

Analysis of Ethylene Glycol and Diethylene Glycol in Oral Syrup Containing Glycerin

Using the Agilent 8890 GC system coupled with the Agilent 5977C GC/MSD



Authors

Praveen Arya and
Prashant Dour
Agilent Technologies, Inc.

Abstract

This study demonstrates the use of an Agilent 8890 GC system coupled with the Agilent 5977C single quadrupole GC/MSD to detect and quantify ethylene glycol (EG) and diethylene glycol (DEG) in oral syrups containing glycerin per United States Food and Drug Administration (USFDA) recommendations.¹ Samples were extracted using methanol, filtered through nylon filters, then followed by GC/MS analysis. Instrument Limit of Quantification (iLOQ) of 0.1 ppm was achieved using internal standard calibration. A solvent-based calibration range was established from 0.1 to 4 ppm.

Instrument parameters

Table 1. GC/MS parameters.

Parameter	Value
GC Parameters	
Inlet Temperature	240 °C
Analytical Column	DB-WAX GC column, 30 m × 0.25 mm, 0.50 µm (p/n 122-7033)
Injection Volume	1 µL
Column Flow	Helium; 1.0 mL/min, constant flow
Injection Mode	Split (20:1)
Oven Program	Start at 130 °C (hold for 4 min), ramp at 17 °C/min to 195 °C (hold for 4 min), then at 35 °C/min to 240 °C (hold for 4 min).
MS Transfer Line Temperature	240 °C
MS Parameters	
SIM Ions	31, 33, 43, 75, 113
Ion Source Temperature	230 °C
Quadrupole Temperature (Q1 and Q2)	150 °C

Experimental

Stock DEG and EG standard preparation (1 mg/mL)

A 100 mg portion of each DEG and EG standard was accurately weighed and transferred to a 100 mL volumetric flask. The solution was diluted to volume with methanol and mixed thoroughly.

Internal standard solution (1 mg/mL)

A 0.1 g portion of 2,2,2-trichloroethanol was accurately weighed and transferred to a 100 mL volumetric flask. The solution was diluted to volume with methanol and mixed thoroughly.

Working QC standard preparation (50 µg/mL)

A 0.5 mL aliquot of the DEG and EG stock standard solution was transferred to a 10 mL volumetric flask. Additionally, 0.10 mL of the internal standard solution was transferred to the same volumetric flask. The solution was then diluted to volume with diluent and mixed thoroughly using a vortex mixer.

Drug product sample preparation

Samples of each product matrix, namely solution, syrup, and suspension, were prepared in 10 mL volumetric flasks by accurately weighing 1.0 g of sample into each flask and adding 0.1 mL of the internal standard solution. The sample solutions were diluted to volume with methanol and mixed thoroughly using a vortex mixer. If solids or suspended material were observed after preparation, the solutions were filtered through a 0.20 µm PTFE syringe filter prior to analysis.

Results

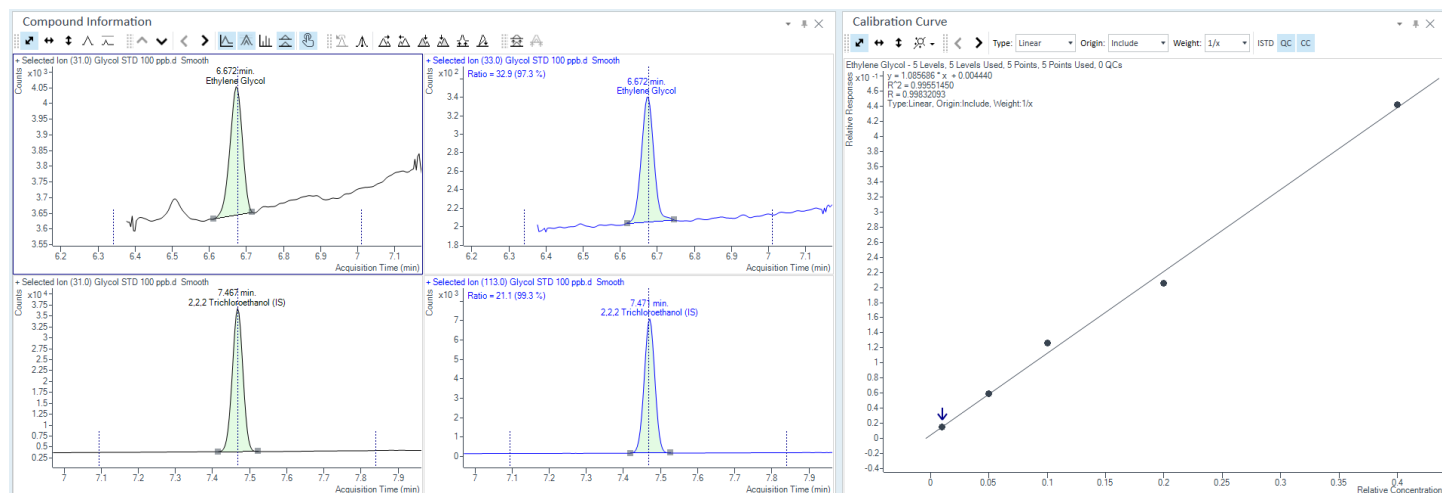


Figure 1. Ethylene glycol peaks at 0.1 ppm level along with IS peaks and calibration curve.

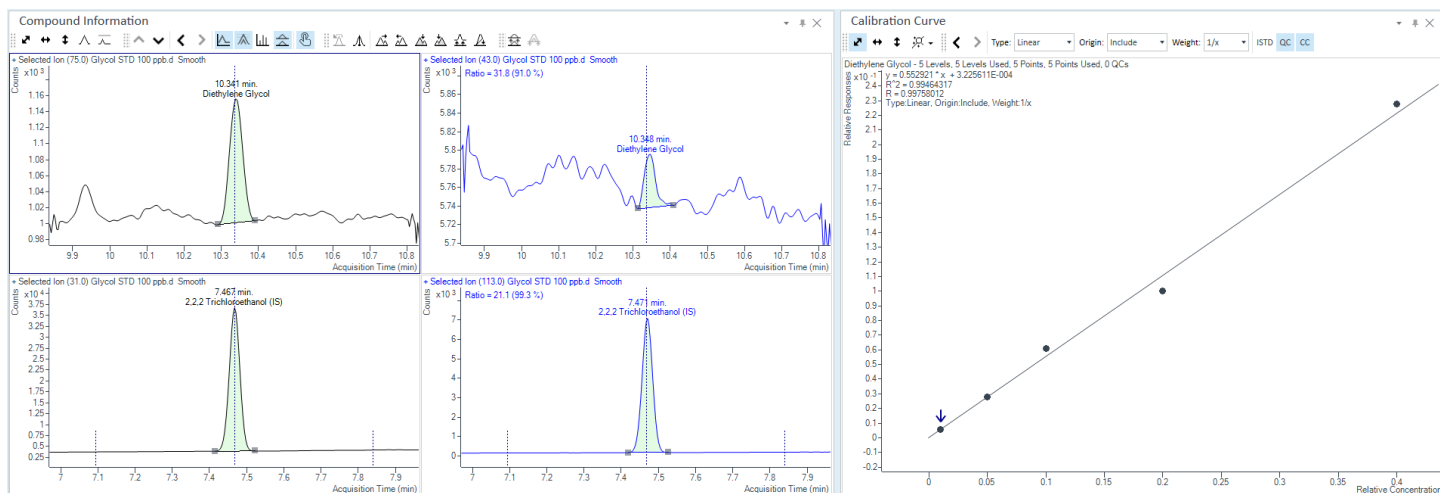


Figure 2. Diethylene glycol peaks at 0.1 ppm level along with IS peaks and calibration curve.

Sample				Ethylene...	Ethylene Glycol Results					Qualifier (33. ...	2,2,2 Trichloroethanol (IS)...		Qualifier (113...
Data File	Type	Level	Dil.	Exp. Conc.	RT	Resp.	Calc. Conc.	Final Conc.	Accuracy	Ratio	RT	Resp.	Ratio
Glycol STD 100 ppb.d	Cal	1	1.0	0.1000	6.672	963	0.0938	0.0938	93.8	32.9	7.467	65864	21.1
Glycol STD 500 ppb.d	Cal	2	1.0	0.5000	6.672	3780	0.5055	0.5055	101.1	34.8	7.464	63733	21.1
Glycol STD 1 ppm.d	Cal	3	1.0	1.0000	6.672	8097	1.1184	1.1184	111.8	34.0	7.464	64334	21.1
Glycol STD_2 ppm.d	Cal	4	1.0	2.0000	6.672	12869	1.8496	1.8496	92.5	33.7	7.467	62698	21.3
Glycol STD_4 ppm.d	Cal	5	1.0	4.0000	6.672	26532	4.0328	4.0328	100.8	33.7	7.467	59990	21.4
Reagent Blank-1.d	Sample		1.0								7.467	59199	21.2
Working Std rep-1.d	Sample		1.0		6.672	308932	51.8383	51.8383		33.9	7.464	54849	21.5
Working Std rep-2.d	Sample		1.0		6.668	309549	52.1583	52.1583		33.9	7.464	54621	21.5
Working Std rep-3.d	Sample		1.0		6.668	305943	52.2154	52.2154		33.9	7.464	53926	21.6
Working Std rep-4.d	Sample		1.0		6.668	303252	52.1311	52.1311		33.9	7.464	53538	21.6
Working Std rep-5.d	Sample		1.0		6.668	297737	52.0107	52.0107		33.9	7.463	52686	21.5
Working Std rep-6.d	Sample		1.0		6.668	296430	51.9729	51.9729		33.9	7.464	52493	21.6
Reagent Blank-3.d	Sample		1.0		6.668	314	0.0086	0.0086			7.464	58536	21.1
spl-1.d	Sample		10.0		6.672	19628	3.3842	33.8418		33.4	7.464	52785	21.3
spl-2.d	Sample		10.0		6.373	0	0.0000	0.0000			7.463	48435	21.6
spl-3.d	Sample		10.0		6.676	10095	1.7236	17.2359		33.9	7.464	52699	21.6
Reagent Blank-4.d	Sample		1.0								7.464	55378	21.1

Figure 3. Ethylene glycol results.

Sample				Diethylen...	Diethylene Glycol Results					Qualifier (43. ...	2,2,2 Trichloroethanol (IS)...		Qualifier (113...
Data File	Type	Level	Dil.	Exp. Conc.	RT	Resp.	Calc. Conc.	Final Conc.	Accuracy	Ratio	RT	Resp.	Ratio
Glycol STD 100 ppb.d	Cal	1	1.0	0.1000	10.341	382	0.0990	0.0990	99.0	31.8	7.467	65864	21.1
Glycol STD 500 ppb.d	Cal	2	1.0	0.5000	10.337	1762	0.4941	0.4941	98.8	34.4	7.464	63733	21.1
Glycol STD 1 ppm.d	Cal	3	1.0	1.0000	10.337	3907	1.0924	1.0924	109.2	39.8	7.464	64334	21.1
Glycol STD_2 ppm.d	Cal	4	1.0	2.0000	10.343	6271	1.8030	1.8030	90.1	39.3	7.467	62698	21.3
Glycol STD_4 ppm.d	Cal	5	1.0	4.0000	10.339	13657	4.1115	4.1115	102.8	38.7	7.467	59990	21.4
Reagent Blank-1.d	Sample		1.0		10.339	0	0.0000	0.0000			7.467	59199	21.2
Working Std rep-1.d	Sample		1.0		10.336	178432	58.8301	58.8301		39.0	7.464	54849	21.5
Working Std rep-2.d	Sample		1.0		10.337	179800	59.5281	59.5281		38.9	7.464	54621	21.5
Working Std rep-3.d	Sample		1.0		10.336	178255	59.7777	59.7777		38.9	7.464	53926	21.6
Working Std rep-4.d	Sample		1.0		10.336	177121	59.8276	59.8276		38.9	7.464	53538	21.6
Working Std rep-5.d	Sample		1.0		10.336	173230	59.4595	59.4595		39.0	7.463	52686	21.5
Working Std rep-6.d	Sample		1.0		10.336	173255	59.6874	59.6874		39.0	7.464	52493	21.6
Reagent Blank-3.d	Sample		1.0		10.331	0	0.0000	0.0000			7.464	58536	21.1
spl-1.d	Sample		10.0		10.331	1399	0.4733	4.7335		30.7	7.464	52785	21.3
spl-2.d	Sample		10.0		10.335	0	0.0000	0.0000			7.463	48435	21.6
spl-3.d	Sample		10.0								7.464	52699	21.6
Reagent Blank-4.d	Sample		1.0		9.928	0	0.0000	0.0000			7.464	55378	21.1

Figure 4. Diethylene glycol results.

Table 2. Results summary for ethylene glycol and diethylene glycol.

	Instrument LOQ (ppm)	%RSD (Area) for Six Replicates of Working Standard	%RSD (IS Area) for Six Replicate Standards
Ethylene Glycol	0.1	1.83	1.81
Diethylene Glycol	0.1	1.58	1.81

Conclusion

A sensitive and robust method was optimized for analysis of EG and DEG in oral syrups containing glycerin. The method uses an internal standard calibration using 2,2,2-trichloroethanol. Instrument LOQ was established at 0.1 ppm level for both EG and DEG. This method meets the requirements per US FDA recommendations for EG and DEG testing.¹ Therefore, this study demonstrates the usefulness of the developed method for routine analysis of oral syrup samples for EG and DEG analysis using GC/MS.

Reference

1. U.S. Food and Drug Administration. *Gas Chromatography-Mass Spectrometry (GC-MS) Method for the Determination of Ethylene Glycol (EG) and Diethylene Glycol (DEG) in Cough, Cold, and Allergy Products Containing Glycerin*. FDA Laboratory Methods 2025. <https://www.fda.gov/media/185817/download>