

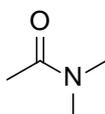
## Monitoring Dimethylacetamide in Complex Water Matrix Using GC-MS/MS (MRM)

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### User Benefits

- ◆ GCMS-TQ8050 NX offers advanced capabilities for the detection of DMAc in water sample.
- ◆ Superior reliability and reproducibility demonstrated.
- ◆ High sensitivity and selectivity when using MRM for detecting and quantitating DMAc.
- ◆ The proposed sample preparation steps successfully cleaned up water sample with complex matrices for GCMS analysis.

### Introduction



Molecular weight: 87.12

**Figure 1.** Chemical structure and molecular weight of N,N-dimethylacetamide (DMAc).

N,N-dimethylacetamide (DMAc), **Figure 1**, is widely used in the various industries:

- In semiconductor sector, it is commonly found in photoresist removal solution for lithography [1].
- It is introduced as electrolyte additives in Li-ion battery to enhance its performance [2].
- It is also heavily used during the production of acrylic fiber in textile industry [3].

As a result, DMAc might be discharged accidentally or illegally to nearby water bodies, hence contaminate freshwater bodies that are meant to produce portable drinking water. DMAc was added to the list of substance of very high concern (SVHC) by EU in 2011 due to its toxicity effect observed on reproduction system [4,5]. A study conducted on rat demonstrated that at 400 mg/kg bw/day, DMAc was capable of causing damage to fetus developmental [5]. In addition, DMAc was also known to cause liver damage [3,5]. In summary, the discharge from industries to the environment, and water bodies near industrial area should be closely monitored for DMAc to safeguard public health.

In this application news, the capability of Shimadzu GCMS-TQ8050 NX will be demonstrated to detect and quantitate DMAc in water sample. The methodology proposed is easily deployed by testing labs, on wide variety of water sample matrices using generic apparatus that are commonly available. Making use the superior sensitivity of GCMS-TQ8050 NX, time consuming step of concentrating the sample after liquid-liquid extraction can be skipped.

### Measurement Conditions

The analysis was performed using Shimadzu GCMS-TQ8050 NX and AOC™-20i+s Plus autosampler (**Figure 2**). Details of the analytical conditions were depicted in **Table 1**.

**Table 1. GCMS Parameters**

<b>Flow Control Mode</b>	Linear Velocity
<b>Linear Velocity</b>	42 cm/s
<b>Injection Mode</b>	Splitless
<b>Injection Port Temp.</b>	200 °C
<b>Injection Volume</b>	1 µL
<b>Carrier Gas</b>	Helium
<b>Column</b>	SH-PolarD Cap. Column (30 m long, 0.25 mm I.D., 0.25 µm df) [P/N: 221-75981-30]
<b>Column Oven Temp. Program</b>	Initial Temp 40 °C (hold for 2 min) - Increase to 210 °C with a rate of 20 °C/min (hold 2 min)
<b>Ion Source Temp.</b>	200 °C
<b>Interface Temp.</b>	200 °C
<b>Solvent Cut Time</b>	4 min
<b>Acquisition Mode</b>	MRM
<b>Event Time (sec)</b>	0.3
<b>MRM Transitions and Collision Energies</b>	87.10 > 45.10, CE 6 (Target ion) 87.10 > 43.00, CE 21 (Reference Ion)



**Figure 2.** GCMS-TQ™8050 NX with AOC™-20i+s Plus.

## ■ Preparation of Standard

### DMAC Standard Stock Solution 1 (10 000 ppm) in DCM

Transfer 100.0 mg of DMAC to a 10 mL volumetric flask, then add 2 mL of dichloromethane (DCM) and homogenize. Top up the volumetric flask to the mark with DCM and vortex the mixture again.

### DMAC Standard Stock Solution 2 (100 ppm) in DCM

Transfer 1 mL of DCM to a 10 mL volumetric flask, then add 100 µL of DMAC Standard Stock Solution 1. Top up the volumetric flask to the mark with DCM and vortex the mixture.

### DMAC Standard Stock Solution 3 (10 000 ppm) in water

Transfer 100.0 mg of DMAC to a 10 mL volumetric flask, then add 2 mL of ultrapure water and homogenize. Top up the volumetric flask to the mark with ultrapure water and vortex the mixture again.

### DMAC Standard Stock Solution 4 (100 ppm) in water

Transfer 1 mL of ultrapure water to a 10 mL volumetric flask, then add 100 µL of DMAC standard Stock Solution 3. Top up the volumetric flask to the mark with ultrapure water and vortex the mixture.

## ■ Calibration Plot

Prepare the Calibration Standard Solutions in accordance with **Table 2**.

## ■ Preparation of Sample

In this application news, a river water sample was used as an example of water matrix to be tested for DMAC using GC-MS/MS. As it might contain many organic and inorganic matters, the complex matrix of river water makes it an ideal candidate to demonstrate robustness of the proposed methodology.

### Sample Preparation (River Water)

Transfer 5 mL of river water to a 15 mL centrifuge tube, then add 100 µL of 1N NaOH . Ensure that the pH of the sample is more than 7. Add 2g of NaCl and vortex the solution for 15 mins. Add 2 mL of DCM to the aqueous mixture and vortex the solution for 1 hour to extract the target analyte (DMAC). Remove the top aqueous layer, and re-extract it with 1 mL of DCM (by vortexing it for 15 mins). Repeat the re-extraction step again with 1 mL of DCM. Combine the organic layers and dry it with Na<sub>2</sub>SO<sub>4</sub>. Transfer the dried combined organic layers to a GC vial for GCMS analysis.

**Table 2. Preparation steps for calibration standard solutions**

Level	Preparation	DCM Volume / µL	Final volume / µL	Final concentration / ppm
5	100 µL from DMAC Standard Stock Solution 2	900	1000	10
4	500 µL from Level 5	500	1000	5
3	100 µL from Level 5	900	1000	1
2	100 µL from Level 4	900	1000	0.5
1	100 µL from Level 3	900	1000	0.1

**Table 3. Results of the system stability for various calibration standards**

Injection	Level	Area	Std. Dev.*	Average	%RSD#
1	1	11278			
2	1	11079			
3	1	11349	319.35	11063	3%
4	1	11306			
5	1	10556			
6	1	10807			
1	3	99385			
2	3	96056			
3	3	99287	1620.78	97771	2%
4	3	98659			
5	3	95658			
6	3	97579			
1	5	922495			
2	5	930291			
3	5	908043	35901.58	894822	4%
4	5	908154			
5	5	854741			
6	5	845206			

\*Results are rounded to 2 decimal places. #Results are rounded to the nearest percentage.

### Sample Preparation (River Water Spiked with 2 ppm DMAc)

Transfer 5 mL of river water to a 10 mL volumetric flask. Add 200  $\mu$ L of DMAc Standard Stock Solution 4. Top up the volumetric flask to the mark with river water and homogenize.

After spiking, the spiked sample was extracted in a similar fashion as the unspiked river water sample mentioned earlier.

## Results and Discussion

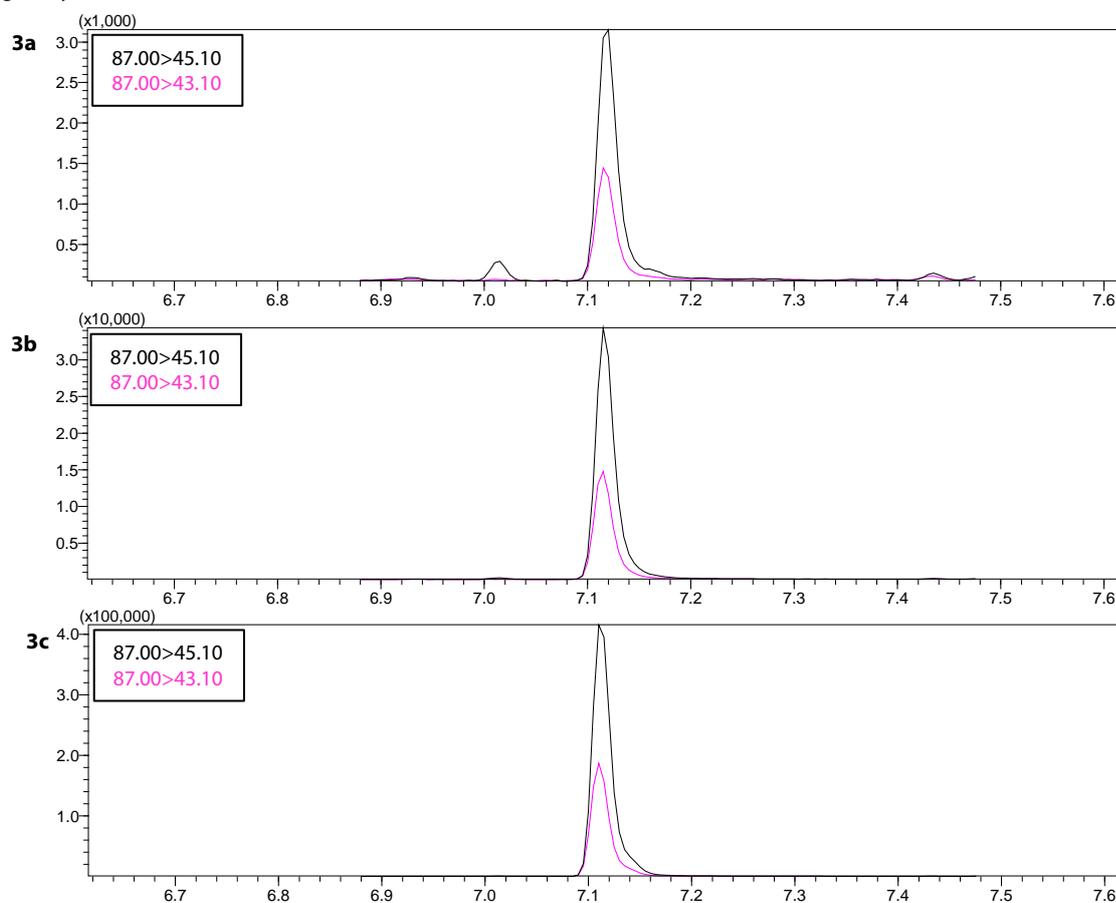
### System Stability

Results of repeated injections ( $n=6$ ) of the Calibration Standards at Level 1, 3 and 5, were used for the evaluation of the system stability. The results obtained were summarized in **Table 3**. It is observed that the peak area %RSD of the repeated injections range only between 2% to 4%.

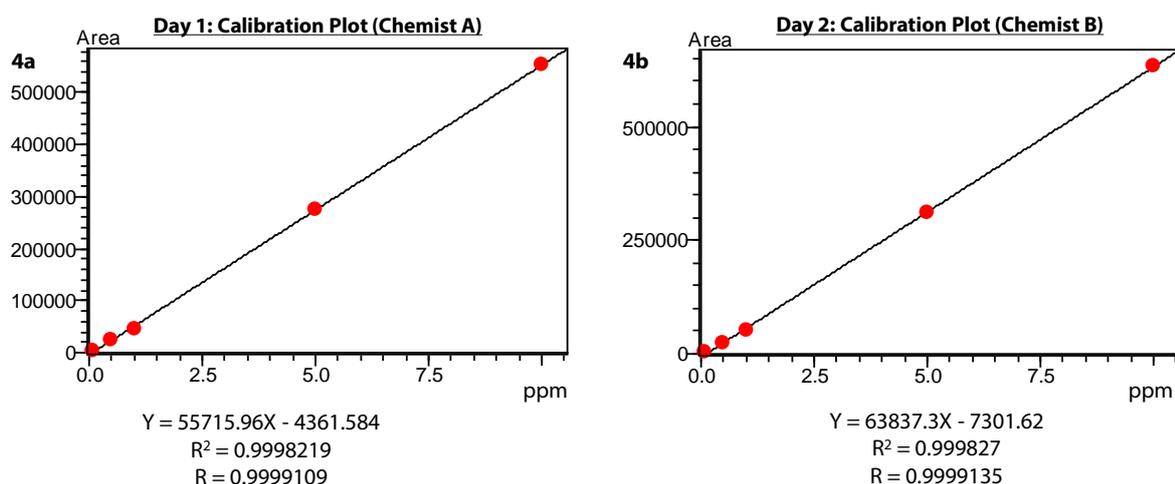
These precision results successfully demonstrated the reliability of Shimadzu instruments, ensuring the generation of consistent and reliable data. **Figure 3a-c** depict the MRM mass chromatograms of the Calibration Standards Solutions. Strong and distinct MRM transitions signals (87.00>45.10 and 87.00>43.10) characteristic of DMAc were observed.

### Calibration Plot

The calibration plots obtained for the spiked experiments are as depicted in **Figure 4a-b**, prepared by 2 different chemists, on 2 different days.  $R^2$  was observed to be at least 0.999 for both of the calibration plots, demonstrating high linearity co-relationship between the area of the peak detected, and the known concentrations of DMAc in the Calibration Standard Solution.



**Figure 3a-c.** MRM mass chromatograms of calibration standards: 0.1 ppm (Level 1), 1.0 ppm (Level 3) and 10 ppm (Level 5) respectively.



**Figure 4a-b.** Calibration plots used for the analysis of the river water sample.

### Quantitation and Accuracy results

Similar to the calibration plots, the river water sample was quantitated in two experiments, conducted by two different chemists, on 2 different days. The extractions were repeated 3 times in parallel (n=3) for each attempt. Such experimental design facilitates the determination of intermediate precision of the protocol to demonstrate the reliability of Shimadzu technology. DMAc was not detected in both attempts. **Figure 5a** depicts the chromatogram for one of the attempts.

To determine the accuracy of our methodology, the experiment was repeated with river water sample spiked with 2ppm of DMAc. The spiked sample then underwent the same sample extraction and analytical process. **Figure 5b** depicts the chromatogram obtained for the spiked sample, and **Table 4** summarizes the results for quantitation, precision (repeatability at n=3) and %Recovery of the experiment. %Recovery of the experiments (n=6) ranges between 111% to 117% were

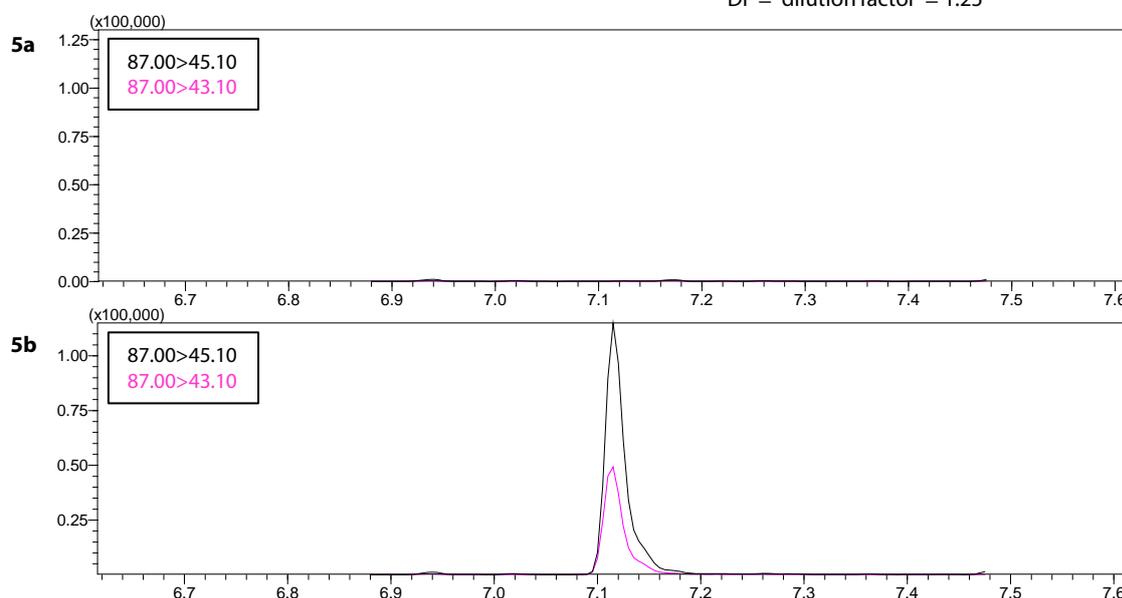
observed. Overall intermediate precision of the experiment (n=6) spreading across the 2 days was observed to be 2% (**Table 5**). This data provide strong evidence demonstrating the proposed protocol has an excellence recovery and robustness for the detection of DMAc. The data also clearly demonstrated GCMS-TQ8050 NX unparallel performance in performing quantitation in complex matrices.

### ■ Calculation

The calculation of final DMAc concentrations detected in the spiked sample in **Table 4** is as followed:

$$\text{Final DMAc concentration (ppm)} = \frac{C}{DF}$$

Where: C = Conc. Obtained from Calibration Plot (ppm)  
DF = dilution factor = 1.25



**Figure 5a-b.** MRM mass chromatograms of unspiked river water and spiked river water (2 ppm DMAc), respectively.

**Table 4. Quantitation, Precision and %Recovery of river water spiked at 2 ppm**

Chemist	Day	Theoretical Concentration /ppm	Conc. Obtained from Calibration plot /ppm	Final Conc. Corrected with Dilution Factor* /ppm	%Recovery#	Average* /ppm	Std. Dev.* /ppm	%RSD#
A	1	2	2.93719	2.350	117%	2.335	0.015	1%
			2.90045	2.320	116%			
			2.91808	2.334	117%			
B	2	2	2.77839	2.223	111%	2.259	0.036	2%
			2.82635	2.261	113%			
			2.86753	2.294	115%			

\*Results are rounded to 3 decimal places. #Results are rounded to the nearest percentage.

**Table 5. Intermediate precision based on data from Table 4**

Theoretical Concentration /ppm	Average* /ppm	Std. Dev.* /ppm	%RSD#
2	2.297	0.048	2%

\*Results are rounded to 3 decimal places. #Results are rounded to the nearest percentage.

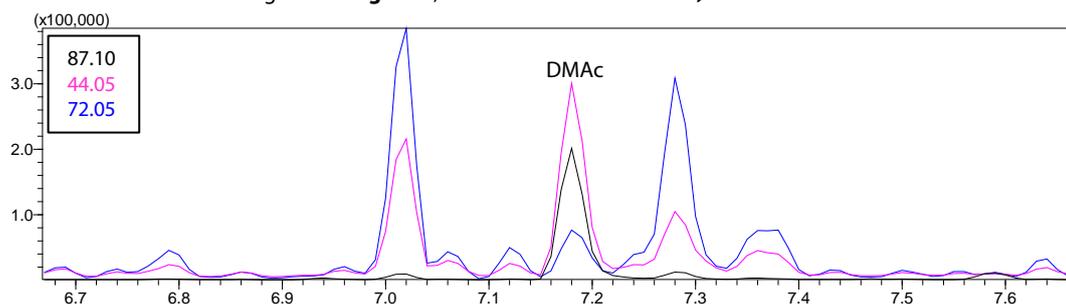
**MRM Selectivity**

During the initial phase of method optimization, the water sample was analyzed using Single Quadrupole GCMS via SIM mode. **Figure 6** depicts DMAc SIM mass chromatograms (sample was spiked with 1ppm of DMAc). As shown, significant background contribution from the matrix was observed. It was also observed that in SIM mode, ion ratio of the reference ions due to the background matrix varies widely. This makes identifying DMAc in water sample with complex matrices challenging.

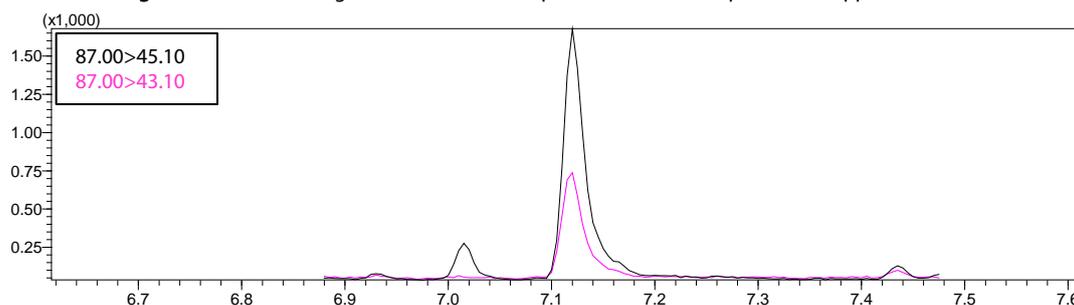
Comparing **Figure 6** and **Figure 7**, the selectivity of using triple quadrupole MRM technique towards the analyte of interest in complex matrix sample becomes apparent. It is worth emphasizing that the amount of DMAc spiked in the sample used to obtain the SIM mass chromatograms in **Figure 6**, was

50 times higher than that of **Figure 7**. The sample in **Figure 7** was obtained by diluting the spiked sample (**Figure 5b**) 100 times in DCM (20 ppb), then analyzed using MRM technique. As shown in **Figure 7**, negligible interferences from background matrix was observed. In fact, it was easier to identify the lower concentration 20 ppb DMAc peak using MRM mode in **Figure 7**, than the more concentrated sample in **Figure 6** using SIM mode. The quality of the chromatogram obtained for **Figure 7** is indistinguishable from those obtained using pure standards (**Figure 3a-c**).

Due to the high selectivity of MRM, and the simple sample preparation procedure using generic labware, wide range of samples of different water sample matrices can be analyzed using the proposed methodology easily. Nevertheless, the %Recovery of different matrices need to be studied.



**Figure 6.** SIM chromatogram obtained for complex water matrices spiked with 1 ppm DMAc.



**Figure 7.** MRM chromatogram obtained for sample in **Figure 5b** diluted 100X (20 ppb DMAc).

**Conclusion**

In this application news, our team has successfully demonstrated that Shimadzu GCMS-TQ8050 NX capability via the detection and quantitation of DMAc in complex matrices. Excellence linearity, selectivity, precision and accuracy of the method have been demonstrated, most importantly, making use of the sensitivity of GCMS-TQ8050 NX, the time-consuming step of concentrating large volume of organic layers before GCMS analysis is avoided.

**Acknowledgement**

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