SHIMADZU
Excellence in Science

Application News

Gas Chromatograph Mass Spectrometer GCMS-QP2020 NX

Screening of Ethylene Glycol and Diethylene Glycol in Medicinal Syrup by GCMS with FASST mode (Part 2 – Improved Method for QC Testing)

Chia Chee Geng, Cynthia Melanie Lahey, Chua Chun Kiang, and Jackie Jackie
Shimadzu (Asia Pacific) Pte Ltd

User Benefits

- GCMS-QP2020 NX delivers high scan speed capabilities for screening analysis
- Fast Automated Scan/SIM Type (FASST) mode enables consecutive collection of scan and single ion monitoring (SIM) data
- Accurately identify and quantify both EG and DEG in medicinal syrup with a single injection
- Superior reliability, reproducibility and selectivity of the results obtained
- Matrix-matched calibration greatly improves %Recovery

■ Introduction

In Part 1 of the application news, we have successfully demonstrated GCMS-QP2020 NX superior capability in screening of ethylene glycol (EG) and diethylene glycol (DEG) in medicinal syrup, using the recommended method by Indonesian BPOM [1]. The method requires minimum sample preparation, making it suitable for laboratories in relevant authorities to screen medicinal syrup from different brands easily, thus making it possible to make rapid assessment on the safety of the medicinal syrup on the market. However, notable matrix effect has been observed, thus affecting the %Recovery of the method. As a result, this approach might not be capable of meeting the stringent QC testing requirements in pharmaceutical industry. Part 2 of the application news intends to address this gap.

To improve the accuracy of the method, our team decided to modify the BPOM method slightly using matrix-matched calibration plot. This slight modification greatly enhances the method selectivity, enabling accurate quantitation of EG and DEG in the presence of complex sample matrices.

In this article, we will be using the exact setup as Part 1. We will examine the usage of the Shimadzu GCMS-QP2020 NX to identify and quantify EG and DEG in medicinal syrup. The analysis will be demonstrated using the Fast Automated Scan/SIM Type (FASST) mode, which enables consecutive operation of scan mode and selected ion monitoring (SIM) mode for accurate qualification and quantitation within a single injection.

Figure 1. Shimadzu GCMS-QP2020 NX with AOC-20i+s Plus

■ Measurement Conditions

The analysis was performed using Shimadzu GCMS-QP2020 NX and AOC-20i+s Plus autosampler (**Figure 1**). Details of the analytical conditions were depicted in **Table 1**, in accordance with the method from the Indonesian national food and drug agency (BPOM) with slight modifications [2]. As the recommended method has minimum sample preparation, modifications were made to enhance the performance and robustness of the system. A capillary column with a 5 m integrated guard column was used to enhance the setup capability to handle a wide range of complex matrices without the risk of losing its performance. Due to the superior sensitivity of GCMS-QP2020 NX, a higher split ratio of 20:1 was used to minimize system contamination from the sample matrix. Event times for Scan and SIM were reduced to 0.2 and 0.1 sec, respectively, to increase the number of data points for better peak shape and integration.

Table 1. GCMS Parameters

Flow Control Mode	Constant Flow
Flow Rate	0.65 mL/min
Injection Mode	Split (Split ratio = 20)
Injection Port Temp.	250 °C
Injection Volume	1 µL
Carrier Gas	Helium
Column	SH-PolarWax column with 5 m integrated guard column (30 m long, 0.25 mm I.D., 0.25 µm film thickness) [P/N: 227-36360-01]
Column Oven Temp. Program	Initial Temp 100 °C (hold for 1 min) - Increase to 130 °C with a rate of 10 °C/min (hold 7 min) - Increase to 240 °C with a rate of 20 °C/min (hold 3 min) - Increase to 250 °C with a rate of 20 °C/min (hold 3 min)
Ion Source Temp.	230 °C
Interface Temp.	240 °C
Acquisition Mode	FASST (Scan/SIM)
Event Time (sec)	Q3 Scan: 0.2 Q3 SIM: 0.1
Scan *m/z* Range	29 to 400 amu
SIM Ions	EG: 31 (target ion) 33 and 62 (reference ions) DEG: 45 (target ion) 75 and 31 (reference ions)

■ Sample Preparation

Medicinal syrup sample preparation

A medicinal sample solution was prepared by transferring 10 mL of the medicinal syrup sample into a 100 mL volumetric flask. To improve dissolution, the medicinal syrup in 50 mL of methanol was sonicated for 5 minutes before topping it up to the mark. The diluted mixture was then filtered with a 0.45 µm PTFE membrane filter. 1 µL filtered sample was then analyzed using GCMS, and only negligible amount of EG was detected, and DEG was not being detected [1]. Thus, this medicinal sample solution was used as a blank sample because endogenous level of EG will be assumed to have negligible contribution to the experimental results. Subsequently, this filtered blank medicinal syrup sample was used for the preparation of the matrix-matched calibration plot (**Table 2**), and in parallel, a separate preparation of spiked samples at corresponding to Level 1 (LOQ) and level 3 of the calibration plot was prepared.

Matrix-matched calibration plot preparation

EG and DEG were purchased from TCI, Japan. Standard solutions of EG and DEG in methanol were prepared by dissolving 100 mg of each in separate 100 mL volumetric flasks. To improve dissolution, sonicate EG and DEG with 50 mL methanol (MeOH) before topping up to the 100 mL mark (1000 ppm standard solution). The 1000 ppm standard solutions were subsequently used for the preparation of a series of various concentrations of calibration standard solutions in 5 mL volumetric flasks in accordance with **Table 2**, topped to the mark with the filtered blank medicinal syrup sample.

Table 2. Preparation of EG and DEG calibration plots in 5 mL volumetric flasks

Level	Ethylene Glycol		Diethylene Glycol	
	Conc /ppm	Amount from 1000 ppm stock/ µL	Conc /ppm	Amount from 1000 ppm stock/ µL
1	6	30	12	60
2	8	40	16	80
3	10	50	20	100
4	12	60	24	120
5	14	70	28	140

■ Results and Discussion

Matrix-matched calibration plot

Matrix-matched calibration plots were obtained by spiking various concentrations of EG (6 to 14 ppm) and DEG (12 to 28 ppm) in the blank medicinal syrup and analyzed them using FASST mode. **Figures 2a** to **2d** demonstrate the linearity of the calibration plot from two separate preparations, having linear fits with R^2 of at least 0.999, for both EG and DEG. The high degree of similarity between the equations of the linearity plot from the two different preparations reflects the robustness and reliability of the method used.

Like Part 1 of the application news, in accordance with the BPOM method, the SIM profiles were used for quantitation. EG was quantitated with the target ion of *m/z* 31 and qualified with the reference ions of *m/z* 33 and 62. On the other hand, DEG was quantitated with the target ion of *m/z* 45 and qualified with reference ions of *m/z* 75 and 31.

%Recovery at levels 1 and 3

Table 3 summarized the result for the %Recovery of the spiked samples using the conventional non-matrix-matched standards

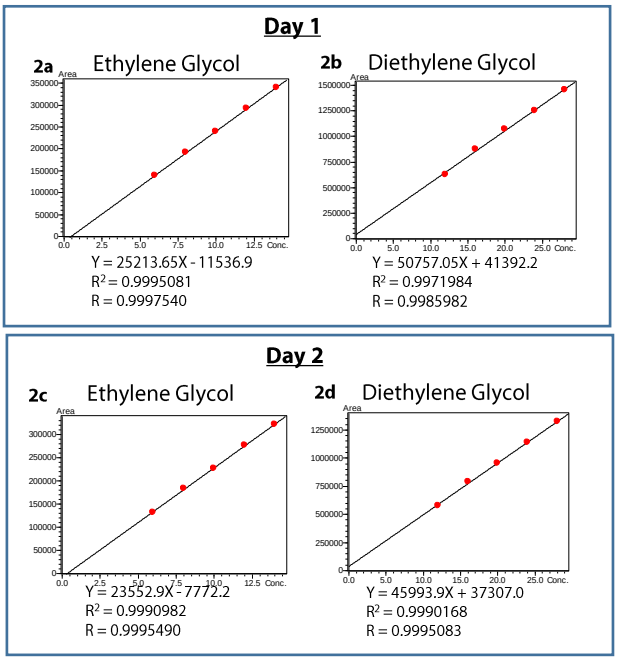

Figure 2a-d. Matrix-matched calibration plots of EG and DEG obtained on separate preparations

calibration plot approach vs matrix-matched calibration plot approach, at level 1 (LOQ) and level 3 concentration levels of EG (6 and 10ppm) and DEG (12 and 20 ppm). For the conventional non-matrix-matched calibration plot approach, %Recovery for EG ranges from 118% to 120%, and 102% to 110% for DEG. Significant positive bias is observed upon attempting to quantify EG and DEG in the spiked sample. This biasness was corrected when using the matrix-matched calibration approach. For the same set of data, using the matrix-matched calibration approach, the %Recovery for EG obtained ranges from 99% to 102%, and 98% to 105% for DEG. The results obtained were also in strong agreement with **Figure 2a** to **2d**, whereby the equations of the separate preparation of the matrix-matched calibration plots on different days shares high degree of similarity.

High degree of precision observed

The high degree of precision observed in **Table 3** is in strong agreement with the observation in Part 1 of the application news. The concentration %RSD (**Table 3**) of the results matrix-match calibration plots obtained were very similar to those of non-matrix-matched. Using the matrix-matched calibration plots, the concentration %RSD obtained ranged from 0.38% to 2.90%. This demonstrates that modifying the method has negligible effect on the precision of the data.

Improving selectivity and accuracy of measurement

As mentioned above, after the modification using the matrix-matched calibration plot to process the data, the %Recovery of the results approaches the ideal value of 100% (**Table 3**). Our team has thus successfully improved the selectivity of the setup that enables us to quantify EG and DEG with a better accuracy. This approach is suitable for QC lab in pharmaceutical industry with previously released batches of uncontaminated finished product that has negligible amount of EG and DEG presence (suitable for use as blank).

The limitation of this approach is the requirement of a corresponding blank matrix (with negligible amount of EG and DEG). In cases where a lab needs to test a diverse range of samples made up of various matrices, such as regulatory agencies or testing laboratories, the approach presented in Part 1 of the application note is more practical [1].

Table 3. Comparison of results using conventional non-matrix-matched calibration plot (spiked in MeOH) with matrix-matched calibration plot approach.

		Non-Matrix-Matched Calibration plot				Matrix Matched Calibration plot			
EG spiked /ppm	DEG spiked /ppm	EG detected /ppm	DEG detected /ppm	%Recovery EG	%Recovery DEG	EG detected /ppm	DEG detected /ppm	%Recovery EG	%Recovery DEG
6	12	7.20433	12.9938	120%	108%	6.11272	12.50618	102%	104%
6	12	7.20901	13.15353	120%	110%	6.11644	12.65962	102%	105%
6	12	7.08610	12.80426	118%	107%	6.01840	12.32410	100%	103%
6	12	7.06675	12.29578	118%	102%	6.00297	11.83565	100%	99%
	%RSD	1.06%	2.91%		%RSD	1.00%	2.90%		
10	20	11.94484	20.35343	119%	102%	9.89412	19.57594	99%	98%
10	20	11.92798	20.42981	119%	102%	9.88068	19.64931	99%	98%
10	20	12.01733	21.17994	120%	106%	9.95195	20.36990	100%	102%
10	20	12.01584	21.47227	120%	107%	9.95076	20.65070	100%	103%
	%RSD	0.39%	2.65%		%RSD	0.38%	2.65%		

Calculation

In this application news, the %Recovery and precision calculations were based on the concentrations of the sample inferred from the linear calibration plot equation, and therefore the final concentrations of EG and DEG in the medicinal syrup were not shown.

Refer to Part 1 of the application news [1] for tips for performing concentration calculations.

■ Conclusion

As a follow-up to Part 1 of the application news, our team showed how we were able to improve the method's selectivity using the matrix-matched calibration plot approach. As a result, we were able to satisfy the demanding QC standards of the pharmaceutical industry for the release testing of finished goods. The highly precise results obtained in this Part 2 is in strong agreement with the observation made in Part 1 of this application news.

Both Parts 1 and 2 of the application news demonstrated that Shimadzu GCMS-QP2020 NX can provide accurate, sensitive, precise, and robust detection of EG and DEG in medicinal syrup with minimum sample preparation. The developed methods are suitable for meeting the stringent requirements of relevant authorities, testing labs, or pharmaceutical quality control.

■ References

1. Chia, C. G. et al, Screening of Ethylene Glycol and Diethylene Glycol in Medicinal Syrup by GCMS with FASST mode (Part 1 – as per Indonesia BPOM Method), Shimadzu Application News No. 04-AD-0283-EN.
2. Metode Analysis Uji Cemaran Etilen Glikol (EG) dan Dietilen Glikol, Badan Pengawas Obat dan Makanan, 24 Oct 2022.

04-AD-0288-EN First Edition: Jan. 2023

Shimadzu Corporation
www.shimadzu.com/an/

SHIMADZU (Asia Pacific) Pte. Ltd,
www.shimadzu.com.sg

Please fill out the survey

Related Products Some products may be updated to newer models.

GCMS-QP2020 NX

Gas Chromatograph Mass Spectrometer

Related Solutions

Food Fraud

Price Inquiry

Product Inquiry

Technical Service / Support Inquiry

Other Inquiry