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Technical Report

Development of the Micro-ESI 8060 Micro-Flow Ionization Unit To Provide Both High Sensitivity and High Robustness

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Abstract:

The Micro-ESI 8060 is an ionization interface optimized for micro-LC/MS systems. By reducing the LC flowrate to between a few and a few tens of microliters per minute, micro-LC/MS systems offer higher ionization and ion-uptake efficiencies, which enables higher sensitivity analyses to be performed.
The Micro-ESI 8060 features an ionization probe whose position and angle is optimized to the mass spectrometer ion inlet. As a result, it achieves both higher sensitivity and higher robustness when performing micro-LC/MS analysis.

Keywords: Micro-ESI 8060, ionization interface, high sensitivity, high robustness, micro-LC/MS

1. Introduction

The Micro-ESI 8060 has been optimized for micro-flowrate ionization using a Shimadzu Nexera Mikros, micro-LC/MS system. The position and angle of the Micro-ESI 8060 ionization probe was optimized with respect to the mass spectrometer ion inlet. Consequently, it achieves both the highest sensitivity and robustness levels in the world. The design is also resistant to contamination, due to the ionization probe position and angle that prevent unwanted liquid droplets from entering the mass spectrometer, while also maintaining the improvements in ionization efficiency and ion uptake efficiency that micro-LC/MS analysis provides.

The Micro-ESI 8060 incorporates the highly regarded cable-free and tube-free design featured in previous ionization interface models. Consequently, it enables stress-free swapping with other ionization units by simply unlocking the quick-release lever, opening the unit, and lifting it up. Furthermore, ESI capillaries can be removed without tools, which make maintenance much easier.

Fig. 1 Nexera Mikros, Micro LC/MS System with Micro-ESI 8060 Ionization Interface

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2. Optimization of Probe Position and Angle

During development of the Micro-ESI 8060, the position and angle of the ionization probe was optimized (Fig. 2). Optimization involved evaluating whether ion intensity increased, whether noise increased significantly, and whether service life decreased as the probe position and angle were adjusted to achieve the best possible balance between ion intensity and robustness.

Fig. 3 shows the relationship between probe angle and ion intensity, given an LC flowrate of 50 µL/min. It shows that if the angle between the ionization probe and the ion inlet is zero degrees, or in other words, when the ionization probe and ion inlet port are positioned opposite each other, then ion intensity is maximized, but noise is significantly increased. In contrast, noise decreases significantly when the ionization probe is oriented at a 30 or 45-degree angle with respect to the ion inlet. The signal-to-noise (S/N) ratio was best when the angle is 30 degrees.

In this way, we determined the Micro-ESI 8060 probe position and angle by evaluating the optimal probe position and angle for a variety of LC flowrates and samples.

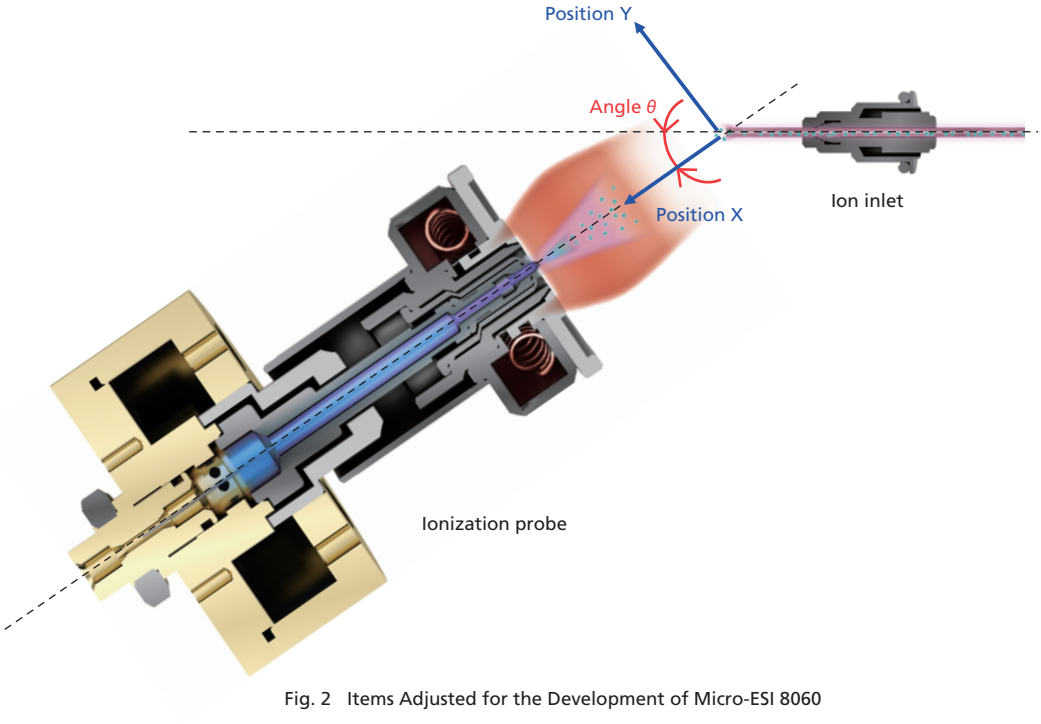

Fig. 2 Items Adjusted for the Development of Micro-ESI 8060

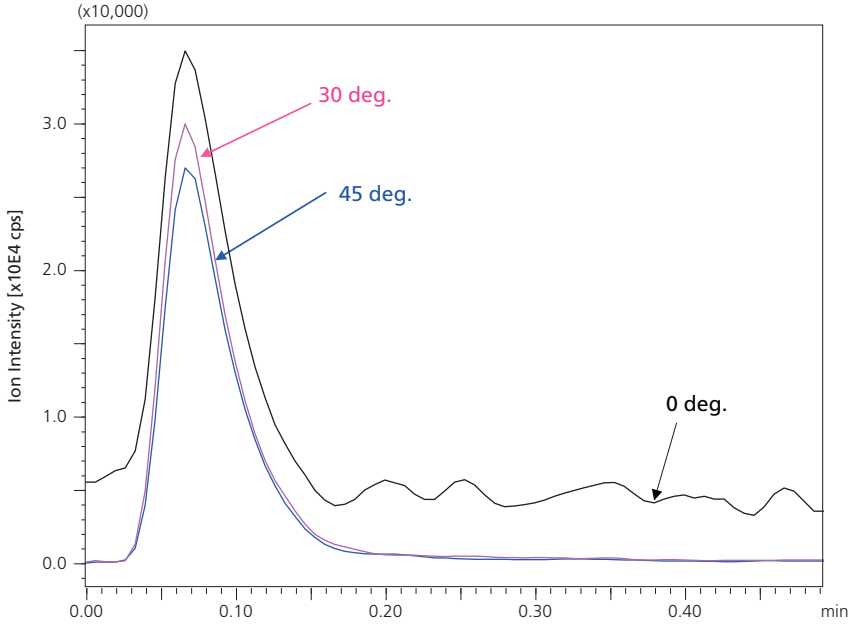

Fig. 3 Relationship Between Ionization Probe Angle Relative to the Ion Inlet and Ion Intensity (LC Flowrate: 50 µL/min)

3. Micro-ESI 8060 Features

3-1. High Sensitivity

As an example of its high sensitivity, a key feature of the Micro-ESI 8060, the following describes results from analyzing five lipid mediator components (LTD4, 20-HETE, 12-HETE, LTB4, and 5,6-DiHETE). The peak intensity for each of the components measured using a micro-LC/MS system (at an LC flowrate of 2 µL/min) with a Micro-ESI 8060 interface was compared to peak intensity measured using a semi-micro-LC/MS system (at an LC flowrate of 400 µL/min) with a standard ESI unit.

As shown in Fig. 4, the ion intensity measured using the micro-LC/MS system with a Micro-ESI 8060 interface was over ten times higher, and for some components up to 33 times higher, than measured using the semi-micro-LC/MS system with a standard ESI unit.

MRM chromatograms of each component are shown in Fig. 5. For each of the components, results from the micro-LC/MS system with a Micro-ESI 8060 interface are shown on the left and the results from the semi-micro-LC/MS system with a standard ESI unit on the right. In each chromatogram, results from injecting the samples are indicated in red and the blanks (blood plasma) in black. The micro-LC/MS system was able to detect all components, even at concentrations that were not detected by the semi-micro-LC/MS system. In the case of LTD4, in particular, the higher sensitivity of the micro-LC/MS system enabled detection of endogenous lipid mediators contained in the blood plasma analyzed as blank samples.

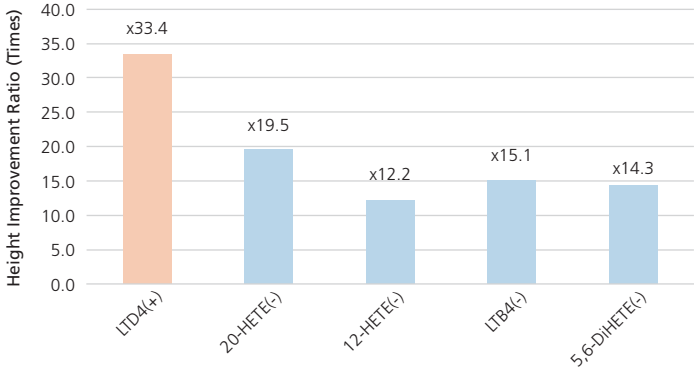

Fig. 4 Increase in Ion Intensity for 5 Lipid Mediator Components Using Micro-LC/MS (LC flowrate: 2 µL/min) Versus Semi-Micro-LC/MS (LC Flowrate: 400 µL/min)

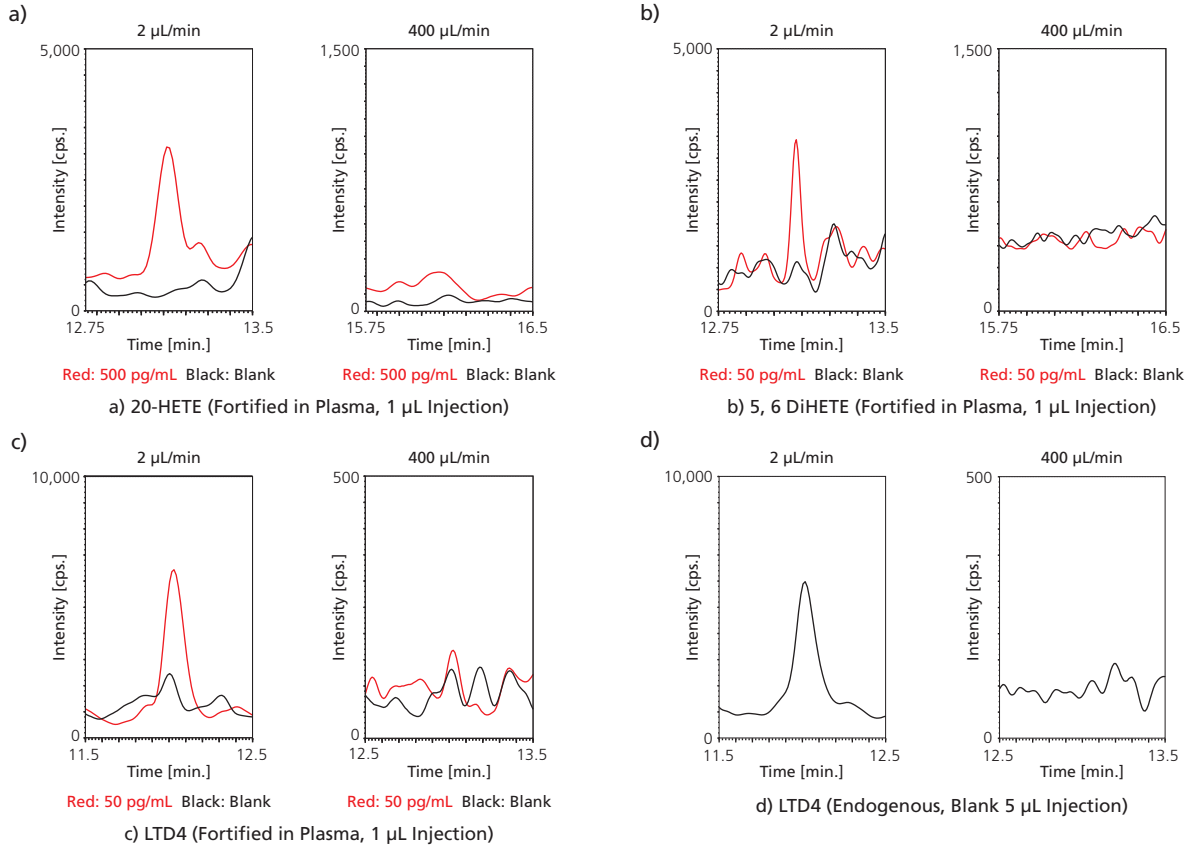

Fig. 5 MRM Chromatograms of Lipid Mediators

3-2. High Robustness

Another key feature of the Micro-ESI 8060 is its outstanding robustness, which is shown by the data in Fig. 6. It is a plot of area values obtained from successively injecting 1500 blank deproteinized blood plasma samples, with QC samples (40 pg/mL nortriptyline) injected after every 50th blank sample. Even after analyzing 1500 blank blood plasma injections, the system achieved an outstanding 4.38 % area repeatability for the QC samples. Note that internal standard correction was not used.

MRM chromatograms from the QC samples analyzed on the 1st, 750th, and 1,500th injections are shown in Fig. 7. Extremely reliable results were obtained, with no peak shape distortion or sensitivity drop between results before and after the successive blank analyses.

The data shows that the optimized probe position and angle of the Micro-ESI 8060 prevents sensitivity drop problems and so on by preventing internal contamination from unwanted liquid droplets getting inside the mass spectrometer.

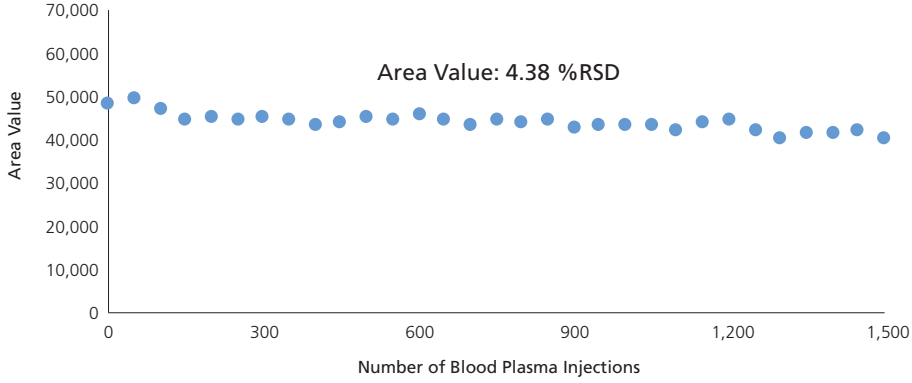

Fig. 6 Area Repeatability for QC Samples (40 pg/mL Nortriptyline)

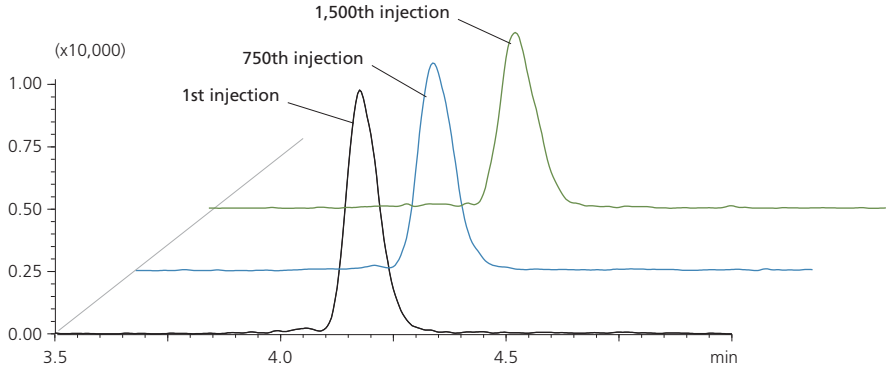

Fig. 7 MRM Chromatograms for QC Samples Analyzed After 1, 750, and 1,500 Injections

4. Conclusion

- The Micro-ESI 8060 maximizes ion uptake efficiency for micro-LC/MS analysis by optimizing the position and angle of the ionization probe with respect to the ion inlet. As a result, it achieves over 30 times higher sensitivity than semi-micro-LC/MS systems equipped with a standard ESI unit.
- Optimizing the ionization probe position and angle prevents contamination caused by unwanted liquid droplets entering the mass spectrometer. This means that the Micro-ESI 8060 provides outstanding robustness even for successive analyses of blood plasma samples.

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