Single-method Quantitation of Chemically Diverse Residual Solvents by Molecular Rotational Resonance:
Application to Peppermint Oil

Abstract

Essential oils are demanding matrices for residual solvent analysis. Their high concentrations of volatile components can complicate chromatographic separations. At the same time, the target solvents themselves span a wide range of volatility and polarity, from volatile compounds to higher-boiling polar solvents such as dimethylformamide (DMF) and ethylene glycol. Covering this range typically requires multiple standard mixtures and analytical runs, and the least volatile solvents are poorly suited to conventional headspace methods. This application note demonstrates a single direct-injection Molecular Rotational Resonance (MRR) method for four chemically diverse residual solvents in peppermint oil. MRR identifies each compound by its unique rotational spectrum, without requiring baseline chromatographic resolution or retention time matching. Each measurement combines quantitation and identity confirmation. Matrix-matched calibrations were linear to 1,000 ppm for all four solvents ($R^2 \geq 0.98$), with repeatability below 10%.

Introduction

Essential oils present a demanding matrix for residual solvent analysis. Steam-distilled and CO_2-extracted oils should contain no residual solvents, so their presence can indicate solvent extraction, synthetic adulteration, or process contamination. For example, DMF can be used to synthesize menthyl acetate from menthol, so trace DMF in peppermint oil may signal synthetic material. The oils themselves complicate detection, since their high concentrations of volatile components crowd chromatographic separations. The solvent panel adds a second challenge. Target solvents span a wide range of volatility and polarity, so conventional headspace GC methods typically require multiple standard mixtures and analytical runs. The least volatile solvents fall outside headspace methods altogether: ethylene glycol is not readily detected under standard headspace conditions, and DMF presents similar, though less severe, challenges. Direct-injection GC or GC-MS avoids this volatility limitation, and essential oils are generally compatible with direct injection. However, these methods still rely on chromatographic resolution for identification, and volatile oil components can co-elute with target solvents and compromise quantitation. Molecular Rotational Resonance (MRR) spectroscopy combines direct injection with structure-specific identification. MRR identifies each compound by its unique rotational spectrum, providing quantitation without requiring baseline resolution from the matrix or other analytes. This application note demonstrates a single direct-injection MRR method for four chemically diverse residual solvents in peppermint oil.

Experimental

Calibration standards were prepared by spiking the four residual solvents into peppermint oil at concentrations up to 1,000 ppm. Standards and samples were analyzed as is, without dilution or other sample preparation. Aliquots of oil in capped 2 mL vials were introduced by programmed temperature vaporization (PTV) direct liquid injection through a SpectrAline cartridge, which transferred the vaporized sample to the MRR spectrometer. Each solvent was quantitated using targeted measurements of its unique rotational transitions. Conditions are summarized in **Table 1**.

Parameter	Setting
Matrix	Peppermint oil, analyzed as is
Calibration range	Up to 1,000 ppm, matrix-matched
Sample introduction	PTV direct liquid injection
Injection volume	10 µL
Cartridge	SpectrAline Stabilwax, 2 m
Temperature program	60 to 220 °C
Carrier gas	Neon (≥99.999%)
Measurement	Targeted MRR quantitation

Table 1. Method conditions

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Results and Discussion

Figure 1 shows matrix-matched calibration curves for four residual solvents in peppermint oil. The panel spans more than 120 °C in boiling point, from cis-1,2-dichloroethene (60 °C) to ethylene glycol (197 °C), and includes both Class 1 and Class 2 solvents. All four were measured using a single direct-injection method, demonstrating the ability to analyze solvents across a broad volatility range without the multiple methods typically required for conventional GC analysis using the standard residual solvent mixtures described in USP General Chapter <467>.

All four calibrations were linear to 1,000 ppm ($R^2 \geq 0.98$), with repeatability below 10% (**Table 2**). Because each targeted rotational transition is unique to its compound, every measurement combines quantitation with identity confirmation. This is most significant for DMF and ethylene glycol, the high-boiling polar solvents that conventional headspace methods do not readily address, which achieved the lowest limits of quantitation in the panel at 10 and 38 µg/mL.

Sensitivity varies across the panel because MRR signal strength depends on each molecule's dipole moment and on how its signal is distributed across rotational transitions. Chlorine-containing molecules divide their signal among isotopic variants and hyperfine components, which accounts for the higher limits of quantitation for the two chlorinated solvents.

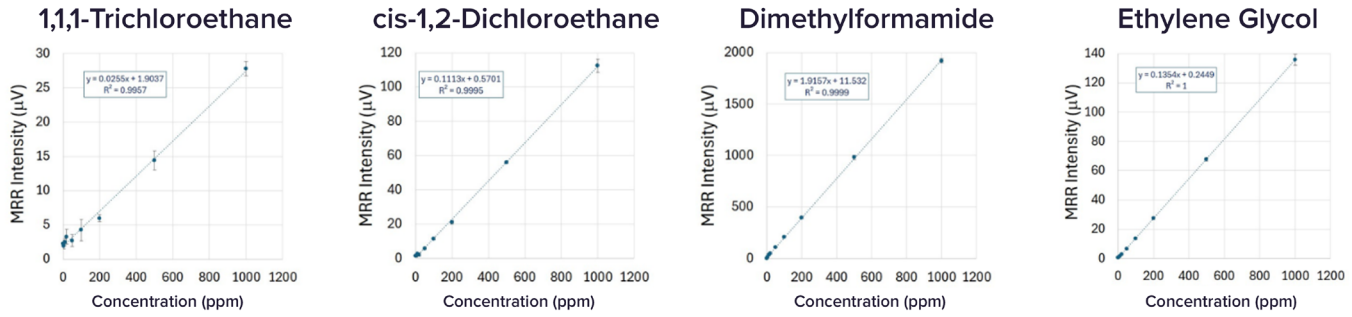


Figure 1. Matrix-matched calibration curves for (a) 1,1,1-trichloroethane, (b) cis-1,2-dichloroethene, (c) dimethylformamide, and (d) ethylene glycol in peppermint oil.

Solvent	Class	R^2	RSD (%)	LOD	LOQ	USP Limit	Criteria Met
1,1,1-Trichloroethane	1	0.99	<10%	186	564	1500	Pass
cis-1,2-Dichloroethene	2A	0.99	<7%	38	114	1870	Pass
Dimethylformamide	2C	0.99	<7%	3	10	880	Pass
Ethylene Glycol	2C	0.99	<10%	12	38	620	Pass

Table 2. Method performance for four residual solvents in peppermint oil. Class indicates the USP <467> class and standard mixture. RSD is repeatability. LOD and LOQ are in µg/mL oil; USP limits are in µg/g. Criteria (USP <467> / ICH): $R^2 \geq 0.9$, RSD ≤ 20%, and LOQ ≤ 50% of the USP limit.

Conclusion

A single direct-injection MRR method quantitated four chemically diverse residual solvents in peppermint oil, spanning volatile chlorinated compounds to high-boiling polar solvents, with linear response to 1,000 ppm and repeatability below 10%. Because each measurement combines quantitation with structure-specific identification, MRR provides confident results without requiring baseline chromatographic resolution or retention time matching, including for DMF and ethylene glycol, which conventional headspace methods do not readily address. The same approach applies to other complex matrices and residual solvent panels that currently require multiple analytical methods.

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