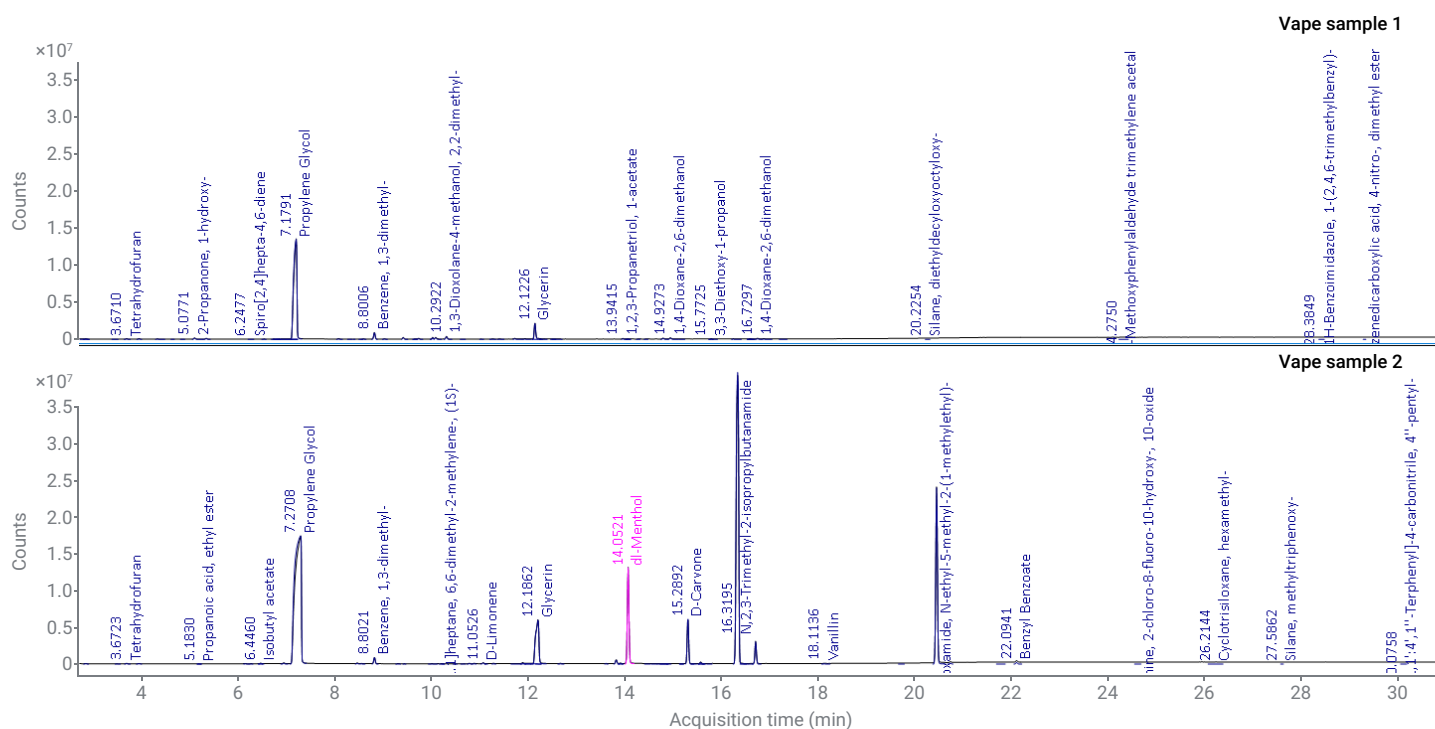


Figure 2. Automated component detection and spectral deconvolution using Agilent MassHunter Unknowns Analysis.

Representative compounds identified in the two commercial e-cigarette liquids are summarized in Table 2. Both samples contained propylene glycol and glycerin as the major carrier solvents. Vape sample 1 was characterized by the presence of flavor-related compounds such as methyl salicylate, *trans*-linalool oxide, and menthol-related alcohols, suggesting a tea- or herbal-inspired flavor profile. In contrast, vape sample 2 contained high levels of DL-menthol,

D-carvone, eucalyptol, and DL-isopulegol, consistent with a mint-dominant formulation. Additional flavoring compounds, including D-limonene and vanillin, contributed to citrus and sweet flavor characteristics. These results demonstrate the ability of Unknowns Analysis to comprehensively characterize both major formulation components and flavor-related constituents in complex e-cigarette liquid matrices from a single GC/MS full-scan acquisition.

Table 2. Representative compounds were identified using Agilent MassHunter Unknowns Analysis in vape samples 1 and 2.

RT (min)	Compound	Category	Component Area	Match Factor
Vape Sample 1				
7.179	Propylene glycol	Carrier solvent	63631537	99.2
9.398	1,2-Propanediol, 1-acetate	Formulation component	474942	99.1
10.007	1,3-Dioxolane-2-methanol, 2,4-dimethyl-	Flavor/formulation component	487266	88.4
10.068	1,3-Dioxolane-2-methanol, 2,4-dimethyl-	Flavor/formulation component	502284	88.7
10.292	1,3-Dioxolane-4-methanol, 2,2-dimethyl-	Flavor/formulation component	817825	97.9
12.123	Glycerin	Carrier solvent	4675357	98
12.203	Benzyl alcohol	Flavor ingredient	91030	89.2
12.509	<i>trans</i> -Linalool oxide (furanoid)	Floral flavor compound	131736	83.2
14.052	Cyclohexanol, 5-methyl-2-(1-methylethyl)-	Menthol-related compound	76238	91.6
14.425	Methyl salicylate	Mint/wintergreen flavor	26055	93.5
Vape Sample 2				
7.271	Propylene glycol	Carrier solvent	167148341	96.4
11.053	D-Limonene	Citrus flavor	348539	96.6
11.27	Eucalyptol	Mint/cooling flavor	94766	89.7
12.186	Glycerin	Carrier solvent	28415112	98.5
13.592	DL-Isopulegol	Mint-related flavor	72650	87.8
14.052	DL-Menthol	Cooling/mint flavor	31102664	98.4
15.289	D-Carvone	Spearmint flavor	13539398	97.8
16.692	Triacetin	Formulation additive	6529711	98.6
18.114	Vanillin	Vanilla flavor	91008	93.7
22.094	Benzyl benzoate	Flavor fixative	541627	94.6

Resolving coeluting compounds through spectral deconvolution

Complex consumer-product samples frequently contain chromatographic regions where multiple compounds elute within a narrow retention-time window. Under such conditions, individual components may be difficult to recognize directly from the TIC.

To evaluate the effectiveness of spectral deconvolution, a crowded chromatographic region was processed using the deconvolution engine within Unknowns Analysis. Figure 3 illustrates an example in which multiple overlapping signals present in the TIC were separated into individual component profiles. This example was generated using a different chromatographic method than the final GC/MS conditions listed in Table 1 and is presented solely to demonstrate the ability of the software to resolve coeluting compounds.

The deconvolution algorithm extracts compound-specific ion patterns and reconstructs individual mass spectra corresponding to the contributing compounds. As a result, compounds that may be partially or completely obscured within the TIC can still be detected and identified.

For complex vaping formulations containing some flavors additives and related compounds, this capability provides a substantial advantage over conventional TIC-based review alone.

Target confirmation using target deconvolution

While broad chemical profiling is important for understanding overall sample composition, many analytical workflows also require confirmation of specific compounds of interest. Target Deconvolution, implemented within MassHunter Quantitative Analysis, enables targeted screening using compound-specific reference libraries. In contrast to non-target workflows that aim to discover unknown compounds, Target Deconvolution focuses on confirming the presence of predefined analytes of interest. The software evaluates spectral agreement between the acquired data and the target library, allowing reliable compound confirmation directly from a full-scan GC/MS dataset.

To demonstrate this capability, menthol and nicotine reference standards were added to the e-cigarette liquid prior to analysis. These compounds were selected because they represent analytically relevant targets for vaping-product investigations.

Menthol is among the most commonly encountered flavor additives in e-cigarette products, whereas nicotine represents an important regulatory and product-classification marker, particularly in markets such as Japan where most commercially available domestic vaping liquids are marketed as nicotine-free.

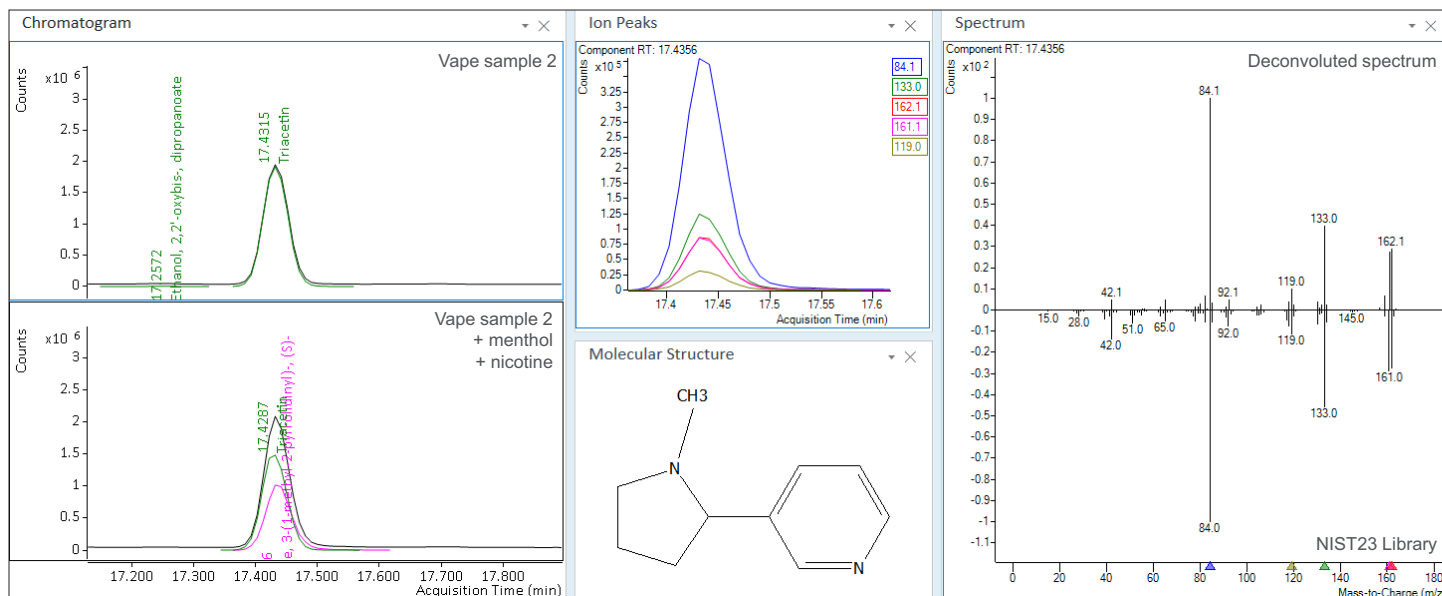


Figure 3. Spectral deconvolution of coeluting nicotine and triacetin in a representative e-cigarette liquid sample. The chromatographic conditions used for this demonstration differ from the final analytical method summarized in Table 1 and are shown here solely to illustrate the deconvolution capability of Unknowns Analysis.

Target Deconvolution was subsequently applied to the same full-scan dataset used for Unknowns Analysis. Unlike traditional targeted methods that may require SIM acquisition or additional analytical runs, Target Deconvolution utilizes the complete spectral information already present in the acquired data file. Figures 4 and 5 show the Target Deconvolution results obtained for menthol and nicotine.

The software successfully extracted characteristic ions associated with menthol, generated a deconvoluted spectrum, and compared the resulting spectral profile against the target library. The agreement between the observed and reference spectra resulted in confident compound confirmation despite the presence of surrounding matrix components. Similarly, nicotine was successfully confirmed using the Target Deconvolution workflow shown in Figure 5.

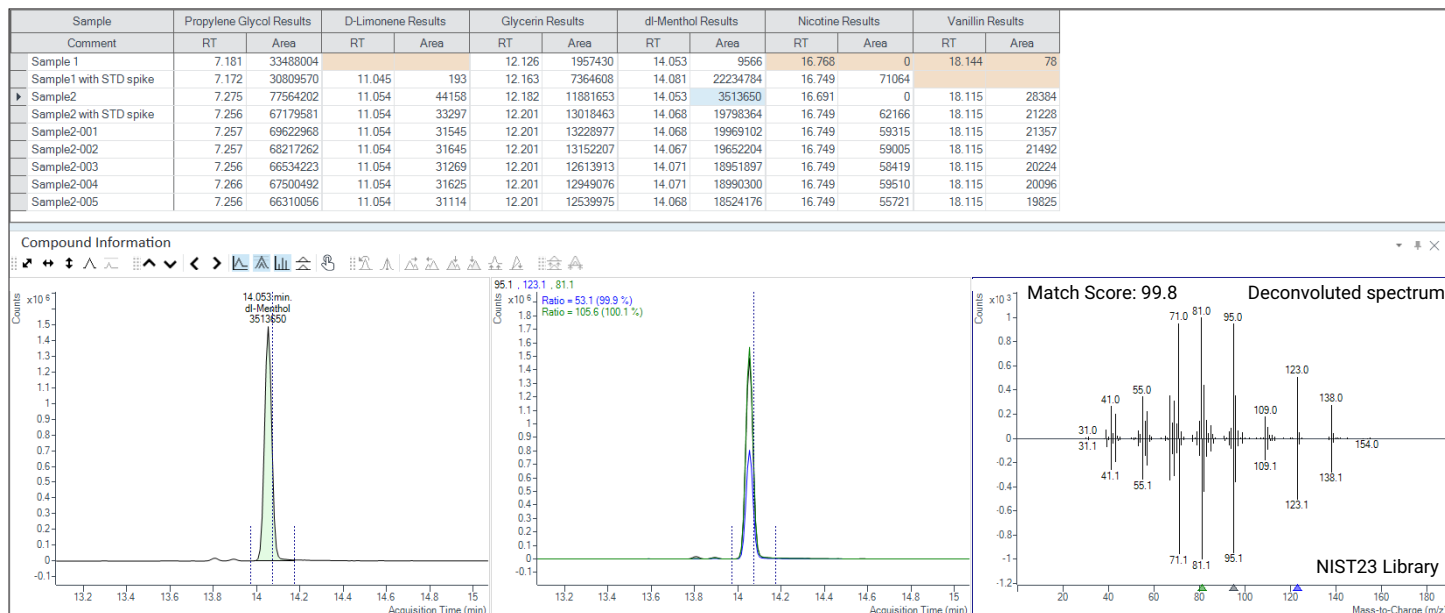


Figure 4. Confirmation of menthol using Target Deconvolution.

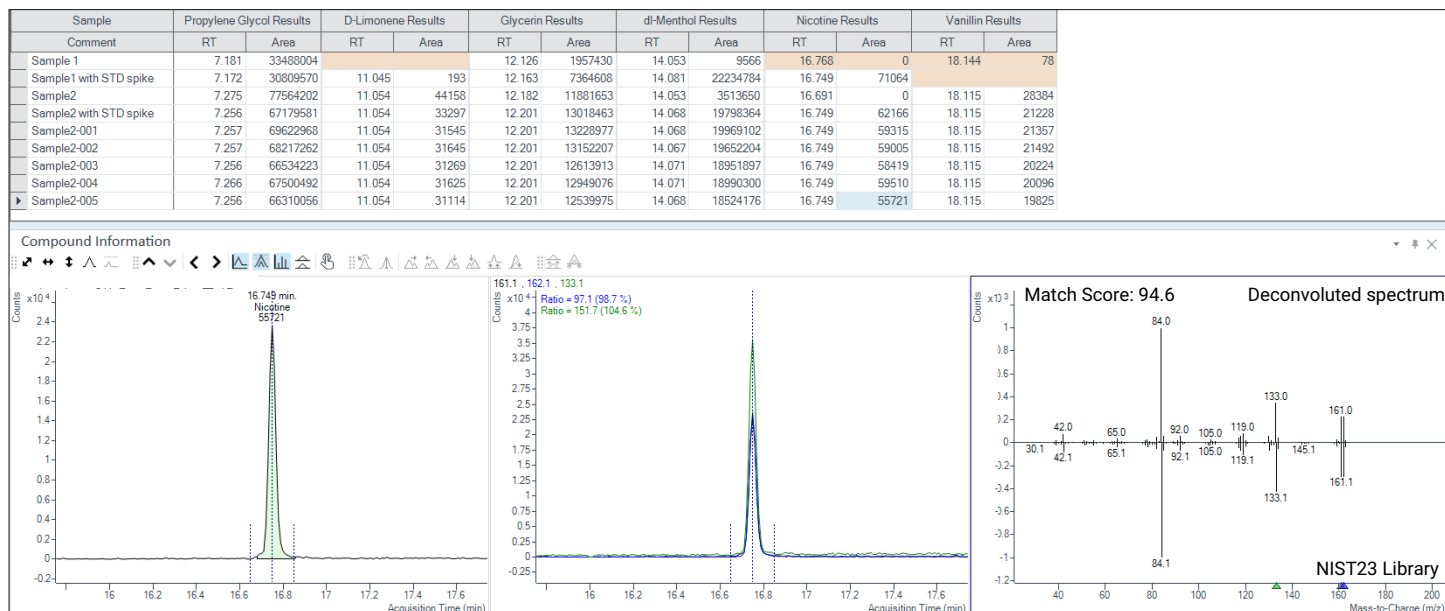


Figure 5. Confirmation of nicotine using Target Deconvolution.

The extracted chromatographic profile and deconvoluted mass spectrum demonstrated excellent agreement with the reference entry. These results illustrate the ability of Target Deconvolution to selectively verify compounds of interest within complex chromatographic environments.

Integrated workflow: Discovery and confirmation from a single dataset

Traditionally, comprehensive screening and confirmation of target compounds are often treated as separate analytical tasks. Non-target workflows focus on discovering unexpected constituents, whereas targeted workflows focus on verifying compounds of known interest.

The present study demonstrates that these objectives can be achieved simultaneously using a single GC/MS full-scan acquisition.

Unknowns Analysis enables comprehensive profiling through automated component extraction, deconvolution, and library searching, providing broad insight into sample composition. Target Deconvolution complements this capability by enabling confident confirmation of selected analytes within the same dataset.

Figure 6 summarizes the integrated workflow employed in this study.

By eliminating the need for multiple acquisition methods or additional sample injections, the combined workflow maximizes the analytical value of each measurement while simplifying data review and increasing confidence in analytical results.

For complex matrices such as e-cigarette liquids, this approach provides an efficient strategy for simultaneously identifying unexpected compounds and confirming compounds of interest, thereby supporting product development, quality control, regulatory investigations, and consumer-product safety studies.

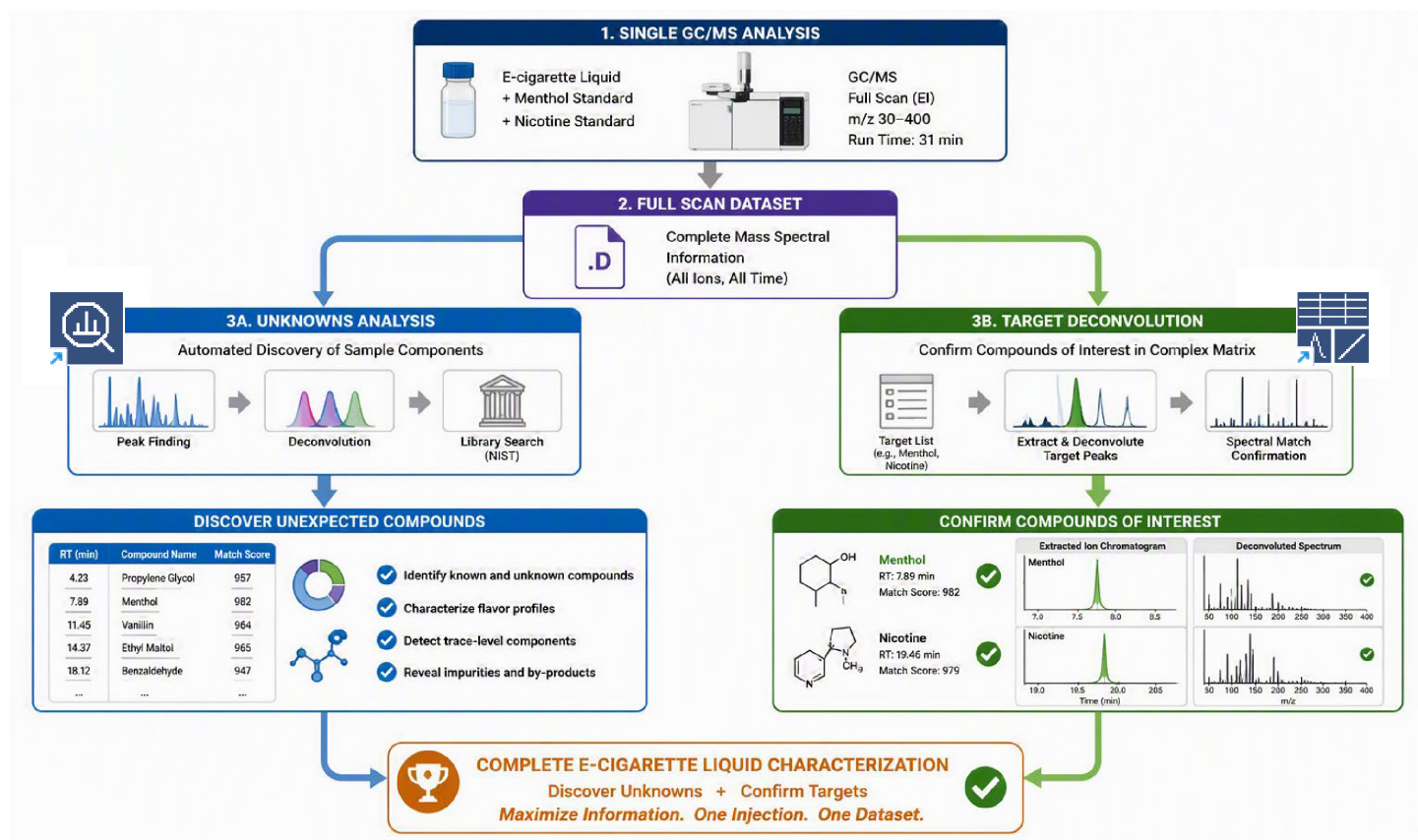


Figure 6. Integrated workflow combining Agilent MassHunter Unknowns Analysis and Target Deconvolution from a single GC/MS full-scan acquisition.

Conclusion

A commercially available e-cigarette liquid was successfully characterized using full-scan GC/MS following simple dilution with dichloromethane. To evaluate both comprehensive screening and targeted confirmation capabilities, menthol and nicotine reference standards were added to the sample prior to analysis.

Unknowns Analysis enabled automated component detection, spectral deconvolution, and library searching, providing comprehensive characterization of the e-cigarette matrix and revealing both major and minor constituents throughout the chromatographic profile. The deconvolution workflow improved the detection and identification of compounds in chromatographically complex regions, demonstrating the value of non-target screening for vaping products that contain flavor-related compounds and formulation additives.

Target Deconvolution was subsequently applied to the same full-scan dataset and successfully confirmed both menthol and nicotine within the fortified sample. By extracting compound-specific spectral information from the complex matrix, the workflow provided confident confirmation of compounds of interest without requiring additional targeted acquisition methods, such as SIM analysis or reinjection of the sample.

The complementary use of Unknowns Analysis and Target Deconvolution demonstrates how a single GC/MS full-scan acquisition can support both discovery of unexpected compounds and confirmation of targeted analytes. This integrated approach maximizes the analytical value of each injection, simplifies data review, and increases confidence in compound identification.

The integrated workflow provides an efficient and information-rich strategy for characterization of complex vaping-product samples using a single GC/MS full-scan acquisition.