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DPiMS™ QT Probe Electrospray Ionization Kit
iMScope™ Imaging Mass Microscope

Application News

Distribution Analysis of Plant Alkaloids in *Narcissus*, by MS Imaging

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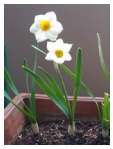
User Benefits

- Qualitative screening using the DPiMS QT kit can be conducted with measurement time of approximately 0.5 min.
- Easily switch between DPiMS QT and iMScope QT.
- Distribution analysis using iMScope QT is expected to improve the efficiency of drug production.

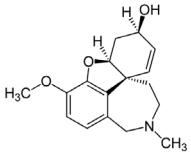
■ Introduction

Plant alkaloids are used in various pharmaceuticals, such as anticancer drugs and analgesics. Among these plant alkaloids, galanthamine is an Amaryllidaceae-type alkaloid with acetylcholinesterase inhibitors used in the treatment of neurological diseases such as Alzheimer's disease. Although the chemical synthesis of galanthamine has been successfully achieved, *Narcissus* is the main source of its production. Research indicates that galanthamine content varies not only with the type of *Narcissus*, but also with the developmental stage and the part of the plant[1)]. Pharmaceutical companies are pursuing plant species with higher galanthamine content to increase pharmaceutical productivity.

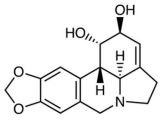
In this study, we were able to quickly confirm the presence of galanthamine in our *Narcissus* sample (Fig. 1) using the DPiMS QT probe electrospray ionization (PESI) kit and the LCMS quadrupole time-of-flight (Q-TOF) mass spectrometer (MS) (Fig. 2). Subsequently, we analyzed the distribution of galanthamine by MS imaging (MSI) using the iMScope QT and the LCMS Q-TOF MS (Fig. 2).



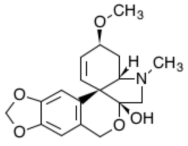
Narcissus Tazetta



Galanthamine
$C_{17}H_{21}NO_3$



Lycorine
$C_{16}H_{17}NO_4$



Tazettiine
$C_{18}H_{21}NO_4$

Fig. 1 Structural Formula of Alkaloids in *Narcissus Tazetta*

■ Sample Preparation and Analysis Conditions

For our sample, we used *Narcissus tazetta* with leaves growing to about 15 cm in length. Galanthamine was extracted with 50% EtOH aq. from freeze-dissolved leaves. The solution was analyzed via the DPiMS QT and the LCMS-9030 (Fig. 2 right). Analytical settings of PESI are shown in Table 1. Data analysis was performed using the LabSolutions Insight Explore™ software. Locations of *Narcissus tazetta* sections are shown in Fig. 3. Frozen leaves and bulbs were sliced to a thickness of 20 µm using a microtome and mounted on indium tin oxide (ITO) coated glass slides. These were coated with a-cyano-4-hydroxycinnamic acid (CHCA) via vapor deposition by using the matrix sublimation apparatus iMLayer™ at a thickness of 0.7 µm.

MSI analysis was performed using the iMScope QT atmospheric MALDI equipped with an optical microscope and the LCMS-9030 (Fig. 2 left). Analytical settings of MSI are shown in Table 2. Data analysis was performed using the IMAGEREVEAL™ MS.

Table 1 Analytical Settings of PESI

Mass spectrometer	
System	: DPiMS QT+LCMS-9030
Polarity	: Positive
DL temp	: 250 ℃
Heat block temp	: 50 ℃
Interface Voltage	: 3.5 kV
MS Range	: *m/z* 50-2,000
Measurement Time	: 0.5 min

Table 2 Analytical Settings of MSI

Mass spectrometer	
System	: iMScope QT+LCMS-9030
Polarity	: Positive
DL temp	: 250 ℃
Heat block temp	: 450 ℃
MS Range	: *m/z* 280-335
Spatial Resolution (Pitch)	: 10 / 25 µm
Laser Diameter Setting	: 1 / 2
Laser Intensity	: 50 / 60
Laser Repetition Frequency	: 20 kHz
Matrix Coating	
System	: iMLayer
Matrix Used	: CHCA
Coating Method	: Deposition with 0.7 µm Thickness

Fig. 2 iMScope™ QT (left) and DPiMS™ QT (right)

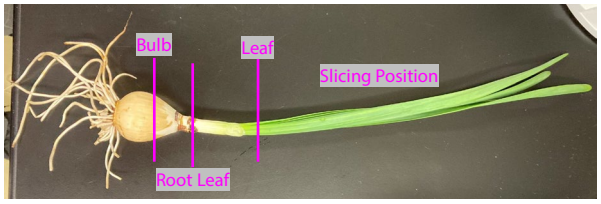


Fig. 3 Locations of *Narcissus tazetta* sections for MS imaging
Narcissus tazetta were grown in soil culture with leaves growing to about 15 cm. Three types of sections were prepared: bulb, root leaf, and leaf cross section.

■ Qualitative Screening of Galanthamine in *Narcissus Tazetta* by DPiMS QT

The mass spectra obtained quickly in only a few tens of seconds from the extracted solution of freeze-crushed *Narcissus tazetta* leaves in positive mode are shown in Fig. 4.

Accurate mass analysis using analysis software confirmed the presence of galanthamine, other plant alkaloids like lycorine and tazettine, the metabolite choline, and sugars composed of hexose were also detected. Plant alkaloids were detected within a mass error of 1 mDa (Table 3).

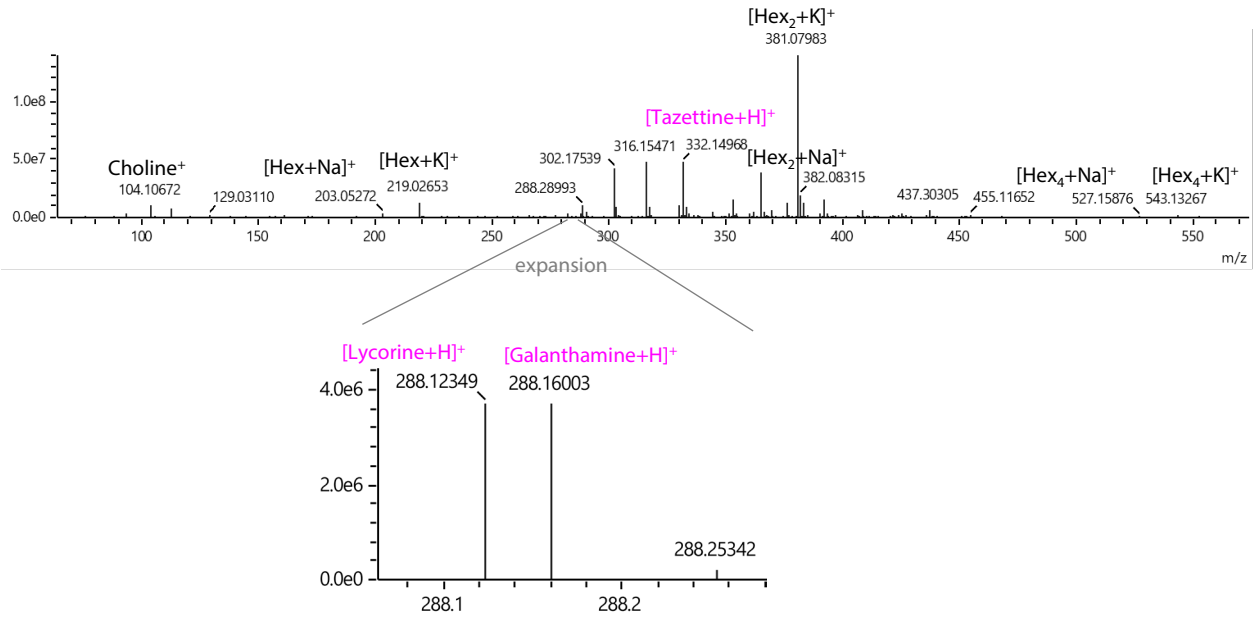


Fig. 4 Mass Spectra of *Narcissus Tazetta* Leaves

Table 3 Mass Accuracy of Alcaloids Detected in *Narcissus Tazetta*

Compounds	Ions	Theoretical *m/z*	Measured *m/z*	Mass Error (mDa)
Galanthamine	$[M+H]^+$	288.1594	288.1600	0.6
Lycorine	$[M+H]^+$	288.1230	288.1235	0.5
Tazettine	$[M+H]^+$	322.1493	322.1496	0.3

■ Distribution Analysis of Galanthamine in *Narcissus Tazetta* by MSI

The distribution of galanthamine, lycorine, and tazettine in sections prepared from the bulb and leaves (two locations) of the *Narcissus tazetta* shown in Fig. 3 was analyzed by MSI. The MS imaging results of a bulb section at 25 µm spatial resolution and 10 µm spatial resolution are shown in Fig. 5, these images were taken with the 5x objective lens. These results showed strong distributions of galantamine, lycorine, and tazettine from all samples. The MS images of the bulb showed that galanthamine was distributed mostly in the section of the bulb that later grows and becomes the leaves, whereas MS images of lycorine and tazettine did not show such distribution, suggesting that the distribution area of plant alkaloids in the bulb differs from species to species, but no such differences in distribution were observed in the leaf cross sections.

■ Conclusion

The combination of PESI and Q-TOF was able to detect galanthamine in *Narcissus* with a high mass accuracy of within 1 mDa. The time required for analysis was significantly reduced compared to that by LC or LC/MS with a measurement time of 0.5 min, suggesting that rapid screening is possible. The specific distribution of galanthamine in narcissus bulbs was confirmed by MS imaging analysis using a combination of iMScope QT and Q-TOF, with the ionization unit replaced from PESI to MALDI. Such distribution analysis enables identification of regions with high galanthamine content, facilitating efficient isolation and purification in the pharmaceutical manufacturing process, and is expected to contribute to the reduction of extraction costs.

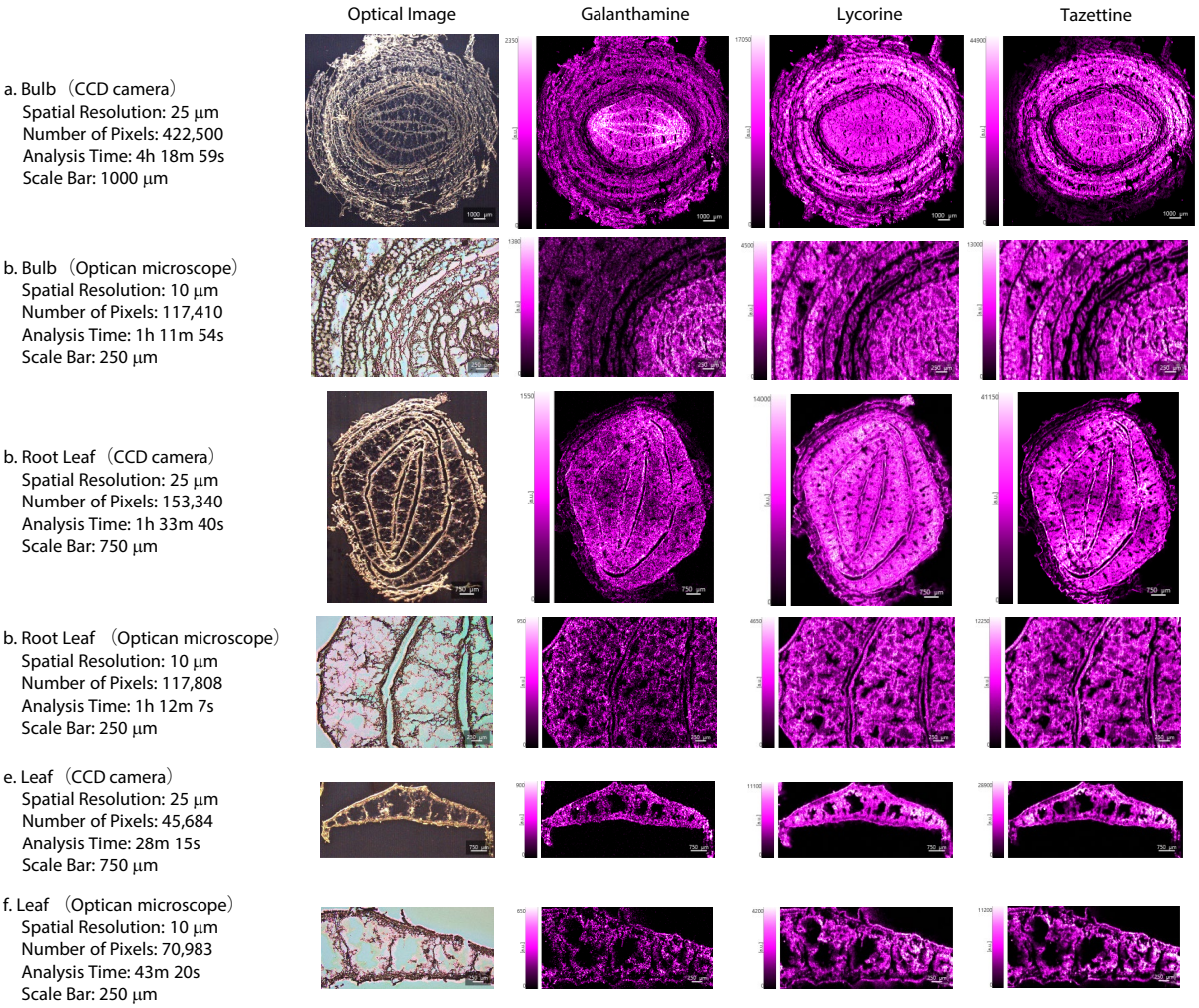


Fig. 5 Mass Images of Alkaloids in *Narcissus Tazetta*

This application news is made and published by rearranging the data from *Mass Spectrom.* 2024;13(1):A0163. For details, please refer to the original paper.

<References>

1) Letter… Planta Med 2003; 69: 1166-1168

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